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Philippe Ciffroy
Alice Tediosi
Ettore Capri *Editors*

Modelling the Fate of Chemicals in the Environment and the Human Body

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Modelling the Fate of Chemicals in the Environment and the Human Body

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Aims and Scope

Since 1980, *The Handbook of Environmental Chemistry* has provided sound and solid knowledge about environmental topics from a chemical perspective. Presenting a wide spectrum of viewpoints and approaches, the series now covers topics such as local and global changes of natural environment and climate; anthropogenic impact on the environment; water, air and soil pollution; remediation and waste characterization; environmental contaminants; biogeochemistry; geoecology; chemical reactions and processes; chemical and biological transformations as well as physical transport of chemicals in the environment; or environmental modeling. A particular focus of the series lies on methodological advances in environmental analytical chemistry.

Series Preface

With remarkable vision, Prof. Otto Hutzinger initiated *The Handbook of Environmental Chemistry* in 1980 and became the founding Editor-in-Chief. At that time, environmental chemistry was an emerging field, aiming at a complete description of the Earth's environment, encompassing the physical, chemical, biological, and geological transformations of chemical substances occurring on a local as well as a global scale. Environmental chemistry was intended to provide an account of the impact of man's activities on the natural environment by describing observed changes.

While a considerable amount of knowledge has been accumulated over the last three decades, as reflected in the more than 70 volumes of *The Handbook of Environmental Chemistry*, there are still many scientific and policy challenges ahead due to the complexity and interdisciplinary nature of the field. The series will therefore continue to provide compilations of current knowledge. Contributions are written by leading experts with practical experience in their fields. *The Handbook of Environmental Chemistry* grows with the increases in our scientific understanding, and provides a valuable source not only for scientists but also for environmental managers and decision-makers. Today, the series covers a broad range of environmental topics from a chemical perspective, including methodological advances in environmental analytical chemistry.

In recent years, there has been a growing tendency to include subject matter of societal relevance in the broad view of environmental chemistry. Topics include life cycle analysis, environmental management, sustainable development, and socio-economic, legal and even political problems, among others. While these topics are of great importance for the development and acceptance of *The Handbook of Environmental Chemistry*, the publisher and Editors-in-Chief have decided to keep the handbook essentially a source of information on "hard sciences" with a particular emphasis on chemistry, but also covering biology, geology, hydrology and engineering as applied to environmental sciences.

The volumes of the series are written at an advanced level, addressing the needs of both researchers and graduate students, as well as of people outside the field of

"pure" chemistry, including those in industry, business, government, research establishments, and public interest groups. It would be very satisfying to see these volumes used as a basis for graduate courses in environmental chemistry. With its high standards of scientific quality and clarity, *The Handbook of Environmental Chemistry* provides a solid basis from which scientists can share their knowledge on the different aspects of environmental problems, presenting a wide spectrum of viewpoints and approaches.

The Handbook of Environmental Chemistry is available both in print and online via www.springerlink.com/content/110354/. Articles are published online as soon as they have been approved for publication. Authors, Volume Editors and Editors-in-Chief are rewarded by the broad acceptance of *The Handbook of Environmental Chemistry* by the scientific community, from whom suggestions for new topics to the Editors-in-Chief are always very welcome.

Damià Barceló
Andrey G. Kostianoy
Editors-in-Chief

Preface

When studying the environment and the impact of human activities on it, we soon realise that we are dealing with a unique system, where the different compartments are strictly interconnected. On the one hand, we are to make simplifications and to fragment reality; on the other one, we see that the environment is a continuum. Exposure assessment of chemicals, as the majority of the branches of applied sciences, draws together several different disciplines. A number of works describe exposure assessment and chemical fate modelling, either in the environment or in the human body. Nevertheless, in our opinion, there is a lack of tools and information enabling investigators to understand and model the complexity of reality and therefore to obtain solutions to practical problems. The fate of chemicals in both the environment and in the human body is a very complex matter, but despite this, models have to be coupled, if we want to assess the behaviour over the whole chain and to hypothesise the possible impacts not only on the environment but also on human health. Only in this way, modelling the fate of chemicals becomes an actual and useful tool to manage the problems connected to the use of chemicals and to take actions to solve or at least to limit them. We strongly believe that the future will necessarily guide policy makers, researchers and all stakeholders to the full integration of exposure assessment.

It is with this challenge in mind that we decided to write a book about modelling the fate of chemicals in the environment *and* the human body. This work is the outcome of many years of experience and of different research activities that have led to the development of MERLIN-Expo, a software for simulating the fate of chemicals in the main environmental systems and in the human body in an integrated way (http://merlin-expo.eu/).

The book is composed of ten chapters. The first chapter considers the challenges of exposure assessment for the future and the evolution of human health and environmental risk assessment. The second chapter is concerned with the SWOT analysis performed to evaluate the potential of MERLIN-Expo and its relevance in legislative frameworks. In the third chapter, the standard documentation of exposure models that was developed in collaboration with CEN (European Committee

for Standardization) is described. Fourth to ninth chapters describe the modelling of different environmental compartments (i.e. surface waters, atmosphere, soil, groundwater, plants, aquatic organisms and mammals). The tenth chapter focuses on the fate of contaminants in humans using a lifetime physiologically based pharmacokinetic model.

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Contents

List of Abbreviations

Acronyms

1D	One-Dimensional
3D	Three-Dimensional
ABL	Atmospheric Boundary Layer
ACF	Atom-Centred Fragment
ADME	Absorption, Distribution, Metabolism and Excretion
AE	Assimilation Efficiency
AF	Assimilation Fraction
AGB	Above-Ground Biomass
ATP	Adenosine Triphosphate
BAF	Bioaccumulation Factor
BC	Black Carbon
BCF	Bioconcentration Factor
BDW	Body Weight
BIC	Bank Identifier Code
BMF	Biomagnification Factor
BSAF	Biota Sediment Accumulation Factor
BSE	Bovine Spongiform Encephalopathy
CAC	Codex Alimentarius Commission
CEC	Cation Exchange Capacity
CEMN	Canadian Environmental Modelling Network
CEN	Comité Européen de Normalisation (French; in English: European Committee for Standardization)
CEP	Canadian Environmental Protection
CERCLA	Comprehensive Environmental Response, Compensation and Liability Act
COMMPS	Combined Monitoring-Based and Modelling-Based Priority Setting
CRA	Comparative Risk Assessment

CRR	Critical Root Radius
CWA	CEN Workshop Agreement
DBH	Diameter at Breast Height
DDT	Dichlorodiphenyltrichloroethane
DRPC	Danube River Protection Convention
DYNAMEC	Dynamic Selection and Prioritisation Mechanism for Hazardous Substances
EC	Elemental Carbon
EC	European Commission
ECB	European Chemicals Bureau
ECHA	European Chemicals Agency
EEA	European Environment Agency
EEA	Environmental Exposure Assessment
EEC	European Economic Community
EFSA	European Food Safety Authority
EIONET-SOIL	European Environment Information and Observation Network for Soil
EMEP	European Monitoring and Evaluation Programme
EPA	Environmental Protection Agency
EPER	European Pollutant Emission Register
EQS	Environmental Quality Standards
ERA	Environmental Risk Assessment
ES	Estonia
ET	Evapotranspiration
EU	European Union
EUPRA	EU Pesticide Risk Assessment
EUSES	European Union System for the Evaluation of Substances
EXAFS	Extended X-Ray Absorption Fluorescence Spectrometry
FAO	Food and Agriculture Organization of the United Nations
FOCUS	Forum for Co-ordination of Pesticide Fate Models and Their Use
FP7	Seventh Framework Programme
GIGO	Garbage In, Garbage Out
GIS	Geographical Information System
GIT	Gastrointestinal Tract
GM	Geometric Mean
GM	Genetically Modified
GMO	Genetically Modified Organism
GPG	General Protection Goal
GSD	Geometric Standard Deviation
GSM	Global System for Mobile Communications
HHRA	Human Health Risk Assessment
IARC	International Agency for Research on Cancer
IBAN	International Bank Account Number
ICPR	International Commission for the Protection of the Rhine
ICRP	International Commission on Radiological Protection

IPCS	International Programme on Chemical Safety
IRA	Integrated Risk Assessment
IRSN	French Institute for Radiological Protection and Nuclear Safety
ISO	International Organization for Standardization
ITS	Integrated Testing Strategy
IVIV	In Vitro In Vivo
JRC	Joint Research Centre
LAI	Leaf Area Index
LCA	Life Cycle Assessment
LCIA	Life Cycle Impact Assessment
LHWA	Little Hocking Water Association
LRAT	Long-Range Atmospheric Transport
LUC	Land Use Coverage
LWC	Liquid Water Content
MCDA	Multi-criteria Decision Analysis
MEA	Millennium Ecosystem Assessment
MSCE	Meteorological Synthesizing Centre – East
MTC	Mass Transfer Coefficient
NGO	Non-governmental Organisation
NHANES	National Health and Nutrition Examination Survey
NRC	National Research Council
NSB	National Standardisation Body
OC	Organic Carbon
ODD	Overview, Design Concepts and Details
OECD	Organisation for Economic Co-operation and Development
OM	Organic Matter
OSPAR	International Convention for the Protection of Marine Systems
PAH	Polycyclic Aromatic Hydrocarbon
PBCDD	Polychlorinated Dibenzodioxins
PBPK	Physiologically Based Pharmacokinetic
PBT	Persistent, Bioaccumulative and Toxic
PBTK	Physiologically Based Toxicokinetic
PCB	Polychlorinated Biphenyls
PDF	Pedotransfer Function
PEC	Predicted Environmental Concentration
PFC	Perfluorinated Compound
PFOA	Perfluorooctanoic Acid
PFOS	Perfluorooctane Sulphonate
PHS	Priority Hazardous Substance
PNEC	Predicted No-Effect Concentration
POC	Particulate Organic Carbon
POP	Persistent Organic Pollutant
ppLFER	Polyparameter Linear Free Energy Relationship
PPP	Plant Protection Product

PRZM	Pesticide Root Zone Model
PS	Priority Substance
PSR	Priority Substances Under Review
QSAR	Quantitative Structure-Activity Relationship
RA	Risk Assessment
RANS	Reynolds-Averaged Navier-Stokes
REACH	Registration, Evaluation, Authorization and Restriction of Chemical Substances
REV	Representative Elementary Volume
RH	Relative Humidity
SCCS	Scientific Committee on Consumer Safety
SCENIHR	Scientific Committee on Emerging and Newly Identified Health Risks
SCHER	Scientific Committee on Health and Environmental Risks
SCS	Soil Conservation Service
SEA	Single European Act
SME	Small and Medium Enterprise
SPG	Specific Protection Goal
SPM	Suspended Particulate Matter
STOA	Science and Technology Options Assessment
SVOC	Semi-volatile Organic Compound
SWOT	Strengths, Weaknesses, Opportunities and Threats
TCDD	2,3,7,8-Tetrachlorodibenzo-*p*-dioxin
TG	Test Guideline
TNO	Netherlands Organisation for Applied Scientific Research
TSCA	Toxic Substance Control Act
TSP	Total Concentration of Suspended Particles
TWA	Time-Weighted Average
UK	United Kingdom
UNECE	United Nations Economic Commission for Europe
US	United States
USDA	US Department of Agriculture
UZ	Unsaturated Zone
vPvB	Very Persistent and Very Bioaccumulative
WFD	Water Framework Directive
WHO	World Health Organization

Symbols

Symbols are defined where they appear in the text.

Evolution and Future of Human Health and Environmental Risk Assessment

Nicoleta Alina Suciu, Silvia Panizzi, Philippe Ciffroy, Antoni Ginebreda, Alice Tediosi, Damià Barceló, and Ettore Capri

Abstract Human Health Risk Assessment (HHRA) and Environmental Risk Assessment (ERA) are well-established regulatory and scientific research fields that support regulatory decision-making in the European Union (EU) and are undergoing constant development. HHRA and ERA are crucial steps for reaching the objectives of Europe 2020, a strategy put forward by the Commission that sets out a vision of Europe's social market economy for the twenty-first century. This chapter aims to describe the basic principles, the evolution and the future challenges of HHRA and ERA.

The first part defines HHRA and ERA and describes the origins of risk assessment and management procedures at an international level. The precautionary principle has always been present in the European Union policies that aim to protect health and the environment.

In the second part, current approaches that characterise risk assessment, such as the tiered approach, are presented. In the future, the implementation of recent scientific developments for the construction of integrated exposure scenarios models is of paramount importance to improve environmental and health risk assessment schemes. Moreover, the evaluation of uncertainties in the modelling

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inputs and outputs and the sensitivity analysis are two key elements to optimise current HHRA and ERA procedures.

Keywords Environmental Risk Assessment • EU policies • Human Health Risk Assessment • Integrated Exposure Assessment • Uncertainty

Contents

1 What Is Human Health and Environmental Risk Assessment?

As defined by the European Commission [1], risk assessment is "A process of evaluation including the identification of the attendant uncertainties, of the likelihood and severity of an adverse effect(s)/event(s) occurring to man or the environment following exposure under defined conditions to a risk source(s). A risk assessment comprises hazard identification, hazard characterization, exposure assessment and risk characterization". Several intermediate steps are required for human health and environmental risk assessments (HHRA and ERA, respectively). First of all a, "problem formulation" is required in order to identify what needs to be assessed, followed by hazard identification. Hazard is commonly defined as "the potential to cause harm". A hazard can be defined as "a property or situation that in particular circumstances could lead to harm" [2]. Exposure assessment describes the intensity, frequency and duration of contact of the hazardous agent with the target [3]. Risk is a more difficult concept to define. Risks represent what people experience of actual harm, as consequence of risk, translated in damages to environmental, life losses and health impacts. Risks have been defined as mental "constructions" [4] created by the mankind who believes that human action can prevent harm in advance.

In HHRA and ERA, the term "risk" is used in three consecutive steps: risk characterisation, risk evaluation and risk management. Risk characterisation "integrates information from the preceding components of the risk assessment and synthesizes an overall conclusion about risk that is complete, informative, and useful for decision makers" [5]. The risk evaluation includes aspects such as choice of technology, social need for the specific risk agent and consideration of possible

substitutions, risk-benefit balances and political priorities, potential for conflict resolution. Traditionally, risk management follows the risk assessment phase.

Risk management refers to the activities of identifying and evaluating alternative regulatory options and selecting among them. Risk management starts with a review of all relevant information which is generated from risk perception studies, economic impact assessments and the scientific characterisation of social responses to the risk source [6]. The traditional view of the risk decision process makes a sharp distinction between two functions, risk assessment (i.e. understanding) and risk management (i.e. action) [7]. According to this approach, the assessment is considered an exclusively scientific process, whereas policymakers and decision makers are responsible for the risk management process. The traditional formulation of risk assessment phases implies a hidden idea of mutual legitimation of science and policy [8] where science determines policy by producing objective, valid and reliable knowledge. Consequently, the risk manager, informed by the scientists, discriminates among values and preferences in order to formulate the correct and rational policy. The need of risk assessment and management is common between many fields and contexts: a multitude of specific cases, frameworks and practices across which it is difficult to generalise, from chemical risks, nuclear risks, to risks arising from the climate changes and the use of biotechnologies.

2 First Steps in Developing Risk Assessment Schemes

At international level, the Codex Alimentarius Commission (CAC), created in 1962 by the United Nations Food and Health Organization (FAO) and the World Trade Organization (WTO), was the first international commission with the aim to protect the health of consumers and to discuss and publish recommended international standards in the field of food safety. The CAC was committed in improving risk analysis procedures related to agricultural and food production, including basic risk assessment carried out by specific committees and their national government counterparts [9].

The US Environmental Protection Agency (EPA) had played a key role in developing first guidance for risk assessment. EPA had been developing risk assessment guidelines primarily for human health: guidance for cancer risk assessment was issued between the 1970s and 1980s (41 Federal Register 21402, 1976; [10]). Each of the guidelines was a product of several years of discussion and review involving scientists and policymakers from EPA, other federal agencies, universities, industry, public interest groups and the general public [11].

The National Research Council (NRC) paradigm for human health risk assessments [10], widely referred to as the "Red Book" can be considered a milestone in the definition of modern risk assessment processes.

The document dealt with the risk of cancer and other health effects associated with exposure to toxic substances: formaldehyde, asbestos and nitrite; its principal

objective was to improve the scientific validity of risk assessment. The Red Book used the term "risk assessment" to mean the characterisation of the potential adverse health effects of human exposures to environmental hazards. Risk characterisation was seen as a summarization of scientific information. This understanding is briefly stated in the Red Book: *Risk characterization is the process of estimating the incidence of a health effect under the various conditions of human exposure described in exposure assessment. It is performed by combining the exposure and dose-response assessments. The summary effects of the uncertainties in the preceding steps are described in this step.*

The Red Book suggested that risk assessment should not only estimate probabilities of clearly defined effects but should also follow a standard methodology approach based on an explicit framework [12]. Formalisation of procedures for ERA began in the 1980s [13, 14], although the ecological risk assessment of chemicals was performed using a hazard assessment paradigm [15, 16]. Barnthouse and Suter proposed in 1986 a framework for ecological risk assessment based on the human health framework. In this case, the ERA framework differed from HRA in some aspects: the hazard assessment was based on a tiered definition, which included defining source terms, describing the environment and choosing the endpoints and not only a pure determination of carcinogenicity of the molecule. It was thus recognised that ERA required more consideration of the nature of the hazard than the HHRA since the receptors were different and their responses were dependent on the characteristic of the environment in which exposure occurs and the nature of the source [12]. Secondly, the scheme was designed as a flow chart which showed the flow of information as a parallel process of analysing exposure and effects and the need for the hazard definition to inform both the exposure and effects assessment [12]. By the late 1980s, emergence and standardisation of tools and methods for conducting ecological risk assessments had begun [17, 18]. In the early 1990s, the US EPA developed the first guidelines for ecological risk assessment [19]. The agency studied existing assessments and identified issues to develop a sound basis for articulating generic guiding principles for the assessment of ecological risks.

The ERA framework developed by EPA [19] included three primary phases: problem formulation, analysis and risk characterisation (Fig. 1). Problem formulation provides a foundation upon which the entire risk assessment depends. It aims at articulating the purpose of the assessment, defining the problem and determining a plan for analysing and characterising the risk [20]. During risk characterisation, the exposure and effects elements are integrated to estimate risk. Risk managers help ensure that risk assessments provide information relevant to their decisions by describing why the risk assessment is needed, what decisions it will influence and what they want to receive from the risk assessor. In turn, risk assessors ensure that scientific information is effectively used to address ecological and management concerns.

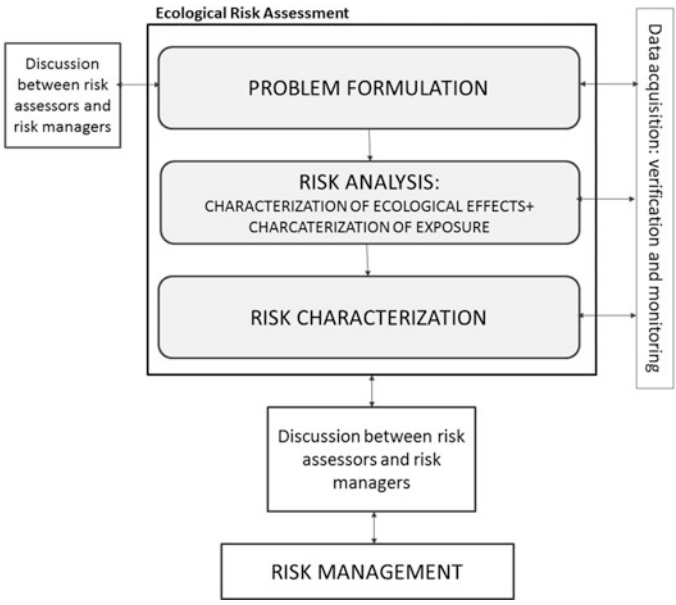

Fig. 1 Framework for ecological risk assessment as developed by EPA (1992, with modifications)

3 Human Health and Environmental Risk Assessment in the European Union

European Union can be considered quite a recent entity, born in 1993 with Maastricht Treaty, when the attempts to go beyond a purely common market as European Economic Community. In a historical sense, it is difficult to speak of a single "European" regulation, because each member state had its own regulation in the field of health and environmental protection, with the exception of some directives that aim to harmonise procedures and requirements among different member state legislations. For example, in 1967, the European Community adopted Directive 67/548/EEC on the classification, packaging and labelling of dangerous substances, which can be considered the first directive which aimed at protecting human health and the environment in the EU [21].

In the area of environmental regulation, the European Union as a unique entity did not have competence since the legislation was left to national governments until 1987 when the Single European Act (SEA) was passed [22].

In the 1970s and 1980s, member states were free to adopt environmental or health measure they wished, as long as such measures were not discriminating. There was no provision in EU law which would oblige a member state to make risk

assessment before taking legislative action; thus some member states decided to ban some chemicals autonomously [23]. Finally, the seventh amendment of Directive 67/548/EEC, Directive 92/32/EEC and the framework Directive 91/414 for the authorisation of pesticides required an evaluation of the potential hazards and risks of notified substances on the basis of a specified data set. These two directives specified the principles for carrying out the risk assessment of chemicals. Since then, the concepts of risk assessment and risk management of substances gradually became firmly established in EU legislation [21].

The Title VII of the SEA dealt with environment and health protection objectives. Indeed starting with 1987 the "action by the Community relating to the environment shall have the following objectives: i) to preserve, protect and improve the quality of the environment, ii) to contribute towards protecting human health, iii) to ensure a prudent and rational utilization of natural resources". Furthermore the "action by the Community relating to the environment shall be based on the principles that preventive action should be taken, that environmental damage should as a priority be rectified at source, and that the polluter should pay. Environmental protection requirements shall be a component of the Community's other policies" (art. 130).

Currently, HHRA and ERA in the EU are carried out by different advisory bodies under specific legal frameworks. A strict separation between the risk assessment phase and the risk management phase, which is competence of the commission, is still present.

The precautionary principle is a key component of health and environmental policies in the EU since the 1970s and is included in EU treaties since the Maastricht Treaty of 1992. At that time, the principle was already present in national and international laws (see Box 1), including agreement to which the community was a party, such as the Rio Declaration. The precautionary principle is mentioned in the environmental chapter of the Lisbon Treaty, together with the principle of prevention (art. 191). In contrast to the legal process in the United States, the precautionary principle has been the primary principle in European Union policies for the health and environment protection [24], and its definition has changed in time. The precautionary principle justifies early action in the case of scientific uncertainty in order to prevent potential harm to human health and the environment. The precautionary principle has been introduced to formulate an approach to the situations where ignorance and indeterminacy dominate the cause-effect relationships [25]. The precautionary principle, by calling for preventive action even when there is uncertainty, by placing the onus ("burden of proof") on those who create the hazard, has stimulated an intense debate about its usefulness and limitations in the scientific community [26–28].

Box 1: The Precautionary Principle in International and EU Treaties

1992 Rio Declaration:

In order to protect the environment, the precautionary principle shall be widely applied by States according to their capacity. Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation.

Treaty on European Union (Maastricht Treaty), 1992:

"Community policy on the environment... shall be based on the precautionary principle and on the principles that preventive actions should be taken, that the environmental damage should as a priority be rectified at source and that the polluter should pay."

EU Treaty (Paragraph 2 of article 191 of the Lisbon Treaty):

Union policy on the environment shall aim at a high level of protection taking into account the diversity of situations in the various regions of the Union. It shall be based on the precautionary principle and on the principles that preventive action should be taken, that environmental damage should as a priority be rectified at source and that the polluter should pay.

Stockholm Convention on Persistent Organic Pollutants (POPs), 2001:

Precaution, including transparency and public participation, is operationalised throughout the treaty, with explicit references in the preamble, objective, provisions for adding POPs and determination of best available technologies. The objective states: "Mindful of the Precautionary Approach as set forth in Principle 15 of the Rio Declaration on Environment and Development, the objective of this Convention is to protect human health and the environment from persistent organic pollutants"**.**

European Environmental Agency, 2013:

"The precautionary principle provides justification for public policy and other actions in situations of scientific complexity, uncertainty and ignorance, where there may be a need to act in order to avoid, or reduce, potentially serious or irreversible threats to health and/or the environment, using an appropriate strength of scientific evidence, and taking into account the pros and cons of action and inaction and their distribution".

The Communication on the Precautionary Principle was issued in 2000 [29] to outline the commission's approach to use the principle and build a common understanding of how to assess, manage and evaluate risks that science cannot fully evaluate. Moreover, the Commission was interested in avoiding unwarranted recourse to the principle as a hidden form of trade protectionism [30]. The Communication clearly assumed again the Red Book philosophy of distinct and separate phases in the risk analysis process: "The precautionary principle should be considered within a structured approach to the analysis of risk which comprises three elements: risk assessment, risk management, risk communication. The precautionary principle is particularly relevant to the management of risk".

In the last decades, the EU bodies have recognised that many European citizens were losing confidence in a poorly understood and complex system to deliver the

policies that they wanted. During the 1990s and early 2000s, food crises, such as BSE, dioxin and biotechnologies had undermined consumer confidence in the safety of the food chain [31]. Consequently, a new European trend in risk governance has emerged: big efforts are made to take into account the new perspective of public and stakeholder-engagement and the implication of the application of the precautionary principle. In this social context, bodies like the European Science and Technology Observatory [32, 33] and European Environment Agency [34, 35] contributed to analyse the shortcomings and new needs in science policies. Some of the work of the European Parliament's Science and Technology Options Assessment unit (STOA) also addresses these new imperatives, and new legal responsibilities are also being introduced, as under the Aarhus Convention [36] and EC Water Framework Directive 60/2000.

The White Paper on governance [37] was born to respond to the mistrust of many of the Union's citizens and to the increasing alienation from politics at global and local level. It sought goals of "good governance", such extended openness, participation, accountability, effectiveness and coherence as important principles of governance [38]. Its aim was to connect governance with food safety issues and argued that the food crisis had undermined consumer confidence in the safety of the food chain.

The creation of European Food Safety Authority (EFSA) (Regulation (EC) 178/2002) was central in the governance reform initiated by the White Paper, as part of the search for good governance forms in the EU context [39], an organisational response to the food scandals which undermined consumer confidence in the safety of the food chain ("...a European Food Authority will enhance the Union's scientific capability, transparency and networking in the area of food safety", [37])

EFSA's Scientific Committee, its Scientific Expert Panels and other expert groups provide "fit-for-purpose and timely advice to risk managers" [40] and develop risk assessments schemes on all matters linked to food and feed safety, including animal health and welfare and plant protection. Moreover, the authority is committed in the risk communication and in increasing transparency towards citizens and stakeholders: "Communicating openly and promptly on its scientific work helps foster trust in EFSA. As well as being transparent, we aim to engage civil society in our risk assessment work and connect with untapped scientific potential" [40]. Rather than being a decision-making body, EFSA provides decision support. All risk-management measures and the operation of food control systems remain the responsibility of the European Commission and member states. EFSA carries out HHRA and ERA for some products authorised under EU food law, such as pesticides, additives in animal feed, or GM food and feed.

Another active European body in this field is the European Commission Joint Research Centre (JRC). The generic risk assessment scheme proposed by EFSA, 2010 in the context of pesticide risk assessment recalls the first EPA publication providing guidance about ERA [19] as well as the Technical Guidance Document for risk assessment developed by JRC in 2003 [41]. Problem formulation is always considered the first fundamental step in the risk assessment, and good communication between the risk assessor and risk manager is stressed [42].

4 Current Practices in Risk Assessment

There are two situations in which risk assessment is required within EU legislation. In prospective risk assessment, the risk must be assessed to anticipate a situation of exposure before taking appropriate measures, such as authorisation of the marketing of a chemical for a set of uses. On the contrary, in retrospective RA, the actual risk is estimated in a real exposure situation (such as the evaluation of the risk of workers, consumers or the environment under the current and/or real use conditions) [43].

In the prospective risk assessment of chemicals, such in the case of pesticides and biocides, a worst-case approach based on conservative hypotheses is carried out applying conservatively chosen assessment factors, scenarios and input parameters to protect human health and the environment.

The integration of information on hazard, exposure and dose-response to provide an estimate of the likelihood that any of the identified adverse effects will occur in exposed people or environmental compartments. Risk characterisation takes place in both human health risk assessments and ecological risk assessments.

In HHRA, the hazard identification is the process of determining whether exposure to a stressor can cause an increase in the incidence of specific adverse health effects (e.g. cancer, birth defects). In the case of chemical stressors, the process examines the available scientific data for a given chemical (or group of chemicals) and develops a weight of evidence to characterise the link between the negative effects and the chemical agent. Exposure can be measured directly but more commonly is estimated indirectly through consideration of measured concentrations in the environment, consideration of models of chemical transport and fate in the environment and estimates of human intake over time [44].

To protect a wide range of nontarget organisms, the environmental exposure in ERA can be measured directly but more commonly is estimated indirectly through consideration of models of chemical transport and fate in the environment. Then, in the risk characterisation phase, the quantitative estimations of environmental exposure (for example, predicted environmental concentrations – PEC) of a substance in the potentially polluted environmental compartments (air/soil/water) are compared to toxicological endpoints (acute or long-term endpoints or Predicted No Effect Concentrations – PNEC), which can be obtained through laboratory tests or more realistic field or semi-field studies.

The tiered approach is the basis of risk assessment schemes that support the registration of chemicals, both in the hazard and exposure estimations. It is based on a hierarchical approach that involves integrated and iterative consideration of exposure and hazard at all phases, with each tier being more refined (i.e. less cautious and more certain) than the previous one but more complex, laborious and cost-intensive [20]. Many risk assessors and public and private organisations have used this approach in risk assessment of chemicals since the 1990s [45–49].

Tiers were defined as “pre-planned and prescribed sets of risk assessments of progressive data and resource intensity” [20]. The outcome of a given tier is to

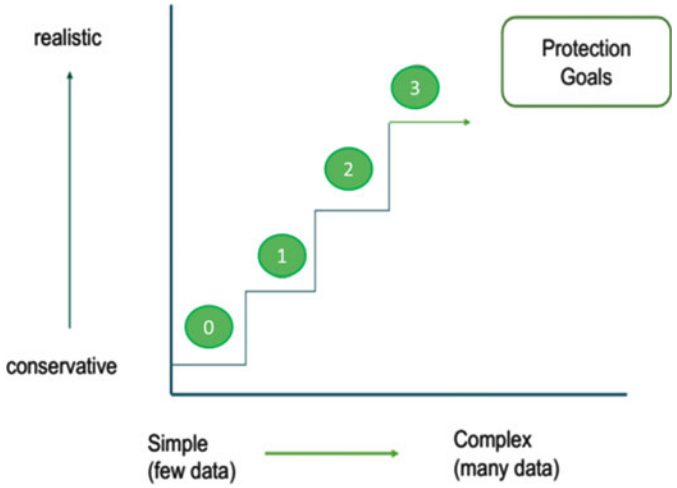

Fig. 2 Tier approach in ERA

either make a management decision, often based on decision criteria, or continue to the next level of effort. Setting up tiered assessments and decision criteria may reduce the need for iteration between risk assessors and managers [20].

According to EFSA PPR Panel, the tiered system needs to be "appropriately protective, internally consistent, cost-effective and increasingly accurate and precise from lower to higher tiers" [50]. The general principles of tiered approaches used in the many current processes of risk assessment are [51] lower tiers are more conservative than higher tiers; higher tiers aim at being more realistic than lower tiers; lower tiers usually require less effort than higher tiers; in each tier, all available relevant scientific information is used; all tiers aim to assess the same protection goal (Fig. 2). First tiers of ERA assess the potential harm on organisms basing on standard laboratory data and simple fate modelling. Because the first-tier assessment is conservative (and considering the often close taxonomic relationship between target species and nontarget aquatic organisms), chemicals frequently do not pass the first tier, and higher-tier assessments, which provides more realistic information, are needed.

When higher-tier assessments are triggered, a traditional approach is to perform fate or effects field experiments (e.g. pond/mesocosm studies) or field monitoring. The higher tiers aim to predict the effects at higher levels of biological and ecological organisation. Recently, the ecological modelling is proposed as a promising tool to assess risk in meaningful terms at population, community, ecosystem levels and possible recovery after harm has been caused [51, 52]. The most appropriate method for estimating population level effects is ecological modelling: population modelling provides essential outputs for choosing among management alternatives and for facilitating cost-benefit assessments [53, 54].

General protection goals (GPGs) for the protection of the environment are only broadly outlined in EU sectorial legislations [55], so that a translation into specific protection goals (SPGs) is required for specific ERA schemes [50].

To be useful for the environmental risk assessment and regulatory decision-making, it is crucial to define clear SPGs and to make them operational by translating them into measurable endpoints. The benefit of doing this is to ensure that the risk assessment is focused on what it needs to be and that the relevance of the data required is optimised, in other words, that the outcome of the risk assessment is actually useful in making regulatory decisions [56].

In recent years, the ecosystem services concept has become adopted as a paradigm for ecosystem management and the sustainable use of natural resources [57]. The "ecosystem services" are benefits that people obtain from ecosystem structures, and they were classified as provisioning, regulating, cultural and supporting services [58]. They are considered effective tools in view of its strength as a communication tool and for the possibility to assign a value to ecosystem services, facilitating a cost–benefit analysis and the decision-making [59, 60].

The EU policies are also integrating the ecosystem service approach into their planning: restoring and preserving ecosystem services is one of the six priorities identified by the rural development pillar in the new proposal for the EU's Common Agricultural Policy [61]. EFSA is currently pushing to increase harmonisation and provide a common methodological framework using ecosystem services to operationalise environmental protection goals including biodiversity in the different EFSA areas (pesticides, GMOs and Feed additives) [42]. Method for deriving SPG options within different legal frameworks is consistent with those proposed for Plant Protection Products in 2010.

The adoption of the tiered approach can be beneficial for mapping ecosystem services. The main advantages of the tiered approach are that it can be adapted to other ecosystem services, it supports the efforts towards a standardised ecosystem services assessment, provides information about relevant variables to be considered in long-term monitoring at different scales and it supports sustainable resource management as it ensures the inclusion of information relevant to decision makers at different levels [62].

5 Future Priorities and Challenges

HHRA and ERA are well-established regulatory and scientific research fields that support regulatory decision-making in the EU and are undergoing constant development. HHRA and ERA play a key role in reaching the objectives of Europe 2020, a strategy put forward by the Commission that sets out a vision of Europe's social market economy for the twenty-first century [63]. One of the main goals of this strategy is environmental protection and ERA helps to inform decision-making in this regard. Significant advances have been made in this field in recent years. The

aim of this paragraph is to briefly discuss some features of future trends in HHRA and ERA approaches.

5.1 Managing Uncertainty Analysis in Risk Assessment

In the last decades, some cases in the field of science and technology policies have showed that management of important issues have to face different stakes, ignorance, social and scientific complexity and uncertainties [34, 35, 64].

Uncertainty is not only absence of knowledge; the general definition given by Walker et al. [65] comprises many dimensions of the concept: "any departure from the unachievable ideal of complete determinism". The uncertainty can be also a situation of inadequate information, as incorrect or unreliable information. What is of fundamental importance can prevail when a lot of information is available, as new information, especially in risk analysis processes, can decrease but also increase uncertainty [66].

Uncertainty can be intended as lack of knowledge or uncertainty due to variability inherent to the system considered (stochastic uncertainty). Two types of uncertainty are therefore distinguished: epistemic and variability uncertainty [65]. The first is due to the imperfection of our knowledge, which may be reduced by more research and empirical efforts, while the latter is due to inherent variability, which is especially applicable in human and natural systems and concerning social, economic, and technological developments. Especially in the case of epistemic uncertainty, additional research may improve the quality of our knowledge and thereby improve the quality of the output. Walker et al. [65] describe uncertainty as manifesting itself at different locations in the model-based water management process. These locations, or sources, may be characterised and localised as follows:

- Context is an identification of the boundaries of the system to be modelled and thus the portions of the real world that are inside the system, the portions that are outside and the completeness of its representation. The model context is typically determined in the problem framing stage and is crucial to the decision support exercise as it clarifies the issues to be addressed and the selection of the outcomes of interest to be estimated by the model.
- Model uncertainty is divided into two parts: model structure uncertainty, which is the uncertainty about the form of the model itself, and the model technical uncertainty, which is uncertainty arising from the computer implementation of the model.
- Inputs to the model are associated with the forces that drive the modelled system.
- Parameter uncertainty is associated with the data and methods used to calibrate the model parameters.
- Model outcome uncertainty is the accumulated uncertainty associated with the model results of interest to the decision maker.

With regard to model uncertainty, it has been argued that often, the complexity of models largely exceeds the requirements for which they are used, and this is also true for complication [28]. They claim that models should not be more complex than they need to be. A model is then "relevant" when its input factors actually cause variation in the model response that is the object of the analysis.

Both policymakers and scientists need to acknowledge and take account the presence of unavoidable uncertainties in the assumptions, methodologies and results of their works. In their work on post-normal science, Funtowicz and Ravetz [67, 68] analysed how the presence of irreducible uncertainty and complexity in many environmental and health policy issues necessitates the development of alternative problem-solving approaches in which science and policy communicate and where uncertainty is acknowledged. Several research groups have dealt with this issue [69–71], but awareness of these methodological biases among many stakeholders appears to be low. When models are designed for the regulatory appraisal of environmental risk, they must be proven capable to deal with uncertainty [72]. Especially when the model is used to drive a choice or a decision, and the importance of the associated uncertainties should be quantified and the relevance of the model ensured. Thus, Saltelli and Funtowicz [28] concluded that in the health and environmental assessments, the assessors and the stakeholders are themselves part of the knowledge production system and should be included in the "extended quality assurance process".

Saltelli et al. [73] proposed a set of rules for sensitivity auditing to be used in contexts where mathematical modelling feeds into a policy context. They assume that an "extended peer community" is identified and involved in the sensitivity auditing of the mathematical modelling. An extended peer community consists not only of persons from academia or with some form of institutional accreditation but of all those with a desire and/or interest to participate in extended peer review processes for the resolution of a specific issue. The proposed rules are 1. Check against rhetoric use of mathematical modelling; 2. Adopt an "assumption hunting" attitude; 3. Detect Garbage In Garbage Out (GIGO), in the extended definition of Funtowicz and Ravetz [67]; 4. Find sensitive assumptions before these find you; 5. Aim for transparency; 6. Do the right sums; 7. Focus the analysis on the key question answered by the model, exploring holistically the entire space of the assumptions.

5.2 Probabilistic and Sensitivity Analysis

Current deterministic approaches in risk assessment attempt to deal with variability and uncertainty by using "worst-case" values for exposure and toxicity and comparing the resulting risk index to a standard threshold value.

However, in complex situations, such as environmental exposure estimations, probabilistic methods represent an essential tool for improving the governance of risks and provide a realistic basis for comparison of the reliabilities of resulting

projections or alternatives [74]. In essence, these methods use distributions to quantify the variability and uncertainty in toxicity and exposure and combine them to produce distributions of predicted impact or risk [75].

The application of probabilistic techniques to the assessment of exposure is traditionally expected to yield a number of benefits including (1) the quantification of the uncertainty associated with model predictions, (2) the identification of the factors which most influence model predictions, (3) the promotion of critical examination of the data and exposure models, (4) the generation of meaningful outputs for subsequent decision-making [76].

Sensitivity analysis (SA) is complementary to uncertainty analysis and provides information on how uncertainty in a model output can be systematically apportioned to different sources of uncertainty in the model input [77]. In other words, sensitivity can be used to identify the important drivers (parameters, processes) mostly contributing to uncertainty and in contrast identify non-influential drivers; it thus identifies priorities in terms of research activities, model refinements and potential countermeasures [78].

One of the biggest challenges for future of HHRA and ERA is to integrate uncertainty considerations into the assessment of exposure, effects or both. In contrast to point estimate risk assessment, the overall objective of the method is to avoid worst-case assumptions and come up with a more realistic assessment of risk. Some limitations can be found in adopting probabilistic approaches, the first one is that these techniques require more data and are more complex. Moreover, they are usually more time demanding and are more difficult to communicate [79].

5.3 Integrated Risk Assessment

One of the main challenges for future developments in risk assessment is a better exploitation of the huge amount of currently existing data on substances and pollutants. In many contexts, it has been stressed that a more integrated approach to risk assessment is part of the solution [80]. The potential benefits of integrated risk assessment (IRA) have been recognised for more than a decade, and the integration of environmental and human exposure assessment was already evaluated in activities as part of a framework on IRA developed under the auspices of the International Program on Chemical Safety (IPCS) of the World Health Organization (WHO), the European Commission (EC), the Organization for Economic Cooperation and Development (OECD) and the US Environmental Protection Agency (US EPA) [81]. However, today no explicit legal mandates for IRA exist, and, so far, EEA and HEA have generally used and developed their own data, methods, scenarios and models in parallel, with poor linkage between them because of historical and scientific reasons [82]. Research and institutions are making efforts to find consistent methodology for both human and environmental risk assessment of chemical mixtures, based on generic approaches and common principles [83, 84]. Indeed, the main scope of two European funded projects, 2 FUN Project

(Full-chain and Uncertainty approaches for assessing health risks in FUture eNvironmental scenarios) and 4 FUN Project (The FUture of FUlly integrated human exposure assessment of chemicals: Ensuring the long-term viability and technology transfer of the EU-FUNded 2-FUN tools as standardised solution) was to develop and standardise an exposure assessment tool which integrates environmental and human exposure assessment. Therefore, after 7 years of research, the MERLIN-Expo tool was developed. The tool is composed of a library of fate models dedicated to non-biological receptor media (surface waters, soils, outdoor air), biological media of concern for humans (e.g. cultivated crops, cow milk, fish seen as foodstuff), as well as wildlife biota (primary producers in rivers, invertebrates, fish). It can calculate bioaccumulation through the aquatic food chain and internal concentrations of chemicals in the human body through PBPK modelling. These models can be linked together to create flexible scenarios relevant for both human and wildlife biota exposure and can be a promising way to better integrate the environmental and human assessments.

New IRA approaches aim to develop methodologies for extrapolating between different individual chemicals and different endpoints in order to bridge gaps in single substance data sets. The use of internal dose in the exposure assessment, complementary to exposure concentrations, is a promising area of cross-fertilisation between ERA and HEA. In silico models like the so-called physiologically based toxicokinetic models (PBTK) have been applied to track the movement of a chemical through the environment and the human body [85]. PBTK models consist of a series of mathematical equations with parameters based on the specific physiology of an organism and on the physicochemical properties of a substance, which are able to describe the absorption, distribution, metabolism, and elimination (ADME) of the compound within this organism. In data-poor situations where exposure data are lacking in a given species, opportunities exist to extrapolate internal concentrations from another species within the same taxa or across taxa, based on toxicokinetics data for human but also for biota, thus extending the potential of these models for the ERA. Current gaps and new opportunities for extrapolating across human and environmental exposure data, models and methods, to support the further development and promotion of the concept of IRA are described in Ciffroy et al. [82].

In regulatory context, the introduction of the concept of integrated testing strategies (ITS) in the preparation phase of Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), Reg. 396/2006 constituted a paradigm shift regarding the use of alternative methods for the hazard assessment of chemical substances. The original Reduce-Refine-Replace (3R) idea of one-to-one replacements of animal tests by in vitro tools was converted into the broader concept of replacing one animal test by the combined use of several nonanimal methods [86]. In an ITS, both non-test and test data may be included. In addition to methods providing data for the physicochemical properties and the human or environmental toxicity endpoint of interest, information theory tools such as (qualitative or quantitative) weight of evidence and consensus modelling can be employed. This

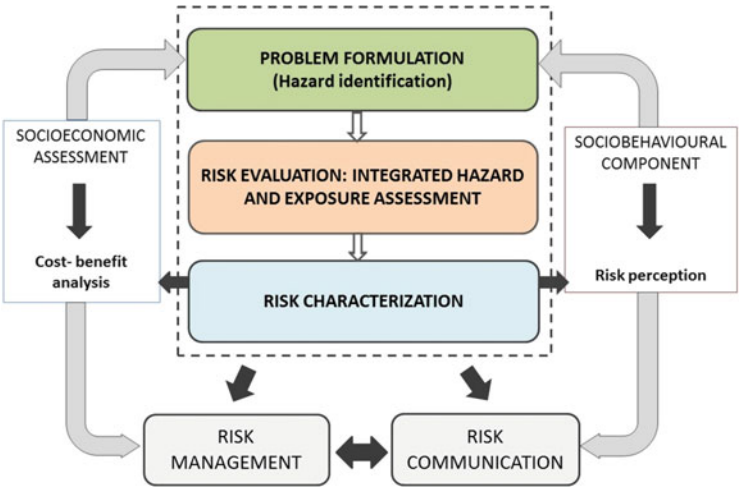

Fig. 3 Conceptual overview of an integrated risk assessment (IRA) ([89], with modifications). The integrated framework consists of three primary assessment phases [81]: (1) the Problem Formulation step (objectives, scope, conceptual model and activities of the assessment are agreed), (2) the evaluation step with the integrated exposure and effects assessment and (3) the Risk Characterisation step (synthesis of exposure and effect information to estimate the risk). Consideration of socio-economic and socio-behavioural impact runs in parallel and informs the problem formulation as well as the risk management and the risk communication processes

will help to unravel the combined information content and to possibly augment the resulting evaluation with a certain level of probability.

The benefit of IRA could expand to the assessment of mixtures. Currently, the risk assessment of chemicals for regulatory purposes does not generally take into account the real exposure to multiple substances but mainly relies on the assessment of individual substances [87]. In these years, big efforts are made by the scientific community and the institutions to identify effects from multiple substances [88] without recurring to further testing on animals.

In the context of IRA, another big challenge is to try to better integrate risk assessment and socioeconomic and socio-behavioural analysis [80]. This requires that risk assessors incorporate the needs and requirements of risk managers. To achieve this, a more concerted effort to translate risk characterisations into assessments of impacts on human health and ecosystem services should be done. Assessment endpoints should be clearly connected to relevant effects and probabilistic expressions of risk are necessary [43].

As outlined by Wilks et al. [89], the nature and extent of integration should be defined at the outset during the problem formulation phase: risk assessors and managers should take into consideration the values, beliefs, political systems and cultural factors, as well as the cost of risk reduction and the benefits of risk mitigation measures to society, thus reinforcing communication, transparency and trust in the risk analysis process (Fig. 3).

An attempt to identify limiting factors in RA processes and to better explore reasons about the gap between risk assessment and risk management was made within the EU FP7 HEROIC project [90]. The survey investigated stakeholder views on factors that could limit the pesticide risk assessment phase linked on how the knowledge is produced and the way the data are used in risk management and in risk communication, also taking into account qualitative factors such as responsibility, trust and behaviours, which could have impact on risk assessment policies. It was concluded that integrations between scientific, socio-behavioural and socioeconomic disciplines may initially increase the complexity but in turn will provide a better and more useful estimation of the risk, reinforce transparency and drive a more efficient use of risk management resources.

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SWOT Analysis of the MERLIN-Expo Tool and Its Relevance in Legislative Frameworks

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Abstract The MERLIN-Expo tool was evaluated using a SWOT analysis, which was based on expert judgement and literature review. A list of criteria was set up containing the major model characteristics, which were divided in general model criteria and relevance model criteria. Relevance model criteria were defined as criteria, which are highly depending on the regulatory framework the model is used in. From the analysis presented above, it appeared that certain regulatory chemical frameworks (e.g. REACH, biocides) are stricter towards their requirements compared to others (e.g. site-specific/local regulatory frameworks). Based on expert judgement, the MERLIN-Expo tool was evaluated using the general and relevance criteria. MERLIN-Expo has many advanced functionalities (such as uncertainty

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analysis, modular approach, dynamic model, combines environmental fate with pharmacokinetics) and models (many fate processes and environmental compartments, different human populations). At the same time, the threat is that current (regulatory) applicability frameworks do not always require these advanced assessment functionalities. The MERLIN-Expo tool appeared to be most suitable for the site-specific assessment as this is the most flexible framework. Based on this analysis, weaknesses of the MERLIN-Expo tool for its use in a certain regulatory framework could also be identified. These weaknesses are at the same time further development opportunities for MERLIN-Expo. On general model characteristics, MERLIN-Expo was identified as a highly documented (both for novice and expert level), transparent, user-friendly tool with regular trainings. Its main treat now is to ensure continuing support and mechanisms for future developmental work and updates.

Keywords Exposure models • MERLIN-Expo • Multimedia models • Regulatory framework • SWOT analysis

Contents

1 Introduction

Chemicals play a major role in modern society, contributing to our well-being and comfort and providing a number of economic benefits. However, many chemicals also pose risks to human health and the environment. Regulatory frameworks are in place in order for chemicals to be used properly, safely and in an environmentally-friendly and healthy manner. Regulatory frameworks exist on an international (focus here is the European level) and national level and/or for specific groups of chemicals such as biocides, agrochemicals, pharmaceuticals and cosmetics. These regulations can require a risk assessment for hazardous substances in order to ensure the safety of the environment and human health indirect via the environment. A risk assessment is a systematic approach to assess potential risks associated with exposure to known or potentially toxic agents.

To accurately evaluate the risk from a chemical, it is necessary to estimate the likely exposure to humans and the environment. Assessment of exposure

concentrations can be done by measurements or by estimation such as model-based computation. Several model-based computation tools are available for this purpose.

MERLIN-Expo has been developed within the 2-FUN project "Full-chain and uncertainty approaches for assessing health risks in future environmental scenarios" and 4FUN project. The MERLIN-Expo tool aims to provide decision-makers with state-of-the-art tools to analyse the current and future trends in environmental conditions and pressures that may lead to health problems. Its main objective is to support the evaluation and ranking of management options through a range of functionalities able to generate outputs of high concern for health risk assessment: building of long-term environmental scenarios, exposure assessment, provision of uncertainty margins and identification of sensitive pathways and risks. The MERLIN-Expo multimedia modelling tool allows the user to assemble several models for a specific scenario, to enter input data and parameter values for selected contaminants, to run deterministic (best- or worst-case estimate) or probabilistic (Monte Carlo) simulations and finally to perform sensitivity analysis.

The main objective of this chapter is to identify the strengths and weaknesses of existing exposure tools (aiming at predicting environmental and human (via the environment) exposure), more in particular the MERLIN-Expo tool (see below) using a SWOT analysis. A SWOT analysis is a structured planning method used to evaluate the Strengths, Weaknesses, Opportunities and Threats.

Reviews of exposure tools have been conducted in the past, but resulting analyses generally remain subjective and qualitative because they are not based on a set of transparent and structured criteria. To overcome this drawback and to facilitate thus an objective and reproducible SWOT evaluation, a comprehensive list of criteria was set up to structure the characteristics of exposure tools. In addition, the applicability of exposure tools towards a certain regulatory framework was assessed based on expert judgement.

2 Methodology

The following frameworks where the use of exposure models is relevant were identified:

- REACH Regulation (No. 1354/2007)
- Plant Protection Products Regulation (No. 1107/2009)
- Biocide Regulation (No. 528/2012)
- Environmental compartment-oriented directives (e.g. Water Framework Directive (WFD, 2000/60/EC))
- Food-oriented regulations/directives (e.g. Food Contact Materials (No. 1935/2004)
- Site-specific assessment (e.g. local contaminations)
- Sustainability assessments (SWOT assessment was conducted for hazard-based approaches such as in Cradle to Cradle; note that the relevancy of the criteria for

risk-based approaches such as LCA with USEtox or GLOBOX would perform better)

In this section, the definition of criteria, their importance following regulatory frameworks and exposure models to be assessed, is further outlined. These are the elements for the subsequent comparative assessment and SWOT analysis.

2.1 Assessment Criteria

In order to perform an objective and reproducible SWOT analysis of the MERLIN-Expo model and currently existing exposure models, a comprehensive list of criteria was set up to structure the assessment of the characteristics of exposure models. Relevant aspects, features and functionalities related to an exposure model were identified and translated into a set of evaluation criteria.

The criteria were in first instance the result of a systematic review of the characteristics of exposure models and models available in the literature (EU FP7 Riskcycle [1], EU FP7 Browse [2–4]; EPA [5]; [1, 6–19]).

Secondly, the requirements of certain chemical regulatory frameworks in which MERLIN-Expo can be used to predict environmental and human (indirect via the environment) exposure were taken into account: REACH (EC 1907/2006), Plant protection products (EC 1107/2009), Biocides (EC 528/2012) were covered. These chemical regulatory frameworks were selected as they are relevant at the EU level in the context of chemical substances management and they deal with different classes of chemicals, which have the potential to cause indirect exposure to humans via the environment. Local/regional regulations are also applicable in the evaluation of chemicals; however, the specificities of these regulations are quite variable and are therefore not taken into account in the assessment criteria.

Finally, expert judgement on relevant aspects for environmental exposure modelling was used to improve the list of criteria. This resulted in a total of 155 criteria. The criteria can be distinguished between general criteria (see Table 1 organised in several lines of evidence) and relevance criteria (Table 2).

- General criteria: general model characteristics not related to a certain (regulatory) applicability framework
- Relevance criteria: specific model characteristics of which the importance is highly dependent on the (regulatory) applicability framework in which the exposure tools are used

In order to support the evaluation of exposure models by selected experts, all the obtained criteria were transformed into the form of yes/no questions. A set of experts was asked to use the resulting questionnaire as a guideline to evaluate each exposure model considered in the comparative assessment, as will be detailed below.

Table 1 Hierarchical structure of the assessment methodology based on lines of evidence, categories, subcategories and questions: general criteria

Line of evidence	Category	Subcategory	Question
Contextual knowledge	Model purpose	Model goal	Are the outputs that the end user is able to calculate clearly defined? (e.g. units, unambiguous definition, etc.)
			Are the potential decisions that can be taken from the model outputs clearly defined? (e.g. screening level assessment, priority setting, labelling, higher exposure tier, etc.)
			Are the regulatory frameworks that the model could be useful for clearly defined? (e.g. REACH, Water Framework Directive, Biocide directive, etc.)
	Model applicability	Spatial and temporal issues	Is the spatial applicability domain clearly defined? (e.g. area and/or volume(s) dimensions, near-field vs global scale, spatial boundaries, minimum spatial resolution)
			Is the temporal applicability domain clearly defined? (e.g. minimum temporal resolution, capability to account for daily/monthly/seasonal variability, etc.)
			Is the capability to simulate dynamic scenarios (e.g. intermittent emissions, accidental emissions) explicitly indicated?
		Chemicals	Are the chemicals (or family of chemicals) for which the model is applicable (and inversely non-applicable) clearly defined?
			If the model is partially applicable for some chemicals, are the applied extrapolation rules indicated? (e.g. read-across, extrapolation from neutral organics to ionic organics, etc.)
Conceptual knowledge	Model structure	Media	Are the media that are included in the model clearly defined?
		Emissions and losses	Are the emissions that can be used as input data in the model clearly

(continued)

Table 1 (continued)

Line of evidence	Category	Subcategory	Question
			defined, e.g. point and/or diffuse sources to surface waters, atmosphere, soils, etc.?
			Are the chemical losses from the system that are governed by transport processes (e.g. advection, diffusion) clearly defined?
			Are the chemical losses from the system that are governed by chemical processes (e.g. degradation) clearly defined?
		Exchange processes	Are the chemical exchanges between media clearly defined?
			Are potential chemical exchanges with other coupled models clearly defined?
	Variables	Forcing variables	Are the meteorological forcing variables (e.g. rain, wind speed, temperature, etc.) that are necessary for the simulation clearly defined (e.g. time and spatial resolution, units, etc.)?
			Are the agronomical and anthropogenic forcing variables (e.g. harvest period, spatial distribution of crops, time and spatial patterns, etc.) that are necessary for the simulation clearly?
			Are the other forcing variables that are necessary for the simulation clearly defined?
		State variables	Are the state variables that are calculated by the model clearly defined (e.g. unambiguous definition, units, etc.)?
			For a given state variable, are the other components of the model that are necessary for its calculation (e.g. parameters, forcing variables, other state variables) clearly and comprehensively defined?

(continued)

Table 1 (continued)

Line of evidence	Category	Subcategory	Question
	Parameters	Parameters	Are the parameters that are necessary for model calculation clearly defined (e.g. unambiguous definition, units, etc.)?
			Are the scenario-specific parameters that must be updated by the end user for each case study clearly identified and distinguished from generic parameters? (e.g. river depth, land use coverage, vegetables production in the investigated region, etc.)
Process knowledge	Scientific background	Process relevance	For each process included in the model, is its relevance justified from the scientific background?
			Does the documentation include a list of processes that are not included in the model, with a justification of their exclusion?
		Alternative and limits	For the model selected for representing a given process, is its applicability domain clearly defined? (e.g. chemicals, spatial and time issues, etc.)
			If relevant, are the alternative models available in the literature for representing a given process presented and critically evaluated?
		Model typology	For each process included in the model, is it indicated (with justification) if this latter is based on mechanistic considerations or empirical relationships (e.g. empirically fitted multilinear relationship between a state variable and parameters)?
			For each process represented in the model, is it indicated (with justification) if this latter is based on steady-state or dynamic assumptions?
	Model equations	Equations	Are model equations clearly and comprehensively documented?

(continued)

Table 1 (continued)

Line of evidence	Category	Subcategory	Question
Numerical knowledge	Initial conditions	Initial conditions	Are the default values proposed for the initial conditions (e.g. concentrations in media at time zero) clearly defined?
			Can the initial values be modified by the end user for each new simulation?
	Forcing variables	Forcing variables	Are the default values proposed for the forcing variables (e.g. atmospheric conditions) clearly defined?
			Can the values for forcing variables be modified by the end user for each new simulation?
	Parameter values source	Calibration	If parameter values were estimated from calibration using empirical data, are the number and origin of the data clearly indicated? (e.g. name and accessibility of the databases, literature references, etc.)
			If the parameter values were estimated from calibration using empirical data, is the uncertainty margin indicated? (e.g. probability density function, mean and standard deviation, quartiles, etc.)
		QSAR* or read-across	If QSAR or read-across are used for deriving parameter values, do they clearly indicate for each chemical if it satisfies the applicability domain?
		**Quantitative structure–activity relationship* models (QSAR models)	If QSAR or read-across are used for deriving parameter values, are the number and origin of the data indicated?
			If QSAR or read-across are used for deriving parameter values, is the goodness of fit (or other indicator of correlation performance) indicated?
		Expert judgement and elicitation	If expert judgement is used for deriving parameter values, is the identity of the expert (or group of experts) clearly indicated?
			If expert judgement is used for deriving parameter values, is the expert(s) justification clearly reminded?

(continued)

Table 1 (continued)

Line of evidence	Category	Subcategory	Question
		Bayesian approach	If parameter values were estimated from a Bayesian approach, are the model assumptions (e.g. prior knowledge) clearly indicated?
			If parameter values were estimated from a Bayesian approach, are the number and origin of the data allowing calculating the posterior distribution clearly indicated? (e.g. name and accessibility of the databases, literature references, etc.)
	Parameter values typology	Default values	If a default value is proposed for each parameter, is it clearly indicated if it corresponds to a conservative value (i.e. for worst-case scenario), mean, mode or best estimate?
			If the default value proposed for each parameter is indicated as being a conservative value (i.e. for worst-case scenario), is it justified that it is actually conservative?
		Probabilistic values	If probabilistic density functions are proposed for all/some parameters, is the database used for generating them clearly identified?
			If probabilistic density functions are proposed for all/some parameters, is the statistical method used for generating them clearly described?
Validation process	Implementation verification	Mathematical verification	Was the correct implementation of equations verified, e.g. against implementation on other models?
			If the model requires numerical solutions, was the numerical scheme verified by comparing simulation results against results obtained analytically and with other numerical solvers?

(continued)

Table 1 (continued)

Line of evidence	Category	Subcategory	Question
	Benchmarking	Benchmarking	Were the simulation results obtained for reference scenarios compared with results obtained for these scenarios using other models?
			When results obtained on reference scenarios differ from those obtained with other models, are these differences justified?
	Validation against actual data	(Bio)monitoring validation	Was the model compared to monitoring data collected on abiotic media (e.g. surface waters, air, soil)?
			Was the model compared to monitoring data collected on biological environmental media (e.g. plants, milk, fish, etc.)?
			Was the model compared to biomonitoring data collected on human material (e.g. blood, urine, hair)?
			Were the differences between deterministic simulation results and actual monitoring data acceptable and/or explainable?
			Were actual monitoring data included in the uncertainty margin given by probabilistic simulation?
User-friendliness	Numerical treatment	Model inputs	Is it possible and easy to change the default values for the forcing variables and parameters?
			Can calculated intermediate results be overwritten, e.g. by measured data?
		Model outputs	Is it possible to export the output, e.g. to Excel, Word, pdf?
			Is it possible to present the outputs in a graphical form?
			Is it possible to present the outputs in a tabular form?
			Does the user have access to intermediate results (e.g. exposure estimate for individual exposure routes)?

(continued)

Table 1 (continued)

Line of evidence	Category	Subcategory	Question
	Checking	Checking	Does the model provide alert messages in case of irrelevant or poorly plausible values for parameters? (e.g. in case of unit mistake)
			Does the model provide error messages in case of impossible simulation, and are these messages clear?
			Is it possible to contact a support (e.g. model developer)?
	Running a simulation	Simulation time	Does the model take shorter than 15 min to run a simulation under deterministic conditions (e.g. without uncertainty analysis)?
			Does the model take shorter than 8 h to run a simulation under probabilistic conditions (i.e. for conducting an uncertainty analysis)?
		Simulation repetition	Is it easy to re-run a previous case study? Will the user be able to reproduce the same results (conservation of previous versions)?
	Training	Training	Is a user manual available?
			Are test examples available and easily accessible (e.g. in the user manual, online, etc.)?
			Is a helpdesk/demonstrator available?
	General	General	Is the model freely available?
			Is the model able to communicate with other software (e.g. input from Excel)?
Scenario relevance	General purpose	Chemicals	Does the model cover the chemical(s) you want to study?
			Can the model perform cumulative exposure assessment for the multiple chemicals you want to study?
			If the chemical you want to study is naturally present, can the model discriminate background and anthropogenic concentrations?
			Does the model cover the formation of metabolites that can be formed from the chemical(s) you want to study?

(continued)

Table 1 (continued)

Line of evidence	Category	Subcategory	Question
Uncertainty/ sensitivity	Uncertainty	Uncertainty process	Does the model allow to define each parameter by the widely used distributions (e.g. (log-) normal, (log-)uniform, discrete, student, etc.)?
			Does the model allow generating random samples for each uncertain parameter by the widely used methods (e.g. Monte Carlo, Latin hypercube)?
			Does the model allow to define correlations between parameters and to rank sample values for respecting such correlations?
			Does the model provide statistical summaries for the probabilistically generated outputs (e.g. mean, percentiles, etc.)?
		Sensitivity process	Does the model cover screening methods to conduct sensitivity analysis (e.g. Morris design, etc.)?
			Does the model cover regression methods to conduct sensitivity analysis?
			Does the model cover variance-based methods to conduct sensitivity analysis (e.g. EFAST, Sobol, etc.)

2.2 *Relevance Criteria Importance for Regulatory Frameworks*

In order to evaluate exposure models towards their compatibility in a certain (regulatory) applicability framework, the relevance criteria were scored on their importance in a certain framework as introduced in Sect. 2. All other criteria were considered to be equally important in all frameworks. The scoring was done based on expert judgement. Every criterion was scored from 1 (not relevant) to 5 (prerequisite) for their importance in a certain framework. The scoring of all relevance criteria is presented in Table 3.

From Table 3, it can be concluded that for site-specific assessment, the majority of the criteria are important (fairly high importance on all criteria). This can be explained because site-specific assessments are in general characterised by more flexibility in the exposure assessment (flexibility that is required for the site specifics of the assessment) and can be used in a variety of circumstances.

Table 2 Hierarchical structure of the assessment methodology based on categories, subcategories and questions: relevance criteria

Category	Subcategory	Question
Exposure population	Exposure to worker	Does the model cover exposure to worker (PPP: worker + operator, REACH: consumer, industrial and professional use)?
	Exposure via the general population	Does the model cover exposure via the general population (PPP: resident + consumer), REACH: indirect via environment)?
	Exposure to subpopulations	Does the model cover exposure to subpopulations (adults, children, etc.)?
Compartments	Ground water	Does the model calculate concentrations in groundwater?
	Surface water	Does the model calculate concentrations in surface water?
	Sediment	Does the model calculate concentrations in sediment?
	Marine water	Does the model calculate concentrations in marine water?
	Soil	Does the model calculate concentrations in soil?
	Pore water	Does the model calculate concentrations in pore water?
	Air	Does the model calculate concentrations in air?
	Human body	Does the model calculate concentrations in the human body?
	Organs	Does the model calculate concentrations in organs?
	Milk	Does the model calculate concentrations in milk?
	Blood	Does the model calculate concentrations in blood?
	Fish	Does the model calculate concentrations in fish?
	Leafy crops	Does the model calculate concentrations in leafy crops?
	Root crops	Does the model calculate concentrations in root crops?
	Livestock	Does the model calculate concentrations in livestock?
	Eggs	Does the model calculate concentrations in eggs?
	Dairy products	Does the model calculate concentrations in dairy products?
	Earthworms	Does the model calculate concentrations in earthworms?
Exposure routes	Oral intake of food and drinks	Does the model cover exposure by oral intake of food and drinks?
	Oral intake of soil or dust ingestion	Does the model cover exposure by oral intake of soil or dust ingestion?
	Inhalation	Does the model cover exposure through inhalation?
	Dermal absorption	Does the model cover exposure by dermal absorption?

(continued)

Table 2 (continued)

Category	Subcategory	Question
Environmental processes	Run-off process	Does the model cover the run-off process?
	Leaching of substances in soil	Does the model cover leaching of substances in soil?
	Volatilization process from water	Does the model cover the volatilization process from water?
	Volatilization process from vegetation	Does the model cover the volatilization process from vegetation?
	Volatilization process from soil	Does the model cover the volatilization process from soil?
	Wet and dry deposition to soil	Does the model cover wet and dry deposition to soil?
	Wet and dry deposition to water	Does the model cover wet and dry deposition to water?
	Wet and dry deposition to vegetation	Does the model cover wet and dry deposition to vegetation?
	Adsorption/desorption processes	Does the model cover adsorption/desorption processes?
	Linear/non-linear sorption	Does the model cover linear/non-linear sorption?
	Sediment burial	Does the model cover sediment burial?
	Sedimentation/resuspension	Does the model cover sedimentation/resuspension?
	Biotic and abiotic degradation	Does the model cover biotic and abiotic degradation?
	Degradation in the air compartment	Does the model cover degradation in the air compartment?
	Degradation in the water compartment	Does the model cover degradation in the water compartment?
	Degradation in the sediment compartment	Does the model cover degradation in the sediment compartment?
	Degradation in the soil compartment	Does the model cover degradation in the soil compartment?
	Bioconcentration of substances	Does the model cover bioconcentration of substances?
	Excretion and degradation by animals	Does the model cover excretion and degradation by animals?
	Food processing step of raw material	Does the model cover the food processing step of raw material?
	Vegetal transpiration process	Does the model cover the vegetal transpiration process?
	Transport of the substance by plant death	Does the model cover transport of the substance by plant death?
	Editable transport factor	Does the model cover an editable transport factor of the substance at harvest of the vegetation (e.g. only roots, complete plant, etc.)?

(continued)

Table 2 (continued)

Category	Subcategory	Question
	Crop interception	Does the model take crop interception into consideration?
	Irrigation	Does the model take irrigation into consideration?
Human processes	Internal absorption of substances	Does the model cover internal absorption of substances in the human body?
	Distribution of substances	Does the model cover distribution of substances in the human body?
	Biotransformation	Does the model cover biotransformation in the human body?
	Excretion	Does the model cover excretion from the human body?
	Bioavailability of a substance	Does the model describe bioavailability of a substance in the human body?(= passage of a substance from the site of absorption into the blood of the general circulation)
	Linear and non-linear saturation process	Does the model describe the linear and non-linear saturation process in the human body?
	Accumulation	Does the model describe accumulation in the human body (i.e. the extent of accumulation reflects the relation between the body-burden compared with the steady-state condition)?
Time	Acute exposure	Does the model cover acute exposure?
	Chronic exposure	Does the model cover chronic exposure?
	Dynamic approach	Is the model based on a dynamic approach?
Spatial resolution	Exposure at the local scale	Does the model cover exposure at the local scale (e.g. 1 km^2)?
	Spatially explicit outputs	Does the model provide spatially explicit outputs (e.g. spatial distribution of contaminant concentration in an area/region)?
	Exposure at a regional scale	Does the model cover exposure at a regional scale (e.g. the Netherlands)?
Metabolites	Formation	Does the model cover the formation of metabolites?
Chemical substance	Organics	Is the model focused on organics in general?
	Inorganic chemicals	Does the model cover inorganic chemicals?
	Metals	Does the model cover metals?
	Cumulative exposure assessment	Can the model perform cumulative exposure assessment of multiple chemicals?
	Background concentrations	Can background concentrations (environmental and human compartments) be taken into account?
Releases	Point source release	Does the model cover point-source release?
	Dispersive release	Does the model cover wide dispersive release?
Plant protection products	Exposure to the bystander	Does the model cover exposure to the bystander (for plant protection products)?
	Exposure to the surface water and air	Does the model cover exposure to the surface water and air via spray drift (for plant protection products)

Table 3 Scoring to importance of relevance criteria according to different frameworks of the assessment methodology based on categories, subcategories and questions: relevance criteria

Question	REACH	PPP	Biocide	Environ. compartment oriented directives	Food oriented directives	Site specific assessment	Sustainability
Does the model cover exposure to worker (PPP: worker + operator, REACH: consumer, industrial and professional use)?	5	5	5	1	1	1	3
Does the model cover exposure via the general population (PPP: resident + consumer), REACH: indirect via environment)?	4	5	4	3	5	4	3
Does the model cover exposure to subpopulations (adults, children, etc.)	1	5	1	1	3	4	1
Does the model calculate concentrations in groundwater?	4	5	4	4	2	4	4
Does the model calculate concentrations in surface water?	5	5	5	4	2	4	4
Does the model calculate concentrations in sediment?	5	5	5	4	2	4	2
Does the model calculate concentrations in marine water?	5	1	3	4	2	4	2
Does the model calculate concentrations in soil?	5	5	5	4	2	4	2
Does the model calculate concentrations in pore water?	4	5	4	3	2	4	1
Does the model calculate concentrations in air?	4	4	4	1	2	4	2
Does the model calculate concentrations in the human body?	2	1	2	1	3	3	1
Does the model calculate concentration in organs?	2	1	2	1	3	3	1
Does the model calculate concentrations in milk?	1	1	1	1	3	3	1
Does the model calculate concentrations in blood?	2	1	2	1	3	3	1

Does the model calculate concentrations in fish?	5	5	5	1	3	4	1
Does the model calculate concentrations in leafy crops?	4	4	4	1	3	4	1
Does the model calculate concentrations in root crops?	4	4	4	1	3	4	1
Does the model calculate concentrations in livestock?	4	1	4	1	3	3	1
Does the model calculate concentrations in eggs?	1	1	1	1	3	3	1
Does the model calculate concentrations in dairy products?	4	1	4	1	3	3	1
Does the model calculate concentrations in earthworms?	5	5	5	2	1	3	1
Does the model cover exposure by oral intake of food and drinks?	5	5	5	2	5	4	3
Does the model cover exposure by oral intake of soil or dust ingestion?	1	1	1	1	2	4	1
Does the model cover exposure through inhalation?	5	5	5	1	1	4	2
Does the model cover exposure by dermal absorption?	5	5	5	1	1	3	2
Does the model cover the run-off process?	5	5	5	4	2	4	2
Does the model cover leaching of substances in soil?	5	5	5	4	2	4	2
Does the model cover the volatilization process from water?	5	3	5	4	2	4	1
Does the model cover the volatilization process from vegetation?	3	5	3	3	2	4	1
Does the model cover the volatilization process from soil?	5	5	5	4	2	4	1
Does the model cover wet and dry deposition to soil?	5	3	5	4	2	4	1

(continued)

Table 3 (continued)

Question	REACH	PPP	Biocide	Environ. compartment oriented directives	Food oriented directives	Site specific assessment	Sustainability
Does the model cover wet and dry deposition to surface waters?	4	3	4	4	2	4	1
Does the model cover wet and dry deposition to vegetation?	3	3	3	3	2	4	1
Does the model cover adsorption/desorption processes?	5	5	5	4	2	4	1
Does the model cover linear/non-linear sorption?	1	5	1	4	2	4	1
Does the model cover sediment burial?	4	4	4	3	2	4	1
Does the model cover sedimentation/resuspension?	4	4	4	3	2	4	1
Does the model cover biotic and abiotic degradation?	5	5	5	4	2	4	2
Does the model cover degradation in the air compartment?	5	5	5	4	2	4	1
Does the model cover degradation in the water compartment?	5	5	5	4	2	4	2
Does the model cover degradation in the sediment compartment?	5	5	5	4	2	4	2
Does the model cover degradation in the soil compartment?	5	5	5	4	2	4	2
Does the model cover bioconcentration of substances?	5	5	5	2	2	4	2
Does the model cover excretion and degradation by animals	1	5	1	1	2	4	1
Does the model cover the food processing step of raw material?	1	5	1	1	4	4	2
Does the model cover the vegetal transpiration process?	1	4	1	2	2	3	1

Does the model cover transport of the substance by plant death?	1	1	1	2	1	3	1
Does the model cover an editable transport factor of the substance at harvest of the vegetation (e.g. only roots, complete plant, etc.)?	1	5	1	1	3	4	2
Does the model take crop interception into consideration?	1	5	1	2	2	4	1
Does the model take irrigation into consideration?	1	5	1	2	2	4	1
Does the model cover internal absorption of substances in the human body?	2	1	2	1	3	4	1
Does the model cover distribution of substances in the human body?	2	1	2	1	3	4	1
Does the model cover biotransformation in the human body?	2	1	2	1	3	4	1
Does the model cover excretion from the human body?	2	1	2	1	3	4	1
Does the model describe bioavailability of a substance in the human body? (= passage of a substance from the site of absorption into the blood of the general circulation)	2	1	2	1	3	4	1
Does the model describe the linear and non-linear saturation process in the human body?	2	1	2	1	3	4	1
Does the model describe accumulation in the human body (i.e. the extent of accumulation reflects the relation between the body-burden compared with the steady-state condition)?	2	1	2	1	3	4	1
Does the model cover acute exposure?	5	5	5	1	4	4	1
Does the model cover chronic exposure?	5	5	5	1	4	4	1
Is the model based on a dynamic approach?	1	3	1	2	2	4	1

(continued)

Table 3 (continued)

Question	REACH	PPP	Biocide	Environ. compartment oriented directives	Food oriented directives	Site specific assessment	Sustainability
Does the model cover exposure at the local scale (e.g. 1 km^2)?	5	5	5	3	1	4	1
Does the model provide spatially explicit outputs (e.g. spatial distribution of contaminant concentration in an area/region)?	2	2	1	5	1	3	1
Does the model cover exposure at a regional scale (e.g. the Netherlands)?	5	2	1	3	3	2	1
Does the model cover the formation of metabolites?	1	5	1	1	4	3	1
Is the model focused on organics in general?	5	5	5	5	5	5	4
Does the model cover inorganic chemicals?	5	5	5	5	5	5	4
Does the model cover metals?	5	5	5	5	5	5	4
Can the model perform cumulative exposure assessment of multiple chemicals?	2	3	2	3	4	4	1
Can background concentrations (environmental and human compartments) be taken into account?	3	2	2	3	1	4	1
Does the model cover point-source release?	5	1	5	4	1	4	1
Does the model cover diffuse release?	1	5	1	4	1	4	1
Does the model cover exposure to the bystander?	1	5	1	1	1	1	1
Does the model cover exposure to the surface water and air via spray drift?	1	5	1	1	1	1	1

As for the REACH/Biocide/PPP chemical regulation, internal (human) concentrations are not taken into account yet; the criteria related to the pharmacokinetic modelling therefore receive a low importance score.

For the environmental compartment-oriented directives and food-oriented directives, the number of important relevance criteria is much smaller as the assessment in these directives is generally focused on a single or smaller amount of compartments and media compared to other regulations that cover a broad range of compartments and where e.g. the exposure of man via the environment is assessed.

Finally, it can be concluded that several criteria proposed are not very important for the sustainability assessment. Models used for sustainability assessment are not always as detailed as the models used for exposure assessment in the proposed regulations. For example, a model used to evaluate pesticide leaching will contain detailed processes on the fate of pesticides in the soil, while sustainability models are more hazard based or consider exposure in broad categories and will therefore not require and contain such detailed processes.

2.3 Exposure Models

To identify the strengths and weaknesses of the MERLIN-Expo model, a comparison was made between the MERLIN-Expo model and existing exposure models. Based on a literature review, 97 exposure models were identified, which could be divided into the following categories: environmental concentration, human intake, dietary exposure, consumer exposure and aggregate or multimedia models. Sixty of the identified models were multimedia models. Based on this list and the expertise of the expert panel, the following exposure models were selected to be included in the comparative assessment: CalTOX, ESCAPE, EUSES, GLOBOX, GREAT-ER, MACRO, MERLIN-Expo, MODULERS, PBPK model, PEARL, STEPS 1–2, TOXSWA and USEtoxs. More information on these models can be found below.

2.3.1 CalTOX

CalTOX is a software model, which was designed to help to assess human health risk levels due to contaminated sites and define remediation soil levels [20]. It was developed for the California Environmental Protection Agency (Cal-EPA). The software can also be used at a regional scale, with continuous emissions in soil, air and water.

2.3.2 ESCAPE

ESCAPE (Estimation of Soil Concentrations After PEsticide applications) is able to calculate the fate of the parent compound and up to two metabolites. ESCAPE

calculates initial, time-related and TW (time-weighted average concentrations) in the soil. It is able to calculate plateau concentrations (background concentrations after many years of pesticide application) (http://www.ime.fraunhofer.de/en/business_areas_AE/Fate_Effects_Agrochem/Exposure_modeling.html).

2.3.3 EUSES

The EUSES (European Union System for the Evaluation of Substances) is a decision-support instrument which enables government authorities, research institutes and chemical companies to carry out rapid and efficient assessments of the general risks posed by chemical substances [21]. EUSES is intended mainly for initial and refined risk assessments rather than for comprehensive assessments. Besides the release estimation, only a few data on substance properties are needed to calculate PECs (Predicted Environmental Concentrations) at Tier 1. The output of EUSES is a quantitative comparison per substance of the results of the effects and the exposure assessments respectively. The system can be used to carry out tiered risk assessments of increasing complexity on the basis of increasing data requirements.

2.3.4 GLOBOX

GLOBOX is a spatially differentiated multimedia fate, exposure and effect model. It is used for the calculation of spatially differentiated LCA characterisation factors on a global scale. It is largely based on the European Union model EUSES version 2.0 (current version is 2.1.2) but can be considered as an extended and more refined elaboration of this model [22].

2.3.5 GREATER-ER

The GREAT-ER model (Geo-referenced Regional environmental Exposure Assessment Tool for European Rivers) is a model for environmental risk assessment and management of chemicals in river basins (www.great-er.org) The GREAT-ER model is designed as an advanced environmental exposure model for chemicals in river basins, for use, e.g. in the European chemicals risk assessment process (REACH) and in the EU Water Framework Directive. The model is implemented as part of a software system that combines a GIS (geographic information system) with fate models to produce a simple and clear visualisation of predicted chemical concentrations and water quality along a river.

2.3.6 MACRO

MACRO is a one-dimensional non-steady state model of water flow and solute transport in structured or macroporous field soils [23]. The primary objectives behind the development of MACRO were to synthesise current understanding of flow and transport processes in structured soils and to develop an easy-to-use physically based simulation model that could be used as a management tool to evaluate the impacts of macropore flow on water flow and solute transport both to surface and groundwaters.

2.3.7 MERLIN-Expo

The MERLIN-Expo software [24] is a decision-support instrument that integrates on the same platform a library of both multimedia and PBPK (physiologically based pharmacokinetics) (including metabolites formation) models, allowing to cover the complete exposure assessment chain (from concentrations in water, air and/or soil to internal dose to target organs and eventually pathology risks). The model thus allows lifetime risk for different human populations (e.g. general population, children at different ages, pregnant women) including exposure through multiple pathways.

2.3.8 MODULERS

MODULERS is a software dedicated to the human health risk assessment performed in the framework of the French regulation for the management of contaminated sites and the chemical emissions of the registered facilities. It has been supported by the French ministry in charge of environment and is mainly intended to be used by consultants and companies. It was developed to improve the practices in the risk assessment studies. In accordance to the principles defined in the French guidance's for risk assessment, it was designed and developed to adapt to various site conditions and deepening levels of studies, to provide a transparent approach and to be helpful in conducting uncertainties analysis.

2.3.9 PBPK

In order to provide a proof of concept on how combining in vitro and in silico methods to predict target organ effects on humans under repeated dose exposure, a PBPK model to predict route to route extrapolation and IVIV (in vitro–in vivo) extrapolations was built by the JRC (Joint Research Center).

2.3.10 PEARL

PEARL (Pesticide Emission Assessment at the Regional and Local scale) is used to evaluate the leaching of pesticides to groundwater, drainage of pesticides to surface waters and persistence of pesticides in topsoil [25]. Primary aim is to support European and Dutch pesticide registration for first and higher-tier assessments. Higher-tier assessments include the interpretation of lysimeter studies for pesticide registration. For assessment of pesticide leaching in the EU evaluation process, PEARL was designed to include all the information relative to the standard groundwater scenarios developed by the FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use).

The model was developed to calculate the concentrations of plant protection products in groundwater in the EU review process according to Council Directive 91/414/EEC.

2.3.11 STEPS 1–2

STEPS 1–2 in FOCUS is a stand-alone Surface water Tool for Exposure Predictions – Steps 1 and 2 for the derivation of PEC values in water and sediment based upon the chosen scenario. The model requires a minimum of input values (molecular weight, water solubility, $DT50_{soil}$, Koc, $DT50_{sediment/water}$, number of applications, application interval and application rate) and is designed to evaluate both active substances and metabolites (http://www.ime.fraunhofer.de/en/business_areas_AE/Fate_Effects_Agrochem/Exposure_modeling.html).

2.3.12 TOXSWA

TOXSWA (TOXic substances in Surface WAters) calculates predicted environmental concentrations in surface water to support the pesticide registration procedures in the Netherlands since 1999 for first and higher-tier assessments (http://www.pesticidemodels.eu/toxswa). Higher-tier assessments include the interpretation of field studies for pesticide registration as well as the interpretation of water-sediment studies to determine transformation rates in water and in sediment.

2.3.13 USEtox

USEtox™ is used for characterising human and ecotoxicological impacts in the framework of the LCIA (Life Cycle Impact Assessment) and the CRA (Comparative Risk Assessment) (www.usetox.org). USEtox calculates characterisation factors for human toxicity and freshwater ecotoxicity. The human toxicity to a chemical is evaluated by estimating the intake fraction, which is derived from the

environmental fate and human exposure, and the human effect factor, which is estimated from the dose-response and the chemical severity. The fresh water ecotoxicity is evaluated by estimating the fate factor and the ecotox effect factor derived from the concentration response and the fraction of species potentially affected. USEtox™ is implemented in Microsoft Excel® and applied for 3000+ organic chemicals and 20+ metal species.

3 Comparative Assessment

Several quantitative (e.g. MCDA (Multi-Criteria Decision Analysis), Weight of Evidence) and qualitative (expert judgement) methods can be used to support a SWOT analysis (e.g. [26, 27]). The main purpose of the MCDA methodology is to rank different models in a relative way. The MCDA methodology appeared very useful to structure the SWOT analysis and could be used in a semi-quantitative matter (see Deliverable 2.4 (2014) of the 4FUN project). Further considerations will here be obtained through a qualitative evaluation of individual models based on expert judgement.

In general, multimedia models receive good scoring for a lot of the general criteria. As far as the relevance criteria are concerned (following applicability frameworks), it can be concluded that the assessed exposure models are least applicable to assess sustainability. The assessed exposure models are less applicable to the food and environmental oriented frameworks because the frameworks cover less compartments/media than REACH, PPP, Biocides and site-specific assessments.

The following observations can be made more specifically for each model:

- *MERLIN-Expo* is assumed to be highly suitable for use in *site-specific assessment*. The MERLIN-Expo model, which is a multimedia model containing a lot of processes and media, contains an environmental exposure model and a model able to calculate internal concentrations of chemicals in the human body (PBPK model). The extensive environmental exposure model and the presence of a pharmacokinetic model lead to a higher score compared to the other models, which in general do not contain a PBPK model. As site-specific assessments are less restricted to regulations and can be very variable depending on national, regional or local requirements, a lot of the relevance criteria might potentially be important. Hence, the combination of both makes the MERLIN-Expo model highly suitable for site-specific assessment. Moreover, given a comprehensive description of many environmental processes, MERLIN-Expo is a versatile and flexible tool for several applications.
- In theory, the *CalTOX* model would fit in the *PPP* regulation as it covers some processes which are important in this regulation such as: it covers exposure to subpopulations, concentrations in pore water, volatilization from vegetation, linear/non-linear sorption, the vegetal transpiration process, crop interception,

irrigation, wide dispersive use and exposure to bystanders. Nonetheless, CalTOX is not completely compliant with the PPP regulation. For example, CalTOX does not cover point-source releases, the formation of metabolites. Moreover, for some compartments, the models to be used are predefined. For example, to determine the concentration in groundwater, PEARL or PELMO should be used.

- *EUSES* is highly suitable for *REACH and biocides* as the model covers a large amount of the relevance criteria which are important for REACH and biocides. It is also the recommended model for use in the REACH regulation and the Biocidal Product Regulation.
- *GLOBOX*, which is more or less based on EUSES, will be mostly suitable for *REACH*; however, it does not contain some essential aspects necessary for REACH: no worker/general population exposure, no concentrations in earthworms, or no local scale. A lot of the background processes available are in compliance with REACH; however the outcome are characterisation factors and not exposure concentrations, which makes this model not applicable for the REACH regulation.
- *MODULERS* contains some PPP specific aspects such as linear sorption, excretion/degradation by animals, food processing, irrigation and wide dispersive release. Moreover it would also be applicable for site-specific assessments, and it is a fairly versatile model.
- *USEtox*, which was also based on EUSES, could be used in the exposure assessment for substances under the REACH regulation. However, similar to GLOBOX, the outcomes are characterisation factors which are useful in LCA (Life Cycle Analysis) frameworks but not useful in REACH.
- *GREAT-ER* is recommended as a higher-tier model for the fate of chemicals in surface water in the REACH regulation. Therefore the model is suitable to cover exposure assessment of surface water for this framework. However, as its use is limited to exposure to water, the model will not further be included in the comparative assessment.
- *PBPK* is a pharmacokinetic model and is therefore focused on determining the internal concentrations in the human body. This model can be useful for site-specific assessment as this type of assessment might take internal concentrations into consideration, which is currently not the case yet for e.g. REACH, PPP and biocides. However, since it does not include any environmental aspect, this model will not further be included in the comparative assessment.
- *MACRO*, *PEARL*, *STEPS 1–2*, *TOXSWA*, *ESCAPE*. All these models are recommended by the authorities for use in the environmental exposure assessment of plant protection products. As they are not multimedia models and therefore less suitable for comparison, these models will not be further discussed.

Table 4 SWOT analysis of the MERLIN-Expo model with a focus on relevance/framework-dependent aspects and processes of models

Strengths		Threats	Weaknesses		Opportunities
General	Detailed		General	Detailed	
Covers internal absorption, distribution of substances, biotransformation, accumulation and excretion in/from the human body and determines concentrations in the human body, organs and blood (PBPK model)		Not all regulations require this		Saturation process in the human body is missing	Implementing the saturation process in the human body
				Bioavailability in the human body is missing	Implement bioavailability in the human body
Applicable for a wide range of chemicals		Not all regulations require this		No speciation and bioavailability processes for metals included	Implement speciation and bioavailability processes for metals
It covers the majority of the processes, media, exposure routes and human populations	Covers bioaccumulation, excretion and degradation by animals	Not all regulations require this	Not all processes, media, exposure routes and human populations are covered	No calculations in groundwater	Implementing a groundwater model
	All ages can be evaluated	Not all regulations require this		No non-linear sorption	Implementing non-linear sorption
	Discriminates between background and anthropogenic concentrations	Not all regulations require this		No sediment burial	Implementing sediment burial
	Covers an editable transport factor of the substance at harvest of the vegetation	Not all regulations require this		No dermal exposure	Implementing dermal exposure

(continued)

Table 4 (continued)

Strengths		Threats	Weaknesses		Opportunities
General	Detailed		General	Detailed	
	Performs cumulative (i.e. parallel) exposure assessment of multiple chemicals	Not all regulations require this		No ageing of chemicals in soil	Implementing ageing of chemicals in soil
				No concentrations in eggs	Implement calculation of concentrations in eggs
				Marine environment and coastal zone not included for fate modelling	Implementing a marine compartment
				No concentrations in earthworms	Implementing equations to calculate earthworm concentrations for secondary poisoning
				No Influence of food processing	Food processing could be included before ingestion
				No formation of metabolites	Implementing metabolite formation cfr. MACRO, PEARL
				No purification of drinking water	Add a purification step before ingestion of surface water
				Inclusion of spray drift	Inclusion of a drift calculator based on Ganzelmeier
				No ingestion of surface water during recreational activities	Insert ingestion of surface water during recreational activities

				No weighted average of human intake at conditions with and without rainfall	Insert weighted average of human intake at conditions with and without rainfall
				Does not contain a model for elimination of chemicals by sewage treatment plants and sludge application on soil	A model for the elimination of chemical by sewage treatment plants can be inserted, e.g. SIMPLETREAT
				No lateral transfer of chemicals	Inclusion of the advection process
				Does not consider occupational and consumer exposure	Implementing an occupational and consumer exposure model
				No indoor air exposure	Implementing an indoor air compartment

Table 5 SWOT analysis of the MERLIN-Expo model with a focus on general model aspects

Strengths		Threats	Weaknesses		Opportunities
General	Detailed		General	Detailed	
QSARs are available to estimate certain parameters		Unreliable results because QSAR predictions can be highly uncertain and/or not applicable			
User-friendly model	User-friendly GUI		Helpdesk and user forum are not available yet		Setting up a helpdesk and user forum
	Easy import/export of data/results			Test examples are not yet available	Include test examples
	Control of out of range of values introduced by the user		Only exposure, no risk assessment		Hazard assessment should be added to calculate risks
	Implemented step-by-step input				
	Graphical visualisation of the results				
Complete documentation for novice and expert	Extrapolation rules are indicated				
	Number and origin of the data used to estimate parameter values from empirical data is clearly indicated		Substance database	Limited quality control of the substance data	Perform quality control or only keep QC data
	Number and origin of the data used to estimate parameter values from empirical data is clearly indicated			Limited range of pollutants in the database	Expand the database

	Applicability domain of QSARs or read-across is well indicated			Requires a relatively large amount of input parameters if the substance is not in the database	Expand the database
	Number and origin of the data used for QSARs or read-across is well indicated				
	Model assumptions using the Bayesian approach to estimate parameter values are clearly indicated				
	Number and origin of the data allowing calculating the posterior distribution of parameter values estimated using a Bayesian approach are clearly indicated				
	Type (conservative, mean, mode or best estimate) of default value is clearly indicated				
	The database used for generating probability density functions of parameters are clearly identified				
Regular trainings are provided		No continuation after termination of the project, low attendance			

(continued)

Table 5 (continued)

Strengths		Threats	Weaknesses		Opportunities
General	Detailed		General	Detailed	
Models were verified	Implementation of equations was verified. Benchmarking with other exposure models was done		Validation		
	Numerical solutions were verified by comparing the results with analytical results or with other number solvers. Model results were compared with monitoring data				
Modular and flexible model	All parameter values can be adopted	Misuse by users, potentially lower acceptability by regulators as it less standardised		Intermediate results cannot be overwritten	Insert functionality were intermediate results can be overwritten by e.g. measured data
	No fixed units		Undefined scope	Not recommended or authorised for use in any regulation yet	Advocacy
	Ability to perform multi-simulations changing the values of one or several parameters			Not fully compliant with the REACH, PPP, Biocide regulation	Make equations/parameters compliant to one of the regulations
	Equations and intermediate results are highly accessible				
	Able to simulate dynamic scenarios	Not all regulations require this	Spatially explicit outputs		Consider implementation of spatially explicit GIS based models

4 SWOT Analysis of the MERLIN-Expo Model

A SWOT analysis involves specifying the objective and identifying the internal and external factors that are favourable and unfavourable to achieve that objective. The objective here is to assess exposure tools aiming at predicting environmental and human (via the environment) exposure. The comparative assessment above is the basis for the SWOT analysis (with particular focus on MERLIN-Expo). An overview of the strengths, weaknesses, opportunities and threats is presented in Tables 4 and 5, for, respectively, relevance/framework dependent aspects of models and for general model aspects.

All identified points were categorised into strengths and weaknesses. Threats and opportunities were determined based on, respectively, strengths and weaknesses, if applicable. Strengths and weaknesses are on their turn divided in general aspects and detailed aspects. Not all identified missing aspects should receive the same importance. For example, concentrations in eggs, soil ingestion, ingestion of meat contaminated via soil ingestion, ingestion of water during recreational activities are of less importance than the inclusion of a groundwater and a marine compartment. Hence, the implementation of each opportunity should be decided on a case-by-case basis.

The general strengths listed below could serve as a basis to market the MERLIN-Expo model as this highlights the added value.

The weaknesses/opportunities can be considered as actions, which can be implemented, if desirable and feasible.

5 Conclusion

MERLIN-Expo has many advanced functionalities (such as uncertainty analysis, modular approach, dynamic model, combines environmental fate with pharmacokinetics) and models (many fate processes and environmental compartments, different human populations). At the same time, the threat is that current (regulatory) applicability frameworks do not always require these advanced assessment functionalities. The MERLIN-Expo tool appeared to be most suitable for the site-specific assessment as this is the most flexible framework. Based on this analysis, weaknesses of the MERLIN-Expo tool for its use in a certain regulatory framework could also be identified. These weaknesses are at the same time further development opportunities for MERLIN-Expo. On general model characteristics, MERLIN-Expo was identified as a highly documented (both for novice and expert level), transparent, user-friendly tool with regular trainings. Its main threat now is to ensure continuing support and mechanisms for future developmental work and updates.

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Standard Documentation of Exposure Models: MERLIN-Expo Case Study

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Abstract At the example of the MERLIN-Expo case study, important aspects of the documentation and of standardisation of chemical exposure models are discussed. A key challenge faced by developers of large or complex chemical exposure models is limited transparency leading to loss of confidence in the applicability of results of the model and other inefficiencies such as lacking interoperability. These inefficiencies can be addressed by standardisation which is explained as a process leading to improved common definitions, transparency and reliability in application. A review of available frameworks on the documentation of exposure models as well other complex models is conducted. The process of arriving at consensus on recommended documentation of exposure models via a workshop process is described, involving representatives from different stakeholders such as scientists, regulators, manufacturers or consultants. Key components of the documentation of chemical exposure models are presented, and a way to structure the communication of the information is proposed. The role of standardisation in supporting research and innovation projects is illustrated.

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Keywords Case study • Complex model • Documentation • Exposure model • Standardisation

Contents

1 Background

1.1 Introduction

MERLIN-Expo is a software supported platform containing multimedia models, pharmacokinetic models and uncertainty and sensitivity analysis tools for the purpose of chemical exposure assessment (for further details on MERLIN-Expo, see the dedicated website http://merlin-expo.eu). A key attraction of MERLIN-Expo is to enable coupling of models among each other, potentially covering the entire exposure path, from release of a chemical across various environmental media and organisms to resulting concentrations of the chemical in specific parts of the human body. Some of the component models of MERLIN-Expo are portrayed in further chapters of this book. In order to take MERLIN-Expo from a prototype to a viable tool that is broadly available, a standard documentation for its component models was developed. The purpose of this MERLIN-Expo case study is to:

- Illustrate key features of the standard documentation and its benefits for chemical exposure model users
- Illustrate the process of standardisation and its role in bridging the gap between innovation and implementation

1.2 The Challenge faced by MERLIN-Expo

One of the key market barriers identified for MERLIN-Expo (and for exposure models in general) was the lack of transparency of its complex models to users. The MERLIN-Expo models and chemical exposure models in general involve indeed a

large set of entities, input data, variables, boundary conditions and underlying hypotheses. This complexity can cause potential outputs with poor operational reproducibility among different users which can lead to lack of confidence in modelling, decision errors and other inefficiencies. The documentation of chemical exposure models often tends to be a mixture of free style general considerations, verbal descriptions of processes, lengthy justifications of the specific model formulations and mathematics, which makes reading exposure model descriptions to choose the right model for a given purpose a cumbersome experience, while the interpretation of results often remains ambiguous.

Poor documentation can be acceptable when models are built for initial or exploratory research or for proof of principle, where no litigation or regulatory action is expected. However, the standardised MERLIN-Expo that intends to reach a wide range of end users (like regulators, industry, SMEs, academia) and to be freely used as a support to policymaking must satisfy higher standards of transparency. To overcome this barrier of non-transparency to third party users, a "standard documentation framework" was developed, providing guidance on what should be the content of an exposure model documentation and how the information is best to be presented. Consequently, documentation of all exposure models on the MERLIN-Expo platform follows this framework.

1.3 Standardisation

There is no single definition for what a standard or standardisation is. The Oxford dictionary offers several definitions, for example, "a required or agreed level of quality or attainment" or "something used as a measure, norm, or model in comparative evaluations" (http://www.oxforddictionaries.com/definition/english/standard). ISO defines a standard as "a document that provides requirements, specifications, guidelines or characteristics that can be used consistently to ensure that materials, products, processes and services are fit for their purpose" (http://www.iso.org/iso/home/standards.htm). Generally speaking, standardisation is a process leading to agreement on common units and definitions to enable communication and exchange between different groups. Most people are aware of standards for country codes (such as UK or ES), for paper size (such as A4), for mobile telephones (such as GSM), for connecting cables (such as USB) or for bank transactions (such as IBAN or BIC), to name but a few illustrations. Since more recent times, standards also provide general recommendations or guidelines to ensure a minimum performance, for example, to ensure safety or protection of the environment. Well-known examples of standards containing such recommendations are hotel rankings from * to ***** or the ISO 9001 on the requirement for quality management systems or the energy efficiency labels on household appliances. Providing common definitions for a better mutual understanding and establishing minimum requirements to ensure safety of use as faced by the prototype of MERLIN-Expo is therefore a situation classically addressed and resolved by standardisation.

Standards are developed on a voluntary basis by those concerned in various ways. For example, they can evolve from tradition or can be developed by a leading company whose methods or product features may become the standard if tacitly accepted and adhered to by others. There are also different groups and platforms that develop standards. Industry associations often develop and recommend a standard (e.g. the Code of Ethics developed by the International Council of Museums) or international organisations such as the WHO or the OECD. In almost all countries there are also official national standardisation bodies (NSBs) which provide platforms open to all individuals and groups for the development of standards (for the list of the European NSBs, see http://standards.cen.eu/dyn/www/f?p=CENWEB:5). The NSBs maintain standing committees of experts (so-called "technical committees") responsible for standardisation in specific areas (e.g. "occupational health" or "ceramic products") which represent a broad cross section of stakeholders from industry and commerce, consulting agencies, academia and research bodies, consumers and labour, NGOs, public authorities and governments. The NSBs together form the European and International Standardisation Organisations, CEN and ISO, respectively. The European Committee for Standardisation (CEN) offers the "CEN workshop", a platform allowing research projects to develop a best practice document as a stepping stone to a European standard, to facilitate interoperability and to facilitate further incremental innovations in the market (see CEN-Cenelec Guide 29 on workshop agreements, http://boss.cen.eu/developingdeliverables/CWA/Pages/default.aspx) [1]. CEN workshops allow European research projects to develop best practice documents in areas of innovation, with little overhead and within a relatively short period of time.

2 Standard Documentation Framework

2.1 Exploratory Research

To start, literature dealing with the documentation of exposure models as well as other complex models was collected and reviewed. The result of the literature search is represented in Table 1.

All of the documents contained some relevant aspects that were used as a resource and reference material for the development of a more general and broadly applicable standard documentation framework for large exposure models.

In particular, Guidance on the development, evaluation and application of environmental models by the US Environmental Protection Agency was a rich resource of material related to the process of creating modelling tools for environmental regulatory modelling, as well as challenges to be faced in making the modelling tool more transparent and reliable for users and policymakers. Documenting environmental models has been highlighted as important step for improving applicability and transparency of a model intended for regulatory decision making. Box 11 of the same document lists recommended elements for

Table 1 Result of literature search on documentation of complex models

Author/source	Title
US Environmental Protection Agency [2]	Guidance on the development, evaluation and application of environmental models
Grimm et al. [3–5]	The "Overview, Design concepts, and Details (ODD)" framework is developed in several consecutive articles: Individual-based modelling and ecology, A standard protocol for describing individual-based and agent-based models, The ODD protocol: A review and first update
Canadian Environmental Modelling Network (CEMN) [6]	Development and application of models of chemical fate in Canada
OECD (Organisation for Economic Co-operation and Development) [7]	Guidance document on the validation of quantitative structure-activity relationship (QSAR) models
Bilitewski et al. [8]	Global risk-based management of chemical activities II, risk-based assessment and management strategies
ISO (International Standardisation Organisation) [9]	ISO/TS 14033. Environmental management – Quantitative environmental information – Guidelines and examples
CEN (European Committee for Standardisation) [10]	CEN/TR 16364. Influence of materials on water intended for human consumption – Influence due to migration – Prediction of migration from organic materials using mathematical modelling
WHO (World Health Organisation) [11]	Principles of characterizing and applying human exposure models

environmental model documentation, but it does not deal in more detail with communication levels for different users that was of interest for the MERLIN-Expo project.

Further analysis showed that several publications by Grimm et al. on the Overview, Design concepts, and Details (ODD) framework also focus on documentation rather than the development or evaluation of models and enable to structure and communicate information about models. However, the ODD framework was developed to be applied for modelling of ecological systems, which contains aspects not relevant for multimedia models while missing others that would be relevant.

A report on Development and application of models of chemical fate published by the Canadian Environmental Modelling Network (CEMN) contains methodology for the ranking of complexity of a model on four levels, which is now commonly used among the environmental model developers and users. However, the categorisation of models by level I–IV may not be so useful for model users who are not familiar with environmental models.

The Guidance document on the validation of quantitative structure-activity relationship (QSAR) model by OECD (Organisation for Economic Co-operation and Development) covers the majority of aspects related to a standard documentation framework. Moreover, it is already an internationally accepted standard and gives stepwise instructions for a very precise way to document the development and

verification of a model. However, it deals only with QSAR models and the proposed approach is not generally applicable to chemical exposure models.

In research work performed by Bilitewski et al. [8], "Global risk-based management of chemical activities II, risk-based assessment and management strategies", nine complex environmental models were described and evaluated by predefined principal characteristics. The principal characteristics could be used to describe exposure models; however, the description for each principal characteristic is lacking detail, and all the information is delivered at the same level and therefore does not provide a framework.

The ISO/TS 14033 from ISO (International Standardisation Organisation) is directly applicable to large exposure models and already constitutes an international standard. However, it is too broad and abstract, providing guiding principles and a process to develop a framework rather than a concrete and detailed framework itself.

The CEN/TR 16364 from CEN (European Committee for Standardisation) provides a concrete standardised modelling procedure relying on a software tool and states the required documentation; however, it is applicable only to a very small area, the migration of organic substances into water.

The WHO (World Health Organisation) report "Principles of characterizing and applying human exposure models" contains collective views of an international group of experts and provides clear and structured recommendations for characterising exposure models but is focusing on human exposure and does not consider aspects for environmental multimedia models.

The approach taken by MERLIN-Expo was to build up on existing knowledge to cover the needs of a wider chemical exposure model community by suggesting a structured documentation framework that would provide necessary model information at different levels of complexity. By doing this the intention was to fill the existing gap in the quality and profile of information given by modellers to final model users that can often have different levels of professional experience. This novel, user-focused, tiered approach is described in more details further in the chapter. Some technical terms and definitions have been adopted from "Guidance on the development, evaluation and application of environmental models" by the US Environmental Protection Agency for the purpose of the standard documentation framework and properly referenced in consequently proposed document.

In order to define the exact structure and sub-elements to propose for standardised documentation framework, in addition to the literature search, a review on currently existing large environmental models and on their documentation was carried out [11–22]. A short summary of the identified components and aspects is presented in Table 2. Initially the work has been focused on large exposure models, but as more information on model components was collected, it has been recognised that the same structure could be applied to a broader range of compartmental models.

As can be seen by a cursory look at Table 2, many very different model components and aspects have to be covered, and communicating them in a

Table 2 Summary of common aspects and components of documentations of complex environmental models

Aspect	Component	Description
General model information	Model developer	Define the identity and contact details of the model developer
	Helpdesk	Indicate if there is an external helpdesk
	Communication with other software	For example, import/export from excel
	Operating systems	For example, Windows, Mac, etc.
	References	Quote the references used to describe the model
Model context	Model approach	Probabilistic/deterministic, empirical/mechanistic, simulation/optimisation, lumped/distributed
	Model range	Define the boundary conditions
	Model complexity	Define the degree of complexity (based on fugacity level)
	Temporal resolution	Describe the static/dynamic approach
	Spatial resolution	Define the spatial resolution of the model (e.g. local, regional, etc.)
	QSAR	Define and describe which QSARs are applied in which part of the model
Model development	Individual/ population	Define if individuals or which part of the population is targeted with the model (worker, general population, division in subgroups, etc.)
	Exposure routes	Describe the possible exposure routes of the model (e.g. ingestion, inhalation, dermal absorption)
	Compartments	Give an overview of all compartments studied and include a graphic representation of the conceptual model
	Environmental processes	Describe the prevailing environmental processes per compartment (e.g. for soil: leaching, run-off, etc.)
	Human processes	State the human processes taking place in the human body (e.g. accumulation, excretion, distribution)
	Exposure time range	Identify whether the model covers acute and/or chronic exposure
	Equations and statements	Define the equations and statements per compartment
	Chemical substance	Outline the chemical range of substances that can be analysed with the model (e.g. metals, organics, etc.) If mixture toxicity is included in the model, define the approach used to assess this Define the origin of background concentrations, if used
	Input parameters	List the input parameters and their units necessary to perform a simulation State which kind of point value is required (e.g. mode, mean, etc.) State which probability distributions can be applied for input values

(continued)

Table 2 (continued)

Aspect	Component	Description
	Default parameters	List the default parameters, their value and origin (reference)
	Risk management measures	Define the use of risk management measures if applicable
Model evaluation	Model validation	Indicate the validation process performed for the selected applications of the model
	Error messages	List the main error messages which might be occurring
	Process time	Provide suggestions on how to speed up the simulation
	Uncertainty	Explain how to display predicted exposure profiles and uncertainties
	Probabilistic approach	Define the different probabilistic approaches possible and their applicability domain
	Sensitivity analysis	Describe the sensitivity analysis to determine key inputs and parameters
Output	Results accessibility	Define how to obtain intermediate results
	Reporting	State the functions to build a report
	Graphs/tables	Define how to build a graphical and tabular output
Model application	Model framework/ purpose	Identify the (regulatory) framework (e.g. REACH, PPP, screening assessment, etc.)
	Scenario analysis	Describe how to run the model with several conditions, assumptions or mathematical approaches

comprehensive way that can easily be understood and is applicable to different types of exposure models can become a very labour-intensive and non-trivial task.

2.2 MERLIN-Expo Standard Documentation Framework

Following the review of literature and of sample documentations, a list of key items was distilled ("low-level structure") that should be covered by a standard documentation of a large exposure model, which then were clustered around topics ("high-level structure"). The list of items and topics was then applied to the documentation of the EUSES model[1] and to the MERLIN-Expo river model and further refined based on the experience, resulting in the framework displayed in Table 3 which provided the framework for documenting all models of MERLIN-Expo.

To tailor the communication to the needs of different users, it was proposed to display the information on levels of increasing detail with specific audiences in mind:

[1]The European Union System for the Evaluation of Substances. See https://ec.europa.eu/jrc/en/scientific-tool/european-union-system-evaluation-substances.

Table 3 MERLIN-Expo standard documentation framework

High-level structure	Low-level structure	Description
Model purpose	Goal	General statement of the model outputs of concern, the stressors and the degree of model accuracy and precision needed. Explanations of what is the purpose of the model
	Decisions or regulatory framework	Identification of the (regulatory) framework to be supported (e.g. REACH, PPP, screening assessment, etc.)
Model context/ applicability	Spatial scale/ resolution	The spatial conditions (extent and resolution) and practical constraints under which environmental data and processes were defined during the model development and over which it should be evaluated. Boundaries or domain, specifying the area or volume (spatial boundary) to which a model application will apply: local, regional, continental or global scale
	Temporal scale/ resolution	The temporal conditions (extent and resolution) and practical constraints under which environmental data and processes were defined during the model development and over which it should be evaluated. Boundaries or domain specifying the time period (temporal boundary) to which a model application will apply
	User community	Define target users if applicable
	Required inputs	List and describe required input data and provide their units of measurement
	Output of interest	To ensure transparency in the output being predicted by a given model, since a given endpoint could be determined by different experimental protocols and under different experimental conditions, including units of measurement
	System limitations	Boundary conditions of the system
	Exposure pathways	The course a chemical takes from a source to an exposed organism. An exposure pathway describes a unique mechanism by which an individual or population is exposed to chemicals at or originating from a site. Each exposure pathway includes a source or release from a source, an exposure point and an exposure route. If the exposure point differs from the source, the transport/exposure medium (such as air) or media (in cases of intermedia transport, such as water to air) are also included
	Exposure routes	The way a chemical or physical agent comes in contact with an organism, i.e. inhalation, ingestion, dermal contact. Describe the possible exposure routes of the model
	Fate, exposure and effect	State if fate, exposure and effect analyses are included or not

(continued)

Table 3 (continued)

High-level structure	Low-level structure	Description
	Chemical considered	Outline the range of chemical substances that can be analysed with the model (e.g. organic pollutants, inorganic pollutants, etc.). If mixture toxicity is included in the model, define the approach used to assess this. Define the origin of background concentrations, if used
	Media considered	An environmental or human compartment assumed to contain a given quantity of the chemical. Quantity of the chemical in the media is governed by inputs/outputs from/to other media and by transformation processes (e.g. degradation): air, water (fresh, ground, sea, etc.), soil, sediment, vegetables, animals, etc. and a graphic representation of the conceptual compartments
	Human population	Define which individuals or part of the population is targeted with the model (worker, general population, division in subgroups, etc.)
	Environmental processes	Describe the prevailing environmental processes per compartment (e.g. for soil: leaching, run-off, etc.)
	Human processes	State the human processes taking place in the human body (e.g. accumulation, excretion, distribution)
Model component	Initialisation	Initial conditions assumed, i.e. what are the initial values of the state variables and is initialisation always the same or changing among simulations?
	Overview input data	Environmental conditions which change over time and space, i.e. precipitation, management (e.g. harvesting regimes)
	State variable	The dependent variables calculated within a model, which are also often the performance indicators of the models that change over the simulation
	Forcing/driving variable	An external or exogenous (from outside the model framework) factor that influences the state variables calculated within the model. Such variables include climatic or environmental conditions (temperature, wind flow, oceanic circulation, etc.)
	Parameters	Terms in the model that are fixed during a model run or simulation but can be changed in different runs as a method for conducting sensitivity analysis or to achieve calibration goals. List the input parameters and their units necessary to perform a simulation. State which kind of point value is required (e.g. mode, mean, etc.). State which probability distributions can be applied for input values. Indicate if QSARs are applied for which parameter in which part of the model

(continued)

Table 3 (continued)

High-level structure	Low-level structure	Description
	Constants	A fixed value (e.g. the gravitational force) representing known physical, biological or ecological activities. List the constants, their value and origin (reference)
	Model structure/ framework	The system of governing equations, parameterisation and data structures that makes up the mathematical model. The model framework is a formal mathematical expression of the concepts and procedures of the conceptual model consisting of generalised algorithms. Detailed explanation of all the sub-models representing the processes listed above in "Process overview and scales", including the parameterisation of the model. All model equations and rules should be presented
Model type	Simulation vs. optimisation	Statement of the model type; simulation vs. optimisation
	Steady-state versus dynamic	Statement of the model type; static (steady-state) (a model providing the behaviour of the state variables assumed to be in immediate equilibrium with all the other interacting state variables or a model providing the long-term or time-averaged behaviour of the state variables) vs. dynamic (a model providing the time-varying behaviour of the state variables)
	Deterministic vs. stochastic	Statement of the model type; deterministic (mathematical model in which the parameters and variables are not subject to random fluctuations, so that the system is at any time entirely defined by the initial conditions chosen) vs. stochastic (model that includes uncertainty and variability in model parameters as a function of changing conditions, spatial and temporal aggregation within the model framework and random variability)
	Lumped vs. distributed	Statement of the model type: solving a set of ordinary differential equations or solving partial differential equations
	Analytical or numerical model	Analytical (a model that can be solved mathematically in terms of analytical functions. For example, some models that are based on relatively simple differential equations can be solved analytically by combinations of polynomials, exponential, trigonometric or other familiar functions) or numerical model (a model that represents the development of a solution by incremental steps through the model domain. Simulations are often used to obtain solutions for models that are too complex to be solved analytically. For most situations, where a differential equation is being approximated, the simulation model will use finite time step (or spatial step) to "simulate" changes in state variables over time (or space))

(continued)

Table 3 (continued)

High-level structure	Low-level structure	Description
	Mode (of a model)	The manner in which a model operates. Models can be designed to represent phenomena in different modes. Prognostic (or predictive) models are designed to forecast outcomes and future events, while diagnostic models work "backwards" to assess causes and precursor conditions
	Screening model	A type of model designed to provide a "conservative" or risk-averse answer. Screening models can be used with limited information and are conservative, and in some cases they can be used in lieu of refined models, even when time or resources are not limited
Model evaluation	Model coding verification	Examination of the algorithms and numerical technique in the computer code to ascertain that they truly represent the conceptual model and that there are no inherent numerical problems with obtaining a solution
	Input data	The accuracy, variability, and precision of input data. The source of parameter default values, as well as probability density functions, should be indicated in the standard documentation protocol, with an explanation of the process of parameter estimation (e.g. expert elicitation, extrapolation, statistical treatment of environmental data)
	Model calibration	If applicable, the general explanation about model calibration
	Model framework/ structure uncertainty	The uncertainty in the underlying science and algorithms of a model. Model framework uncertainty is the result of incomplete scientific data or lack of knowledge about the factors that control the behaviour of the system being modelled. Model framework uncertainty can also be the result of simplifications necessary to translate the conceptual model into mathematical terms
	Model predictivity	The predictivity of a model, determined by using an appropriate test set. There is no absolute measure of predictivity that is suitable for all purposes, since predictivity can vary according to the statistical methods and parameters used in the assessment: • Indication in test set is independent from training set (if relevant) • Provide details on full test set • Representativeness of test set

(continued)

Table 3 (continued)

High-level structure	Low-level structure	Description
	Uncertainty analyses	Investigation of the effects of lack of knowledge or potential errors on the model (e.g. the "uncertainty" associated with parameter values). When combined with sensitivity analysis (see definition), uncertainty analysis allows a model user to be more informed about the confidence that can be placed in model results. Uncertainty analysis can be qualitative or quantitative
	Sensitivity analysis	The computation of the effect of changes in input values or assumptions (including boundaries and model functional form) on the outputs [23]; the study of how uncertainty in a model output can be systematically apportioned to different sources of uncertainty in the model input [24]. By investigating the "relative sensitivity" of model parameters, a user can become knowledgeable of the relative importance of parameters in the model

Level 1 – **Basic knowledge**
Provides a general overview for end users who trust model developers on scientific, numerical and mathematical issues

Level 2 – **Process knowledge**
Targeted towards end users, who want to have a clear understanding of the scientific background and foundations of the model

Level 3 – **Numerical knowledge**
Targeted towards end users, who want to have a clear vision of all the parameter values included in the model, to better capture the assumptions related to the parameterisation of the model

Level 4 – **Mathematical knowledge**
For end users who want to deeply understand the equations that translate the processes described at level 2

3 CEN Workshop

3.1 CEN Workshop "MERLIN-Expo"

After developing the MERLIN-Expo standard documentation framework, the project team decided to take standardisation on documentation one step further to integrate the perspectives and requirements of other stakeholders outside the consortium, such as regulators or potential users of the MERLIN-Expo tool. With the aim to create a platform for standardisation that would integrate other stakeholders, it was decided to set up a CEN workshop. The MERLIN-Expo standard

documentation framework would be provided as a basis for the workshop along with the sample documentation of the first documented model ("River model") from the MERLIN-Expo tool. On this basis, the workshop should then develop a standard documentation of chemical exposure models.

The CEN workshop was publicly advertised and also communicated to CEN technical committees dealing with chemicals, inviting participation specifically from public administrators and regulators dealing with risk assessment and chemicals and from producers of chemicals/manufacturers using chemicals. The kick-off meeting of the workshop took place on July 2, 2014, in Brussels. The following members participated in the CEN Workshop (in bold are the participants from outside the MERLIN-Expo consortium that were new to the project):

- Aeiforia Srl, Federico Ferrari and Gabriella Fait
- ARCHE cvba (Assessing Risks of Chemicals), Frederik Vedonck
- Electricité de France S.A. (EDF), Philippe Ciffroy
- **European Commission's Joint Research Centre (JRC), Stylianos Kephalopoulos, Alicia Paini and Anita Radovnikovic**
- **European Food Safety Authority (EFSA), Jean Lou Dorne**
- Facilia AB, Rodolfo Avila Moreno
- **Federal Institute for Risk Assessment (BfR), Gerhard Heinemeyer**
- **French Institute for Radiological Protection and Nuclear Safety (IRSN), Marie Simon-Cornu**
- Institut National de l'Environnement Industriel et des Risques (INERIS), Céline Brochot
- **Netherlands Organisation for Applied Scientific Research (TNO), Wouter Fransman**
- Università Cattolica del Sacro Cuore, Ettore Capri and Nicoleta Suciu

The objective of the workshop was to agree on minimum requirements for the amount and type of information to be provided on exposure models along with guidelines for the structure and presentation of the information within a timeframe of little more than 1 year. The resulting workshop agreement (CWA) was expected to facilitate a more rigorous formulation of exposure models, to improve the comparability between different exposure models, their transparency and the understanding by users.

In a first step, the MERLIN-Expo standard documentation framework was transferred into the standard format foreseen by CEN for European standards (CEN/CENELEC [25] Internal Regulations Part 2), including a clear definition of the scope and applicability of the standard and a section on terms and definition to be used consistently throughout. The body of the text of the framework was changed from descriptive to prescriptive, rephrasing the text to contain requirements and recommendations rather than descriptions or rationales. The latter renders a standard easy to use by giving clear instructions.

At the core of the workshop process to deliver the workshop agreement were cycles of reviews and comments by participants of the workshop until a general consensus had been reached on a draft text. For example, there were long discussions on the terms and definitions section on what individual terms like "exposure"

or "model" should designate in the context of exposure models or what "basic knowledge" was meant to contain on a chemical exposure model. Important new perspectives have been integrated from participants from outside the MERLIN-Expo project, from the point of view of consumer exposure models and worker exposure models, both frequent applications of chemical exposure models outside environmental multimedia models.

The draft workshop agreement was then submitted to a public review, inviting comments from anyone outside the workshop. The most detailed comments were received from the Federal Institute for Occupational Safety and Health in Germany. After giving full consideration to the comments received from public review, the workshop agreement was formally accepted on by the participants of the workshop.

Below is a reproduction of the scope of the workshop agreement and of its table of content.

Scope This CEN Workshop Agreement (CWA) establishes terms and definitions for exposure models and their elements, specifies minimum requirements for the amount and type of information to be documented on exposure models and proposes a structure for communicating the documentation to different users.

This document is applicable to the documentation of a wide range of exposure models (quantitative and nonquantitative), including:

- Environmental models describing the fate of chemicals in different media such as soil, air or water
- Environmental models describing the chain of chemicals from the environment to humans, in particular via food (e.g. plants and animals), drinking water and other pathways
- Human exposure models (occupational, consumers) including toxicokinetic models but excluding toxicodynamic models

The documentation of the coupling of different exposure models that were developed independently and that can cause consistency issues is not the focus of this CWA. However, this CWA is applicable to models (or sub-models) originally designed to be consistently coupled.

Excluded from the scope of this document are issues of:

- Model coding and translation into software
- Hazard assessment and risk assessment
- Source characterisation
- Legislation dependent aspects of exposure assessment such as tiered approaches and exposure assessment reporting

(continued)

3.2 The CEN Workshop Agreement CWA 16938

While much of the content of the CEN workshop agreement was contained in one form or another in the original MERLIN-Expo standard documentation framework, it gained in breadth and precision through the workshop process integrating comments from outside stakeholders. Sample documentations of a consumer exposure model (“Evaporation model” from ConsExpo; https://www.advancedreachtool.com/) and of a worker exposure model (ART; https://stoffenmanager.nl/) in the format of the workshop agreement were contributed by participants from outside the MERLIN-Expo project. There is a clear scope for the standard and definitions that are consistent to terminology in related international standards.

The CEN Workshop Agreement CWA 16938 [26] “Standard documentation of chemical exposure models” is the first standard for documenting chemical exposure models and is now available for other model developers to use.[2] It can help model developers with more user-friendly formulating their own models and with documenting them for others. Should other model developers follow this standard, it will be easier for model users to compare and evaluate models, broadening the

[2]The CEN Workshop Agreement “Standard documentation of chemical exposure models” can be obtained from any of the national standardisation bodies in Europe. For a list see http://standards.cen.eu/dyn/www/f?p=CENWEB:5:::NO:::.

applicability for chemical exposure models. In addition, the improved transparency in the model standard documentation can help regulators to accept use of new exposure models.

The CEN workshop agreement will be periodically reviewed and can be revised integrating the experience of others, and it may also become the basis for a European or International standard on documentation of exposure models. The workshop agreement provided a useful tool for dissemination of the results of research carried out by MERLIN-Expo on standard documentation.

Through the process of standardisation via the CEN platform, the MERLIN-Expo project was able to better understand and engage with the particular requirements of potential users of MERLIN-Expo as well as the requirements of regulators, thereby gaining useful information for the further refining and improvement of the MERLIN-Expo tool. In areas of research and development that stand to benefit from standardisation, a multistakeholder workshop (including users and regulators) can be an excellent tool for co-development of new products and services.

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Modelling the Fate of Chemicals in Surface Waters

Philippe Ciffroy

Abstract A good knowledge and modelling of the fate of chemicals in surface waters is essential for achieving a holistic risk assessment approach. This chapter describes the processes that should be considered in models simulating the fate of chemicals in natural waters. The first section describes the exchange of chemicals between the dissolved and particulate phases in water and sediments, as well as the simulation of suspended particulate matter concentration. The second section describes mechanistic modelling of chemical exchange between the overlying water column and bottom sediments that results from deposition and/or resuspension of contaminated particles. The third section describes the diffusion of chemical at the interface between surface water and sediment porewater that is classically based on a two-film diffusion description. The fourth section describes absorption and volatilization of semi-volatile substances at the air-water interface that are generally modelled according to the stagnant boundary theory. The fifth section describes processes responsible for degradation (i.e. hydrolysis, photolysis, biodegradation) that are generally aggregated in a global loss rate.

Keywords Degradation • Deposition • Desorption • Diffusion • Distribution coefficient • Modelling • Resuspension • Sediment • Sediment rating curve • Sorption • Surface waters • Suspended particulate matter

Contents

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1 Introduction

Several European policies regulate the anthropogenic use of hazardous substances and their release into surface waters. Some of these regulations define a set of critical substances, which should be submitted to detailed assessments and monitoring. For example, the European Water Framework Directive (WFD) defines holistic basin-scale assessments and establishes a list of 'priority substances', selected among those presenting a 'significant risk to, or via, the aquatic environment'. For selecting these substances, several criteria were taken into account: intrinsic toxicity, persistence and bioaccumulation as well as the monitored and/or modelled concentrations in the aquatic environments. Thus, about 820,000 monitoring data from waters and sediments from all member states were analysed and combined with data related to production, use and distribution of chemicals in the environment. Priority chemicals were identified from a *co*mbined *m*onitoring-based and *m*odelling-based *p*riority *s*etting (COMMPS) process. Three categories of substances were thus defined: (1) priority hazardous substances (PHS), for which discharges into the environment must cease or phase out in the delay of 20 years after the adoption of the WFD; (2) priority substances under review (PSR), which can be incorporated into the PHS list after further investigation; and (3) priority substances (PS), submitted to progressive reduction of discharges into the environment.

Regional conventions also regulate the use and discharge of chemicals into surface waters for specific European areas. For example, the international convention for the protection of marine systems (OSPAR) gathers representatives of 15 contracting parties and the European Commission and is the current instrument guiding international cooperation on the protection of the marine environment of the north-east Atlantic. The hazardous substances strategy sets the objective of preventing pollution of the maritime area by continuously reducing discharges, emissions and losses of hazardous substances. A 'dynamic selection and prioritization mechanism for hazardous substances' (DYNAMEC) was set up for the identification of substances of priority concern. It was based on persistency,

bioaccumulation and toxicity screening for many potential substances of concern, as well as information related to emissions and/or concentrations in the environment. Regulations were also set up for the regulation of freshwaters. Thus, the Danube River Protection Convention (DRPC) gathers seven countries and forms the overall legal instrument for cooperation on transboundary water management in the Danube river basin. The DRPC includes measures to reduce the pollution loads entering the Black Sea from sources in the Danube river basin. The DRPC established its own list of priority substances, gathering many substances listed in the WFD, but also specific substances for which monitoring in the Danube river system is required (e.g. metals like arsenic, chromium, copper and zinc; pesticides like DDT, malathion, parathion). Similarly, the International Commission for the Protection of the Rhine (ICPR) gathers five countries and supports all coordinating work for the entire Rhine river basin district. It must control that target values for substances relevant to the Rhine traced in water, suspended matter, sediments and organisms will be sustainably respected.

Despite such extensive regulation and technological advances, chemicals continue however to threaten aquatic biota. Many streams and rivers are ecologically impaired or threatened with significant losses in biodiversity, which compromise the future provisioning of vital ecosystem services [1]. For example, Malaj et al. [2] extracted data from the Waterbase database [3] and reviewed concentrations for 233 chemicals in 4,000 monitoring sites in Europe. They compared these levels with ecotoxicological thresholds for three species (algae, invertebrate and fish) and concluded from this comprehensive analysis that organic chemicals were likely to exert chronic long-term effects on sensitive species in 42% of the sites. Besides, as most monitoring programmes considered only included a subset of targeted chemicals, this assessment likely underestimates the actual risk. Pesticides, tributyltin, polycyclic aromatic hydrocarbons (PAHs) and brominated flame retardants were identified as the major contributors of the predicted effects. Besides, protection of freshwater ecosystems from chemicals is not only essential for preserving biodiversity but also for maintaining ecosystem services like the production of clean drinking water at an acceptable cost and recreational values.

This background demonstrates the pivotal role of surface waters in environmental and human health risk assessments. Considering that ~100,000 organic chemicals are currently in daily use and may enter freshwater ecosystems via different routes [4], a better knowledge and modelling of the fate of chemicals in natural waters is then essential for achieving a holistic assessment approach.

Among the processes governing the fate of chemicals in aquatic systems, the exchanges at the interface between water and particles play an essential role. The residence time of chemicals in surface water streams is indeed strongly affected by their interactions with suspended particulate matter (SPM) and settlement in sedimentation zones. In particular, sediments can act as a temporary or long-term sink for pollutants. Besides, the uptake of chemicals by aquatic organisms depends on their speciation, especially on the partition between the dissolved and particulate phases, both in the overlying water column and in bottom sediment. The accumulation of chemicals in bottom sediments is important for organisms for which

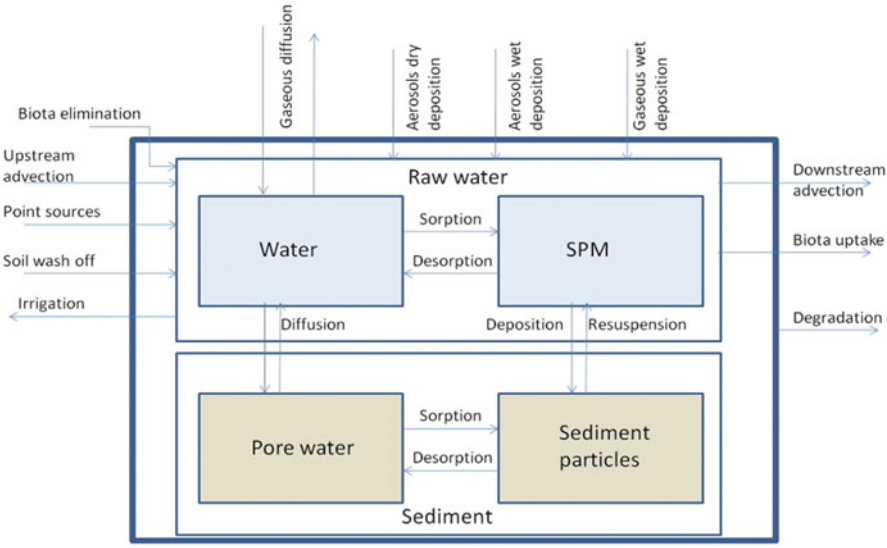

Fig. 1 Media, loading inputs, losses and exchanges considered in the MERLIN-Expo 'surface waters' model

sediment represents the habitat compartment, i.e. benthic organisms, especially those playing the essential role of decomposition in freshwater communities. The fate of chemicals in surface waters can also be affected by other processes like diffusion at the interface with atmosphere or degradation. The aim of this chapter is to review and describe the main processes governing the fate of chemicals in surface waters and particularly those implemented in the MERLIN-Expo model (Fig. 1).

2 Sorption/Desorption Between Water and Particles

2.1 Process Description

Exchanges of contaminants between the dissolved and the particulate phases in surface waters govern their flux to atmosphere and sediments because (1) only contaminants associated with particles can physically deposit to bed sediment and inversely be resuspended from bed sediments; (2) instead, only dissolved contaminants can exchange by diffusion at the water-'sediment porewater' interface; and (3) only dissolved contaminants can exchange by diffusion at the water-atmosphere interface.

Most of the fate models assume that exchange of chemicals between surface water and SPM, and between sediment porewater and sediment particles, is equilibrated. Such exchanges can thus be described by a distribution (or partition)

coefficient, generally noted K_{d_SPM} and K_{d_sed}, respectively (in $m^3\ g^{-1}$), expressed as the concentration ratio at equilibrium between the particulate phase and the dissolved phase. Under this assumption, chemical concentration in the dissolved and particulate phases can be calculated as follows:

$$C_{dis\_water} = \frac{C_{water}}{1 + K_{d,SPM} \cdot SPM} \quad (1)$$

$$C_{SPM} = \frac{K_{d,SPM} \cdot C_{water}}{1 + K_{d,SPM} \cdot SPM} \quad (2)$$

where C_{dis_water} (mg m^{-3}) is the concentration of the chemical dissolved in river water, C_{SPM} (mg g^{-1}) is the concentration of the chemical associated with SPM, C_{water} (mg m^{-3}) is the concentration of the chemical in raw river water, SPM (mg g^{-1}) is the suspended particulate matter, and $K_{d,SPM}$ ($m^3\ g^{-1}$) is the distribution coefficient between SPM and water.

Organic carbon is assumed to be the main particulate media interacting with hydrophobic chemicals potentially present in surface waters. Considering this assumption, distribution coefficients are generally related to the water-organic carbon partition coefficient K_{oc} (representing the ratio at equilibrium of the chemical between particulate organic carbon and water, respectively) and to the fraction of organic matter f_{OM} in particles (when K_{d_SPM} and K_{d_sed} are expressed in $m^3\ g^{-1}$):

$$K_{d,SPM} = 10^{-6} \cdot f_{OM,SPM} \cdot 10^{\log 10\_K_{oc}} \quad (3)$$

and

$$K_{d,sed} = 10^{-6} \cdot f_{OM,sed} \cdot 10^{\log 10\_K_{oc}} \quad (4)$$

where $K_{d,sed}$ ($m^3\ g^{-1}$) is the distribution coefficient between sediment particles and sediment porewater, $f_{OM,SPM}$ (dimensionless) is the fraction of organic matter in SPM, $f_{OM,sed}$ (dimensionless) is the fraction of organic matter in sediments, and K_{oc} (dimensionless) is the water-organic carbon partition coefficient.

Equilibrium and hydrophobic assumptions can be disputable in some cases. When equilibrium condition between water and SPM is not respected, e.g. just upstream of a point release, the model must then be considered with caution. In such a case, exchanges between water and SPM should be described by non-equilibrium kinetics, using sorption and desorption kinetic rate constants. Parameter values for such kinetic rates are however scarce in the literature. Besides, the hydrophobicity assumption is disputable for ionizable compounds because interactions with particles result from lipophilic but also from electrical partitioning equilibriums [5, 6].

2.2 Water-Organic Carbon Partition Coefficient for Organic Chemicals

Despite limitations indicated above, the water-organic carbon partition coefficient K_{oc} remains in many cases an essential parameter in fate models. Because experimental K_{oc} data are not available for all chemicals in use, numerous correlations have been developed relating K_{oc} to molecular descriptors. Such QSAR models tend to be developed for specific groups or classes of chemicals and can therefore be adapted for some classes of chemicals only. Many QSAR models able to derive K_{oc} values for neutral organics are described in the literature (e.g. [7–12]; and others). They differ in the parameters used for describing chemicals (e.g. octanol-water partition coefficient K_{ow}, molecular weight, connectivity index, molecular E-state indices, fragment constants, structural factors) and in the databases used as training and predictive sets, respectively, and defining the applicability domain. Franco and Trapp [5] and Franco et al. [6] developed also a QSAR model for ionizable compounds (monovalent organic acids and bases). The classical K_{ow} model was applied, but the K_{ow} value accounts for the distribution of the chemical between neutral and ionic forms (depending on pH), according to the Henderson-Hasselbalch relationship. A summary of some of these QSAR models is presented in Table 1, showing the variety of approaches used for predicting K_{oc} for various classes of chemicals.

2.3 Fraction of Organic Matter in SPM and in Sediments

The other parameter used for calculating the distribution coefficients K_{d_SPM} and K_{d_sed} is the fraction of organic matter f_{oc} in particles. Organic carbon is indeed considered to be the main sorbing phase in water and sediments for neutral organic compounds. In fact, for non-neutral organics, which typically have a $\log(K_{ow})$ greater than 4, affinity to organic matter tends to be much stronger than to mineral surfaces and the sorption to these latter can be neglected. Organic matter in surface waters is however highly variable. Organic carbon content can indeed be divided between amorphous, soft or new and condensed, old or black carbon. Besides, SPM in rivers can originate from different sources: endogenous, bed resuspension and allochthonous. The organic fraction in SPM generally depends on the relative importance of these sources: for low SPM concentrations, the organic fraction in SPM is large and essentially phytoplanktonic; for higher SPM concentrations, the organic fraction is less abundant and essentially allochthonous [13]. As for organic matter in water, different sources of particulate organic carbon (POC) to sediments influence organic matter content. In lakes, for example, pelagic community processes influence the flux of organic matter to benthic communities. For higher flow rate conditions, organic fraction can essentially be allochthonous. Despite such variability in organic matter sources and quality, fate models generally consider organic carbon as a unique sorbing phase. Abril et al. [14] provide a good overview

Table 1 Several QSAR models available for predicting water-organic carbon partition coefficient (K_{oc}) of chemicals

Source	Descriptors	No. of data in the training set	MSE	Applicability domain
Sabljic et al. [10]	1: Topological index 1χ	81	0.26	Predominantly hydrophobics[a] – 3–22 atoms of carbon or halogens with $1 < \log K_{oc} < 6.5$
	1: Octanol-water partition coefficient K_{ow}	81	0.45	Predominantly hydrophobics
		390	0.56	Nonhydrophobics[b] with $-2 < \log K_{ow} < 8$
		54	0.40	Phenols, anilines, benzonitriles, nitrobenzenes with $1 < \log K_{ow} < 5$
		216	0.42	Acetanilides, carbamates, esters, phenylureas, phosphates, triazines, triazoles, uracils with $-1 < \log K_{ow} < 8$
		36	0.39	Alcohols, organic acids with $-1 < \log K_{ow} < 5$
		21	0.34	Acetanilides
		13	0.4	Alcohols
		28	0.49	Amides
		20	0.34	Anilines
		43	0.41	Carbamates
		20	0.24	Dinitroanilines
		25	0.46	Esters
		10	0.58	Nitrobenzenes
		23	0.34	Organic acids
		24	0.37	Phenols, benzonitriles
		52	0.34	Phenylureas
		41	0.45	Phosphates
		16	0.38	Triazines
		15	0.48	Triazoles
Schüürmann et al. [11]	Molecular weight, bond connectivity, molecular E-state, 24 fragment corrections representing polar groups, one indicator for nonpolar and weakly polar compounds	457 (and 114 compounds used in the prediction set)	0.47	Neutral organics (except for partial ionization of acids and bases at soil pH) with atom types C, H, N, O, P, S, F, Cl, Br

(continued)

Table 1 (continued)

Source	Descriptors	No. of data in the training set	MSE	Applicability domain
Tao et al. [12]	74 fragment constants and 24 structural factors	430 (and 162 compounds used in the prediction set)	0.37	Organics with K_{oc} over 7.65 log units
Huuskonen [7, 8]	12 structural parameters (connectivity index 1χ, 11 atom-type E-state indices)	143 (and 58 compounds used in the prediction set)	0.40	Organic pesticides (with logK_{oc} ranging from 0.42 to 5.31)
Poole and Poole [9]	4 descriptors	131	0.25	
Franco and Trapp [5] and Franco et al. [6]	3 descriptors or conditions (octanol-water partition coefficient K_{ow}, pKa, pH)	44 (10 acids, 12 bases, different pH)	0.32	Ionizable monovalent organic acids and bases

[a]Defined as molecules containing only C, H and halogen (F, Cl, Br, I)
[b]Defined as all the molecules that contain other atoms than C, H and halogen (F, Cl, Br, I). Does not imply anything about their lipophilicity

of organic matter content in European rivers: they collected data on nine European rivers (Sado, Douro, Gironde, Loire, Thames, Scheldt, Rhine, Ems, Elbe) during 19 monitoring campaigns, representing 410 POC values. Data reported by Abril et al. [14] show that organic fraction in SPM may vary over a wide range according to rivers and seasons, e.g. from 3% in the Gironde river to about 20% in the Loire river, modifying the fate of organic chemicals in such rivers.

2.4 Distribution (or Partition) Coefficient for Metals

For metals, $K_{d,\mathrm{SPM}}$ and $K_{d,\mathrm{sed}}$ values are generally obtained from empirical measurements. However, they may depend on many environmental factors and/or experimental conditions, as described by Ciffroy et al. [15] in his review related to radioactive isotopes of metals. The main factors influencing $K_{d,\mathrm{SPM}}$ and $K_{d,\mathrm{sed}}$ values are:

- pH. pH modifies the speciation of solid surface sites and the speciation of competitive ions in water. Adsorption to SPM and sediment particles can generally be represented by a sigmoid curve, with sudden increase in adsorption occurring over a narrow range of 1–2 pH units. The observed metal sorption behaviour can be interpreted in terms of interaction of dissolved metals with deprotonated sites on the particle surface. The importance of pH in the choice of relevant $K_{d,\mathrm{SPM}}$ and $K_{d,\mathrm{sed}}$ is particularly crucial for elements that show steep slopes in the range of natural pH found in freshwaters (typically 6–7).

- Equilibration time. Numerous studies have shown that the sorption of metallic trace elements on natural particles resulted from several kinetic processes, involving rapid but also slow processes (e.g. oxidation processes, inner sphere complexation and migration of cation in the clay structure).
- Nature of particles. SPM and sediments gather contrasted type of particles such as clay, carbonates, oxides and hydroxides and organic matter including living cells, such as phytoplankton. The partitioning of a given metal is highly dependent on the composition of the particulate pool. The degree of reversibility also highly depends on the distribution of the metal of concern among these different types of particulate ligands.
- Concentration of complexing ligands and/or competitors in the dissolved phase. The concentration of complexing ligands and/or competitors in the dissolved phase (e.g. analogue ions or dissolved organic matter) largely influences the $K_{d,\mathrm{SPM}}$ and $K_{d,\mathrm{sed}}$ values. Experiments conducted in estuarine waters where significant salinity gradients are observed demonstrated the effect of ionic strength on $K_{d,\mathrm{SPM}}$ values.
- And other factors like biological activity.

An extended literature review of $K_{d,\mathrm{SPM}}$ and $K_{d,\mathrm{sed}}$ values was conducted by Allison and Allison [16]. Approximately 245 articles and reports were reviewed and a total of 1,170 individual K_d values were obtained after filtering process (e.g. studies using pure mineral phases were rejected; only data obtained at low total metal concentrations (i.e. at usual natural concentrations) were accepted). For a particular metal in SPM or bottom sediment, the degree to which the literature sample is truly representative of the population of metal partition coefficients was dependent on the number of sample points, the actual variability of important medium properties that influence partitioning and how well this variability is represented in the sample. When there were too few representative data points in the sample to have confidence in the descriptive statistics, alternative approaches were used like analogies between media (i.e. derivation of K_ds for SPM from those observed from soils using a regression relationship), geochemical speciation modelling (using geochemical speciation models like MINTEQ) or expert judgement. In absence of site-specific data, the literature review performed by Allison and Allison [16] may provide a useful dataset for estimating generic PDFs of $K_{d,\mathrm{SPM}}$ and $K_{d,\mathrm{sed}}$ for several metals.

3 Variability of the Suspended Particulate Matter Concentration

3.1 Process Description

Sorption and desorption processes depend on the intrinsic affinity of chemicals with particles but also on the quantity of these latter in surface waters. Indeed, the number of available sorption sites is directly related to SPM concentration. An

accurate prediction of the time dependence of SPM in surface waters is then essential for the estimation of transfer of chemicals in aquatic systems.

Empirical relationships such as the so-called sediment rating curves are often used for estimating the effect of discharge on SPM at a given location in a river. They reflect the increase of SPM during flood events. Thus, the selected model assumes that SPM at any time is linearly related to flow rate in log-log coordinates:

$$\log(\mathrm{SPM}) = \log(a_{\mathrm{SPM}}) + b_{\mathrm{SPM}} \cdot \log(\mathrm{Flow}_{\mathrm{river}}), \tag{5}$$

where a_{SPM} and b_{SPM} (dimensionless) are parameters that depend on the river concern, the location and eventually the season and $\mathrm{Flow}_{\mathrm{river}}$ ($\mathrm{m}^3\ \mathrm{s}^{-1}$) is the flow rate of the river.

The inaccuracy of sediment rating curves in some cases was highlighted in different publications. According to statistical considerations linked to back transformation of log values, the sediment load is likely to be underestimated when the least squares regression on logarithms is used for fitting the model [17, 18]. Correction factors were thus introduced by several authors to correct this bias [19]. Besides, log-transformed data on sediment loads and discharge sometimes result in concave or convex relationships rather than linear. In such cases, nonlinear models were tested and it was shown that they can in some cases significantly improve the fitting [20]. Furthermore, differences in sediment availability between the beginning and the ending of a flood event generally result in hysteresis effects [21, 22], not taken into account by sediment rating curves. Finally, for a given river, rating curve parameters can show high inter-annual or inter-seasonal variability [21, 23]. One strategy to overcome these limitations is to modify the sediment rating equation itself, e.g. by introducing correction factors accounting for non-linear relationships, sediment depletion following flood events, etc. More complex models can thus be found in, for example, Moog and Whiting [24], Morehead et al. [21] or Ciffroy et al. [25].

3.2 *Intercept and Slope of the SPM-Flow Rate Relationship*

As a sediment rating curve is an empirical relationship, the intercept and slope of the SPM-flow rate relationship, i.e. a_{SPM} and b_{SPM}, have no physical meaning. Nevertheless, some physical interpretation is sometimes proposed to them. The a_{SPM} coefficient can represent an index of erosion severity because high a_{SPM} values indicate intensively weathered materials, which can easily be transported [26, 27]. The b_{SPM} coefficient represents the erosive power of the river, with large values being indicative for rivers where a small increase in discharge results in a strong increase in erosive power of the river.

By nature, the a_{SPM} and b_{SPM} coefficients depend on the river basin and its erosivity characteristics. The estimation of these parameters depends on the availability of data, i.e. on the availability of simultaneous measurements of flow rates and SPM. When a long-term monitoring campaign is available with both

measurements of flow rates ($Flow_{river}$) and SPM, a_{SPM} and b_{SPM} values can be estimated by fitting the model using the least squares regression on logarithms. For estimating the uncertainty of these parameters (i.e. for defining the a_{SPM} and b_{SPM} PDFs), a bootstrap procedure can be used, as those described in Rustomji and Wilkinson [28]. At the opposite, if no measurement at all is available, the a_{SPM} and b_{SPM} values can be estimated by analogy with rivers that present long-term monitoring data on flow rates and SPM. A good literature source is the study published by Syvitski et al. [29], who estimated a_{SPM} and b_{SPM} values for 57 gauging stations located on 49 American rivers. Applying multiple regressions to the data and using several explanatory variables, they propose several relationships to predict a_{SPM} and b_{SPM} best estimates from different sets of basin properties, like mean annual flow rate, mean annual sediment load, latitude, mean annual air temperature, basin relief or peak flow anomaly (i.e. ratio of the annual peak flow rate to the mean flow rate). Some of these variables like latitude do not have a physical control on SPM, but they represent a proxy for climate variables. The percentage of the variance explained (R^2) is included for each formula allowing to derive uncertainty factors. The intermediate situation is when only few monitoring data are available. In this case, the a_{SPM} and b_{SPM} values can be estimated by a Bayesian approach, merging prior knowledge and monitoring data. For example, a_{SPM} and b_{SPM} values for 'similar' rivers or locations which were monitored over years or decades can be used as 'prior knowledge' and provide expected orders of magnitude on a_{SPM} and b_{SPM}. Such prior information can be given by formulae proposed by Syvitski et al. [29]. A Bayesian approach can be selected to combine this source of information with monitoring data because it is well adapted to build posterior PDFs when theoretical prior knowledge is available and when only a limited set of experimental data is available. To illustrate such SPM-flow rate relationships, two examples related to French rivers are presented in Fig. 2. Different slopes in SPM-flow rate dependence can be observed, showing contrasted effects of the increase of flow rates, especially during floods. The uncertainty in the prediction is related to the number of monitoring data available for calibrating the a_{SPM} and b_{SPM} values. The SPM-flow rate relationship is then highly site-dependent and must be adapted by end users before any site application (Fig. 2).

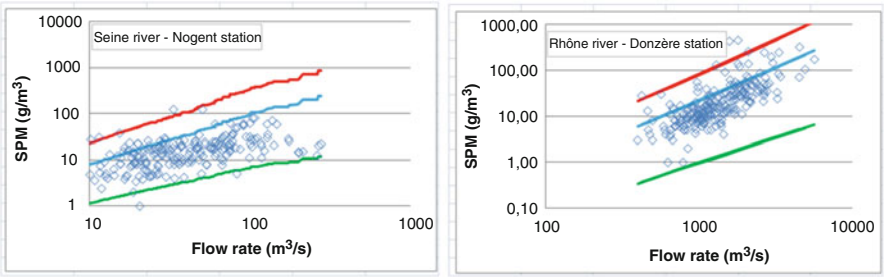

Fig. 2 Relationship of SPM-flow rate measured and calculated for different French rivers (from P. Ciffroy, personal communication). The *three curves* represent the mean SPM-flow rate relationship, as well as the 5th and 95th percentiles

4 Deposition and Resuspension of Particles and Associated Chemicals to and from Bed Sediment

4.1 Process Description

Exchange of chemicals between the water column and bottom sediments can result from deposition of contaminated particles and inversely from resuspension of contaminated particles previously accumulated in bottom sediments.

Mechanistic dynamic models based on physical assumptions were developed in sediment science. Two conflicting paradigms were proposed for mechanistically representing deposition and resuspension of cohesive sediments: (1) the 'exclusive' paradigm suggests that deposition and resuspension do not occur at the same time; (2) the 'simultaneous' paradigm allows deposition and resuspension to occur at the same time. These two paradigms were discussed by Ha and Maa [30] and Winterwerp [31].

For both paradigms, modelling of the deposition of fine cohesive particles (and associated chemicals) is based on the assumption that the gravitational settling velocity of particles (governed by their density and granulometry) plays the dominant role. It is then assumed that the deposition flux of particles is proportional to the SPM concentration and that the proportionality factor is settling velocity (W_s, in m s^{-1}). Besides, the exclusive paradigm considers that deposition flux of particles increases when flow velocity (reflected by bed shear stress τ, in Pa) decreases and that particle deposition can occur only when the bed shear stress is below a given threshold (the 'critical shear stress for deposition' τ_d, in Pa). These assumptions are generally translated by Krone's relationship:

$$\begin{aligned} F_d &= \mathrm{SPM} \cdot W_s \cdot \left(1 - \frac{\tau}{\tau_d}\right) \qquad if \quad \tau < \tau_d \\ F_d &= 0 \qquad\qquad\qquad\qquad\qquad\quad if \quad \tau > \tau_d \end{aligned} \tag{6}$$

where F_d (g particles m^{-2} s^{-1}) is the deposition flux of particles.

Modelling of the resuspension of fine cohesive particles (and associated chemicals) is based on the assumption that the bed shear stress exerted by the flow plays the dominant role, i.e. that resuspension is facilitated for high bed shear stress (e.g. during flood events). It is then assumed that the resuspension flux of particles increases with the bed shear stress exerted by the flow. Resuspension is assumed to become negligible when the bed shear stress exerted by the flow is below a bed shear stress threshold, i.e. the critical shear stress for resuspension τ_r (in Pa). These assumptions are generally translated by Partheniades' relationship:

$$\begin{aligned} F_r &= e \cdot \left(\frac{\tau}{\tau_r} - 1\right) \qquad if \quad \tau > \tau_d, \\ F_r &= 0 \qquad\qquad\qquad\quad if \quad \tau < \tau_r \end{aligned} \tag{7}$$

where e (g particles m^{-2} s^{-1}) is the maximum erosion rate and F_r (g particles m^{-2} s^{-1}) is the resuspension flux of particles.

Besides, some resuspension models can also integrate a consolation rate to simulate the fact that resuspension becomes more limited for deeper consolidated sediment layers. This assumption is supported by experimental observation, where an increasing resistance to erosion was observed according to consolidation conditions and thus to sediment depth [32–36].

Bed shear stress (τ) is assumed to depend on water density, acceleration due to gravity, hydraulic radius (which can be assimilated to the river depth) and mean water velocity.

Other alternative models are also proposed in the literature. They are based on steady-state assumptions, considering that permanent deposition and resuspension occur simultaneously and can be described by constant rates. This approach leads to a permanent net deposition, without any net resuspension period (i.e. deposition minus resuspension = constant positive value). Such a steady-state assumption is not realistic for many rivers submitted to seasonal variations in the flow rate leading to temporal cycles of net deposition/resuspension (especially driven by floods). Besides, to compensate the continuous accumulation of sediments resulting from a constant positive net deposition, models generally include a burial process, old sediments being considered as inactive and assimilated to a sink compartment. The model is then highly dependent on the choice of the active sediment depth and on the burial rate. Thus, it appeared that the simplicity of the steady-state approach needs to be compensated by the addition of processes that are not easily parameterized (i.e. the 'burial' process).

An example of application of the MERLIN-Expo dynamic model simulating particle dynamics in rivers is presented in Fig. 3. It can be observed that deposition of SPM and associated accumulation of particles in bottom sediments occur during low flow rate periods, while rapid resuspension occurs during floods leading to a decrease in particles accumulated in sediments. Chemicals associated with particles follow the same kind of behaviour. This example demonstrates why a dynamic modelling of deposition and resuspension processes is important for predicting the potential accumulation and transport of chemicals in surface waters.

4.2 Settling Velocity of Particles

Settling is the process by which particles settle to the bottom of a liquid and form sediment. There are two main forces enacting upon any particle that is considered individually in water: gravity and a drag force that is due to the motion of the particle through water. Gravity is not affected by the particle velocity, whereas the drag force is a function of the particle velocity. For a particle at rest, no drag force will be exhibited, which causes the particle to accelerate due to the applied force. When the particle accelerates, the drag force acts in the direction opposite to the particle motion, retarding further acceleration. As the particle increases in velocity,

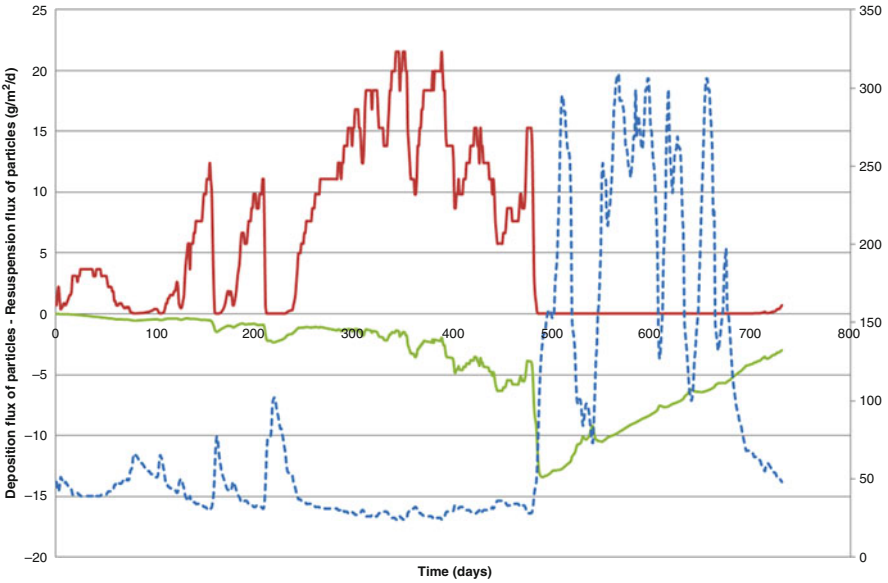

Fig. 3 Dynamics of SPM and bottom sediments in the Seine river during 2 years simulated by MERLIN-Expo. The *blue line* (right *y* axis) represents flow rate (in $m^3\ s^{-1}$, Nogent station). The *red* and *green lines* (left *y* axis) represent deposition flux of SPM (positive) and resuspension flux of sediments (negative)

the drag force and the applied force will approximately equate, causing no further change in the particle velocity. This velocity is known as the *settling velocity* of the particle.

The settling velocity of the particle is affected by many parameters, i.e. anything that will alter the particle's drag. Hence the terminal velocity is most notably dependent upon particle size, the shape (roundness and sphericity) and density of the particle as well as viscosity and density of the fluid. For noncohesive particles at low concentrations, settling velocity can be calculated by the Stokes law which describes the settling velocity of uniform small spheres in the viscous Reynolds number regime, i.e. settling velocity is proportional to particle excess density and to the square of its diameter.

However, particles interacting with chemicals are generally cohesive and thus form aggregates (mud flocs) characterized by size and settling velocity potentially quite different from the individual particles. Settling velocity can then be quite different from those calculated for individual particles. In these conditions, it can be more relevant to determine W_s estimates by in situ measurements. Several experimental methods are possible for estimating W_s values, e.g. use of sediment traps or other sensors (e.g. [37–40]), measurements of vertical gradients of SPM and application of the Rouse profile (e.g. [25]), flume experiments (e.g. [37, 41]) and long-term monitoring of SPM concentrations in a river (e.g. [42, 43]).

4.3 Critical Deposition and Resuspension Shear Stress

There is general agreement that bottom shear stress exerted by currents is the dominant force causing deposition and resuspension of particles. Even if several mathematical formulations were proposed to simulate deposition and resuspension process, they are all based on two parameters called 'critical shear stress for deposition' and 'critical shear stress for resuspension' (or erosion critical shear stress). By definition, deposition occurs only when the bed shear stress is below the critical shear stress for deposition. The definition of the critical shear stress for resuspension may be more ambiguous [36]. It can be defined as the stress at which initiation of motion first occurs, or at which significant erosion occurs. These differences in interpretation can lead to significant differences in derived parameters.

Critical shear stress for deposition and critical shear stress for resuspension are influenced by site-specific characteristics like particle size distribution, particle density, cohesiveness, water content and biological disturbance or binding. Several experimental methods are possible for estimating parameter values: flume or erosion chamber experiments, long-term monitoring of SPM concentrations in a river and in situ measurements of bed strength.

A review of values available in the literature shows that the critical shear stress for deposition generally ranges between 0.05 and 0.4 N m^{-2}, while the critical shear stress for resuspension generally ranges between 0.1 and 1 N m^{-2}.

5 Diffusion Between Water and Sediment Porewater

5.1 Process Description

Deposition/resuspension and diffusion participate in parallel to the exchanges between the overlying water column and the sediment. The diffusion of contaminants at the interface surface water-sediment porewater is classically based on a two-film diffusion description, where the transport into the sediment is assumed to happen through two layers of resistance: the first layer represents the laminar water-side film and the second one sediment-side boundary layer. According to these assumptions, the diffusive flux at the surface water-sediment porewater interface can be simulated according to Fick's law, i.e. by taking into account the concentration gradient between the two compartments and a global mass transfer factor $MTC_{water\text{-}sed}$. This latter is estimated according to the assumption that it results from two resistances in series by analogy with Ohm's law and considering that a diffusion coefficient is equivalent to the inverse of a resistance.

The first resistance represents the resistance to diffusion on the upper part of the water-sediment interface. For organics, it is calculated by the ratio of the boundary layer thickness below water δ_w by the effective diffusion coefficient of

the chemical in pure water D_{water} that is assumed to depend on its molar mass. For metals, the effective diffusion coefficient of the chemical in pure water is an empirical value. The boundary layer thickness below water δ_w corresponds to the thickness where diffusion occurs at the water-sediment interface because of the fluid viscosity.

The second resistance represents the resistance to diffusion on the lower part of the water-sediment interface. For organics, it is calculated by the ratio of the boundary layer above sediment δ_{sed} by the effective diffusion coefficient of the chemical in pure water corrected by a tortuosity factor according to the Millington and Quirk law. The boundary layer thickness above sediment δ_{sed} corresponds to the thickness where diffusion occurs within the sediment. Generally speaking, the Millington and Quirk law states that tortuosity depends on porosity ϕ and water content θ according to

$$\text{Tortuosity} = \frac{\theta^{10/3}}{\phi^2} \tag{8}$$

As sediments are water-saturated, the mass transfer coefficient $\text{MTC}_{\text{water-sed}}$ describing diffusion of organic chemicals between water and sediment porewater is given by

$$\text{MTC}_{\text{water-sed}} = D_{\text{water}} \cdot \frac{{\phi_{\text{sed}}}^{4/3}}{\delta_{\text{sed}} + \delta_w \cdot {\phi_{\text{sed}}}^{4/3}} = \left(\frac{M_{O_2}}{M_{\text{molar}}}\right)^{0.5} \cdot D_{O_2,\text{water}} \cdot \frac{{\phi_{\text{sed}}}^{4/3}}{\delta_{\text{sed}} + \delta_w . {\phi_{\text{sed}}}^{4/3}} \tag{9}$$

where $\text{MTC}_{\text{water-sed}}$ (m d^{-1}) is the mass transfer coefficient from water to sediments, D_{water} (m^2 d^{-1}) is the diffusion coefficient of the chemical in water, $D_{O_2,\text{water}}$ (m^2 d^{-1}) is the diffusion coefficient of dioxygen in water, M_{O_2} (g mol^{-1}) is the molar mass of dioxygen, M_{molar} (g mol^{-1}) is the molar mass of the chemical, ϕ_{sed} (dimensionless) is the porosity of sediment, δ_{sed} (m) is the boundary layer thickness above sediment, and δ_w(m) is the boundary layer thickness below water.

Sørensen et al. [44] conducted a critical analysis of a generic compartmental description to represent the diffusion process at the water-sediment interface. The relative contributions of physical (i.e. particle deposition) and diffusive processes, respectively, were assessed. They concluded that under transient conditions, diffusion is an important exchange pathway only during a limited time scale, just after the start of emission, because of large gradients at the sediment surface. However, as time progresses, the diffusion-induced flux rapidly decreases, as the concentration gradients at the top of the sediment decreases. In contrast, deposition-resuspension of particle-bound contaminant is not governed by gradients at the sediment-water interface and thus generally becomes predominant over long time scales. It can then be considered that it is relevant to include diffusion in multimedia

modelling only in some cases, e.g. for transient short-term conditions (like accidental conditions). It must also be underlined that bioturbation is not taken into account in the model presented above, while it may induce a vertical mixing of water and sediment solids and thus enhance diffusive transfer.

5.2 *Boundary Layer Thickness Below Water and Above Sediment*

The diffusive boundary layer below water (δ_w) represents the interface zone between water and sediment when there is a relative movement. It is generated by the fluid viscosity: when a fluid runs along a fixed wall, the velocity at the wall is zero, while it is the flow velocity at a distance where no influence occurs. Velocity varies then from zero to a maximum and the distance separating these velocities defines the boundary layer below water. The boundary layer thickness below water δ_w is inversely dependent on the spatial mean water velocity in the water column and depends on the bed roughness.

In theory, the boundary layer thickness below water δ_w can be estimated from water velocity and interface roughness. For example, Sørensen et al. [44] defines a hyperbolic relationship between the boundary layer thickness below water and the flow velocity. It is however difficult to define the value of this parameter for a specific natural system because water velocity and bed roughness highly vary in time and space. The range of values generally found for common flow velocities and reported by Sørensen et al. [44] allows to propose a generic range for representing the boundary layer thickness below water, from 0.05 to 1 mm.

The diffusive boundary layer above sediment (δ_{sed}) represents the interface zone between water and sediment when there is a gradient of concentration within the sediment. The boundary layer thickness above sediment δ_{sed} depends on sediment properties like porosity, bulk density as well as on bioturbation. Sediment-side data related to diffusion are often difficult to interpret due to natural sediment heterogeneity (e.g., small-scale variations in porosity and grain size). Variations in sediment chemical levels are generally site-specific because of sediment heterogeneity, while more uniform concentrations are maintained by lateral advection and mixing in the water column, which provide an averaging effect on localized influences [45]. Only poor data are then available about the boundary layer thickness above sediment. Most of the data are related to O_2 or nutrient diffusion in sediment rather than to trace elements. By default, data monitored for O_2 can then be used to define values for this parameter. In particular, Bryant et al. [46] determined the sediment-side boundary layer for several sediments from high-resolution profile microsensors and found a range varying from 1 to 9 mm.

6 Diffusion Between Water and Atmosphere

6.1 Process Description

Some pollutants that are highly volatile (or semi-volatile organic compounds, SVOCs) can be emitted from waterbodies and the transfer from water to atmosphere can be a significant contribution to the mass balance of the chemical in freshwater.

Absorption/volatilization of semi-volatile substances at the air-river interface is generally modelled using the stagnant boundary theory (two-film model), the chemical being assumed to diffuse across two layers (stagnant water layer and stagnant air layer) characterized by two resistances in series. According to this approach, the net flux from freshwater to the atmosphere ($F_{\text{water-atm}}$, in mg m^{-2} s^{-1}) is driven by the difference in gaseous concentration between air and surface water according to Fick's law. The gaseous concentration of the substance in river water is assumed to be in equilibrium with the dissolved concentration ($C_{\text{dis,water}}$). This equilibrium is simulated by the adimensional Henry's law constant H/RT. Thus, the flux of chemical from water to atmosphere is given by

$$F_{\text{water-atm}} = \text{MTC}_{\text{water-atm}} \cdot \left(\frac{H}{RT} \cdot C_{\text{dis, water}} - C_{\text{gas\_atm}} \right), \tag{10}$$

where T (K) is the temperature, R (Pa m^3 mol^{-1} K^{-1}) is the universal gas constant, H (Pa m^3 mol^{-1}) is Henry's law constant, $C_{\text{dis\_water}}$ (mg m^{-3}) is the concentration of the chemical dissolved in river water, $C_{\text{gas\_atm}}$ (mg m^{-3}) is the gaseous concentration in the atmosphere, and $\text{MTC}_{\text{water-atm}}$ (m d^{-1}) is the mass transfer coefficient at the water-atmosphere interface.

The first resistance represents the resistance to diffusion on the upper part of the interface (i.e. in above atmosphere). A 'gas film mass transfer coefficient' ($\text{MTC}_{\text{water-atm\_g}}$, in m d^{-1}) can be calculated according to the approach proposed by Schwarzenbach et al. [47] that relates this latter to wind velocity u_{wind} at height 10 m (in m s^{-1}). $\text{MTC}_{\text{water-atm\_g}}$ is also assumed to depend on the chemical molar mass, according to the following relationship:

$$\text{MTC}_{\text{water-atm},g} = 864 \cdot (0.2\ u_{\text{wind}} + 0.3) \cdot \left(\frac{M_{H_2O}}{M_{\text{molar}}} \right)^{0.3} \tag{11}$$

The second resistance represents the resistance to diffusion on the lower part of the interface (i.e. in water). A 'water film mass transfer coefficient' ($\text{MTC}_{\text{water-atm\_w}}$, in m d^{-1}) can be calculated according to the approach proposed by Wanninkhof et al. [48] and Hornbuckle et al. [49] that also relates this coefficient to wind velocity at height 10 m [50]. $\text{MTC}_{\text{water-atm\_w}}$ is also assumed to depend on the Schmidt number of the chemical, which is assumed to be linearly related to the

squared root of its molar mass. According to these assumptions, the water film mass transfer coefficient can be calculated as follows:

$$\mathrm{MTC}_{\text{water-atm},w} = 0.108 \cdot (u_{\text{wind}})^{1.64} \cdot \left(\frac{M_{\mathrm{CO}_2}}{M_{\text{molar}}}\right)^{0.25} \tag{12}$$

where M_{CO_2} (g mol^{-1}) is the molar mass of carbon dioxide.

Other empirical formulae were proposed in the literature to calculate the film mass transfer coefficients (e.g. see [50]). A comparison could then be made with those proposed here to evaluate the robustness of the evaluation for the specific scenario under investigation.

The total mass transfer coefficient ($\mathrm{MTC}_{\text{water-atm}}$) is then given by

$$\mathrm{MTC}_{\text{water-atm}} = \frac{R \cdot T_{\text{river}} \cdot \mathrm{MTC}_{\text{water-atm},w} \cdot \mathrm{MTC}_{\text{water-atm},g}}{R \cdot T_{\text{river}} \cdot \mathrm{MTC}_{\text{water-atm},w} + H \cdot \mathrm{MTC}_{\text{water-atm},g}}$$

6.2 Henry's Law Constant

Henry's law constant is the main parameter depending on the chemical that is used to calculate the diffusive exchange at the atmosphere-water interface. It represents the ratio between vapour pressure and solubility of the chemical, corrected by temperature. It describes the capability of the chemical substance to partition between air and water in a binary system. It is expressed here in Pa m^3 mol^{-1}. When divided by the gas constant R and by temperature (in Kelvin), the adimensional Henry's law constant is obtained. Henry's constant can also be defined in the literature as the ratio between the chemical concentration in aqueous phase and the partial pressure in the gaseous phase. Under the terminology 'Henry's constant', both types of values can then be found in the literature. Henry's law constants are also often converted to dimensionless air-water partition coefficients by invoking the ideal gas law: $K_{\text{aw}} = \frac{H}{RT}$, where R is the universal gas constant and T is the system temperature (°K).

Henry's law constant depends on temperature. Values are generally estimated for 25°C. Henry's law constant typically increases with increasing temperature and is calculated according to the Van't Hoff equation often used to model the temperature dependence.

Because experimental data for Henry's law constant H are not available for all chemicals in use, several QSAR models have been developed relating H to molecular descriptors like bond descriptors [51–54], to estimate the temperature dependency of Henry's law constant in water for organic compounds from the 2D structure. Other models based on the estimation of both water solubility and vapour pressure are also available. A summary of some of these QSAR models is presented in Table 2.

Table 2 Several QSAR and read-across models available for predicting Henry's law constant H

Source	Descriptors	No. of data in the training set	MSE
Meylan and Howard [53][a]	59 chemical bonds	345 (and 74 compounds used in the prediction set)	0.46
Viswanadhan et al. [54]	QSAR model based on solvation free energy. The method (ALOGS) uses an extensive atom classification scheme	265 (and 26 compounds used in the prediction set)	0.86
Abraham et al. [51]	5 descriptors (excess molar refraction, dipolarity/polarizability, effective hydrogen-bond acidity and basicity, McGowan characteristic volume)	408	0.15
Kühne et al. [52]	46 substructure fragments. Temperature dependency of H in water for organic compounds from the 2D structure	456	0.21

[a]Chemical classes in Meylan's database with indication of the number of chemicals: alkanes 16; alkenes 20; alkynes 7; acids, aliphatic ***6***; alcohols 18; aldehydes 17; esters 27; ethers 16; epoxides 2; ketones **9**; halomethanes 22; halothanes 20; halopropanes 11; halobutanes **9**; other haloalkanes 4; haloalcohols 5; haloalkenes 12; aliphatic amines 13; nitriles ***5***; other aliphatic nitrogen compounds 11; aliphatic sulphur compounds 8; five-member aromatic rings 3; pyridines 12; benzene and alkylated; benzenes 13; halogenated benzenes 12; anilines 3; Phenols 8; biphenyls 3; polyaromatics 13; other aromatics 14; pesticides 6

7 Degradation

Several processes can contribute to the degradation of a chemical in water and sediments and to the formation of metabolites: biodegradation, photolysis, and hydrolysis. In water, a major degradation pathway is aerobic biodegradation. Microbial degradation can be attenuated by anaerobic conditions, suboptimal temperature and suboptimal pH. For some compound classes (e.g. alkyl halides, carboxylic acids and organophosphate esters), hydrolysis is an important abiotic degradation process. Indirect photolysis may take place in the aqueous surface layer via sunlight-excited dissolved organic matter. Photolysis involves light intensity and is then dependent on water depth and light penetration.

The processes indicated above are considered individually in some specific models dedicated to freshwaters (e.g. Aquatox). However, such an approach requires a lot of parameters that are poorly available for most of the chemicals. That is why individual processes responsible for degradation (i.e. hydrolysis, photolysis, biodegradation) are not distinguished in many models, but they are added into an aggregated loss rate. Degradation processes are then simulated by pseudo first-order degradation rates (i.e. degradation proportional to the concentration of contaminants in the media).

The parameter estimation can, for example, be based on the method published by Kühne et al. [55], who developed a read-across approach for estimating degradation rates of chemicals in water and sediments. Kühne's method is based on the

assumption that molecular susceptibility for abiotic and biotic degradation is associated with certain structural features; properly designed similarity measures between substances provide reasonable guidance to relate similarity in structure to similarity in degradability. Similarity between substances is based on the atom-centred fragment (ACF) method. From this method, extrapolation about medium-specific semi-quantitative half-lives may be conducted from existing data to compounds where respective information is missing.

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Modelling the Fate of Chemicals in the Atmosphere

Vincent Loizeau, Yelva Roustan, Nora Duhanyan, Luc Musson-Genon, and Philippe Ciffroy

Abstract Atmosphere is an important component of the whole ecosystem because it directly interacts with all the other media, i.e. soil, surface waters, vegetation and biota. This chapter describes the processes that should be considered in models simulating the fate of chemicals in the atmosphere. The first section describes model approaches able to simulate the long-range transport of chemicals in the atmosphere. The second section describes the partition of chemicals between gaseous and particulate phases in the atmosphere. Two approaches, respectively, based on liquid vapour pressure and octanol-air partition coefficient are presented. The third section describes chemical reactions occurring in the atmosphere, driven by photolysis and reactions with photooxidants like the hydroxyl radical OH. The forth section describes dry deposition of both gaseous and particulate chemicals on the earth surface. Dry deposition is driven by aerodynamic, quasi-laminar sublayer and canopy resistances. The calculation of these latter is presented here in detail. The fifth section describes wet deposition of both gaseous and particulate chemicals on the earth surface, driven by rainout (in-cloud) and washout (below-cloud) scavenging.

Keywords Advection • Aerodynamic resistance • Atmosphere • Below-cloud scavenging • Canopy resistance • Dry deposition • Hydroxyl radical • In-cloud scavenging • Long-range transport • Modelling • Partition between gas and particles • Photooxidants • Quasi-laminar sublayer resistance • Wet deposition

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Contents

1 Introduction

Atmosphere is an important component of the whole ecosystem because it directly interacts with all the other media (i.e. soil, surface waters, vegetation, biota). Furthermore, it is an important repository of anthropogenic emissions.

Humans enter in contact with atmospheric pollutants primarily by inhalation and, to a lesser extent, by dermal contact. Air pollution may have both acute and chronic effects on human health, affecting a number of different systems and organs. For example, polychlorinated biphenyls (PCBs) and pesticides may be associated with thyroid toxicity, effects on immune, reproductive, nervous and endocrine systems, and cancer effects including breast cancer [1–4]. Epidemiologic studies have linked dioxin exposure to increased mortality caused by ischemic heart disease [5]. These chemicals can also lead to developmental delays in children [2, 4, 6]. Dioxins were found to be transferred from the mother to the foetus via the placenta, affecting growth and development of the central nervous system of the foetus [7]. In spite of all these studies, mechanisms of action, adverse effects and dose-response relationships for many of these chemicals are poorly understood, so questions remain as to the health impacts of these exposures.

The concentration of chemicals in atmosphere is governed by four types of processes: (1) emissions from natural or anthropogenic sources, (2) transport by advection or diffusion, (3) chemistry (i.e. transformation of parent compounds into by-products) and (4) deposition on earth surface (both on bare soils and vegetation). Emission is the source term for atmosphere; chemistry can be a source (chemical production of by-products) or a loss (chemical removal of a parent compound) term; deposition is a loss term, and transport contributes to the chemical spatial redistribution.

Modelling the fate in the atmosphere of chemicals that are persistent and/or volatile is relevant. Such chemicals are often called persistent organic pollutants

(POPs). After their emission, they may be transported over long distances, eventually by successive phases of advection-deposition-reemission. This phenomenon is called as "grasshopper effect" [8]. The process of reemission is largely governed by temperature. It results in a global transport from equatorial regions to polar regions where an accumulation of POPs is observed [9]. Therefore, chemical concentration is not determined only by local sources of emission but also by transport from remote locations. This implies that an independent willingness for reducing emission of one country will not automatically lead to an atmospheric pollution decrease. On the contrary, a coordinate international environmental policy is required to reduce the effects of this kind of chemicals on human health. The international community has called for actions to reduce and eliminate production, use and releases of POPs. To that end, two international legally binding instruments have been negotiated and concluded: the Protocol to the regional UNECE (United Nations Economic Commission for Europe) Convention on Long-Range Transboundary Air Pollution on Persistent Organic Pollutants and the global Stockholm Convention on POPs. These instruments establish international regimes for initial lists of POPs (16 in the UNECE Protocol and 12 in the Stockholm Convention). The 179 countries who ratified the Stockholm Convention accepted to reduce or prohibit POP uses by adopting some specific actions of regulation.

Chemicals can be emitted in the atmosphere by natural sources like forest fires or volcanic eruptions. However, they are mainly emitted by anthropogenic activities through various sectors: transport (e.g. road, railroad, waterway, aerial), industry (e.g. power plants, chemistry, incinerators, steel industry), agriculture (e.g. fertilisers, breeding) and residential sector (e.g. heating, phytosanitary products). Chemicals can also enter the atmosphere from secondary sources (eolian erosion, resuspension of particles, reemissions from soil, vegetation or surface waters). Estimation of emission inventory is a very difficult exercise to achieve because there are many sources of uncertainty. It includes inaccuracy in values of activity data and emission factors, measurement errors, lack of relevant data, omissions and non-representativeness. EPER is the European Pollutant Emission Register – i.e. the European-wide register of industrial emissions into air and water. It gives access to information on the annual emissions of approximately 9,200 industrial facilities in 15 member states of the EU mostly for the year 2001 and approximately 12,000 facilities in the 25 member states of the EU and Norway for the year 2004. In order to improve the quality of the reported data, a review is jointly carried out by the cooperative programme for monitoring and evaluation of the long-range transmission of air pollutants in Europe (EMEP) and the European Environment Agency (EEA). It allows the identification of potential problems in reported emissions.

A wide range of models of different complexity exists to simulate the transport and fate of chemicals in the atmosphere. The simplest ones are box models. They assume that chemicals are homogeneously distributed in the considered part of the atmosphere and they only compute a balance between gains (emissions) and losses (deposition, chemical reactions) of chemicals. Gaussian models are often used to determine the concentration of plumes from point sources like smokestacks.

Relying on stationary assumptions, they diagnose that the air chemical dispersion has a normal probability distribution. These kinds of simple models are generally inadequate to describe the transport of chemicals at regional or global scale, according to the level of precision that is required. More complex models discretise vertically and horizontally the domain under consideration. A 3D transport equation is then resolved to compute chemical concentration at each time step and in every cell of the mesh. Meteorological models can be used to determine fields like temperature, wind or precipitations.

The aim of this chapter is to review and describe the main processes governing the fate of chemicals in the atmosphere and models able to simulate them. The first section describes the transport of chemicals by advection and turbulent diffusion in the atmosphere. The second section is related to the partition between particulate and gaseous phases in the atmosphere. This partition depends on several intrinsic or meteorological parameters, and it affects the deposition on surfaces. The third section describes the chemical reactions in both particulate and gaseous phases. The two last sections describe the interactions between soil and other media, i.e. gaseous exchanges, particulate and wet depositions.

2 Transport in the Atmosphere

2.1 Process Description

Theoretically, the fluid-chemical coupled system should be solved simultaneously by the reactive Navier-Stokes equations: this is called as "online coupling". However, in practice, a dilution assumption is often considered: chemical evolution is assumed to have negligible influence on mass fluid. Evolution of meteorological fields and chemical concentration are then decoupled: this is referred as "offline coupling". In a preprocessing step, meteorological models determine fields like pressure, temperature and wind velocity. These latter are then used to solve chemical transport equation.

Horizontal advective transport is driven by wind fields: chemicals are transported by air mass movements. Longitudinal wind (West-East) is typically about 10 m s^{-1}, and latitudinal wind (South-North) is lower (approximately 1–2 m s^{-1}). This determines characteristic time scales for the transport by advection: 1 or 2 months for hemispheric mixing and transport from midlatitudes to poles or equatorial regions [10]. At synoptic scales, vertical pressure gradient is compensated by gravity and then vertical winds are much lower (about 3 or 4 orders of magnitude) than horizontal winds.

Molecular diffusion is too weak (kinematic viscosity of approximately 10^{-5} $m^2 \cdot s^{-1}$) to have an influence on chemical dispersion, except near the soil-air interface (few millimetres).

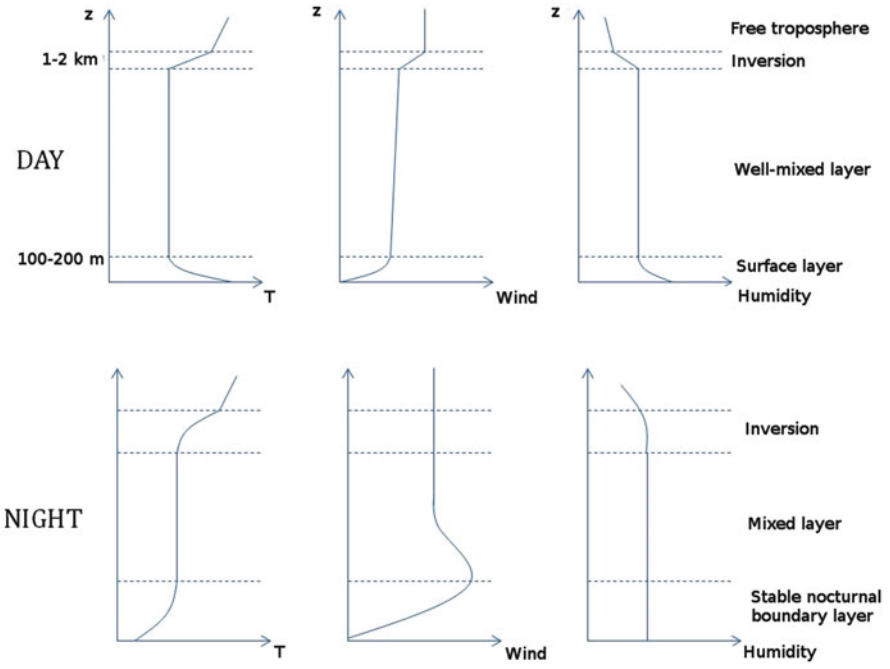

Fig. 1 Typical profiles of temperature, wind and humidity over land in midlatitudes

Vertical mixing occurs by turbulence phenomenon, which is related to boundary layer effects [11]. These effects have dynamic (vertical wind shear stress) and thermal (vertical gradient of temperature due to soil temperature cycles) origins. Turbulence mainly takes place in the atmospheric boundary layer (ABL) that is defined as the layer in interaction with surface (approximately 1 km thick). During the day, soil is heated by solar radiation. Then the ABL is heated by turbulent mixing (the ABL is unstable). During the night, soil is cooled and thermal transport does not occur (the ABL is stable) (Figs. 1 and 2). Turbulence shows then a diurnal variation. Turbulence is characterised by eddies of various characteristic sizes. It is impossible to represent all these scales in a model. An empirical approach is then often used: all physical variables are decomposed in an average term and a fluctuation around this average. Navier-Stokes equations are rewritten with this decomposition. This kind of model is called RANS (Reynolds-Averaged Navier-Stokes) model because it is based on time-averaged equations of motion for fluid flow. The decomposition leads to correlations between fluctuations. These terms need to be quantified to solve the RANS equation: this is the closure problem. Various models are then available to close these equations. For example, the Boussinesq hypothesis [12], based on the concept of eddy viscosity, leads to express the fluctuations correlation as a function of the mean variables by introducing

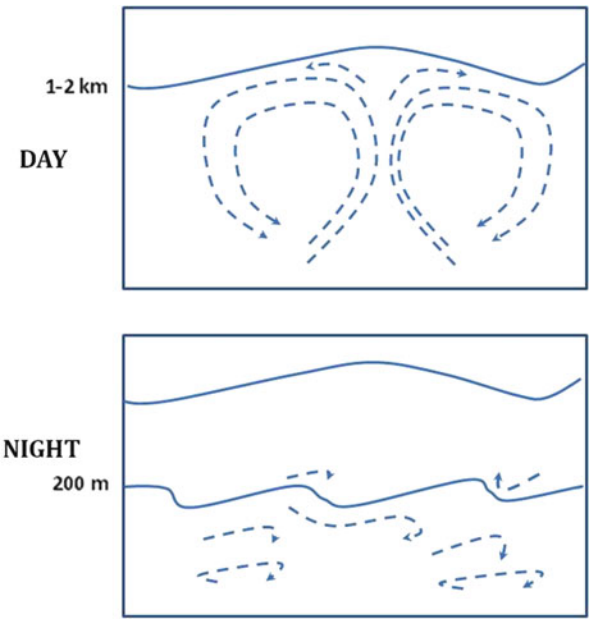

Fig. 2 Typical ABL eddy structure and circulation in the day and night

turbulent diffusion coefficients. The detailed description of such coefficients is out of the scope of this book and can be found in dedicated works [13, 14].

Finally, the transport equation can be written as:

$$\frac{dC_{\text{air}}}{dt} = -\text{div}\,(UC_{\text{air}}) + \text{div}\,(K\nabla C_{\text{air}}) + \text{Sources} - \text{Losses} \quad (1)$$

where C_{air} (g m^{-3}) is the atmospheric concentration, K is the turbulent diffusion tensor (coefficients of the tensor are given in m^2 s^{-1}) and U (m s^{-1}) is the mean speed of the flow over the ABL.

3 Partition Between Gaseous and Particulate Phases

3.1 Process Description

Chemicals may partition between gas and particulate phases in the atmosphere. Since chemical transformation and deposition in the gas phase differ from that in the particulate phase, the partitioning is a key factor for simulating the fate of chemicals in the atmosphere [15]. The rationale of partitioning models is to predict the compound distribution between particulate and gaseous phases from knowledge of its basic physico-chemical properties. In theory, models are strictly applicable only within a group of structurally related substances. Most models were thus

developed for (semi-)volatile, non-polar organic chemicals that interact with organic matter predominately by dispersive interactions. The group of (semi-) volatile, non-polar organic chemicals includes many persistent organic pollutants, for example, many halogenated aromatic compounds.

The distribution of organic non-polar chemicals between gas and particle phases was first considered by Junge [16, 17], who investigated the transport of biocides and PCBs in the atmosphere, and was discussed by Pankow [18]. Assuming that chemicals adsorb to active sites on the surface of particles, the Junge-Pankow adsorption model uses the subcooled liquid vapour pressure (P_{vs} in Pa) as a correlation parameter for gas/particle interactions and is based on the linear Langmuir isotherm to predict the fraction ϕ of chemical onto particles:

$$\varphi = \frac{c\theta}{P_{vs} + c\theta} \tag{2}$$

where ϕ (dimensionless) is the fraction of chemical onto particles; P_{vs} (Pa) is the subcooled liquid vapour pressure; c (Pa m) is a parameter depending on the molar mass of the pollutant, on the nature of the particles and on the temperature (assumed to be 0.17 Pa m according to [17]); and θ is the surface of particles ($m^2\ m^{-3}$).

Subcooled liquid vapour pressure at ambient temperature T can be expressed from vapour pressure at reference temperature $P_{vs}{}^0$ (298 K):

$$P_{vs}(T) = P_{vs}^0 \cdot \exp\left[-a_p\left(\frac{1}{T} - \frac{1}{T_0}\right)\right] \tag{3}$$

where a_P is the vapour pressure coefficient depending on temperature.

The distribution of chemicals between particulate and gaseous phases can alternatively be described by the particle-gas partition coefficient K_P ($m^3\ \mu g^{-1}$ particles), which is related to fractions of chemicals in gas (C_{gas}) and particles (C_p), respectively, and to the total concentration of suspended particles (TSP in μg particles m^{-3}). The fraction ϕ of chemical onto particles is related to particle-gas partition coefficient K_P as follows:

$$\varphi = \frac{K_P \cdot \mathrm{TSP}}{K_P \cdot \mathrm{TSP} + 1} \tag{4}$$

For calculating K_P, it may be assumed that chemical partitions through an absorption process in the aerosol organic matter (OM) rather than by physical adsorption onto the surface of particles [19]. Partitioning coefficients normalised to the OM content were taken as a basis for an absorption model. For example, Harner and Bidleman [20] studied partition of PCBs, PAHs and PCNs in air and proposed the following empirical relationship for predicting K_P:

$$\log K_P = \log K_{OA} + \log f_{om} - 11.91 \quad (5)$$

where K_P (m^3 μg^{-1} particles) is the particle-gas partition coefficient, K_{OA} (dimensionless) is the octanol-air distribution coefficient and f_{om} (dimensionless) is the fraction of organic matter in the particle phase.

To judge the suitability of these two alternative approaches (based on P_{vs} or K_{OA}) in determining the gas-particle partition of chemicals, some studies regressed these two parameters against K_P [20–24]. In some studies, K_{OA} was found to explain better than P_{vs} the observed variability of K_P within a compound class and between compound classes, whereas other studies found no evidence for such difference in fit [25]. The authors concluded that it is meaningless to compare P_{vs} and K_{OA} because of the large uncertainty of both these two descriptors. Indeed, differences in the fit of regression equations observed in various studies are largely due to differences in the quality and consistency of the physico-chemical data sets. K_{OA} data set is more consistent than that of P_{vs} because the same method of measurement is often used. On the contrary, vapour pressure data set is less homogeneous because of the multitude of methods and investigators involved in their generation.

Other considerations can help to make a choice between these two methods. The vapour pressure method implies the use of a different reference state for each chemical, whereas the use of K_{OA} makes octanol the common reference phase for all chemicals [25]. Furthermore, K_{OA} can be determined by direct experimental measurement, whereas subcooled liquid vapour pressure P_{vs} has to be derived from measured solid vapour pressure data, introducing additional uncertainty.

There are some evidences that gas-particle partition is influenced by both adsorption and absorption processes. Lohmann and Lammel [26] found that absorption to organic matter is not sufficient in accounting for the observed PAH sorption to particles. They suggested that a combination of absorption into organic matter and adsorption to black carbon and other matrices occurs in the atmosphere. In contrast to organic matter, the black carbon surface is limited, and non-linearity can be expected: as the concentration increases, the black carbon sites are saturated, and absorption into organic matter becomes more important. Götz et al. [27] proposed a model based on polyparameter linear free energy relationships (ppLFERs) to take into account both absorption and adsorption. In this model, the partition coefficients for absorption into aerosol bulk phases and adsorption on the various aerosol surfaces are calculated separately and then combined to calculate K_P. For non-polar compounds, the authors found high correlation between K_{OA} model and theirs. On the contrary, for polar compounds and aerosols with low organic matter content, differences were observed.

3.2 Organic Matter in the Atmosphere

The K_{OA} approach requires the estimation of the fraction of organic matter in the atmosphere (f_{om}), as well as the total concentration of suspended particles (TSP). The determination of atmospheric organic carbon (OC) is however subject to several artefacts: during prolonged sampling, adsorption of gaseous organic compounds on filters or evaporation of gaseous organic material from particles collected on filters can generate positive or negative artefacts in the OC measurement. Organic compounds that can be associated with ambient fine aerosols have a wide range of different physical and chemical properties, and carbon is also present under atmospheric elemental and/or black carbon (EC/BC, mainly produced by fuel combustion and biomass burning); OC charring during analytical protocols can lead to an overestimation of EC/BC and an underestimation of OC concentrations [28]. Conversion of OC to OM (organic matter) is also a critical factor of uncertainty. A factor of 1.4 has commonly been applied for this purpose both in urban and rural areas even if the source contribution of organic matter varies from site to site and also by season. Reviewing conversion factors reported in the literature, Turpin and Lim [29] concluded that 1.6 ± 0.2 was a better estimate for urban areas, whereas 1.9–2.3 were suggested for aged aerosols and 2.2–2.6 for aerosols originating from biomass burning [28].

Yttri et al. [28] performed an extensive monitoring campaign for 12 European rural and two urban background sites within the EMEP (European Monitoring and Evaluation Programme) and thus provided a good picture of atmospheric organic matter variability in Europe. They found that PM_{10} concentration ranged from about 8–41 μg m^{-3}, with the highest levels observed at the most urban influenced sites and with wintertime concentrations higher than summertime ones. The annual mean contribution of OM to PM_{10} ranged from about 9–37%, without any systematic seasonal effect. These values provide relevant levels that can be used when modelling the partitioning of chemicals in the atmosphere.

4 Chemical Reactions

Chemicals are subject to transformations in the atmosphere. These reactions can occur either in gaseous or particulate phases. They determine the residence time of chemicals in the atmosphere. These reactions include photolysis and reactions with atmospheric photooxidants like the hydroxyl radical (OH), the nitrate radical (NO_3) and ozone (O_3) [30]. Generally, the reaction with OH radicals is the most important [31]. The concentration of OH is subject to seasonal and diurnal variations since its major tropospheric source is the photochemical cleavage of ozone by sunlight. Reaction with ozone is generally of secondary importance.

The degradation process is described by a first-order equation:

$$\left(\frac{dC_{\text{air}}}{dt}\right)_{\text{chemical}} = -\left(\phi\lambda_{\text{part}} + (1-\phi)\lambda_{\text{gas}}\right)C_{\text{air}} \tag{6}$$

where ϕ (dimensionless) is the fraction of chemical onto particles and λ_{part} (s^{-1}) and λ_{gas} (s^{-1}) are the degradation constants in particulate and gaseous phases, respectively.

Degradation of particulate phase is more difficult to estimate. Photodegradation in the atmosphere is generally faster for the compounds in the gas phase than for the compounds associated to particles. However it is generally assumed to be negligible for pollutants mostly present in gaseous phase since the other degradation processes are dominant. Some works (e.g. [32]) proposed some estimation of photodegradation rates for various chemicals based on QSAR approaches.

Degradation in gaseous phase being dominated by reaction with hydroxyl radical, only this reaction is generally considered [15]. λ_{gas} is expressed as:

$$\lambda_{\text{gas}} = \lambda_{\text{OH}}\,[\text{OH}] \tag{7}$$

where λ_{gas} (s^{-1}) is the reaction rate constant of the chemical in gas, λ_{OH} ($m^3\ mol^{-1}\ s^{-1}$) is the reaction rate constant with hydroxyl radical and [OH] (mol m^{-3}) is the atmospheric hydroxyl radical concentration.

[OH] is a very short-lived (about 1 s) free radical, and its concentration in the atmosphere cannot presently be measured at the regional to global scale directly by in situ or remote sensing techniques. Large-scale average concentrations can, however, be inferred indirectly from long-term global measurements of the trace methyl chloroform gas (CH_3CCl_3) because OH is the major destruction mechanism for this gas [33]. As ozone and other chemicals emitted by anthropogenic activities are sources of OH radicals in the atmosphere, the concentration of these latter has shown long-term evolution, with increasing concentrations until 1993 followed by a significant decrease [34]. At short term, OH concentration also depends on meteorological fields like temperature (T), pressure (P) and solar radiation (RS), and this dependence can be expressed as:

$$[\text{OH}] = \frac{PN_A}{RT}[\text{OH}]_{\text{ref}} \quad \text{if} \quad \text{RS} > 2\ \text{W m}^{-2}\ \text{s}^{-1} \tag{8}$$

where N_A is the Avogadro constant, P is the pressure (Pa), R (J K^{-1} mol^{-1}) is the universal gas constant and $[\text{OH}]_{\text{ref}}$ (ppt) is the average mean concentration of hydroxyl radical. This reference average mean [OH] concentration can be obtained by EMEP database [35]. According to this equation, hydroxyl radical is present only during the suntime.

Midday photostationary-state OH concentrations range from 10^7 to 10^6 species cm^{-3} or less, depending on ambient levels of ozone, water vapour and UV solar radiation. The NO_3 radical concentration in the lower troposphere is generally one order of magnitude larger than for OH. The reaction rate constant λ_{OH} can be calculated according to Arrhenius equation:

$$\lambda_{\mathrm{OH}} = A \exp\left(-\frac{E_a}{RT}\right) \tag{9}$$

where E_a (J mol^{-1}) is the activation energy of the reaction with hydroxyl radical and A (m^3 mol s^{-1}) is a constant depending on the chemical as well as E_a.

On the basis of existing experimental data for the tropospheric degradability of organic compounds, approaches based on QSAR were alternatively investigated for predicting half-lives (or degradation rates) of chemicals in the atmosphere [36]. The literature provides about 500 rate constants for organic compounds in the gas-phase reaction with the OH radical and about 150 for the reaction with the NO_3 radical. Many QSAR models have been published that correlate spectroscopic (e.g. ionisation energies) or thermodynamic (e.g. bond dissociation energies, number of hydroxyl groups, of hydrogen atom donors for H-bonds) with the reaction rate constant of organic chemicals with OH and/or NO_3 and/or ozone free radicals (e.g. [37–42]).

5 Dry Exchanges Between Atmosphere and Surface

5.1 Dry Exchanges of Gaseous Chemicals

The dry exchanges of gaseous chemicals between the atmosphere and the earth surface (bare soil, vegetation and/or surface water) can be seen as the composition of a dry deposition (or absorption) flux and a (re)emission flux [43]. It does not include deposition governed by precipitations or fog (see Sect. 6). The exchange flux of gaseous chemicals can be explained by the capture (deposition flux) or the release (reemission) of chemicals by the surface. For the gaseous phase, the concentration gradient that appears above the surface (bare soil, vegetation and/or surface water) generates a diffusive flux in the atmosphere and a deposition of chemicals on earth surfaces. Gaseous deposition of chemicals has been deeply investigated for pollutants like ozone or nitrogen oxides, but the simultaneous consideration of deposition and reemission is relatively specific to the POPs that require consistent mass-budget modelling in the different compartments of the environment.

Considering by convention that the exchange is oriented upwards, the dry exchange flux of gaseous chemicals, $F_{\mathrm{dry},g}$ (expressed e.g. in µg m^{-2} s^{-1}), can be written as:

$$F_{\mathrm{dry},g} = -K_{\mathrm{dry},g} \times \left(C_{\mathrm{gas,atm}} - C_{\mathrm{gas,surface}}\right) \tag{10}$$

where $K_{\mathrm{dry},g}$ (m s^{-1}) is the global diffusive transfer coefficient; $C_{\mathrm{gas,atm}}$ (µg m^{-3}) is the chemical gaseous concentration at a given reference height, z_{ref}, in the atmosphere; and $C_{\mathrm{gas,surface}}$ (µg m^{-3}) is the gaseous concentration in air at the interface

between atmosphere and earth surface (air layer in contact with water, vegetation or bare soil, including interstitial air in soil).

According to assumptions selected for the model, $C_{\text{gas,surface}}$ can be directly related to the global concentration in exposed surface (see the chapters "Modelling the Fate of Chemicals in Surface Waters" and "Modelling the Fate of Chemicals in Soils") or determined through the resolution of a dynamical representation of exchanges between the air and the exposed surface. In the framework of atmospheric dispersion modelling, the reference height z_{ref} typically ranges from a few metres up to a few tens of metres, depending of the vertical resolution of the atmospheric transport model. For being consistent with the theoretical framework of dry deposition velocity, z_{ref} has to remain in the surface layer. The transfer coefficient $K_{\text{dry},g}$ integrates all the different mechanisms involved in the mass transfer. Such mechanisms are commonly integrated within a "resistance" scheme, which is based on three resistances in series representing specific diffusive mechanisms. In the upper layer, atmospheric turbulence is assumed to govern the transport via the aerodynamic resistance R_a, while in the underlying quasi-laminar layer, Brownian diffusion, inertial impaction and interception are supposed to be predominant processes, which are grouped into a quasi-laminar resistance term R_b. The surface or canopy resistance $R_{s,g}$ combines all uptake processes involving individual elements of the surface (soil, vegetation, surface water). In summary, the global diffusive transfer coefficient $K_{\text{dry},g}$ can be expressed as:

$$K_{\text{dry},g} = \frac{1}{R_a + R_b + R_{s,g}} \tag{11}$$

where R_a, R_b, and $R_{s,g}$ (in s m^{-1}) are, respectively, the aerodynamic resistance, the quasi-laminar sublayer resistance and the surface (or canopy) resistance for gases.

5.1.1 Aerodynamic Resistance

The aerodynamic resistance R_a represents the transport by turbulent diffusion between the reference height z_{ref} and the quasi-laminar sublayer. It does not depend on the chemical properties. The R_a formulation is classically derived from the Boussinesq eddy viscosity model. R_a can be defined as the integral of the inverse of the turbulent viscosity:

$$R_a = \int_{z_0}^{z_{ref}} \frac{1}{\nu_t} dz \tag{12}$$

where z_0 (m) is the roughness height that depends on ground coverage and season. It corresponds to the height where the mean horizontal velocity is zero. It varies typically from 5 mm for lakes or seas to 2 m for forest soils; z_{ref} (m) is the reference height; ν_t (m^2 s^{-1}) is the turbulent viscosity.

According to the Prandtl mixing length assumption [44], R_a may be expressed as a function of the friction velocity u_* and the Von Karman constant κ that describes the logarithmic velocity profile of a turbulent flow:

$$R_a = \frac{1}{\kappa u_*} \ln\left(\frac{z_{ref}}{z_0}\right) \tag{13}$$

where u_* (m s^{-1}) is the friction velocity, which depends on the shear stress at the flow boundary, and κ (dimensionless) is the Von Karman constant, typically 0.41.

This formulation is valid for thermally neutral conditions but has to be enhanced to take into account the thermal stability of the surface layer [45].

5.1.2 Quasi-Laminar Sublayer Resistance for Gas

Within the quasi-laminar sublayer (i.e. close to the surface), molecular diffusion governs the transfer of the chemical gaseous species. Modelling and experimental studies suggest that "near-surface" resistance, R_b, is strongly influenced by the chemical diffusivity. Model formulations for R_b are then generally derived from empirical fitting and rely on molecular diffusivity of the species of concern.

For instance, Hicks et al. [46] propose the following expression above homogeneous vegetated land surface:

$$R_b = \frac{2}{\kappa u_*} \left(\frac{Sc}{\mathrm{Pr}}\right)^{2/3} \tag{14}$$

where Sc (dimensionless) is the Schmidt number, i.e. the ratio between the momentum diffusivity (kinematic viscosity) and the molecular diffusivity (both in m^2 s^{-1}), u_* (m s^{-1}) is the friction velocity, κ (dimensionless) is the Von Karman constant and Pr (dimensionless) is the Prandtl number, i.e. the ratio between the momentum diffusivity and the thermal diffusivity (both in m^2 s^{-1}).

The Prandtl number for air (typically about 0.72) was introduced in the relationship as a correcting factor because basic observations were primarily for heat transfer. This expression can be adapted for surfaces based on bluff roughness elements that are impermeable to the flow [47] or for open waters [48]. More refined representations of dry deposition flux propose a multilayer approach [49–51] instead of a "big leaf" approach. In this case, R_b is no more determined globally for the whole canopy but derived as a function of the height z. Wu et al. [51] proposed the following generic formulation for R_b:

$$R_b(z) = C \frac{\mathrm{Re}(z)^r \mathrm{Sc}^s}{\kappa u*} \tag{15}$$

where C (dimensionless) is an empirical constant that can be fitted ($\approx$2), r and s are exponents derived for different assumptions on the flow around the leaves (r typically ranges from 0 to 0.5 and s from 0.5 to 0.7) and Re(z) (dimensionless) is the Reynolds number of the flow and can be determined by:

$$\mathrm{Re}(z) = \frac{U(z) \cdot D_L}{\nu} \tag{16}$$

where $U(z)$ (m s^{-1}) is the wind speed in the canopy, D_L (m) is the length scale of the leaves and ν (m^2 s^{-1}) is the kinematic viscosity.

5.1.3 Canopy Resistance

The surface (or canopy) resistance, $R_{s,g}$, is supposed to represent all the relevant capture or release pathways from the exposed surface. When the surface is covered by vegetation, it includes gaseous exchange processes with plants through cuticle or stomata. Resistances associated to biological pathways (via leaf stomata and cuticle) are detailed in the chapter "Modelling the Fate of Chemicals in Plants". A concern for the atmospheric model is that effective resistances for plants are generally expressed per unit area of foliar surface, i.e. they are simulated for an individual plant perspective rather than for the global atmosphere perspective. In the context of atmospheric modelling, the relevant units for resistances are those expressed per unit horizontal area of the earth surface. The extrapolation from individual plants to canopy (like forests) is based on leaf area index (LAI). For many canopies (e.g. crops), LAI scaling is adequate, while forests may need additional correction factors. Plant resistance depends indeed on radiation and may be affected by shading. LAI can then be partitioned into sunlit and shaded plant fractions, globally in the framework of "big leaf" model or as a function of height in a multilayered model [46, 49–53]. The surface resistance $R_{s,g}$ can also integrate an in-canopy aerodynamic resistance (R_{ac}) and the subsequent ground resistance (R_{ground}) [53]. R_{ac} does not depend on chemical species while, R_{ground} does. Wesely [54] specified a constant R_{ac} for forest canopies, and Erisman et al. [55] suggested a formula as a function of canopy height and friction velocity. Zhang et al. [53] suggested the following relationship for the in-canopy aerodynamic resistance R_{ac}, where the effect of canopy height is implicitly included in the parameter $R_{\mathrm{ac},0}$ and the friction velocity u_*:

$$R_{ac} = \frac{R_{ac,0} \cdot LAI^{1/4}}{u_*} \tag{17}$$

where $R_{\mathrm{ac},0}$ (s m^{-1}) is a reference value for in-canopy aerodynamic resistance that is tabulated in Zhang et al. [53] for different Land Use Coverage (LUC), $R_{\mathrm{ac},0}$ values can seasonally change to reflect the change of canopy structure at different times of

the growing season, LAI (m^2 leaf m^{-2} soil) is the leaf area index and u_* (m s^{-1}) is the friction velocity.

The ground resistance R_{ground} can be considered separately for different surface types (water, ice, snow, soil), and it can be derived from resistances evaluated for bare soils (see the chapter "Modelling the Fate of Chemicals in Soils").

5.2 Dry Exchanges of Particles

For particles, the dry exchange flux between atmosphere and earth surface is expressed as the product of a deposition velocity by the atmospheric concentration in the particulate phase:

$$F_{dry,p} = -v_{dry,p} \times C_{part,atm} \tag{18}$$

where $F_{dry,p}$ (mg m^{-2} s^{-1}) is the dry flux of chemical between atmosphere and earth surface, $v_{dry,p}$ (m s^{-1}) is the deposition velocity and $C_{part,atm}$ (mg m^{-3}) is the chemical concentration in atmospheric particles.

This is the same kind of equation as for the gaseous phase, considering implicitly that the concentration in particulate phase at the surface is equal to zero. The dry deposition velocity of particles can be expressed by resistances to deposition as for gases, but there is an additional term corresponding to the gravitational settling velocity. The following global formulation was proposed by Venkatram and Pleim [56]:

$$v_{dry,p} = \frac{v_{grav}}{1 - e^{-v_{grav}\left(R_a + R_{s,p}\right)}} \tag{19}$$

where v_{grav} (m s^{-1}) is the gravitational settling velocity and R_a and $R_{s,p}$ (s m^{-1}) are, respectively, the aerodynamic resistance and the surface (or canopy) resistance for particles.

For small particles (typically diameter <20 μm), the gravitational settling velocity, v_{grav}, that assumes an equilibrium between the weight of the particle (its buoyancy is generally neglected) and the drag force due to viscosity (Stokes' law) can be given by:

$$v_{grav} = \frac{d_p^2 \rho_p g}{18 \mu_{air}} \tag{20}$$

where d_p (m) is the particle diameter, ρ_p (kg m^{-3}) is the particle mass density, g (m s^{-2}) is the gravitational acceleration and μ_{air} (kg m^{-1} s^{-1}) is the dynamic viscosity.

This expression has to be corrected for small particles (below 1 μm) by the Cunningham slip correction factor. For larger particles, the Stokes law is no longer valid, and a drag coefficient has to be included [57]. The contribution of

gravitational deposition depends on the size of particles. For particles larger than a few micrometres, gravitational settling has to be taken into account ($v_{dry,p}$ tends to v_{grav} when the particle diameter increases), but for smaller particles ($v_{dry,p}$ tends to $1/(R_a + R_{s,p})$ when the particle diameter decreases), the other mechanisms are expected to be largely predominant.

The aerodynamic resistance R_a is similar to those estimated for gaseous deposition. The surface resistance for particles $R_{s,p}$ represents the other mechanisms that can lead to particle capture. Three mechanisms are generally considered [58, 59]: the collection due to Brownian diffusion (i.e. process by which aerosol particles move randomly due to collisions with gas molecules), the collection due to impaction (related to the inertia of the particles) and the collection due to interception (related to the size of the particles). Several authors [60–62] separately consider each of these three processes for calculating $R_{s,p}$:

$$R_{s,p} = \frac{1}{u_*(\varepsilon_{br} + \varepsilon_{im} + \varepsilon_{int})} \tag{21}$$

where u_* (m s^{-1}) represents the friction velocity and ε_{br}, ε_{im}, and ε_{int} (dimensionless) are collection efficiencies for the Brownian diffusion, inertial impaction and interception, respectively.

Brownian diffusion is generally considered as the most efficient process for ultrafine particle (less than 100 nm in diameters). Several relationships can be found in the literature for calculating the collection efficiency for the Brownian diffusion, the simplest one being related to the Schmidt number [62]:

$$\varepsilon_{br} = Sc^{\gamma} \tag{22}$$

where Sc (dimensionless) is the Schmidt number and γ (dimensionless) is an empirical parameter depending on the earth surface (typically, $\gamma = 2/3$ for vegetated surfaces).

Impaction and interception are predominant for particles between 100 nm and few μm. Impaction represents the following process: an aerosol particle transported by the flow towards an obstacle cannot, when its inertia is too large, follow the flow deviation in the vicinity of the obstacle. Thus the particle collides with the obstacle surface and remains on its surface. The parameter governing impaction process is the Stokes number, St. It has different forms according to the type of surface considered. For instance, for vegetated surfaces, Slinn [61] writes it as:

$$St = \frac{v_{grav} \cdot u_*}{g \cdot A} \tag{23}$$

where St (dimensionless) is the Stokes number, v_{grav} (m s^{-1}) is the gravitational settling velocity, u_* (m s^{-1}) is the friction velocity, g (m s^{-2}) is the gravity constant and A (m) is the characteristic radius of collectors (typically leaves for vegetative canopies) that depends on Land Use Coverage (LUC) [62].

Thus, ε_{im} can be calculated as:

$$\varepsilon_{\text{im}} = \left(\frac{\text{St}}{\alpha + \text{St}}\right)^2 \tag{24}$$

where α (dimensionless) is a coefficient depending on LUC. As mentioned in Zhang et al. [62], other parameterisations are proposed in the literature, sometimes for specific LUC.

Interception occurs if the particle passes an obstacle at a distance shorter than its physical dimensions. This is especially important for large particles. Interception efficiency ε_{int} depends on particle diameter and on the characteristic radius of collectors A. A simple relationship is proposed as:

$$\varepsilon_{\text{in}} = \frac{1}{2}\left(\frac{d_p}{A}\right)^2 \tag{25}$$

where d_p (m) is the diameter of particles.

In some models, more than one length scale is considered for collectors, and a radius for "small" collectors is introduced to quantify the interception by vegetative hairs [61].

The global collection efficiency is sometimes weighted by a correction factor, R, to take into account the possible rebound of particles larger than few micrometres following the collision with dry surface. The generic formulation for this coefficient proposed by Slinn [61] is:

$$R = \exp\left(-b\sqrt{\text{St}}\right) \tag{26}$$

where R (dimensionless) is a correction factor for global collection efficiency, St (dimensionless) is the Stokes number and b is a coefficient to fit ($b \sim 1$).

Considering all these processes, the global dry velocity for particles follows trends similar to those presented in Fig. 3 with highest values for ultrafine and coarse particles and lowest values in the middle region of the diameter range.

More recent models [64–66] explore more deeply the role played by the turbulence in the canopy. As for gaseous chemicals, multilayer models could be useful to improve the representation of the collection efficiency.

6 Wet Deposition

Water is one of the main components of the atmosphere. Its proportion in air is variable (up to 3%), and it can be found in gaseous, liquid or solid forms. It is an efficient agent to clean the atmosphere from many of its chemicals. In atmospheric dispersion models, wet deposition refers to the mechanism leading to the removal

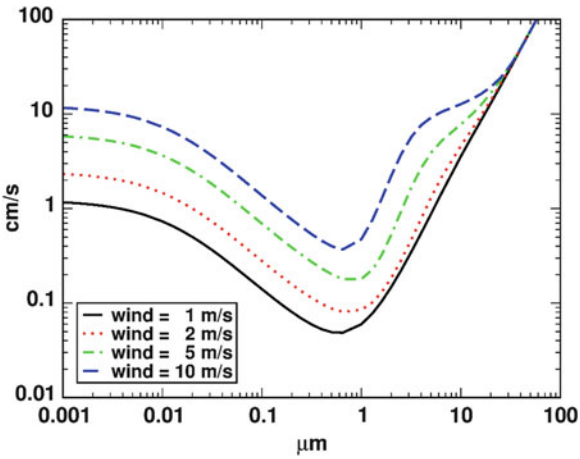

Fig. 3 Typical trends for global dry velocity of atmospheric particles (from [63])

of chemicals from the atmosphere by precipitating hydrometeors or fog. The models of wet flux related to fog are similar to those used for the dry deposition of particles (see, for instance, [67] for a review of this topic). Chemicals are captured by particles of condensed water (droplets, snowflakes and hailstones) which grow to become hydrometeors (rain, snow and hail). These latter precipitate and chemicals are deposited on the earth surface. If the capture occurs when the condensed water is aloft in the atmosphere, the phenomenon is called rainout or in-cloud scavenging. If it occurs during the fall of the condensed water to the ground, it is called washout or below-cloud scavenging. Both processes are generally represented in atmospheric dispersion models by scavenging coefficients which are used to determine a removal rate of the atmospheric concentration:

$$\left(\frac{dC_{\text{air}}}{dt}\right)_{\text{wet}} = -\left[\varphi \cdot \left(\lambda_{\text{part,ic}} + \lambda_{\text{part,bc}}\right) + (1-\varphi) \cdot \left(\lambda_{\text{gas,ic}} + \lambda_{\text{gas,bc}}\right)\right] \cdot C_{\text{air}} \quad (27)$$

where $\left(\frac{dC_{\text{air}}}{dt}\right)_{\text{wet}}$ (mg m^{-3} s^{-1}) is the variation in concentration of the chemical in air due to wet deposition, C_{air} (mg m^{-3}) is the concentration of the chemical in air, ϕ (dimensionless) is the fraction of chemical onto particles and $\lambda_{\text{part,ic}}$, $\lambda_{\text{part,bc}}$, $\lambda_{\text{gas,ic}}$ and $\lambda_{\text{gas,bc}}$ (s^{-1}) are the different scavenging coefficients, respectively, for particles rainout (in-cloud) and washout (below cloud) and for gases rainout and washout (see Sect. 3.1).

A wide range of parameterisations are proposed in the scientific literature to determine these coefficients [68–70]. Currently there is no scientific consensus to discriminate between them. To follow the distinction between rainout and washout, the first step is to determine where the different coefficients are applied and then where the clouds are. Some of the models proposed in the literature embedded an implicit diagnosis of the cloud presence [71]. For models providing only a removal coefficient, the cloud diagnose can be performed using the relative humidity vertical profile or the cloud liquid water content [72].

6.1 In-Cloud Scavenging

In-cloud scavenging happens during the formation of rain clouds and in their lifetime in the sky. First, water vapour condenses around particles which then play the part of cloud condensation nuclei. This is called nucleation scavenging. Second, the remainder of the particles in the interstitial air (between the droplets) is captured by collision with the cloud droplets. The gases present in the interstitial air can also diffuse towards and dissolve inside the cloud droplets. Third, the droplets grow by condensation and coalescence to become raindrops. Fourth, during their fall and before they reach the bottom of the cloud, the raindrops capture by collision many cloud droplets also loaded with chemicals. The final amount of chemical collected by the cloud droplets before they fall below the cloud is attributed to the in-cloud part of wet scavenging.

In-cloud scavenging is difficult to parameterise because data sets are poor and aqueous-phase chemistry should be taken into account. That is why most of the parameterisations of in-cloud scavenging coefficient are simple empirical formulations that only depend on the rain intensity. For instance, as reported by Webster and Thomson [73], Maryon et al. [74] proposed the following formulations for convective (Eq. 28) and large-scale (Eq. 29) rains, respectively:

$$\lambda_{\text{part,ic}} = 3.36.10^{-4} P^{0.79} \tag{28}$$

and

$$\lambda_{\text{part,ic}} = 8.4.10^{-5} P^{0.79} \tag{29}$$

where $\lambda_{\text{part,ic}}$ (s^{-1}) is the scavenging coefficient for particles rainout (in-cloud) and P is the intensity of rain (in mm h^{-1}).

Other parameterisations can be based on the relative humidity or the water content of the atmosphere. Roselle and Binkowski [72] proposed, for instance:

$$\lambda_{\text{ic}} = \frac{1 - \exp\left(-\frac{\tau_{\text{cloud}}}{\tau_{\text{washout}}}\right)}{\tau_{\text{cloud}}} \tag{30}$$

with

$$\tau_{\text{washout}} = \frac{\text{LWC} * h_{\text{cloud}}}{P}. \tag{31}$$

where λ_{ic} (s^{-1}) is the scavenging coefficient, respectively, for particles or gas rainout (in-cloud), τ_{cloud} (s) is a time scale representative of the lifetime of the cloud, τ_{washout} is the time needed to drain the cloud water at the precipitation rate P, LWC ($m_{\text{water}}^{3}\ m_{\text{air}}^{-3}$) is the liquid water content within the cloud, h_{cloud} (m) is the vertical extension of the cloud and P (here in m s^{-1}) is the intensity of rain.

This formulation is supposed to be applied to the chemical mass in aqueous phase regardless of its gaseous or particulate form; then for this kind of model, the concentration in aqueous phase has to be assessed before the determination of the removal rate from the atmosphere.

6.2 Below-Cloud Scavenging of Gas

The mechanism of below-cloud wet scavenging has been investigated for many years. Theoretical and semiempirical formulations for the scavenging coefficients of gases and particles have been derived [75, 76] to represent the microphysical processes that lead to the capture of chemicals by falling raindrops. Below-cloud wet scavenging, being generated in part by impaction process, first depends on the raindrop radius R_{drop} (that governs the probability of collision with chemicals present in the atmosphere). Raindrop radius can be represented by probability distributions (e.g. Gamma functions) or by their average diameter. Several parameterisations exist for the representative diameter of raindrops of the form:

$$R_{\text{drop}} = AP^B \tag{32}$$

with A and B ranging from 0.2 to 0.97 and from 0.16 to 0.25 according to [57].

Scavenging efficiency also depends on raindrop falling velocity U_{drop}, which can be computed as a function of raindrop radius. If raindrop radius is represented by its average diameter (instead of a radius distribution), Sportisse [57] established that the scavenging coefficient for gas is given by:

$$\lambda_{\text{gas},bc} = \frac{6\theta_{\text{rain}} D_g Sh}{(R_{\text{drop}})^2} \exp\left(-\frac{6D_g Sh \cdot z}{U_{\text{drop}} R_{\text{drop}}^2} \frac{H}{RT}\right) \tag{33}$$

where $\lambda_{\text{gas,bc}}$ (s^{-1}) is the scavenging coefficient for gas washout (below cloud), θ_{rain} (dimensionless) is the liquid water content for rain (volume of falling water per volume of air), D_g ($\text{m}^2\ \text{s}^{-1}$) is the molecular gas-phase diffusivity for the scavenged gas, Sh (dimensionless) is the Sherwood number (see below), R_{drop} (m) is the raindrop diameter, U_{drop} ($\text{m}\ \text{s}^{-1}$) is the raindrops falling velocity, H (atm mol^{-1} L) is the Henry constant, R (0.0831 atm mol^{-1} L K^{-1}) is the universal constant for ideal gases, T (K) is the air temperature and z (m) is the distance from the cloud base.

The exponential term represents the loss of scavenging efficiency due to the mass pollutant load of the raindrops during their fall. For a highly soluble species, this term can be neglected.

The Sherwood number describes the fact that the mass transfer in the falling raindrop is not only due to gas-phase diffusivity. It is calculated by the Reynolds and Schmidt numbers:

$$\mathrm{Sh} = 2 + 0.6\mathrm{Re}^{1/2}\mathrm{Sc}^{1/3} = 2 + 0.6\left(\frac{U_{\mathrm{drop}}R_{\mathrm{drop}}}{\upsilon_{\mathrm{air}}}\right)^{1/2}\left(\frac{\upsilon_{\mathrm{air}}}{D_g}\right)^{1/3} \tag{34}$$

where Re (dimensionless) is the Reynolds number, Sc (dimensionless) is the Schmidt number and υ_{air} is the kinematic viscosity in air (typically 1.5×10^{-5} m^2 s^{-1}).

6.3 Below-Cloud Scavenging of Particles

For particles, the below-cloud scavenging describes the fall of drops that have intercepted particles. Unlike gases, the solubility is no more relevant. A semiempirical parameter, $E(R_{\mathrm{drop}}, r_{\mathrm{part}})$, called the collision efficiency, is introduced to calculate the scavenging coefficient for particles:

$$\lambda_{\mathrm{part,bc}} = \frac{3}{2}\frac{E \cdot P}{R_{\mathrm{drop}}} \tag{35}$$

where $\lambda_{\mathrm{part,bc}}$ (s^{-1}) is the scavenging coefficient for particle washout (below cloud); E (dimensionless) is the collision efficiency, which depends on the raindrop diameter R_{drop} and on the particle diameter r_{part}; and P (here in m s^{-1}) is the intensity of rain.

The collision efficiency represents the ratio between the number of collisions between raindrops and the number of particles present in the scavenged volume. As for the dry deposition of particles, three mechanisms, i.e. Brownian diffusion, interception of particles and impaction, can be considered to express the collision efficiency as:

$$E = \frac{4}{Pe}\left(1 + 0.4 \cdot Re^{1/2} \cdot Sc^{2/3}\right) + 4k\left(k + \frac{1 + 2vk}{1 + v \cdot Re^{-1/2}}\right) + \left(\frac{S - S_*}{S + C}\right)^{3/2} \tag{36}$$

where Pe (dimensionless) is the Péclet number (Pe = Re·Sc), k (dimensionless) is the ratio between particle and droplet diameters ($k = r_{\mathrm{part}}/R_{\mathrm{drop}}$) and S, S_* and C are empirical coefficients relating maximum raindrop fall velocity and relaxation time of particles.

The first term represents Brownian diffusion (random movement of particles leading to their collect by raindrops)*;* the second term corresponds to the interception of particles falling in the vicinity of raindrops (it depends more on particle's geometry than on its mass); the third term describes the impaction of particles too big to follow the streamlines. Other processes could be also relevant [77]. A detailed description of the collision efficiency can be found in Wang et al. [70]. Similarly to the case of the in-cloud scavenging, more empirical formulation are also widely used to determine the below-cloud scavenging coefficients [68].

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Modelling the Fate of Chemicals in Soils

Philippe Ciffroy

Abstract A good knowledge and modelling of the fate of chemicals in soil is essential for achieving a holistic risk assessment approach. This chapter describes the processes that should be considered in models simulating the fate of chemicals in natural soils. The first section describes the exchange of chemicals between soil particles and soil porewater. The second section describes downward infiltration of dissolved chemicals in the soil depth profile. It requires the simulation of water mass balance in soil that is assumed to be governed by inputs/outputs of water in the soil system, i.e. rainfall, irrigation, evapotranspiration, downward infiltration and upward capillarity. A retardation factor incorporates adsorption of chemicals on soil particles. The third section describes absorption and volatilization of SVOCs at the air-soil interface, which can be simulated using the stagnant two-film model. The forth section describes bioturbation in soils, i.e. the disturbance of soil layers by biological activity. The fifth section describes diffusion of chemicals along the vertical soil profile that is governed by the general 1D transport model. The sixth section describes wash-off of chemicals from soils, i.e. the transport of chemicals in water flowing over the soil surface and finally reaching surface water systems. The seventh section describes processes responsible for degradation (i.e. hydrolysis, photolysis, biodegradation), which may be aggregated in a global loss rate.

Keywords Advection • Bioturbation • Degradation • Desorption • Diffusion • Infiltration • Modelling • Retardation factor • Soil • Soil porewater • Sorption • Wash-off • Water mass balance

Contents

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1 Introduction

Soil is the foundation of all terrestrial ecosystems, in particular those providing agricultural and forestry services. It is the structural medium for supporting the terrestrial biosphere and for providing food to humans. Ecosystem services provided by soil are linked to its key functions, in particular production of biomass and provision of habitat for many species contributing to genetic diversity. Degradation of soils, in particular those generated by chemical contamination, may lead to declines in soil fertility, modifications in soil organic matter and loss of biodiversity.

Among the perturbations affecting soils, the massive inputs of chemical substances presenting potential toxic effects can play a predominant role. Contamination issues range from local sites to global scales. Contaminated sites, especially the megasites, have become an issue of major concern due to their worldwide occurrence and the related extensive environmental and socioeconomic impacts [1, 2]. In Europe, there are over 20,000 large and complex contaminated sites presenting complex pollutant mixtures. But also, during recent decades, trace contaminants have been distributed so widely that even soils in remote regions show increased levels of certain chemicals of anthropogenic origins. For example, toxic compounds have been detected in remote Arctic environments. Chemicals residing in soils of developed countries can indeed volatilize and be transported over long-range distances, demonstrating that the soil contamination issue is a worldwide problem.

Chemicals can enter the soil by a number of pathways, and their behaviour and fate in soils can differ according to their source. In particular, agrochemicals and plant protection products (PPP) are widely used in intensive agriculture and can

reach the soil in a variety of ways: direct application to the soil (e.g. soil fumigant, herbicides like atrazine or simazine), spray that is not intercepted by the target plant and decay and decomposition of plant tissues that have been exposed to pesticide applications. Sewage sludges and other wastes can be recycled in agriculture as fertilizers and soil amendments. Trace elements are introduced into the soil also through waters used for irrigation, especially wastewaters. Finally, atmospheric deposition from industrial and urban emissions can be an important point source of chemicals for soils. Once emitted, trace elements may travel long distances in either gaseous form or in particle phase before deposition and can be dispersed over large areas from the point of release.

Toxic effects of contaminants present in soils can affect species living in such media. This is of great importance because a large proportion of the ecosystem services provided by soils comes from the soil biotic community and soil biodiversity is critical to ecosystem functioning and sustainable land management [3]. The main soil functions that are performed by soil organisms are decomposition (e.g. of cellulose or lignin), elemental transformations (e.g. nitrification, denitrification), bioturbation (e.g. by earthworms), microsymbiosis (e.g. mycorrhiza) and plant biomass production.

Soil quality can also affect human health. Humans can indeed be exposed to soil contamination through several pathways [4]. First, humans can ingest soil either involuntarily or deliberately. Young children (especially until 12–18 months) are especially vulnerable to this exposure pathway because of hand-to-mouth activity. This exposure pathway is generally called “pica,” and it can be applied to any form of abnormal ingestion which involves substances that are not normally regarded as edible. Some foods are also often contaminated with soil particles that could be consumed if foods are not properly washed. Soil can also be inhaled because human activity (e.g. soil cultivation) can disseminate particles in the above-ground atmosphere. But exposure pathways involving soil contamination are also indirect. Soils are indeed in interaction with the hydrosphere. Erosion, surface runoff, flooding (leading to water movement sideways through the soil into a watercourse) and leaching can affect surface- and/or groundwater quality. For example, soils are indirectly a potential source of drinking water contamination by pesticides. Soil is also in interaction with above-ground plants which provide food crops for human consumption. The entry of chemicals, which are present in the terrestrial environment, into human food chains is indeed controlled in the long term by their uptake by plant roots. For many chemicals, exposure to chemicals via ingestion of food products is a predominant pathway, and the transfer from soil to crops has to be properly evaluated (see chapter “Modelling the Fate of Chemicals in Plants”).

This background demonstrates the pivotal role of soils at different horizons in environmental and human health risk assessments. A better knowledge and modelling of the fate of chemicals in soils is then essential for achieving a holistic assessment approach. The fate of chemicals in soils can be affected by several processes like interaction at the water-particles interface, diffusion at the interface with atmosphere, within-soil diffusion and advection, bioturbation or degradation. The aim of this chapter is to review and describe the main processes governing the

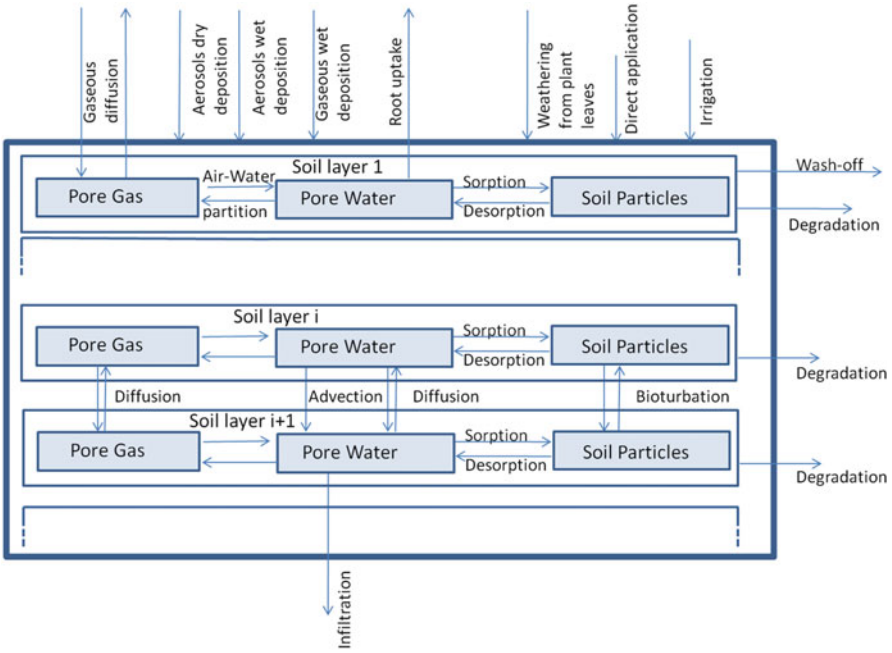

Fig. 1 Media, loading inputs, losses and exchanges considered in the 'superficial soil' model (some processes like dry, wet and gaseous atmospheric depositions, as well as Root uptake, are described in chapters "Modelling the Fate of Chemicals in the Atmosphere" and "Modelling the Fate of Chemicals in Plants")

fate of chemicals in soils and implemented in the MERLIN-Expo model (Fig. 1). The chapter is limited to processes occurring in superficial soil, i.e. in the first tenths of centimeters corresponding to the root zone of typical plants. For processes occurring in the vadose zone (i.e. unsaturated zone between superficial soil and groundwater table) and in groundwater itself, the reader has to refer to chapter "Modelling the Fate and Transfer of Substances Discharged Into Soil Unsaturated Zones and Water Tables".

2 Sorption/Desorption Between PoreWater and Soil Particles

2.1 Process Description

Exchanges of contaminants between the dissolved (i.e. porewater) and the particulate phases of soil govern their flux towards atmosphere and deeper soil layers because (1) only dissolved contaminants can exchange by diffusion (except bioturbation) along the vertical soil profile, (2) only dissolved contaminants can move by

advection towards deeper soil layers together with water advective movement, (3) only gaseous contaminants, which are assumed to be in equilibrium with the dissolved phase, can exchange by diffusion at the soil-atmosphere interface.

Exchanges of contaminants between porewater and soil particles are assumed to be equilibrated and thus described by a distribution (or partition) coefficient $K_{d,soil}$, expressed as the concentration ratio between the particulate phase and the dissolved phase, respectively. Similarly to what described for surface waters, organic carbon is assumed to be the main particulate media interacting with hydrophobic chemicals present in soil. Considering this assumption, distribution coefficients are generally related to the water-organic carbon partition coefficient K_{oc} and to the fraction of organic matter $f_{OM,soil}$ in soil:

$$K_{d,soil} = 10^{-6} \cdot f_{OM,soil} \cdot 10^{\log 10\_K_{oc}} \quad (1)$$

The limitations indicated in chapter "Modelling the Fate of Chemicals in Surface Waters", which regard equilibrium and hydrophobic assumptions, are also valid here.

2.2 Water-Organic Carbon Partition Coefficient for Organic Chemicals

Description of water-organic carbon partition coefficient K_{oc} is provided in chapter "Modelling the Fate of Chemicals in Surface Waters".

2.3 Fraction of Organic Matter in Soils

Organic carbon is considered to be the main sorbing phase in soil for neutral organic compounds. In fact, for nonneutral organics, which typically have a $\log(K_{ow})$ greater than 4, affinity to organic matter tends to be much stronger than to mineral surfaces, and the sorption to these latter can be neglected. Organic carbon content in soils can be divided between amorphous, soft or new and condensed, old or black carbon. Organic matter content in soils also depends on natural backgrounds as well as on anthropogenic activities (e.g. land use coverage, wet zone management). For example, to be used as agricultural, land peat soils have been drained and lost soil organic carbon. Moreover, the composition of organic carbon in soil can vary substantially and influence sorption. Finally, the organic carbon content alone as the descriptor of soil composition is then not sufficient to predict the soil-water distribution of chemicals that do not exclusively sorb to organic matter [5]. Despite these limitations and even if subdivisions in types of organic matter can be relevant

Table 1 Organic fraction (%) in soils in several European countries (from [6]) and French regions (from [7])

Country	Number of cells	Best estimate (%)	Standard deviation (%)
Austria	55,329	2.7	3.3
Bulgaria	14,101	2.1	1.0
Denmark	42,919	2.0	1.5
Estonia	13,379	3.5	4.6
Ireland	1,322	13.3	14.1
Italy	30,521	3.1	2.3
Netherlands	29,866	3.5	2.6
Norway	14,249	3.2	3.1
Poland	220,090	2.6	4.0
Serbia	1,181	2.0	1.6
Slovakia	26,959	1.3	1.1
Switzerland	105	4.5	5.6
France – Brittany		2.5	1.2
France – Alsace		2.5	1.2
France – Provence		1.2	0.1

for non-ionic organics, organic carbon is generally considered as a unique sorbing phase in fate models.

Panagos et al. [6] reviewed organic content in soils ($f_{OM,soil}$) of different European countries (at a large national scale). They collected data using the European Environment Information and Observation Network for soil (EIONET-SOIL). Data submitted by participating countries and presented in Panagos et al. [6] are their best estimate and represent an official point of view. Each participating country provided monitoring data on the basis of a grid of 1 km × 1 km cells and for 30 cm soil depth. For data at a regional scale, specific national monitoring programs can be consulted. For example, data were collected in the frame of a French program aiming at mapping soil properties at local scales. These data are freely available and can be consulted on the website www.gissol.fr. Mean and extreme values can thus be calculated for each French region. Data proposed by Panagos et al. [6] are reported in Table 1. They are assumed to follow normal distributions. Three examples of default values extracted from the French program Gissol [7] are also provided in Table 1. This illustrates natural variability of organic matter content in soils at a national or regional scale with values ranging from 1.2 to 13.3%.

3 Water Mass Balance in Soil and Loss by Infiltration

3.1 Process Description

The vertical movement of pore water in soils leads to downward infiltration (drainage or leaching) of dissolved chemicals that thus reach deeper soil layers and the vadose zone. In many models, a constant advection velocity of chemicals is considered, whatever meteorological and soil conditions. The downward infiltration of water in soil is however highly variable because it depends on soil moisture; and therefore advection velocity is time-dependent.

Water mass balance in soil is assumed to be governed by inputs/outputs of water in the soil system, i.e. rainfall, irrigation, evapotranspiration, infiltration downwards water flux and capillarity upwards water flux. Water content in soil can be dynamically calculated from the mass balance resulting from these input/loss contributions.

Rainfall and irrigation are considered as forcing variables given by meteorological and agricultural data. If monitoring data are not available for evapotranspiration, predictive models described in the literature may be used. For example, the Penman-Monteith or Penman-FAO models [8] calculate potential evapotranspiration ET_p from several variables, e.g. the latent heat of vaporization, volumetric latent heat of vaporization, rate of change of saturation specific humidity with air temperature, net irradiance, ground heat flux, specific heat capacity of air, dry air density, vapour pressure deficit, or specific humidity, conductivity of air, conductivity of stoma, and psychrometric constant. All these variables are generally difficult to measure and are poorly available. A simpler model based on accessible variables can then be preferred like the Turc's equation that provides an estimation of potential evapotranspiration at a monthly time scale from air temperature T_{air} and solar radiation Ig. Actual evapotranspiration ET_a can be obtained from potential evapotranspiration corrected by a cultural coefficient. If the Turc's relationship is used, this gives:

$$ET_a = K_c.ET_p = K_c.0.4.\frac{T_{\text{air}}}{T_{\text{air}} + 15}.\frac{Ig + 50}{30} \tag{2}$$

where ET_a (mm d $^{-1}$) is the actual evapotranspiration, ET_p (mm d^{-1}) is the potential evapotranspiration, K_c (dimensionless) is the cultural coefficient, T_{air} (°C) is the temperature in atmosphere and Ig (cal cm^{-2} s^{-1}) is the global solar radiation.

In order to calculate the infiltration velocity v_{adv} (and thus the quantity of water infiltrating to deeper soil layers), water quantity in soil over the investigated depth (here the root depth) can be subdivided into three different fractions (Fig. 2):

1. The excess water fraction, exceeding 'water content at field capacity' (θ_{fc}). 'Water content at field capacity' is defined as the amount of soil water content held in the soil after excess water has drained away. It can be assimilated to the maximum water content in soil.

Fig. 2 Schematic representation of the different fractions of water contents in soil

2. The 'optimal yield' fraction, where water is readily available by plants to reach maximal yields and corresponding to water content between 'water content at stress' (θ_{stress}) and 'water content at field capacity' (θ_{fc}). In dry soils, water has a low potential energy and is strongly bound by capillary and absorptive forces to the soil matrix and is less easily extracted by the crop. When the potential energy of the soil water drops below a threshold value (θ_{stress}), the crop is said to be water-stressed.
3. The 'water content at wilting point' (θ_{wp}) is defined as the minimal point of soil moisture the plant requires not to wilt.

According to water content in soil, different processes can be initiated: (1) downward water flux (i.e. infiltration) can be assumed to occur preferentially for excess water, i.e. for the fraction exceeding field capacity (i.e. when $\theta > \theta_{fc}$); (2) if water content is in the water stress zone (i.e. when $\theta < \theta_{stress}$), evapotranspiration is limited. Calculating the water mass balance in soil by taking into account the inputs and outputs described above allows then to evaluate the loss of water by infiltration.

3.2 Water Contents at Field Capacity and at Wilting Point

As defined above, soil water content at field capacity (θ_{fc}) and soil water content at wilting point (θ_{wp}) are key parameters for estimating water mass balance in soils. θ_{wp} can also be defined as the water content at -1500 J/kg of suction pressure, or negative hydraulic head.

Several pedotransfer functions were developed to predict θ_{fc} and θ_{wp} from soil physical properties. A review is proposed in Donatelli et al. [9], and the variables used for predicting soil water contents in several pedotransfer functions are reported in Table 2. These latter show that the water content thresholds can be influenced by soil texture (clay, silt, sand content), organic matter and/or bulk density. Baes and Sharp [10] reviewed also a lot of values obtained on soil from different textures and proposed mean and extreme values for four different textures (Table 3). Thus, when poor information is available about soil properties, parameter estimation can be based on the ranges proposed by Baes and Sharp [10]. If information is available on sand content, clay content, organic matter content and/or bulk density, most of pedotransfer functions referenced in Table 2 can be

Table 2 Variables used in several pedotransfer functions for calculating water contents at field capacity and at wilting point (from [9])

Pedotransfer function	Variables used for calculating soil water contents at field capacity and at wilting point
Brakensiek-Rawls	Sand content, clay content, organic matter content, bulk density
Hutson	Clay content, silt content
British soil service	Clay content, silt content, organic matter content, bulk density
Baumer	Sand content, clay content, cationic exchange capacity (CEC), bulk density
Manrique	Sand content, clay content, bulk density

Table 3 Mean and range of soil water content (dimensionless) at field capacity and at wilting point collected by Baes and Sharp [10] for different soil textures

	Water content at field capacity (dimensionless)			Water content at wilting point (dimensionless)			
Soil texture	Number of soils analysed	Mean	Standard deviation	Observed range	Mean	Standard deviation	Observed range
Silt loams	76	0.345	0.051	0.24–0.45	0.13	0.046	0.06–0.30
Clay and clay loams	33	0.36	0.063	0.26–0.45	0.22	0.049	0.14–0.32
Sandy loams	24	0.22	0.064	0.12–0.33	0.077	0.044	0.03–0.16
Loams	17	0.32	0.051	0.23–0.39	0.13	0.04	0.08–0.17
All soils	154	0.32	0.088	0.12–0.45	0.13	0.076	0.03–0.33

used. Such information can be available in specific national monitoring programs; for example, such data are made available on www.gissol.fr for all the French regions at a small spatial resolution.

4 Retardation Factor and Advection Within Soil

4.1 Process Description

As described above, water infiltration in soil is responsible for downward chemical movement along the soil profile. However, because the chemical is partly sorbed on the solid phase, only the dissolved phase is assumed to move along the depth profile, resulting in a retardation factor. In other words, the retardation factor incorporates the adsorption of chemicals on the particulate soil phase and must then be included in the advection transport equation of chemicals within the soil profile. Assuming that the partitioning of the chemical is described with a linear isotherm, the retardation factor $f_{\text{retardation}}$ is a dimensionless parameter defined as the amount by which a chemical is held back by the soil in comparison to the water

velocity. In other words, how much the flow of the chemical is delayed as compared to flow of the infiltrating water.

The fate of the chemical within the soil depth profile because of advection process can be described by 1D general transport equation. Because advection (or infiltration) applies only to the dissolved phase, the transport equation is under the form:

$$\frac{\partial C_T}{\partial t} = -v_{\text{adv}} \frac{\partial C_W}{\partial z} \tag{3}$$

where $C_T(z,t)$ is the total concentration of the chemical in soil and $C_w(z,t)$ is the concentration of the chemical in porewater, both expressed in mg m^{-3}, and v_{adv} (m s^{-1}) is the water advection velocity.

To homogenize the above-mentioned equation, total soil concentration C_T is expressed as the sum of the three phase concentrations:

$$C_T = \theta C_W + aC_G + \rho_{\text{solids}} C_S \tag{4}$$

where θ (dimensionless) is the soil water content, a (dimensionless) is the soil gas content, ρ_{solids} (kg dw m^{-3}) is the soil particles dry density, C_G (mg m^{-3}) is the concentration of the chemical in soil gas and C_S (mg kg^{-1} dw) is the concentration in soil particles.

Considering that water, gaseous and solid phases are assumed to be in equilibrium, i.e.:

$$K_D = f_{\text{OM,soil}} K_{\text{OC}} = \frac{C_S}{C_W} \tag{5}$$

and

$$K_{\text{AW}} = \frac{H}{\text{RT}_{\text{soil}}} = \frac{C_G}{C_W}, \tag{6}$$

where K_D (m^3 g^{-1}) is the distribution coefficient between soil particles and soil porewater, K_{AW} (dimensionless) is the air-water partition coefficient, $f_{\text{OM,soil}}$ (dimensionless) is the fraction of organic matter in soil, K_{OC} (dimensionless) is the water-organic carbon partition coefficient, H (Pa m^3 mol^{-1}) is the Henry's law constant and R (Pa m^3 mol^{-1} K^{-1}) is the universal gas constant.

Combining these equations, the differential equation can be rewritten:

$$\frac{\partial C_T}{\partial t} = -v_e \frac{\partial C_T}{\partial z} \tag{7}$$

where v_e is the effective advection velocity (m d^{-1}).

The effective advection velocity v_e is then defined as:

$$v_e = \frac{v_{\text{adv}}}{f_{\text{retardation}}}, \tag{8}$$

with v_{adv} as the advection water velocity and $f_{\text{retardation}}$ the water phase retardation factor defined as:

$$f_{\text{retardation}} = \rho_{\text{solids}} K_D + \theta + aK_{\text{AW}} \tag{9}$$

The retardation factor can thus be calculated from soil properties (bulk density, water content and air content) and chemical partition coefficients (soil-water and air-water partition coefficients).

It has to be noted that in some publications, another formulation of the retardation factor can be found under the form $f_{\text{retardation}} = 1 + \frac{\rho_{\text{solids}} K_D}{\theta}$. In this case however, the air content is not taken into account while it can be important for some organic chemicals.

5 Diffusion Between Soil and Atmosphere

5.1 Process Description

Some pollutants that are highly volatile (or semi-volatile organic compounds – SVOCs) can be emitted from soil surfaces to atmosphere. Reemission processes are important for SVOCs because such compounds are subject to long-range atmospheric transport (LRAT) occurring through a series of deposition-reemission events at the soil surface-air interface. This periodic movement of pollutants between soil and atmosphere has been termed the 'grasshopper effect' [11]. Grasshopper effect was put in evidence through several observations. For example, emissions into the environment of some pollutants like PCBs (polychlorinated biphenyl) showed historical variations, with hot spots in the 1950s and 1960s and emission restrictions in the 1970s resulting in a decrease in deposition to soil surfaces. Monitoring data and model simulations evidenced that by the early 1990s atmospheric concentrations were reduced sufficiently to invert the direction of flux at the atmosphere-soil interface, soil becoming a source of PCBs towards atmosphere [12–16]. It was also hypothesized that the 'grasshopper effect' is driven by temperature and soil organic matter; this results in global fractionation and accumulation of SVOCs in polar regions [13]. The latitudinally segmented inventory that was observed for some pollutants in soils [17] supports this assumption and gives evidence for fractionation of SVOCs. Finally, concentrations of SVOCs in air vary diurnally and seasonally [18, 19]. In particular, a decrease in soil concentration is observed during the warmer period of the day, corresponding to an equivalent increase in air, showing a dynamic behaviour of SVOCs at the air-soil interface.

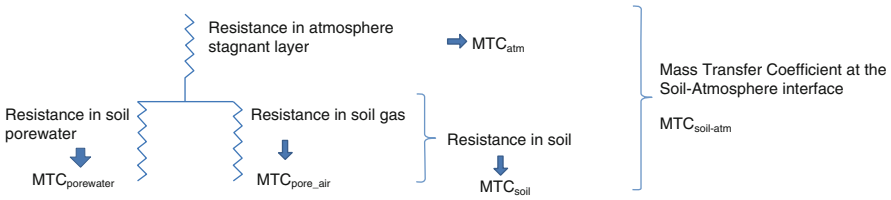

Fig. 3 Conceptual representation of resistances involved in diffusion process at the soil-atmosphere interface

Absorption/volatilization of SVOCs at the air-soil interface can be modelled using the stagnant boundary theory (two-film model), the chemical being assumed to diffuse across two layers (stagnant soil layer and stagnant air layer) characterized by two resistances in series; the soil resistance results itself of the combination of two resistances in parallel representing resistances in soil porewater and in soil gas, respectively (Fig. 3). According to this approach, the net flux from soil to the atmosphere is driven by the difference in gaseous concentration between air and surface soil according to the Fick's law.

The first resistance represents the resistance to diffusion on the upper part of the interface (i.e. in the thin boundary layer in atmosphere over the soil surface). A mass transfer coefficient in atmosphere (MTC_{atm}) can be calculated by dividing the diffusion coefficient of the chemical in air (D_{gas}) by the boundary layer thickness in atmosphere (δ_{atm}). Suggested values for air-side diffusion layer thickness δ_{atm} vary from 1 mm [20] to 5 mm [21]. For organics, the effective diffusion coefficient of the chemical in air is assumed to depend on its molar mass:

$$MTC_{atm} = \frac{D_{gas}}{\delta_{atm}} = \frac{D_{H2O\_gas}}{\delta_{atm}} \cdot \left(\frac{M_{H2O}}{M_{molar}}\right)^{0.5} \tag{10}$$

where MTC_{atm} (m d^{-1}) is the mass transfer coefficient from soil to atmosphere, D_{gas} (m^2 d^{-1}) is the diffusion coefficient of the chemical in gas, D_{H2O_gas} (m^2 d^{-1}) is the diffusion coefficient of water in gas, M_{H2O} (g mol^{-1}) is the molar mass of water, M_{molar} (g mol^{-1}) is the molar mass of the chemical and δ_{sed}(m) is the air-side boundary layer thickness.

In the soil, two resistances are involved in parallel, representing diffusion within the soil in either water-filled pore space or air-filled pore space. These two resistances are described by two parameters: the mass transfer coefficient in soil porewater ($MTC_{porewater}$) and the mass transfer coefficient in soil pore air (MTC_{pore_air}). These coefficients are estimated as described by Millington and Quirk [22], taking into account a tortuosity factor limiting diffusion in soil. Generally speaking, the Millington and Quirk's law states that tortuosity in water depends on porosity ϕ (dimensionless) and water content θ (dimensionless) according to:

$$\text{Tortuosity} = \frac{\theta^{10/3}}{\phi^2}. \tag{11}$$

The boundary layer thickness in soil δ_h corresponds to the thickness where diffusion occurs within the soil at the soil-atmosphere interface; in many models, it is assumed to correspond to the thickness of the first soil layer (i.e. order of magnitude of one centimeter):

$$\text{MTC}_{\text{porewater}} = \frac{D_{\text{water}}}{\delta_h}.\frac{\theta^{10/3}}{(a+\theta)^2}.\frac{\text{RT}_{\text{soil}}}{H} = \frac{D_{\text{O2\_water}}}{\delta_h}.\left(\frac{M_{\text{O2}}}{M_{\text{molar}}}\right)^{0.5}.\frac{\theta^{10/3}}{(a+\theta)^2}.\frac{\text{RT}_{\text{soil}}}{H}, \tag{12}$$

and

$$\text{MTC}_{\text{pore\_air}} = \frac{D_{\text{gas}}}{\delta_h}.\frac{a^{10/3}}{(a+\theta)^2} = \frac{D_{\text{H2O\_gas}}}{\delta_h}.\left(\frac{M_{\text{H2O}}}{M_{\text{molar}}}\right)^{0.5}.\frac{a^{10/3}}{(a+\theta)^2} \tag{13}$$

where $\text{MTC}_{\text{porewater}}$ (m d^{-1}) is the mass transfer coefficient in soil porewater, $\text{MTC}_{\text{pore\_air}}$ (m d^{-1}) is the mass transfer coefficient in soil gas, D_{water} (m^2 d^{-1}) is the diffusion coefficient of the chemical in water, D_{gas} (m^2 d^{-1}) is the diffusion coefficient of the chemical in gas, $D_{\text{O2\_water}}$ (m^2 d^{-1}) is the diffusion coefficient of dioxygen in water, $D_{\text{H2O\_gas}}$ (m^2 d^{-1}) is the diffusion coefficient of water in gas, M_{O2} (g mol^{-1}) is the molar mass of dioxygen, M_{H2O} (g mol^{-1}) is the molar mass of water, M_{molar} (g mol^{-1}) is the molar mass of the chemical, δ_h (m) is the boundary layer thickness in soil, a (dimensionless) is the soil gas content, θ (dimensionless) is the water content in soil, H (Pa m^3 mol^{-1}) is the Henry's law constant and R (Pa m^3 mol^{-1} K^{-1}) is the universal gas constant.

Finally, the global mass transfer coefficient $\text{MTC}_{\text{soil-atm}}$ (in m d^{-1}) is calculated according to the Ohm's law related to resistances in series and in parallel, considering that a diffusion coefficient is equivalent to the inverse of a resistance:

$$\text{MTC}_{\text{soil-atm}} = \frac{\left(\text{MTC}_{\text{porewater}} + \text{MTC}_{\text{pore-air}}\right).\text{MTC}_{\text{atm}}}{\left(\text{MTC}_{\text{porewater}} + \text{MTC}_{\text{pore-air}}\right) + \text{MTC}_{\text{atm}}} \tag{14}$$

As indicated above, the 'grasshopper effect' is in part driven by temperature. To reflect this effect of temperature in the exchanges at the soil-atmosphere interface, the dependence of the Henry's law constant can be included in the model. The enthalpy of volatilization can then be used to consider the temperature dependence of air-water partition coefficient (e.g. [23]):

$$K_{AW}(T) = \frac{H(T_0)}{RT_0}.\exp\left[\frac{-\Delta H_{volatilization}}{R}.\left(\frac{1}{T}-\frac{1}{T_0}\right)\right] \quad (15)$$

where $K_{AW}(T)$ (dimensionless) is the air-water partition coefficient at temperature T (in K), $H(T_0)$ (Pa m^3 mol^{-1}) is the Henry's law constant at the reference temperature T_0 (in K), R (Pa m^3 mol^{-1} K^{-1}) is the universal gas constant and $\Delta H_{volatilization}$ (J mol^{-1} or Pa m^3 mol^{-1}) is the enthalpy of volatilization.

It must be indicated also that other combinations of resistances were proposed in the literature. Thus, the deposition to the surface can be assumed to be controlled by three resistances in series (aerodynamic, quasi-laminar layer and surface resistances). A deposition velocity is thus computed from these three resistances and allows calculating dry deposition of gaseous pollutants [24]. The fugacity approach described in detail above offers however the advantage of taking into accounts both deposition and volatilization of gaseous pollutants.

5.2 Henry's Law Constant

Description of Henry's law constant H is provided in chapter "Modelling the Fate of Chemicals in Surface Waters".

6 Bioturbation

6.1 Process Description

Bioturbation refers to the disturbance of soil layers by biological activity. Some species (e.g. earthworms) disturb the soil by burrowing and feeding, enhancing the transport of chemicals in this compartment. Animals move indeed through the soil to obtain nutrients and water or to seek protection from predators or environmental variability. In doing so, they penetrate the soil vertically and horizontally. Bioturbation was showed to be a significant soil-mixing vertical process in many situations [25, 26].

Bioturbation can thus be seen as the process responsible for the sorbed phase transport of chemicals in soil depth. Vertical sorbed phase transport in the soil was shown to have a major impact on predicted soil concentrations, the state of equilibrium and the direction and magnitude of the chemical flux between air and soil.

McLachlan et al. [27] and Cousins et al. [28] suggested incorporating the bioturbation process as an additional diffusion process, representing the vertical sorbed phase transport. This process was then assimilated to a diffusion component in the solid phase. By analogy with diffusion in gas and water phases, bioturbation

can then be represented by a vertical diffusion coefficient $D_{\text{bioturbation}}$. This coefficient applies exclusively to the chemical concentration on particles.

6.2 Bioturbation Diffusion Coefficient

The bioturbation diffusion coefficient is abusively included in the diffusion transport equation because it does not refer *stricto sensu* to diffusion but to mechanical disturbance of soil by organisms. On a physical point of view, it refers to soil turnover rates that generate particles movement over the soil depth. By nature, the bioturbation diffusion coefficient is highly dependent on the fauna that occupies soil. Most studies were conducted with earthworms that are a main contributor to bioturbation. The value of the bioturbation diffusion coefficient can be estimated by two methods.

The first one is based on the assumption that the transport of lipophilic organic chemicals is expected to be closely linked to the transport of soil carbon. This assumption is supported by the expected preferential sorption of lipophilic organic chemicals to soil organic matter. Some studies investigated the transport of carbon in soils (Elzein and Balesdent, cited in [27]), providing thus orders of magnitude for $D_{\text{bioturbation}}$ (i.e. from 2.7×10^{-7} to 4.1×10^{-6} m^2 d^{-1}).

The second one is based on the evaluation of a characteristic path length of soil organisms and of the mass of soils moved annually by soil organisms (essentially earthworms) by unit area (or soil turnover rates). The combination of such information allows calculating an estimated value for $D_{\text{bioturbation}}$. Rodriguez [29] collected 25 values of bioturbation diffusion coefficients for earthworms that can be used for fitting a range for this parameter. According to this approach, $D_{\text{bioturbation}}$ would range from 10^{-8} to 3×10^{-6} m^2 d^{-1}.

7 Diffusion Within Soil

7.1 Process Description

Diffusion within soil (i.e. along the vertical soil profile) is governed by the general 1D transport model and is directed according to the concentration gradient within soil (Fick's law). Diffusion occurs in the three soil phases. Because diffusion coefficients are different for the gaseous, dissolved and particulate forms of the chemical, the transport equation is under the form:

$$\frac{\partial C_T}{\partial t} = \left[D_{\text{gas}} \frac{\partial^2 C_G}{\partial z^2} + D_{\text{water}} \frac{\partial^2 C_W}{\partial z^2} + \rho_{\text{solids}} . D_{\text{bioturbation}} \frac{\partial^2 C_S}{\partial z^2} \right] \tag{16}$$

where C_T (mg m^{-3}) is the total concentration of the chemical in soil, C_W (mg m^{-3}) is the concentration of the chemical in porewater, C_G (mg m^{-3}) is the concentration of the chemical in soil gas, C_S (mg kg^{-1} dw) is the concentration in soil particles, ρ_{solids} (kg dw m^{-3}) is the soil particles dry density, D_{gas} and D_{water} (m^2 s^{-1}) are the diffusion coefficients of the chemical in gas and water, respectively, and $D_{\text{bioturbation}}$ (m^2 s^{-1}) is the bioturbation diffusion coefficient.

To homogenize the above-mentioned equation, total soil concentration C_T is expressed as the sum of the three phase concentrations as described in Eq. (4). Thus, the diffusion equation can be rewritten:

$$\frac{\partial C_T}{\partial t} = D_T \frac{\partial^2 C_T}{\partial z^2} \tag{17}$$

where D_T is the effective diffusion coefficient applicable to the total chemical concentration in soil, with:

$$D_T = \frac{K_{\text{AW}} D_{\text{gas}} + D_{\text{water}} + \rho_{\text{solids}} K_D D_{\text{bioturbation}}}{f_{\text{retardation}}} \tag{18}$$

Diffusion occuring in a porous media like soil differs from diffusion in free water and pure gas. Effective diffusion coefficients in gas and water D_{gas} and D_{water} are then defined from diffusion coefficient in pure phases corrected by a tortuosity factor to account for the reduced flow area and increased path length of diffusing gas and water molecules in soil, as described in Eqs. (11)–(13).

8 Wash-off from Soils to Surface Waters

8.1 Process Description

Wash-off of chemicals designates the transport of contaminants in water flowing over the soil surface and finally reaching surface water systems (rivers and/or lakes). It includes runoff of dissolved contaminants and erosion of contaminated soil particles. Wash-off from watersheds is a loss process from soils and can be a significant secondary input into surface waters because these latter collect water and particle fluxes from potentially wide areas, especially during rainfall.

Several approaches are possible to simulate wash-off. One of them is based on global wash-off rate constants λ_{washoff} directly relating concentrations in soils and inputs into surface waters. Such global rate constants were fitted especially in the

field of radioecology where nuclear accidents represent a good source of tracers for following global transfer from watersheds to surface water systems. For example, global wash-off rate constants were calibrated using datasets collected after the Chernobyl accident for a wide range of European rivers. The Chernobyl accident corresponds indeed to a single atmospheric pulse with well-known spatial mapping of soil contamination and follow-up of river contamination during short and long periods after the deposit allowed to fit global transfer functions from watersheds to freshwater systems [30].

Some other models consider also transfer functions, but directly from rainwater to freshwaters, shunting thus the soil system. For example, the SimpleBox multimedia model assumed that a constant proportion of rainwater directly reaches freshwater systems and that this fraction is in immediate equilibrium with soil. Such models directly connect rainwater to freshwaters through a constant transfer rate and shunt many processes actually occurring in natural soil systems.

Other empirical models take into account short kinetic and spatial variations in the rainfall regime to simulate the loss of runoff water from soil during a given meteorological event. For example, the PRZM multimedia model incorporated the 'SCS runoff curve number approach' developed by USDA [31]. This approach calculates the soil depth impacted by runoff according to the rainfall event and to an empirical parameter (called 'curve number') implicitly accounting for landscape characteristics (like hydrologic soil group, slope of the field and land use coverage). This approach is mechanistically relevant because wash-off is by nature intermittent as it is related to the rainfall regime: it increases after heavy rainfall, floods and snowmelt. Besides, it can show high spatial variability, even at small scales, because it depends on the slope of the field and on its cover. However, this approach is essentially used at a local scale (rather than at a watershed scale) to predict the loss of water, particles and eventually associated chemicals from a field; it requires several information related to slope and land use of the field that are not easily accessible in many situations.

8.2 Global Wash-off Rate Constant

The global wash-off rate constant $\lambda_{washoff}$ gathers both liquid wash-off (when chemicals are transported in soluble phase) and solid wash-off (when chemicals are transported in particulate phase). It considers wash-off as a continuous process although it is by nature intermittent (linked to individual rainfall events). The global wash-off rate constant has the inverse dimension as the half-life, i.e. time needed to reduce by a factor 2 the concentration of chemicals in soils. As reported by Garcia-Sanchez [30] for radionuclides, $\lambda_{washoff}$ can mainly be explained by soil texture, chemical affinity for soil particles and observation time scale.

Accidental releases of radionuclides in the atmosphere (bomb-derived and Chernobyl fallouts) provide good estimations of wash-off processes. Inputs in the atmosphere and deposition on soils can indeed be quantified with a relative good

Table 4 Wash-off rate constants derived by Garcia-Sanchez [30] for several radionuclides

Radionuclide	Number of data	Process	Range (in d^{-1})
^{137}Cs	62	Liquid wash-off	1.8×10^{-7}–5.5×10^{-5}
	11	Solid wash-off	2.4×10^{-7}–3.3×10^{-4}
	18	Total wash-off	10^{-7}–2.7×10^{-5}
^{90}Sr	28	Liquid wash-off	1.8×10^{-6}–1.4×10^{-4}
	14	Total wash-off	1.8×10^{-7}–3×10^{-6}
^{241}Am	2	Solid wash-off	2.7×10^{-7}–5.5×10^{-7}
^{7}Be	1	Solid wash-off	5.5×10^{-5}
^{210}Pb	2	Solid wash-off	9×10^{-7}–2×10^{-6}
	4	Total wash-off	9×10^{-7}–3.4×10^{-6}
Pu	36	Solid wash-off	5.5×10^{-8}–1.6×10^{-5}
	3	Total wash-off	2.7×10^{-7}–3.3×10^{-6}
^{131}I	1	Total wash-off	3×10^{-4}
^{103}Ru	1	Total wash-off	5.5×10^{-5}

precision. Besides, radionuclides are substances that were followed on long-term in many European watersheds and associated rivers. Garcia-Sanchez [30] compiled and unified the existing information on radionuclide wash-off flux dynamics from atmospherically contaminated watersheds. Published wash-off quantifications were gathered in a database. Reported wash-off quantifications covered many situations (e.g. sites, wash-off processes, radionuclides and time scales) accumulated since 1960. Data obtained on radionuclides cover a wide range of chemical behaviours (in term of solubility and interaction affinity with soil particles, including mobile elements like strontium (Sr) and iodine (I) and very poorly mobile ones like plutonium (Pu)) and provide then a range of potential values that can be found for all the chemicals discharged onto soils, including organics. Data collected by Garcia-Sanchez [30] are summarized in Table 4 and show that $\lambda_{washoff}$ may range from 5×10^{-8} to 3×10^{-4} d^{-1}.

9 Degradation

9.1 Process Description

As described in chapter "Modelling the Fate of Chemicals in Surface Waters", degradation of chemicals in soils can be driven by hydrolysis, photolysis and/or microbial degradation. Such processes are considered individually in some specific models. In other models, they are not distinguished but added into an aggregated loss rate assuming linear first-order kinetics.

In soils, temperature is assumed to be one of the main factors influencing the degradation rate of chemicals. A possible approach for relating half-life of a given substance and temperature is to introduce a coefficient, generally noted *Q10*, which

represents the ratio between the rates at 20° and 10°C. This approach is those generally used for plant protection products [32]. The effect of temperature on degradation can also be described by the Arrhenius equation which gives the degradation rate coefficient as a function of the temperature and the activation energy E_a. This approach requires however the determination of the activation energy E_a for each substance.

9.2 Global Degradation Half-Life in Soil at 25°C

Description of degradation half-lives is provided in chapter "Modelling the Fate of Chemicals in Surface Waters".

9.3 Degradation Increase Factor

As indicated above, it was proposed in the literature to introduce a coefficient, called degradation increase factor, and noted *Q10* to relate the half-life of a given substance and temperature. The theory behind the determination of *Q10* values is based on the Arrhenius relationship, which relates a chemical reaction rate constant with temperature and activation energy E_a. Activation energy theoretically depends on the substance under investigation and on a diversity of biotic processes occurring in soils.

Q10 parameter values were estimated by EFSA [32] through an exercise dedicated to plant protection products (PPP). A review of literature was undertaken for collecting data on activation energies, considering some filtering criteria (e.g. poor storage conditions of soils, non-reliable testing designs, half-life shorter than 1 day as considered as less accurate, half-life greater than twice the study duration). The resulting dataset was then checked by experts to eliminate possible anomalies. Finally, the dataset contained 99 data representing 53 pesticide compounds. EFSA used the Arrhenius equation to analyse these data. E_a values were then converted into $Q10$ values. Data thus collected allowed to derive a geometric mean (GM = 0.95) and geometric standard deviation (GSD = 0.25) for the *Q10* parameter.

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Modelling the Fate and Transfer of Substances Discharged into Soil Unsaturated Zones and Water Tables

Mohamed Krimissa, Cécile Couégnas, Philippe Bataillard, and Valérie Guérin

Abstract This chapter highlights the complexity of water and chemical phenomena that control the behaviour of contaminants in the unsaturated zone (UZ). Numerous mechanisms are involved in fixing these elements in soils, and many are not fully understood. This area of study is characterised by their hierarchy, or the predominance of one mechanism over another, depending on the bio-physico-chemical conditions of the environment. Understanding this hierarchy requires site analysis and measurements which currently are not always carried out.

Nevertheless, estimating the potential risk of a moderately contaminated site in the medium and long term, determining its future use, predicting groundwater quality and optimally managing contaminated excavated material (waste and polluted soil) all require a good understanding of pollutant behaviour in time and space.

Keywords Reactivity of chemicals • Unsaturated zone • Water flow

Contents

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1 Introduction

The unsaturated zone (UZ) is a medium that is often neglected in risk assessment studies. Yet the role of this zone is of particular interest. Low pollutant mobility can cause accumulation in surface areas, increasing the risk of transfer to the biosphere. High migration can lead to pollutants down to the groundwater.

Two types of mechanisms have to be taken into account to explain the behaviour of chemical substances discharged into soil and water tables: hydrological and bio-physico-chemical processes. These mechanisms are largely the same in UZ and in water tables. UZs are not distinguished from water tables by particular mechanisms but only by the physico-chemical conditions found there. In this chapter we will focus on UZs.

UZs are areas in which the interstices in the soil and rock are not completely filled with water. UZs thus extend from the ground surface to the top of the water table. This zone can be subdivided into a sub-surface layer corresponding to the soil horizons (the "soil" zone) and geological strata corresponding to the series of rock formations between the soil zone and the water table. Due to its position between the ground surface and the water table, the UZ affects the behaviour of chemicals in the environment, particularly in terms of retention and mobility.

As the UZ may be submitted to several biological and chemical mechanisms, it can act both as a buffer zone in the transfer of elements from the surface to water tables and as a pollution release zone. The migration of a reactive solute through unsaturated ground results simultaneously from the flow and retention processes to which the solute is submitted. Percolation in the UZ is a complex process because of the succession of its layers, but also because of the structure of some of these layers (possibly with preferential flow paths). Comprehensive modelling of solute transport in the UZ thus requires coupling hydrodynamic models and physico-chemical interactions.

2 Water Flow in the UZ

2.1 Water Flow and Soil Porosity

A prerequisite for modelling chemical transport in the UZ is a good understanding of water movement in this system. The UZ is a porous media, containing both water and air in varying proportions depending on the surface input (precipitation-evaporation balance) and the materials that make up the UZ (the degree to which

water can pass through them). Water flow first depends on soil "effective" or "efficient" porosity, i.e. porosity that actually contributes to percolation. Efficient porosity may be associated to (1) micropores (or textural porosity) in which percolation is very slow due to the strong influence of capillary action and adsorption. This type can be described by laws such as the Richards' equation [1]. Here the flux is considered as primarily diffusive; (2) macropores (or structural porosity) in which percolation is rapid and little capillary action is involved. In this latter case, the flow does not follow the same laws as with micropores. Percolation is considered as primarily convective. Water remains longer in micropores, favouring slow chemical reactions. This can cause a delay in the transfer of chemicals or even long-term binding. In contrast, the rapid percolation in macropores reduces the possibility of chemical binding.

2.2 Water Balance and Flow

In groundwater risk analysis, one of the main variables to be determined is the water flow passing through the UZ. To do this, one must first determine the water inputs and outputs to/from the soil, i.e. the amount of precipitation straight onto the site, from which the amount of evapotranspiration and run-off must be subtracted. The capacity of the ground to let water pass through also depends on its initial moisture. The drier the soil, the lower the absorption rate. Vertical water circulation (and water table replenishment) can only take place if usable soil reserves (the quantity of water retained by capillary action or still water) are exceeded. Heavy rain after a period of drought thus does not penetrate the ground as easily as a heavy rain after a wet period and causes water puddles or run-off.

Part of the precipitated water returns to the atmosphere by evaporation either directly from the ground or by plant transpiration. This water uptake by direct evaporation and plant evaporation is known as evapotranspiration or ET. Different methods of varying complexity can be used to calculate ET (Table 1). Most of these equations require knowledge of a certain number of climatic variables. The choice of one equation over another depends on the availability of meteorological data and the geographic location of the study area. The available equations may be very general as is the case for Turc's [2] and Thornthwaite's [3] equations or, conversely, they may only be regionally applicable like those proposed by Primault [4], Penman [5] and Penman-Monteith [6]. To date, the most commonly used equations are certainly those of Thornthwaite [3] and Turc [2].

The infiltration capacity or infiltrability of soil is its water absorption capacity. It is defined as the maximum flow that the soil is able to absorb through its surface. Infiltration capacity partially limits percolation. When the degree of inflow exceeds this capacity, water stagnates on the surface if the field is flat and trickles down the surface of sloping ground. Run-off is typically a non-linear process characterised by threshold effects. The occurrence of run-off depends on the physical state of the surface (roughness, clay crust, compaction, vegetation) and the initial moisture of the ground surface. The run-off coefficient is the ratio between "net rainfall",

Table 1 Some evapotranspiration equations

Name	Thornthwaite	Turc	Penman
Characteristic	Potential evapotranspiration per month or decade	The formula depends on whether the average humidity (U_m) is $>$ or $<$50%	
Formula	$\mathrm{ET} = 16\left(\frac{10\theta}{I}\right)^a \cdot F(\lambda)$	If $U_m > 50\%$ $\mathrm{ET}_{\mathrm{mm/10\,days}} = 0.13\frac{\theta}{\theta+15}\left(R_g + 50\right)$ If $U_m < 50\%$ $\mathrm{ETP}_{\mathrm{mm/10\,days}} = 0.13\frac{\theta}{\theta+15}\left(R_g + 50\right)\left[1 + \frac{50-U_m}{70}\right]$	$E = \frac{1}{L}\frac{R_n\frac{F'\theta}{\gamma}}{1+\frac{F'\theta}{\gamma}} + E_a\frac{1}{1+\frac{F'\theta}{\gamma}}$ $R_n = I_{g_a}(1-a)\left(0.18 + 0.62\frac{h}{H}\right)$ $-\sigma\theta^4(0.56 - 0.08\sqrt{e})\left(0.1 + 0.9\frac{h}{H}\right)$
Variables to be taken into account	ET in mm/year θ: average temperature measured under shelter during the reporting period a: $6.75 \times 10^{-7}I^3 - 7.71 \times 10^{-5}I^2 + 1.79 \times 10^{-2}I + 0.49$ I: annual heat index, the sum of twelve monthly heat indices i $i = \left(\frac{\theta}{5}\right)^{1.514}$ $F(\lambda)$ = correction coefficient, dependent on the latitude and the month, provided by reference tables	U_m: average humidity θ: average temperature measured under shelter during the reporting period R_g: overall solar radiation $R_g = I_{g_a}\left(0.18 + 0.62\frac{h}{H}\right)$ (cal/cm^2/day) h: actual sunshine duration H: maximum possible duration of insolation (length of the astronomical day) I_{ga}: direct solar radiation in the absence of atmosphere, I_{ga} and H are tabulated according to latitude and date	L: latent heat of water evaporation (59 cal/cm^2 for 1 mm of water equivalent) R_n: Net radiation (cal/cm^2/day) E_a: potential evaporation of the air $E_a = 0.26(e_w - e)(1 + 0.4V)$ γ: Psychometric constant ($\gamma \cong 0.65$) θ: Air temperature under shelter (K) σ: 1.19×10^7 (cal/cm^2/day/K) I_{ga}: solar radiation in the absence of atmosphere (cal/cm^2/day) h: actual sunshine duration H: length of the astronomical day e: water vapour pressure measured in mbar under shelter e_w: maximum water vapour pressure for temperature θ in mbar V: mean wind speed measured at 10 m above the evaporating surface (m/s) $F'\theta$: gradient of the maximum water vapour pressure curve

i.e. the flow rate leaving the surface under consideration and the "gross rainfall". This coefficient depends on, e.g. the impermeability of the surface and the watershed slope. The more impermeable the ground, the greater the run-off. The run-off coefficient varies according to the surface. For flat surfaces, the value is around 2 for farmland, 10 for compacted sand and from 40 to 90 for bitumen.

2.3 Water Movement

Water percolation in a porous medium takes place in the network of empty interstitial pores of the solid phase. A detailed microscopic description of the porous medium is difficult due to the geometric complexity and spatial heterogeneity related to the structure. The texture of the medium is also important. The scale generally used to study water percolation and solute transport is the representative elementary volume (REV) scale. REV is defined as the smallest volume of a porous medium over which a measurement can be made that will yield a value representative of the whole. Once this change of scale is achieved, the porous medium can be considered as a continuous medium.

Everything related to fluid circulation refers to the concept of permeability. Porosity and permeability are two different yet related concepts: porosity is a necessary condition for the existence of permeability. Porosity is generally recorded ω in the REV as the ratio of the volume of voids to the total volume. The voids in the porous medium may contain varying amounts of water, introducing the concepts of water content θ and of saturation S_t, respectively, corresponding to the ratio of water volume to the total volume and the ratio of water volume to the volume of voids. A saturated medium is one in which the entire void volume is occupied by water. We then have $S_t = 1$ and $\theta = \omega$. The medium is unsaturated if $S_t < 1$. In reality, a porous medium contains both water and air (it never reaches $S_t = 0$ or $S_t = 1$). It is therefore customary to introduce residual water content θ_r as well as the saturated water content θ_s. We then have $\theta_s \geq \theta \geq \theta_r$. Effective saturation $\Theta = (\theta - \theta_r)/(\theta_s - \theta_r)$ is then introduced, giving a saturation value varying between 0 and 1.

Groundwater movement is driven by potential gradient: water flows from points of high potential towards those of lower potential. Darcy [7] introduced the concept of hydraulic head, expressing the total potential of water as energy per unit of weight. The hydraulic head of an incompressible fluid subjected only to the action of gravity is defined by:

$$H = \frac{u^2}{2g} + \frac{p}{\rho g} + z \tag{1}$$

where u (m/s) is the fluid velocity at the point considered, p (Pa or N/m^2) is the fluid pressure, ρ (kg/m^3) is its density, and z (m) is the altitude of the point considered.

Flow velocities in porous media are low enough to ignore the first term. This only leaves a pressure term $h = P/\rho g$ and a gravitational term z. Subsequently, we denote that $H = h + \delta_g z$, where h represents pressure and δ_g is an integer equal to 1 if gravity is taken into account and 0 if it is not.

Darcy established empirically that there is proportionality between water velocity and hydraulic head gradient in a porous medium. Considering multidimensional flow and a non-isotropic medium, water velocity may then be calculated by the following tensor product:

$$\underline{\boldsymbol{v}} = -\underline{\underline{\boldsymbol{K}}}\,\underline{\nabla H} \tag{2}$$

where $\underline{\underline{\boldsymbol{K}}}$ (m/s) is the permeability tensor and $\underline{\nabla H}$ is the hydraulic gradient (m/m). The permeability tensor $\underline{\underline{\boldsymbol{K}}}$ is constant in a saturated medium but depends on the water content in a non-saturated medium. We then write:

$$\underline{\underline{K}} = k_r \underline{\underline{K_s}} \tag{3}$$

where $\underline{\underline{K_s}}$ (m/s) is the permeability tensor in a saturated medium (constant inside a given environment) and $k_r = k_r(h)$ is the relative permeability.

Noting source term S representing volume flow, we can write:

$$\frac{\partial(\rho\theta)}{\partial t} + \underline{\nabla}\left(\rho \underline{v}\right) = \rho S \tag{4}$$

As the water density is assumed to be constant, this equation can be simplified as (the conservation of mass equation):

$$\frac{\partial\theta}{\partial t} + \underline{\nabla} \cdot \underline{v} = S \tag{5}$$

By coupling Eq. 5 (i.e. the equation describing mass conservation) with Darcy's law (Eq. 2), the Richards' equation is obtained:

$$\frac{\partial\theta}{\partial t} = \underline{\nabla}\left(\underline{\underline{K}} \cdot \underline{\nabla}\left(h + \delta_g z\right)\right) + S \tag{6}$$

Assuming the existence of a local differential relationship between θ and h, capillary capacity $C = \frac{d\theta}{dh}$ can be introduced and two other formulations of the equation can be obtained: the h formulation and the θ formulation:

$$C\frac{\partial h}{\partial t} = \underline{\nabla} \cdot \left(\underline{\underline{\boldsymbol{K}}} \cdot \underline{\nabla}\left(h + \delta_g z\right)\right) + S \tag{7}$$

$$\frac{\partial \theta}{\partial t} = \underline{\nabla} \cdot \left(\underline{\underline{\boldsymbol{K}}} \cdot \left(\frac{1}{c} \cdot \underline{\nabla \boldsymbol{\theta}} + \delta_g \underline{\nabla \boldsymbol{z}} \right) \right) + S \tag{8}$$

The θ formulation cannot be used in a saturated medium because then $C = 0$. In a saturated medium, water content θ and permeability are constant, so the Richards' equation is linear and elliptical. On the other hand, in an unsaturated medium, $\underline{\underline{K}}$ and C both depend on h. The equation is then non-linear and parabolic.

To obtain these equations, we had to introduce the permeability tensor $\underline{\underline{K}}$ and the capillarity capacity C, which are not constant in an unsaturated medium. Thus, two other equations are needed to solve the problem. These two relationships are known as (1) the retention law, linking effective saturation Θ and suction ψ ($\Theta(\psi)$), and (2) the permeability law, linking hydraulic conductivity K to water content θ or to suction ψ, ($K(\psi)$). These laws are based on semi-empirical or statistical relationships. In practice, in order to describe soil's hydrodynamic characteristics, we generally try only to apply parameterized mathematical functions that reduce the description of the ground to a few variables rather than go through a large number of measuring points. Some of these functions are based on the soil's physical characteristics; others are purely empirical. The most frequent functions found in the literature are shown in Table 2 for the retention curve and in Table 3 for hydraulic conductivity.

Flow laws are only valid for media presenting a homogeneous porous texture; it then excludes preferential flow. Full description of the UZ therefore requires implementation of dual porosity models. Such models, based on water balances, are used by agronomists (the MACRO model, [15]). However, they are never used in site risk assessments or for testing contaminated soils. Preferential flows may be indirectly taken into account by choosing a higher permeability value than those

Table 2 Retention curves (according to [8], where ψ: suction, Θ: effective saturation)

Authors	Equations	Definitions of the variables
Gardner [9, 10]	$\Theta = \frac{1}{1+q\psi^n}$ $\psi = a\theta^{-b}$	q: adjustment parameter related to air inlet pressure n: adjustment parameter relating to the gradient at the inflection point of the retention curve a and b empirical constants
Brooks and Corey [11]	$\Theta = (\psi_a/\psi)^{\lambda}$ $\Theta = \frac{\theta-\theta_r}{\theta_s-\theta}$	θ_r: residual (or irreducible) water content θ_s: water content at saturation (effective porosity) ψ_a: air inlet pressure λ: pore size distribution index
Visser [12]	$\psi = \frac{a(n-\theta)^b}{\theta^c}$	n: porosity of the material b, c: adjustment variable
Van Genuchten [13]	$\theta = \theta_r + \frac{\theta_s-\theta_r}{(1+(\alpha\psi)^n)^m}$	Θ: effective saturation, as in the Brooks and Corey equation α, n, m: soil parameters, related to capillary fringe height for α (cm^{-1}) and to particle size distribution for n and m^2, with $m = 1 - 1/n$

Table 3 Hydraulic conductivity (according to [8])

Authors	Equations	Definitions of the variables
Gardner [9, 10]	$k(\psi) = k_s \cdot \exp(\alpha \cdot \psi)$ $k(\psi) = \frac{a}{(b + \psi^m)}$ $k(\psi) = \frac{k_s}{(1 + \psi/\psi_m)}$	α: constant depending on the nature of the soil a, b and m: empirical constants ψ_m: matric suction in which $k = 0.5k_s$ (k_s: saturation permeability m/s)
Brooks and Corey [11]	$k(\psi) = k_s \left(\frac{\psi_a}{\psi}\right)^m$ for $\psi \leq \psi_a$ $k(\psi) = k_s$ for $\psi \leq \psi_a$	m: constant characteristic of the soil ψ_a: air inlet pressure
Van Genuchten [13] derived from Mualem	$k(\theta) = k_s \sqrt{\Theta} \left[1 - \left(1 - \Theta^{1/m}\right)^m\right]^2$	Θ and m have the same meaning as they do in van Genuchten's equation $\Theta(\psi)$ k_s: saturation permeability (m/s)
Campbell [14] and Brooks and Corey [11]	$k(\theta) = k_s \left(\frac{\theta}{\theta_s}\right)^\beta$	β: adjustment variable, assumed to be $\beta = (1 - m)/m + 3$ when used with the van Genuchten retention curve

measured in laboratory and by making some assumptions about the proportion of fast percolation.

One of the current challenges is to express transfers in the root zone as simple equations. Evaporation and uptake by vegetation (combined under the term evapotranspiration) actually complicates the flow. According to Alaoui and Eugster [16], water escapes evapotranspiration below the root zone (that is to say below a depth of 70 cm) in grassland.

From a hydrological point of view, it is conceivable to use tools developed by agronomists for the surface part of the soil structure, where conventional models have their limits, and to use their results as input data for modelling "deeper" UZs that more closely resemble the conditions of isotropic porous mediums.

3 Reactivity of Chemicals in the UZ

Speciation of chemicals, i.e. their distribution and exchange dynamics between soil phases, govern their transport in the UZ. To describe the behaviour of chemicals in soil and subsoil, driving processes must be observed at three different spatial scales: the molecule scale, the soil aggregate scale and finally the UZ scale. It is precised that this paragraph is specifically dedicated to trace metals.

3.1 Chemical Mechanisms at the Molecular Level

With EXAFS (extended X-ray absorption fluorescence spectrometry), element and molecule fixation mechanisms in the soil and the subsoil are becoming better

understood. As this technique is non-destructive, relationships that vary over time can be monitored. In particular, the potential path of a metallic ion from solution to the core of a mineral consists of several steps:

(1) Outer sphere complex formation. In this complex, there are no chemical bonds with functional surface groups because the ions in solution maintain their hydration sphere. Interaction is mainly driven by electrostatic forces, which keep chemicals on the surface of the particle. Such adsorption is not very specific and ions involved in this process are easily interchangeable and therefore relatively mobile.
(2) Inner sphere complex formation. The interacting ion loses a part of its hydration sphere and forms a chemical bond with sites on the mineral surface. The strength of the bond depends on the electronic structure of the adsorbed ion and the ligand to which it is attached. Inner sphere complexation is also called specific adsorption or chemisorption.
(3) Precipitation can occur directly in solution. Precipitation may occur when the solubility limit of the chemical species is exceeded. Precipitation can also be initiated on the surface of other minerals through the adsorption of a nucleus. Some phases can also incorporate trace elements into their matrix by co-precipitation.
(4) Diffusion in the crystal lattice. Once adsorbed on the surface, a cation may diffuse into the crystal lattice and fill gaps in it or replace the ions already present. This process will occur if the ionic radius of the particular cation is close to the size of the cavity or to the substituted cation.

Most of these processes (e.g. dissolution, precipitation, complexation, oxidation) are based on a set of elementary reactions, each of them representing a stage of the reactive process. This distinction is important because it helps to link the kinetics of the process: some elementary reactions are limiting in terms of velocity. Moreover, the formulation of these reactions can provide an input for mechanistic modelling.

Numerous terms are used in the literature for the chemical mechanisms involved in trace mineral element mobility, particularly with regard to surface interactions (although the problem also arises for "co-precipitation"). For example, Blanc et al. [17] mention a "cation exchange" mechanism while other authors refer to "adsorption", "adsorption in the strict sense", "non-specific adsorption" or even "physisorption". For a second term "surface complexation" used by Blanc et al. [17], it is common to see the terms "specific adsorption" or "chemisorption" when the ion is retained to the surface by the formation of a chemical bond. Calvet [18] chooses to use the terms ions "adsorbed with or without complexation". Sposito [19] refers to "highly selective adsorption". This mass of terms does not help to clarify matters related to contaminant behaviour in soils and complicates the task of the teacher.

For soil scientists, the concept of soil "Cation Exchange Capacity" (CEC), or "cation exchange", originates from a set of mechanisms. CEC and exchangeable cations are primarily measurable variables. CEC is the maximum quantity of an element which can be exchanged with another under specified conditions. It will be

used as an input variable for the models. Given the protocol used (adding a highly-charged excess cation in a soil/water suspension), it is highly likely that some surface complexes and some precipitates will also be destabilised.

Ultimately, taking into account this complexity and the numerous elementary reactions, it appears more consistent to use the term "adsorption" to describe the fixation of an ion on a surface without chemical bonding and the term "surface complexation" when a chemical bond exists with solid surface groups. In terms of mobility, adsorbed ions are easily and thus potentially more mobile than ions in complexation for which the strength of the bond depends on the electronic structure of the ion and the ligand to which it is fixed.

Finally, the term "sorption" is used in English-speaking environments. This term is highly generic, designating any process in a liquid/solid interface leading to a phase change of the solute ([20], cited by [21]).

3.2 Chemical Behaviour at the Aggregate Scale

Microporosity results from the organisation of minerals and soil organic matter in aggregates and the structure of porous rocks in the UZ. The heterogeneity of porous media combined with slow transport in a microporous system results in spatial variability in chemical conditions at the scale of the grain size. Consequently, what eventually happens to trace elements (like trace metals) may be influenced by the structure of the medium itself in the absence of flow. Adsorption moves the ionic species from the solution to the surface of the soil components (e.g. clays, iron oxides, organic matter), and subsequently "ageing" (maturing) processes move adsorbed elements from the surface to the depth of the solid phase. The mechanisms involved are diffusion in the surface micropores, diffusion in the solid lattice, ionic species trapping by pore closure following precipitation of a mineral phase and formation of stable organic complexes.

The dynamics of the soil components must also be taken into account in order to understand and predict the dynamics of trace elements. For example, an organic compartment with highly variable characteristics over time (seasonal addition of fresh organic matter, humification and gradual mineralisation) has a strong impact on chemical speciation. It acts directly on this speciation as a trap but also indirectly influences what happens to chemicals by modifying the chemistry of the soil solution, for example, changing pH, releasing mineral and organic solutes due to decay and rendering colloidal macromolecules soluble.

3.3 Behaviour of Chemicals at a UZ Scale

As described in the two last paragraphs, many chemical reactions, as well as soil structure, govern the behaviour of chemicals at a millimetre scale. In order to move

on to the UZ scale, we must also consider the physical and chemical conditions of the site along with the soil profile and underlying bedrock. These conditions depend on the mineralogy of the materials, the presence or absence of organic matter, the form of land use or even the site topography and the climate.

Chemical variables (e.g. Eh, pH, solute concentrations, osmotic force) will directly determine numerous reactions. But they themselves depend on the mineralogy of the solid, the microbial activity and the water content of the system. The climate and the structure of the material also influence the water status and bacterial activity.

Although knowledge of basic mechanisms is required for anticipating changes in transfer of chemicals in the UZ, their hierarchy, i.e. their expression in terms of physico-chemical conditions, must also be understood. This is why site data collection on a case-by-case basis is an essential step. Currently, it is too often inadequate in risk studies of contaminated sites as data collection is generally limited to the determination of total chemical levels. This characterisation phase should also provide the basic variables for understanding the physico-chemical conditions that trace elements will encounter, including pH, Eh, grain size, organic matter content, carbonate content and generally chemical analyses on solid and liquid samples collected on site or obtained after imposed leaching.

4 Modelling of Transfer in Unsaturated Zones

4.1 Typology of Models Combining Transport and Chemistry

Natural environments have a high degree of physical and chemical complexity which increases further in the presence of chemicals. Interactions between the different chemical and physical processes are often coupled and non-linear. A better understanding of the causal relationships between transport and reactive processes is therefore required in order to understand the transfer of chemicals to water tables.

Subsoil water percolation can be simulated by a number of hydrogeological simulation codes. In addition, field measurements are performed to estimate water table height variation and to measure certain key variables such as permeability or porosity. Numerous calculation codes can simulate transport in saturated zones. Fewer codes allow for integrating transport in the UZ. The implementation of such models requires acquiring additional characteristic variables of the environment (e.g. retention curve, permeability at saturation). Furthermore, models must take into account the reactivity of the permeated rocks and soil in order to describe the transfer of trace elements and not limit themselves to mere transport. Full understanding of the chemical behaviour of trace elements requires characterisations or even laboratory experiments providing data about chemical reactivity (e.g. distribution coefficients, characterisation of solid phases, microorganism action).

There are currently two types of model:

(1) General transport models, where the modelling of chemistry is simplified: dynamics of chemicals is modelled using simplified chemistry (taking into account a sorption coefficient and occasionally solubility limits), with possible bacterial decline. These are used to simulate percolation (diffusion, dispersion and convection) in saturated and unsaturated porous mediums in two and/or three dimensions and two axisymmetric dimensions. A common way to incorporate chemical reactivity in transport is to introduce a "delay coefficient" (or "retardation factor") R, defined as the amount by which a chemical is held back by the soil in comparison to the fluid velocity. Codes such as MARTHE [22], PORFLOW [23], HYDRUS1D-3D [24, 25] or FEFLOW [26] can take into account the sorption phenomena with a delay coefficient or with non-linear isotherms, with or without kinetics.
(2) Combined chemical transport model, where chemistry is mechanistically described. Combining geochemistry and transport takes into account chemical speciation over time in the investigated environment. The most elaborate of these models also take into account porosity changes due to precipitation/dissolution and their effects on percolation and the transport of chemical species. Among the geochemical codes coupled with transport codes are PHREEQC [27] and CHESS [28]. CHESS is coupled with a transport code in the HYTEC platform [28]. The PHREEQC code has been coupled with HYDRUS1D [24], MODFLOW [29], HST3D [30] and MARTHE [22].

However, there are only a very limited number of available codes able to combine both geochemical calculations and UZ transport simultaneously. Each code has its particularities: some work only in one dimension (1D), while others do not take all potential equilibrium reactions and/or gas phase transport into account. In all cases, their implementation is more complex and more expensive than the empirical "delay coefficient" approach. Moreover, this latter approach is common in risk assessments dedicated water resources.

4.2 The "Delay Coefficient" Approach

Beyond the use of literature values, several strategies may be considered to collect delay coefficients: (1) from field data, (2) from batch experiments in laboratory and (3) from column experiments in laboratory.

First delay coefficients may be derived from the extent of the chemical plume with respect to the source, characterised in the course of field investigations (iterative blocking). Specifically, drilling is carried out downstream from the source to collect and analyse water from the water table. In doing so, the extent of the plume is determined. The delay coefficient of the chemical under investigation is calculated from the age of the source and the flow velocity of the water table. The results thus obtained are then compared to those found in the literature in order to

avoid potential errors. Once determined, the delay coefficient R is taken into account by the flow model in order to predict the future extent of the plume in the absence of any interventions.

The delay coefficient can also be calculated from batch sorption isotherms performed in laboratory ("static conditions") or by means of percolation columns ("dynamic conditions"). Batch studies are frequently used as they are relatively easy to implement. They involve putting a known quantity of soil in contact with a well-controlled chemical solution for a specified period of time. A batch series is performed with increasing concentrations of chemicals in order to plot curves as follows:

$$C_{\text{solid}} = f\left(C_{\text{liquid}}\right) \tag{9}$$

where C_{solid} (mg/kg) is the concentration of chemical in the solid and C_{liquid} (mg/l) is the concentration in the solution after equilibrium.

Sorption is temperature dependent. As experiments are carried out at constant temperature, the curves are referred to as "isotherms". Soil reactivity is expressed by a sorption constant derived from experimental curves. Depending on the model used, other variables will also be derived, such as the maximum adsorption concentration (Langmuir model) or adsorption intensity (Freundlich model).

The column method takes longer and is more expensive, more complex to implement and gives results that are more difficult to interpret [31]. However, it is recommended for determining distribution and delay coefficients as it allows the transfer of chemicals in the presence of hydrodynamic effects (e.g. dispersion, colloidal transport) and chemical processes (e.g. presence of multiple species, reversibility) to be characterised, unlike the batch method. The principle involves collecting and analysing a solution with an initially known composition after percolation through a soil column.

In the case of modelling results using the Freundlich formalism, the delay coefficient R is expressed by the following equation [32]:

$$R = 1 + K_F \frac{d}{\omega} n C_{\text{solid}}^{n-1} \tag{10}$$

where d is the bulk density of the soil (kg/m^3) and ω is its kinematic porosity (dimensionless). These variables should be determined from site data or from the literature. K_F is a coefficient related to adsorption capacity (m^3/kg), and n is an empirical factor calculated by the model, with a value below 1.

The Freundlich model assumes that the solid is a heterogeneous surface having a "multi-site" surface defined by an adsorption energy continuum and described by an exponential distribution. This hypothesis results in the equation by adding the empirical factor n. On a phenomenological level, this means that at high concentrations, the same cation has more difficulty being adsorbed since high-affinity sites are already occupied by one of its congeners. Note that R is dependent on the concentration in solution. The lower the solute concentration in the solution, the

higher the R value. This reflects the idea that adsorption is dependent on surface site energy: adsorption is more effective when a large number of sites with high energy are available.

In most studies, n is taken to be 1; the dependence of the concentration on the delay factor no longer appears. The isotherm is linear and the formalism of distribution coefficient K_d is found.

$$C_{\text{solid}} = K_d \cdot \left(C_{\text{liquid}}\right) \quad \text{and} \quad R = 1 + K_d \frac{d}{\omega} \tag{11}$$

This direct proportionality between adsorbed concentrations and concentrations in solution is generally verified in the presence of low concentrations (around a few mg/l).

These models are based on adsorption theory and must be handled with care. Empirical isotherms are determined according to a specific protocol and on a specific soil media. The data cannot be isolated from this context and are therefore not readily usable for another site. In addition, data are determined under simple conditions in which some effects, like competition or kinetics, are not systematically taken into account. Data depend on pH, ionic strength and temperature. In principle, these formalisms do not allow the simulation of scenarios in which environmental conditions vary over time. This approach is therefore not sufficient for describing contaminant behaviour in the UZ.

4.3 The Mechanistic Approach

The mechanistic approach is based on the description of the main reactions that occur between the solid and the liquid phases and which are specifically combined into computer code with fluid transport [33]. Whichever model is chosen, variables describing the initial chemical composition in water and solids, as well as the physico-chemical conditions of the medium, are required. The models are based on thermodynamics, which by nature allow describing reactions at equilibrium through coefficients that do not depend on experimental conditions. In some cases, kinetics of elementary reactions may be incorporated.

The most sophisticated tools take into account acid-base reactions, redox reactions, surface complexation, ion exchange and precipitation/dissolution of chemical species present in soils and aquifers. From the initial description of the environment, the model is used to calculate chemical speciation, i.e. the distribution of elements in the liquid and solid phases. Ultimately, calculation results provide access to a distribution of elements in the complex system.

The possibility of breaking mechanisms down into multiple elementary reactions has been discussed above. At present, many reaction sequences are unknown

and geochemical modelling is based on "overall" chemical reactions that are actually a series of elementary reactions [19]. These are studied on a macroscopic scale (beaker scale), while the basic mechanisms can only be studied on a molecular scale. Macroscopic mechanisms are more or less fully outlined in many publications [17, 21, 34–36]. For example, Blanc et al. [17] distinguish the following mechanisms likely to control the concentration of dissolved contaminants: precipitation/dissolution, surface complexation, cation exchange, surface precipitation and co-precipitation.

Surface precipitation and co-precipitation are distinguished from simple precipitation as they are considered to play an important role in soil contaminant fixation. From a kinetic point of view, the presence of a surface promotes precipitate formation. However, unless empirical correction is applied to the equilibrium constant value of the precipitate, the models do not yet allow these distinctions. Most of them therefore consider the three following mechanisms: precipitation/dissolution, surface complexation and cation exchange.

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Modelling the Fate of Chemicals in Plants

Philippe Ciffroy and Taku Tanaka

Abstract Consumption of contaminated fruits, vegetables and/or cereals may be a significant exposure route for human exposure to chemicals. This chapter describes the processes that should be considered in models simulating the fate of chemicals in plants. The first section describes modelling approaches able to simulate the uptake of chemicals from soil to root and their subsequent transport through the xylem flow. This process is governed by the transpiration stream, driving the movement of dissolved chemicals in the continuum soil-root-stem-leaves/storage organs. Section 2 describes the transport of chemicals in the phloem system, which is responsible for distributing the products of photosynthesis from the leaves to the rest of the plant. Section 3 describes diffusion of chemicals from soil to tubers, which are botanically seen as a part of the stem. The transport of chemicals inside the tuber is driven by partition coefficients, water and gas contents, and diffusion coefficients in water/gas pores. Section 4 describes diffusive exchanges between leaves and air through both the stomata and cuticle pathways. Diffusion is driven by several permeabilities in series and/or in parallel within the leaf structure. Section 5 describes processes responsible for deposition and interception of chemicals on above-ground plant. Wet particle deposition is driven by rain events while dry deposition is driven by gravitational deposition of aerosols. Both the fractions of dry and wet deposits intercepted by leaf can be related to the interception fraction and the above-ground biomass (or leaf area index). Section 6 describes partition of chemicals between plant and plant water. Section 7 describes specific electrodiffusive processes for electrolytes. Such processes have to account for the distribution of the chemical among neutral and dissociated species and for electrical potential across the membrane. Section 8 describes data available for bioaccumulation of metals in plants.

Keywords Bioaccumulation modelling • Cuticle pathway • Diffusion between leaves and air • Diffusion from soil • Electrolytes uptake and transport •

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Interception • Partition • Phloem flow • Plants • Stomata pathway • Transpiration stream • Xylem flow

Contents

1 Introduction

Exposure to chemicals via ingestion of food products can be a predominant pathway which must be taken into account for assessing health risk to environmental pollution. For example, pesticides are widely used to ensure high crop yields. In 2003, the use of plant protection products (PPPs, i.e. herbicides, insecticides, fungicides and other pesticides) in agriculture amounted to about 220,000 tons in the EU15 [1]. A large proportion of PPP is applied on crops like fruit and vegetables; for example, fungicides are widely used in vineyards. By nature, pesticides are deliberately released into the environment for controlling undesired organisms such as weeds, fungi and insects. Pesticides are biologically active compounds, and they are a significant source of diffuse pollution for nontargeted organisms. They might cause long-term health implications in humans. In general, consumption of food products and especially of fruits and vegetables is then the main exposure route for human exposure to pesticides. Food is also considered to be the major source of human exposure for other types of chemicals, e.g. PAHs, since grains, fruits and vegetables may be contaminated from atmospheric deposition and interception, as well as from root uptake. About 90% of the human dioxin and PCB exposure is also estimated to occur through food. In this latter case, contamination of food is primarily caused by air emissions from industry and incinerators. Contamination of fruit, vegetables and cereals (including beverages containing fruits) is thus of concern for human exposure because they are one of the most

frequently consumed food groups. Besides, because they are mainly consumed raw or semi-processed, they are expected to contain high levels of chemicals compared to other food groups.

Fruit and vegetables are submitted to various routes of contamination for chemicals, e.g. intentional spray application on leaves, intentional direct application to soil (e.g. soil fumigants, herbicides, sewage sludge and other wastes recycled in agriculture as fertilisers and soil amendments) followed by root uptake, atmospheric deposition and interception by leaves and irrigation of crops, especially with waste waters. Once in contact with contaminants, several physiological processes occur in plants, leading to chemical bioaccumulation and distribution among several organs (roots, stem, leaves and storage organs like fruits). Dynamics of chemicals in plants is thus governed by transpiration stream and water transport in xylem; phloem flux from leaves to storage organs; gas exchange through leaves' cuticle and stomata; partition of chemicals between organ components like water, lipids, gas or carbohydrates; diffusion between soil water and roots; and, finally, growth. As demonstrated by this broad list of processes, the interactions in the soil-air-vegetation system are quite complex. The purpose of this chapter is to review the main processes driving dynamics of contaminants in this system and to describe the main parameters to be taken into account in modelling soil-air-plant transfers.

2 Transpiration Stream and Xylem Flow

2.1 Process Description

Xylem flow, which is driven by plant transpiration, is a key process in the transfer of chemicals from soil to root. Indeed, thanks to their extremely high surface, roots take up water and minerals from soil porewater. Water and minerals move from soil to the root structure through capillary spaces between the cortex cells (outermost layer of root cells, bounded on the outside by the epidermis and on the inside by the endodermis) (Fig. 1). The endodermis is a semipermeable membrane (composed of a waxy barrier called Casparian strip) that discriminates some molecules and controls the composition of the transpiration stream. Contrary to nutrients that are taken up actively, there is no evidence of active uptake for most chemicals. Water (and potential associated toxins) can reach the xylem flow through several pathways: it can enter the apoplast, i.e. the free space outside the plasma membrane creating a continuum of adjacent cells, or it can follow the symplast and transmembrane pathways, i.e. the network of cell cytoplasms. The xylem sap is the conductive system for the transpiration stream, and it is located in the central cylinder of the roots and stem. Water and substances dissolved within the xylem sap rise upwards against gravity to the leaves. This upwards movement is governed by the gradient in water potential (high potential in the soil and no potential in leaves)

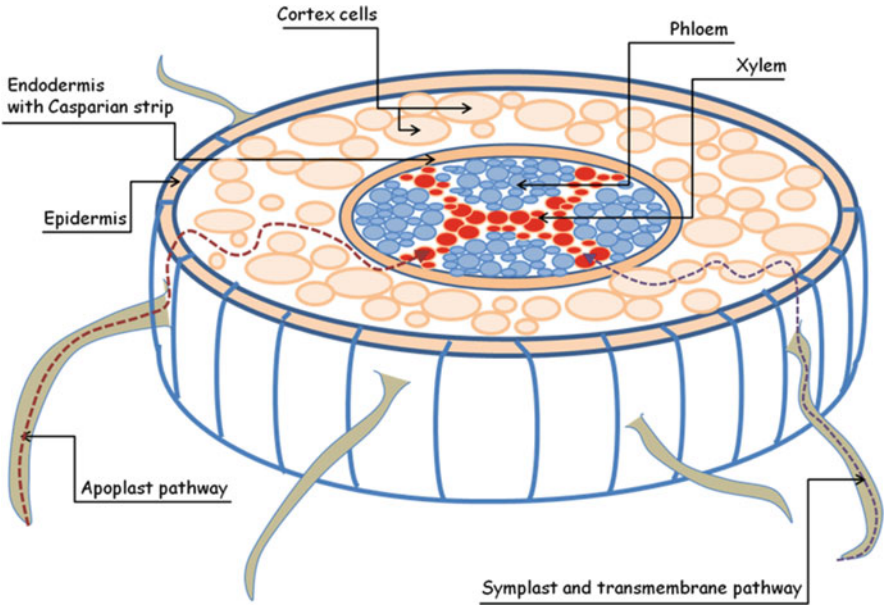

Fig. 1 Structure of the root system – interaction with soil, xylem and phloem

that is created by the controlled water loss through stomata. Water loss by the plant through stomata is known as transpiration.

According to the above description, the uptake of chemical from soil to root is governed by the transpiration stream that drives the movement of dissolved chemicals in the continuum soil-root-stem-leaves/storage organs. Transpiration alone is not commonly measured. Instead, it is common to measure or estimate evapotranspiration, i.e. the sum of soil evaporation and plant transpiration. It is then needed here to derive plant transpiration from evapotranspiration. The partition of actual evapotranspiration between soil evaporation and plant transpiration is governed by the solar radiation that can actually reach the soil and that can be spent as latent energy to evaporate water from soil surface. The fraction of solar radiation that can reach soil decreases with the increase of leaf area, generally represented by the leaf area index (LAI, i.e. the one-sided leaf area per unit ground surface area, in m^2 leaf m^{-2} soil). Thus, Sau et al. [2] and López-Cedrón et al. [3] proposed a model which partitions potential evapotranspiration (ET_p) to potential soil evaporation and potential plant transpiration, based on the Ritchie approach [4, 5]. This model estimates plant transpiration according to:

$$\text{Transpiration} = 0.001 \times ET_a \times [1 - \exp(-\alpha_{\text{extinction}} \times \text{LAI})] \quad (1)$$

where Transpiration (m d^{-1}) is the plant transpiration, ET_a (mm d^{-1}) is the actual evapotranspiration, LAI (m^2 leaf m^{-2} soil) is the leaf area index, $\alpha_{\text{extinction}}$ (dimensionless) is the extinction factor.

Kool et al. [6] describe some alternative models for estimating evaporation/transpiration partitioning. These are categorised into mechanistic (M) and empirical (P) approaches or analytical (A) and numerical (N) models. Kool et al. [6] categorise the following models using the symbols above: Shuttleworth-Wallace (MA), ENWATBAL (MN), Cupid-DPEVAP (MA), SWEAT (MN), TSEB (MA), FAO dual Kc model (PA) and HYDRUS-1D (MN). Among these models, FAO dual Kc model [7] is the most common model used to partition evaporation and transpiration, as it requires relatively few parameters (e.g. wind speed at 2 m height, relative humidity) compared to other models. It subdivides the total evapotranspiration into a plant component ET_{plant} and a soil component ET_{soil}; the plant component is expressed as:

$$ET_{plant} = ET_{tot}\left\{K_{plant,table} + \left[0.04(u_2 - 2) - 0.004(RH_{min} - 45)\left(\frac{h_p}{3}\right)^{0.3}\right]\right\} \quad (2)$$

where ET_{plant} (mm d^{-1}) is the plant component of evapotranspiration, ET_{tot} (mm d^{-1}) is total evapotranspiration, $K_{plant,table}$ (dimensionless) is a value found in the literature that has been measured experimentally, u_2 (m s^{-1}) is mean daily wind speed at 2 m height over grass, RH_{min} (%) is the mean daily minimum relative humidity and h_p (m) is the mean plant height.

The FAO dual Kc model is however empirical and pre-defined crop factors (i.e. $K_{plant,table}$) are not always applicable to sites in different contexts.

The approach presented in Eq. (1) is also empirical but requires less parameters than the FAO dual Kc model. Therefore, this approach can be useful when weather data such as wind speed and humidity are not available, or when crop-specific data are not tabulated. A difficulty in the approach may be to give a right value of the extinction factor.

Once the transpiration stream is evaluated, the xylem influx of chemicals from soil to root and the outflux of chemicals from root to stem can be estimated. It is assumed that only chemicals that are dissolved in soil porewater can contribute to xylem influx, while only chemicals that are present in the root water phase can reach the stem system, i.e.:

$$\text{Xylem\_influx} = \text{Transpiration} \times \frac{1}{Kd_{soil}} \times C_{soil} \quad (3)$$

where Xylem_influx (mg m^{-2} d^{-1}) is the transfer of the chemical of concern from soil to root, Transpiration (m d^{-1}) is the plant transpiration, Kd_{soil} (m^3 kg^{-1}) is the distribution coefficient of the chemical between soil particles and soil porewater (see the chapter 'Modelling the Fate of Chemicals in Soils') and C_{soil} (mg kg_{dw}^{-1}) is the concentration of the chemical in the soil root zone (on dry mass basis).

$$\text{Xylem\_outflux} = \frac{\text{Transpiration}}{K_{\text{root\_water}} \times m_{\text{root}}} \quad (4)$$

where Xylem_outflux (d^{-1}) is the loss rate from root to above-ground plant system through xylem, $K_{\text{root\_water}}$ ($m^3\ kg_{fw}^{-1}$) is the partition coefficient between root and water (see Sect. 7) and m_{root} ($kg_{fw}\ m^{-2}$) is the mass of root per unit area of soil.

It has to be highlighted that, although transpiration stream is generally the main driving process that governs the transport of chemicals from soil to roots, some models do not consider xylem flow dynamics and apply the equilibrium partitioning approach for calculating the distribution of chemicals between soil and root (i.e. the ratio between concentration in root and in soil respectively is assumed to be constant). Such approach has been questioned for lipophilic chemicals in some studies [8–11]. Comparing results from the equilibrium approach and the dynamic root model [11] to measured concentrations of benzo(a)pyrene in root crops shows that the equilibrium approach gives a concentration in roots that is three orders of magnitude higher than the measured value. Instead, the estimate from the dynamic model based on transpiration stream lies in the same order of magnitude as the measured value [8]. Consequently, the approach in which the uptake of chemical from soil to root is based on the transpiration flow rate and the chemical distribution between root and soil appears to be more robust.

However, it must be highlighted that the current root uptake mechanism by xylem flux is consistent for lipophilic neutral chemicals but not necessarily for ionisable and dissociating chemicals. For these latter substances, the uptake of chemicals into roots is usually slower than that of water. The application of the current model for ionisable and dissociating compounds would then be conservative. To be more realistic, it is necessary to introduce correction factors that represent the reduced uptake for such substances (see Sect. 9).

2.2 The Extinction Factor

In Eq. (1), $\alpha_{\text{extinction}}$ represents the extinction factor for total solar irradiance which functions as partitioning radiant energy between canopy and soil surface, that is, as partitioning evapotranspiration between soil evaporation and plant transpiration. $[1 - \exp(-\alpha_{\text{extinction}} \times \text{LAI})]$ is a shielding factor representing the ratio of radiation intercepted by the vegetation. The extinction factor can be simulated by taking into account several factors like the incident radiation direction (given, e.g. by the zenithal angle) and the effective LAI (depending on green and senescent leaves) [12]. However empirical values can also be found in the literature. Thus, Tahiri et al. [13] indicate that measured values of the extinction coefficient vary from about 0.3 to 1.5 depending on crop species and stand types (external structure of the plants). Values less than 1.0 are often found for non-horizontal leaves or clumped leaf distributions, while values greater than 1.0 are common for horizontal leaves or more regular arrangements in space. A literature review reported in Sau et al. [2]

indicated values ranging from 0.44 for corn to 0.79 for cowpea. Sau et al. [2] recommend testing lower values (about 0.5) in a wide range of crops and environments. In summary, a mid value of 0.7 can be selected as a best estimate, with a variability range between 0.3 and 1.5.

2.3 Leaf Area Index at Harvest

Leaf area index (LAI) represents the one-sided leaf area (m^2) per unit ground surface area (m^2) and is an important parameter in plant models, as it influences transpiration rates. LAI at harvest has been estimated for a variety of plants and trees and can be found in various databases. For example, Asner et al. [14] built a database of LAI, categorising the data into different plant types (e.g. crops, deserts, grasslands, plantations, wetlands), and then made statistical analyses for each category. For example, they calculated normal distributions representing LAI in crops and grasslands that can be used as generic values for exposure models. Breuer et al. [15] collected also many LAI values over different plant crops. However neither of the two studies records or specifies LAI values of fruit trees. LAI values relevant for fruit trees can be found in Stephan et al. [16] who estimated LAI values for different types of apple cultivars.

2.4 Mass of Root Per Unit Area of Soil

The calculation of xylem flux from root to fruit trees requires the estimation of the mass of root per unit area of soil (Eq. 4). This parameter is not easily measurable (at least during the tree life) and is generally not measured because of its poor economic interest. The estimation of this parameter can then be based on some assumptions.

It may be first estimated that the below-ground biomass of mature fruit trees (and more generally of trees) represents about 20% of the total tree biomass. According to data presented in Drénou [17], this percentage ranges from 14 to 27%. Allometric relationships were also proposed to estimate the above-ground tree biomass (AGB) (that represents about 80% of the total biomass according to the assumption above) from more easily parameters like the trunk diameter at breast height (DBH) and/or the tree height. A lot of allometric relationships have been proposed for a wide variety of trees (i.e. [12, 18, 19]). The use of such allometric relationships allows to estimate the above-ground tree biomass. Finally, the surface occupied by roots (used to convert total root mass into mass of root per unit area of soil) can be estimated by the 'critical root radius' (CRR) that is an estimation of the lateral root extension below ground. The classical method to evaluate the CRR (in cm) is to multiply the DBH (in cm) by a factor 20 (relationships are generally given in feet and inches and were converted in cm here).

3 Phloem Flow

3.1 Process Description

A fraction of chemicals accumulated in storage organs (like fruits) is originated from the xylem transport from roots to storage organs (see Sect. 2) but also from the phloem flow originating from leaves. According to Bromilow and Chamberlain [20], the total volume of xylem flow in plants is 50–100 times greater than phloem flow. It indicates that the importance of phloem flow is minor. However, for storage organs like fruits, the phloem flow dominates; hence this process has to be included in fate models. Unlike xylem, the cells that make up phloem are living at maturity and can carry materials both up and down the plant body. Phloem is comprised of sieve elements, which are arranged end to end to form passageways to organic compounds. The movement in phloem is then multidirectional, whereas, in xylem cells, it is unidirectional (upwards). Phloem is responsible for distributing the products of photosynthesis, such as amino acids and carbohydrates, from the leaves to the rest of the plant. Despite their different functions, xylem and phloem streams are however neighboured and then a diffusive exchange may occur between these transport systems (Fig. 1). For this reason, Trapp [21] assumed no difference between chemical concentration in phloem and in xylem flows, respectively. As discussed in Sect. 2, the xylem flow is driven by the transpiration stream (transpiration); instead, the phloem flow is driven by fruit growth. The xylem flow goes into both leaves and fruits. The fraction of the xylem flow directed to the fruits to that directed to leaves is assumed to be proportional to the respective surface areas. The xylem flow into the fruits can thus be calculated from the transpiration stream multiplied by the fraction directed to fruits. The phloem flow into the fruits can be calculated according to Trapp [21]. Phloem sap has high dry matter content, about 10%, that remains in the fruit. Therefore, it may be assumed that the total phloem flow into the fruits over the growth period is about 10 times the dry mass of the fruits. The daily phloem flow into the fruits can be obtained by dividing the total phloem flow with the growth period.

4 Diffusion from Soil to Tubers

4.1 Process Description

The term ‘tuber’ is used here to describe structures derived from stems only (‘tuber’ can also describe structures derived from stems and roots). According to this definition, a tuber like potato is botanically seen as a part of stem. At the top sides, a stem tuber forms shoots that grow into typical stems and leaves, and at the under sides, it produces roots. The below-ground stem tuber is a short-lived storage and regenerative organ, and offspring or new tubers are attached to a parent tuber.

In particular, potato has all the parts of a normal stem, including nodes and internodes. The inside of a tuber has the typical cell structures of any stem, including a pith, vascular zones, and a cortex. It can then be assumed that a tuber has no connection with the root system and the transpiration stream, and diffusive mass transfer from soil can be considered as a main process contributing to the accumulation of hydrophobic compounds in tubers like potato. The accumulation of chemicals in potato may also occur via translocation downwards via phloem. However, for hydrophobic organic compounds, the translocation via phloem can be assumed to be negligible [22]. The uptake of hydrophobic organic pollutants into potato is, therefore, most likely to take place from soil by diffusion through the peel of potato. According to Trapp et al. [23], the accumulation of chemicals in potatoes can then be estimated using the diffusion coefficients for water and gas.

The partition of chemicals inside the tuber between dry matter, water and gas is governed by partition coefficients and by water and gas contents:

$$f_{w\_\text{tuber}} = \frac{\theta_{\text{tuber}}}{K_{\text{tuber\_water}}} \tag{5}$$

$$f_{g\_\text{tuber}} = \frac{G_{\text{tuber}}}{K_{\text{tuber\_water}}} \times K_{\text{AW}} \tag{6}$$

where f_{w_tuber} (dimensionless) is the fraction of the chemical in tuber water, f_{g_tuber} (dimensionless) is the fraction of the chemical in tuber air, θ_{tuber} (L $\text{kg}_{\text{fw}}^{-1}$) is the water content of tuber, G_{tuber} (L $\text{kg}_{\text{fw}}^{-1}$) is the air content of tuber, $K_{\text{tuber\_water}}$ (L $\text{kg}_{\text{fw}}^{-1}$) is the partition coefficient between tuber and water and K_{AW} ($\text{m}^3\ \text{m}^{-3}$ or dimensionless) is the partition coefficient between air and water.

The diffusion coefficients in water/gas pores of the tuber (D_{w_tuber} and D_{g_tuber}, respectively) are derived from diffusion coefficients in water and air (D_{water} and D_{gas} respectively) together with tortuosity factors (T_{w_tuber} and T_{g_tuber}, respectively) that account for a slower diffusion in water and air pores of the potato than in pure water and air [23]. Tortuosity factors are calculated according to the Millington and Quirk's law (see the chapters 'Modelling the Fate of Chemicals in Surface Waters' and 'Modelling the Fate of Chemicals in Soils'). Diffusion coefficients of the chemical in water and gas are related to its molar mass. Diffusion coefficients in water/gas pores can then be expressed as:

$$\begin{aligned} D_{w\_\text{tuber}} &= T_{w\_\text{tuber}} \times f_{w\_\text{tuber}} \times D_{\text{water}} \\ &= \frac{\theta_{\text{tuber}}^{10/3}}{\left(\theta_{\text{tuber}} + G_{\text{tuber}}\right)^2} \times f_{w\_\text{tuber}} \times D_{\text{O}_2,\text{water}} \times \sqrt{\frac{M_{\text{O}_2}}{M_{\text{molar}}}} \end{aligned} \tag{7}$$

$$D_{\text{gas\_tuber}} = T_{g\_\text{tuber}} \times f_{g\_\text{tuber}} \times D_{\text{gas}}$$
$$= \frac{G_{\text{tuber}}^{10/3}}{(\theta_{\text{tuber}} + G_{\text{tuber}})^2} \times f_{g\_\text{tuber}} \times D_{\text{H}_2\text{O, gas}} \times \sqrt{\frac{M_{\text{H}_2\text{O}}}{M_{\text{molar}}}} \quad (8)$$

where D_{w_tuber} ($\text{m}^2\ \text{s}^{-1}$) is the diffusion coefficient of the chemical in tuber water; D_{g_tuber} ($\text{m}^2\ \text{s}^{-1}$) is the diffusion coefficient of the chemical in tuber gas; D_{water} ($\text{m}^2\ \text{s}^{-1}$) is the diffusion coefficient of the chemical in water; D_{gas} ($\text{m}^2\ \text{s}^{-1}$) is the diffusion coefficient of the chemical in gas; $D_{\text{O}_2\text{, water}}$ ($\text{m}^2\ \text{s}^{-1}$) is the diffusion coefficient of dioxygen in water; $D_{\text{H}_2\text{O, gas}}$ ($\text{m}^2\ \text{s}^{-1}$) is the diffusion coefficient of the water in gas; T_{w_tuber} and T_{g_tuber} (dimensionless) are the tortuosity factors in tuber water and gas, respectively; f_{w_tuber} (dimensionless) is the fraction of the chemical in tuber water; f_{g_tuber} (dimensionless) is the fraction of the chemical in tuber air; θ_{tuber} ($\text{L kg}_{\text{fw}}^{-1}$) is the water content of tuber; G_{tuber} ($\text{L kg}_{\text{fw}}^{-1}$) is the air content of tuber; M_{molar} (g mol^{-1}) is the molar mass of the chemical of concern; M_{O_2} (g mol^{-1}) is the molar mass of dioxygen; and $M_{\text{H}_2\text{O}}$ (g mol^{-1}) is the molar mass of water.

The total diffusion coefficient in tuber structure is then the sum of diffusion coefficients in water and gas pores. The depuration rate $k_{\text{depuration}}$ can then be deduced from a radial diffusion model, assuming that the tuber can be represented by a sphere [21], while the uptake rate k_{uptake} is calculated from phase equilibrium:

$$k_{\text{depuration}} = \frac{23 D_{\text{tuber}}}{(R_{\text{tuber}})^2} \quad (9)$$

where D_{tuber} ($\text{m}^2\ \text{d}^{-1}$) is the diffusion coefficient in tuber and R_{tuber} (m) is the tuber radius.

$$k_{\text{uptake}} = k_{\text{depuration}} \times K_{\text{tuber\_water}} \quad (10)$$

The estimation of the partition coefficient between tuber and water is given in Sect. 7.

5 Diffusive Exchange Between Plants and Air

5.1 Process Description

Some pollutants, especially those that are highly volatile (semi volatile organic compounds, SVOCs), can be exchanged between above-ground plant surfaces (in particular leaf surfaces) and the atmosphere. Water lost from the transpiration stream and CO_2 required for photosynthesis are exchanged at the leaf-air interface through stomata (Fig. 2). Stomata are pores formed by a pair of cells which can open and close to control the exchange between a plant and the environment.

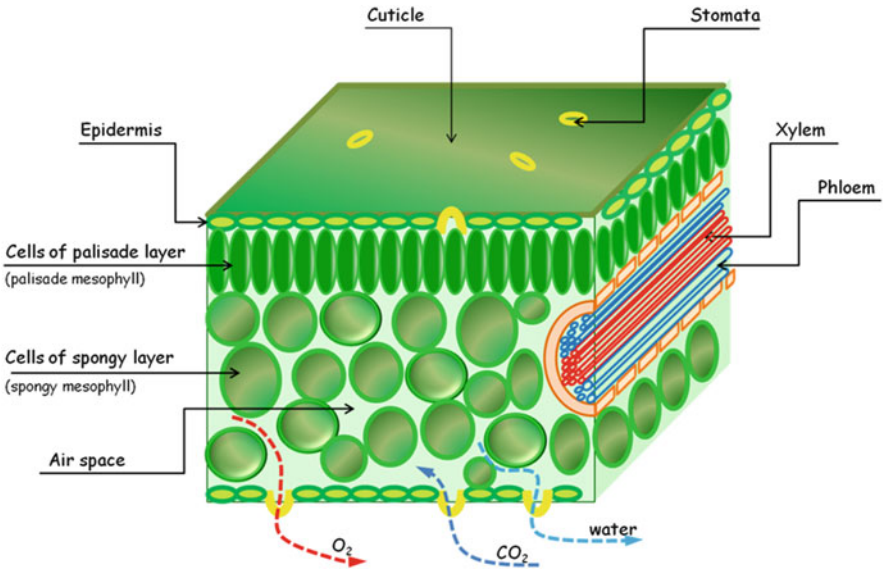

Fig. 2 Leaf structure and interaction with air

Although stomata occur on all aerial parts of the primary plant body, they are most abundant on leaves. Stomata are present on both sides of leaves but are more frequent on their underside surface. In grass, however, stomata are usually present in equal numbers on both sides due to the positioning of the leaf towards the sun. Stomata are surrounded by guard cells that open and close the stomata, depending on the plant's needs. Stomata generate thus a pathway, but also a resistance to the transfer of chemicals between leaves and surrounding air. Leaf surface is also covered by an effective waxy barrier to water movement called cuticle. The waxy cuticle restricts diffusion through the leaf so that water vapour and other gases must enter and exit via leaf stomata. The waxy cuticle in most plants thus prevents gases exchange although this depends on the thickness and composition of the cuticle. It is however estimated that a small fraction (about 5%) of water loss from leaves occurs via the cuticle.

Considering this background related to plant physiology, it can be assumed that diffusion of chemicals between air and leaf is controlled by the conductance of leaf. The diffusive uptake (or loss in case of negative variation) of chemicals by leaf from the air can be expressed as:

$$\frac{dm_{\text{leaf}}}{dt} = A_{\text{leaf}} \cdot g_{\text{leaf}} \left(C_{\text{air}} - \frac{C_{\text{leaf}}}{K_{\text{leaf\_air}}} \right) \tag{11}$$

where m_{leaf} (mg m^{-2} soil) is the mass of chemical per unit surface of soil, A_{leaf} (m^2 leaf m^{-2} soil) is the leaf surface area par unit surface of soil, g_{leaf} (m^3 air m^{-2} leaf d^{-1}) is the conductance of leaf, C_{air} (mg m^{-3}) is the concentration of the chemical in air, C_{leaf}

(mg kg_{fw}^{-1}) is the concentration of the chemical in leaf and K_{leaf_air} (m^3 kg_{fw}^{-1}) is the partition coefficient between leaf and air (that may be calculated from leaf-to-water and water-to-air partition coefficients). If the exchanges are reported per unit area of soil (i.e. $\frac{dm_{leaf}}{dt}$ in mg m^{-2} soil d^{-1}), the leaf surface area A_{leaf} is expressed in m^2 leaf m^{-2} soil and corresponds to 2×LAI (up and downside leaf surface area).

The leaf conductance g_{leaf} is related to the leaf permeability. The difference between conductance and permeability is that the former is related to concentrations in the gas phase (expressed in m^3 air m^{-2} leaf d^{-1}), while the latter is related to concentrations in water (expressed in m^3 water m^{-2} leaf d^{-1}). Reasoning in terms of conductance or permeability is then equivalent. The relationship relating conductance and permeability is then:

$$g_{leaf} = \frac{P_{leaf}}{K_{AW}} \tag{12}$$

where g_{leaf} (m^3 air m^{-2} leaf d^{-1}) is the conductance of leaf, P_{leaf} (m^3 water m^{-2} leaf d^{-1}) is the permeability of leaf and K_{AW} (m^3 m^{-3}) is the partition coefficient between air and water.

The leaf permeability P_{leaf} is estimated by considering that several resistances control the exchange between plant and air, i.e. cuticle resistance, air boundary layer resistance and stomata resistance [24]. Some models consider also inside-leaf resistances in water and cell wall.

The permeability of the cuticle ($P_{cuticle}$) and air boundary layer (P_{air}) (and eventually in the water layer (P_{water}) and the cell wall (P_{cell_wall})) can be aggregated as total permeability of cuticle pathway ($P_{cuticle\_tot}$), assuming that these resistances act in series [8], i.e.:

$$P_{cuticle\_tot} = \frac{1}{(1/P_{air} + 1/P_{cuticle})} \tag{13}$$

where $P_{cuticle\_tot}$ (m^3 water m^{-2} leaf d^{-1}) is the total permeability of cuticle, P_{air} (m^3 water m^{-2} leaf d^{-1}) is the permeability in the air boundary layer and $P_{cuticle}$ (m^3 water m^{-2} leaf d^{-1}) is the permeability of cuticle.

The transport of neutral organic compounds across the cuticle is a dissolution-diffusion process [25, 26]. Kerstiens [27, 28] reviewed several models able to predict cuticle permeability according to chemical properties like octanol/water partition coefficient and/or octanol/air partition coefficient and/or boiling point and/or molar volume. For example, Kerler and Schönherr [29] proposed the following empirical relationships (which are equivalent) for predicting cuticle permeability or conductance of *Citrus aurantium*:

$$\log P_{cuticle} = 0.704\ \log K_{ow} - 11.2, \tag{14}$$

or

$$\log g_{\text{cuticle}} = -0.296\ \log K_{\text{ow}} + \log K_{\text{oa}} - 11.2 \tag{15}$$

where P_{cuticle} (m^3 water m^{-2} leaf d^{-1}) is the permeability of cuticle, g_{cuticle} (m^3 air m^{-2} leaf d^{-1}) is the conductance of cuticle, K_{ow} (dimensionless) is the octanol-water partition coefficient and K_{oa} (dimensionless) is the octanol-air partition coefficient.

Kerstiens [28] tested another alternative model assuming that the cuticle permeability P_{cuticle} depends on the octanol/air partition coefficient K_{oa} and on the LeBas molar volume V_m, according to:

$$\log P_{\text{cuticle}} = [0.67 - 1]\ \log K_{oa} - 0.45\ [7 - 12]\quad V_m - 9.92 \tag{16}$$

where the numbers in square brackets represent the uncertainty range of the regression coefficients, K_{oa} (dimensionless) is the octanol-air partition coefficient and V_m (L mol^{-1}) is the LeBas molar volume.

After (or before) the chemical has crossed the cuticle, the next resistance is provided by the air boundary layer around the leaf. A resistance of 200 s m^{-1} can be estimated as typical for a chemical with a molecular mass of 300 g mol^{-1} for the air boundary layer [8, 30]. The ratio of square molar masses M_{molar} is used to derive the permeability in air for any chemicals:

$$P_{\text{air}} = 86400 \times K_{\text{AW}} \times \frac{\sqrt{300}}{200 \times \sqrt{M_{\text{molar}}}} \tag{17}$$

where P_{air} (m^3 water m^{-2} leaf d^{-1}) is the permeability of in the air boundary layer, K_{AW} (dimensionless) is the air-water partition coefficient and M_{molar} (g mol^{-1}) is the molar mass of the chemical of concern.

As indicated above, the other pathway allowing exchanges between plant and surrounding air is the stomata pathway. The permeability of the stomata pathway P_{stomata} (m^3 water m^{-2} leaf d^{-1}) for a given chemical is directly related to the permeability for water, the correction factor depending on the compound molar mass M_{molar}. Nearly all the water transpired by plants is lost through the stomata as water vapour diffusion via cuticle can be neglected. Then, the stomata conductance for water can be estimated from the transpiration stream and the leaf area index, LAI. If the leaf is assumed to be water saturated, the transpiration stream can be estimated by:

$$\begin{aligned}\text{Transpiration} &= 2 \times \text{LAI} \cdot g_{\text{H}_2\text{O}}(C_{\text{H}_2\text{O,leaf}} - C_{\text{H}_2\text{O,air}}) \\ &= 2 \times \text{LAI} \cdot g_{\text{H}_2\text{O}} \cdot C_{\text{H}_2\text{O,sat}}(1 - \text{rh})\end{aligned} \tag{18}$$

where *Transpiration* (m d^{-1}) is the plant transpiration, *LAI* (m^2 leaf m^{-2} soil) is the leaf area index, $g_{\text{H}_2\text{O}}$ (m^3 air m^{-2} leaf d^{-1}) is the conductance of leaf for water, $C_{\text{H}_2\text{O,leaf}}$ (m^3 water m^{-3} leaf) is the water content in leaf, $C_{\text{H}_2\text{O,air}}$ (m^3 water m^{-3}

leaf) is the water content in air, $C_{H_2O,sat}$ (m^3 water m^{-3}) is the water content at saturation and *rh* (dimensionless) is the relative humidity in air.

The permeability of stomata for the chemical can then be obtained as:

$$P_{Stomata} = g_{Stomata} \times K_{AW} = g_{H_2O} \times \sqrt{\frac{M_{H_2O}}{M_{molar}}} \times K_{AW} = \frac{\text{Transpiration}}{2 \times LAI \times (1 - rh) \times C_{H_2O\_sat}} \times \sqrt{\frac{M_{H_2O}}{M_{molar}}} \times K_{AW} \quad (19)$$

where $P_{Stomata}$ (m^3 water m^{-2} leaf d^{-1}) is the permeability of the stomatal pathway for the chemical, $g_{Stomata}$ (m^3 air m^{-2} leaf d^{-1}) is the conductance of the stomatal pathway, K_{AW} (m^3 m^{-3}) is the partition coefficient between air and water, M_{molar} (g mol^{-1}) is the molar mass of the chemical of concern and M_{H_2O} (g mol^{-1}) is the molar mass of water.

An additional resistance is also considered for fruits for representing the diffusive pathways in the inner structure of the fruit. Diffusion coefficients of the chemical in water and gas pores of fruit tissues are calculated exactly as for diffusion in tuber tissues (described in Sect. 4). The permeability P_{tissue} of fruit tissue is given by:

$$P_{tissue} = \frac{D_{fruit}}{\Delta_{fruit}} \quad (20)$$

where D_{fruit} (m^2 d^{-1}) is the diffusion coefficient in fruit and Δ_{fruit} (m) is the diffusion path length in fruit. The diffusion path length in fruit represents the thickness of the layer in fruit tissue relevant for diffusion, and the order of magnitude is 0.01 m according to Trapp [21].

The permeabilities in cuticle, stomata and eventually tissue can then be combined assuming that these two pathways act in parallel, i.e.:

$$P_{tot} = P_{cuticle\_tot} + P_{stomata} + P_{tissue} \quad (21)$$

where P_{tot} (m^3 water m^{-2} leaf d^{-1}) is the total permeability in plant organ (leaf or fruit), $P_{cuticle\_tot}$ (m^3 water m^{-2} leaf d^{-1}) is the total permeability of cuticle, $P_{Stomata}$ (m^3 water m^{-2} leaf d^{-1}) is the permeability of the stomatal pathway and P_{tissue} (m^3 water m^{-2} leaf d^{-1}) is the permeability of tissue.

It has to be highlighted that the model presented above estimates the gaseous diffusion by calculating time-dependent and chemical-specific permeability of plant tissue, whereas other models (e.g. TGD and CSOIL) apply a fixed gas deposition rate.

6 Deposition and Interception of Chemicals on Above-Ground Plant

6.1 Process Description

Some experimental observations showed that the fraction of atmospheric contaminants intercepted by plants (essentially leaves) is not negligible and should be taken into account in mass budget calculations. For example, several experiments were conducted with radionuclides as tracers of atmospheric aerosols (e.g. [31–36]) and showed that, under some conditions (e.g. high leaf area index), the main part of chemicals that are deposit from air to surfaces is intercepted by plants. For organic pollutants, the relative importance of intercepted particles versus gaseous diffusion depends on the partitioning in the atmosphere between aerosols and gas phase. The interception of particulate dry or wet deposits can play a predominant role for some organic chemicals mainly associated to atmospheric particles (e.g. PAHs) [37, 38]. It is then justified to include this process in the modelling of leaf contamination.

Wet particle deposition is driven by rain events, while dry deposition is driven by gravitational deposition of aerosols. Both the fractions of dry and wet deposits intercepted by leaf can be quantified by the Chamberlain's relationship [39]. This relationship relates the interception fraction (i.e. the ratio between the intercepted quantity and the total deposited quantity) and the above-ground biomass and involves a parameter called interception coefficient, i.e.

$$f_{\text{Interception}} = 1 - \exp\left[-\mu_{\text{Interception}} \times m_{\text{leaf}} \times (1 - \theta_{\text{leaf}})\right] \tag{22}$$

where $f_{\text{Interception}}$ (dimensionless) is the dry or wet interception fraction onto leaves, $\mu_{\text{Interception}}$ ($m^2\ kg_{dw}^{-1}$) is the interception coefficient for dry or wet deposits, m_{leaf} is the mass of leaf per unit area of soil ($kg_{fw}\ m^{-2}$ soil) and Θ_{leaf} is the water content of leaf ($L\ kg_{fw}^{-1}$).

This relationship reflects the fact that the interception fraction increases as the plant grows (and the surface of leaves increases). For example it was implemented in the urban multimedia model developed by Diamond et al. [40] (only for dry deposits). The Chamberlain's model was experimentally supported for pasture grass and other leafy crops. For cereals however, Pröhl and Hoffman [35] proposed a more appropriate normalisation by LAI, i.e.:

$$f_{\text{Interception}} = 1 - \exp\left[-\mu_{\text{Interception}} \times \text{LAI}\right] \tag{23}$$

where $f_{\text{Interception}}$ (dimensionless) is the dry or wet interception fraction onto leaves, $\mu_{\text{Interception}}$ ($m^2\ kg_{dw}^{-1}$) is the interception coefficient for dry or wet deposits and LAI (m^2 leaf m^{-2} soil) is the leaf area index.

Similarly, for wet deposits, Müller and Pröhl [41] proposed a relationship accounting for the LAI and the rainfall intensity (used in the urban multimedia model developed by Diamond et al. [40]):

$$f_{\text{Interception\_wet}} = \frac{\text{LAI} \cdot S}{R}\left[1 - \exp\left(-\frac{\ln 2}{3 \cdot S} \cdot R\right)\right] \tag{24}$$

where S (dimensionless) is a retention coefficient and R (mm) is the of rainfall amount. The term $\left[-\frac{\ln 2}{3 \cdot S}\right]$ is based on the assumption that 50% of the maximum storage capacity of the leaf is reached for a rainfall amounting to three times that of this storage capacity. However, when this equation is applied, $f_{\text{Interception\_wet}}$ can be greater than unity for low rainfall, which is unrealistic.

The models presented above propose a macroscopic description of the interception process. Some more complex models tried to subdivide the global interception process into different consecutive and/or competitive subprocesses governing the interactions of chemicals with plant leaves [42, 43] (see the chapter 'Modelling the Fate of Chemicals in the Atmosphere'), i.e. (1) Brownian diffusion, affecting very fine particles and representing the deposition through the boundary layer surrounding the leaves; (2) 'interception', for particles following the streamline of the flow field and interacting with the leaves according to their diameter; (3) impaction, representing the collision of a particle against an obstacle; (4) sedimentation, representing the gravity movement of particles; and (5) rebound. Petroff et al. [42, 43] propose an integrated model combining each of these processes. However, such a complex mechanistic model remains quite difficult to parameterise.

6.2 *Interception Coefficient for Dry/Wet Deposits*

The interception coefficient $\mu_{\text{interception}}$ represents the empirically derived interception (absorption) coefficient for dry/wet deposits. The interception coefficient for wet deposits can be used to calculate both the interception of wet deposits of aerosols and the interception of irrigated water.

Queguiner et al. [44] conducted a comprehensive literature review about foliar interception coefficients for particulate metals (dry deposits) and for dissolved metals (wet deposits). Since it was found that data obtained from the literature review were heterogeneous in terms of the data sources, plant species, aerosols granulometry and chemicals, each data point was assigned a score according to its quality. The generation of probability density functions was then made through a direct weighted bootstrap procedure. Queguiner et al. [44] assumed that interception coefficients for dry and wet deposits follow log-triangular distributions, i.e. T (Min = 0.16, Max = 14, Mode = 1.51) for dry deposits and T (Min = 0.25, Max = 11.5, Mode = 1.68) for wet deposits.

7 Partition Between Plant and Plant Water

The processes previously described generally require the estimation of the partition of the chemical between plant organ and plant water. Thus, the following partition coefficients are needed for describing several plant systems: $K_{\text{tuber\_water}}$, partition coefficient between tuber and water; $K_{\text{root\_water}}$, partition coefficient between root and water; and $K_{\text{fruit\_water}}$, partition coefficient between fruit and water.

As an example, the determination of the partition coefficient between tuber and water, $K_{\text{tuber\_water}}$, is discussed hereafter. Similar relationships can be derived for roots and fruits, but the carbohydrate content can be neglected for these latter organs.

For calculating the partition coefficient between tuber and water $K_{\text{tuber\_water}}$ (L $\text{kg}_{\text{fw}}^{-1}$), it may be assumed that tuber is composed of water, carbohydrate, traces of lipids and gas phase. $K_{\text{tuber\_water}}$ is then defined as the ratio of the concentration in all the tuber phases (water phase, lipids, carbohydrate and gas phase), to the concentration in the water phase of tuber. $K_{\text{tuber-water}}$ can be estimated from:

$$K_{\text{tuber\_water}} = \theta_{\text{tuber}} + CH_{\text{tuber}} \times K_{\text{CH\_water}} + L_{\text{tuber}} \times \delta_{\text{density\_OW}} \times \left(10^{\log 10\text{Kow}}\right)^{\delta_{\text{solubility\_lipids\_tuber}}} + G_{\text{tuber}} K_{\text{AW}} \quad (25)$$

where θ_{tuber} (dimensionless) is the water content in tuber, CH_{tuber} (L $\text{kg}_{\text{fw}}^{-1}$) is the carbohydrate content in tuber, $K_{\text{CH\_water}}$ (dimensionless) is the partition coefficient between carbohydrate and water, L_{tuber} (kg $\text{kg}_{\text{fw}}^{-1}$) is the lipid content in tuber, $\delta_{\text{density\_OW}}$ (L kg^{-1}) is a correction factor for density difference between water and *n*-octanol, $\log K_{\text{ow}}$ is the octanol-water partition coefficient (in log 10), $\delta_{\text{solubility\_lipids\_potato}}$ is an empirical correction factor for differences between solubility in octanol and sorption to tuber lipids (dimensionless), G_{tuber} (L $\text{kg}_{\text{fw}}^{-1}$) is the air content of tuber and K_{AW} ($\text{m}^3\ \text{m}^{-3}$ or dimensionless) is the partition coefficient between air and water.

8 Specific Processes for Electrolytes

The uptake and transport behaviour of neutral and mainly hydrophobic organic compounds can be adequately described with the theory described in the previous chapters. For electrolytes (called also ionic, ionisable, dissociating or charged compounds), transfers between environmental compartments (e.g. liquid-solid partition, soil-to-plant transfer) are partially governed by lipophilic interactions, but also partially by ionic interactions. For example, pharmaceuticals are mostly bases, but also acids and amphoters and many of them do not fit with models based on hydrophobicity. Many herbicides and pesticides are also electrolytes. Pesticides are indeed selected to specifically reach some target organs in the plant according to

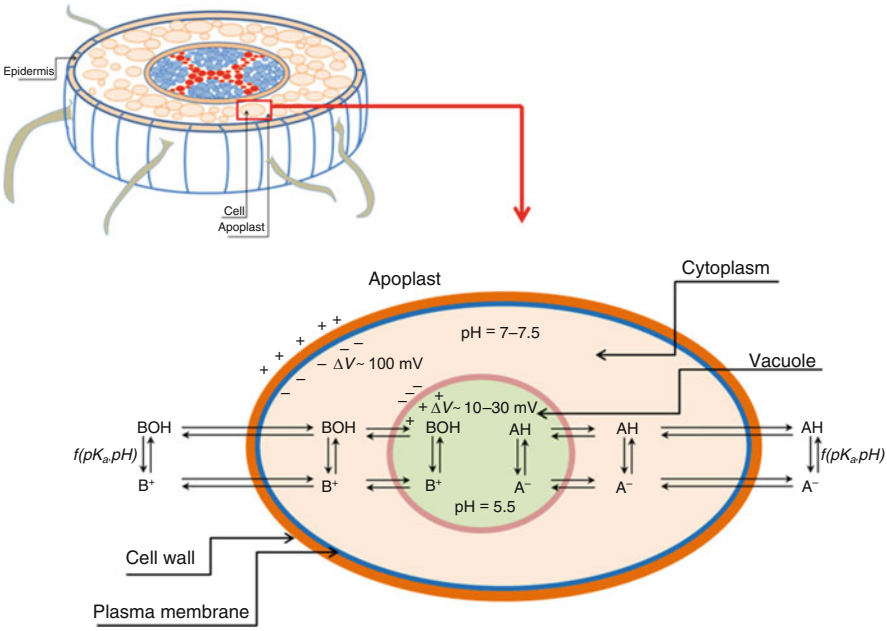

Fig. 3 Structure and processes governing uptake of ions into a cell

their acid/base properties. Herbicides preferentially target growing parts of the plant via phloem. As phloem pH is about 8, weak acids can accumulate in this organ and exert their action on plant. Fungicides preferentially target plant xylem, whose pH is about 5.5. This can explain that most fungicides are weak bases. For electrolytes, additional processes have then to be taken into account [45–48].

Weak acids and bases are simultaneously present in a given media according to acid/base reaction, i.e.:

$$\mathrm{BOH} \leftrightarrow \mathrm{B}^+ + \mathrm{OH}^- \quad \text{or} \quad \mathrm{AH} \leftrightarrow \mathrm{A}^- + \mathrm{H}^+$$

Amphoters combine these two reactions. The chemical under study is then partially under a neutral form (indicated hereafter by the index 'n') and partially under a dissociated form (indicated hereafter by the index 'd'). The respective distribution of the chemical activities among neutral and dissociated compounds (a_n and a_d) is given by the Henderson-Hasselbalch equation:

$$\log\left(\frac{a_d}{a_n}\right) = \pm(\mathrm{pH} - \mathrm{p}K_a), \text{with } a \text{ sign } (+) \text{ for acids and } (-) \text{ for bases.} \qquad (26)$$

pH will thus govern the distribution of the chemical in different plant structures that show different pH (Fig. 3). Thus, most of the cytosol is water and pH of the intracellular fluid is in the range 7–7.5. Instead, because of carboxylic acids

(e.g. citric, oxalic and malic acids), the vacuole shows acidic pH in the range 5–5.5 typically. A proton motive force is thus created allowing the transport of nutrients into and out of the vacuole.

Every cell is enclosed in a biomembrane, which has the structure of a lipid bilayer with many types of large molecules embedded in it. Because it is made of lipid molecules, the plasma membrane has a high electrical resistivity, in other words a low intrinsic permeability to ions. This is why ions are assumed to diffuse slower than neutral compounds. The plasma membrane combines resistance and capacitance. Resistance arises from the fact that the membrane impedes the movement of charges across it and acts thus as a resistance. But the lipid bilayer is thin and accumulation of charged particles on one side gives rise to an electrical potential that moves oppositely charged particles towards the other side. As the membrane is thin (about 7–8 nm), a high electric potential can be generated across the membrane (about 100 mV). The electrical attraction or repulsion of electrolytes at the charged biomembranes drives the exchange of electrolytes across it. At equilibrium, diffusive and electrical forces counterbalance, so that there is no net ion flow across the membrane. This means that the transmembrane voltage exactly opposes the force of diffusion of the ion, such that the net current of the ion across the membrane is zero and unchanging. The equilibrium potential of a particular ion is given by the Nernst equation:

$$\ln\left(\frac{a_{d,\text{out}}}{a_{d,\text{in}}}\right)_{\text{equ}} = \frac{z E_{\text{eq}}\ F}{R\ T} \tag{27}$$

where E_{eq} (V) is the equilibrium potential for the ion, R is the universal gas constant (8.314 J K^{-1} mol^{-1}), T is the absolute temperature (K), z is the number of elementary charges of the ion, F is the Faraday constant (96,485 C mol^{-1} or J V^{-1} mol^{-1}), $a_{d,\text{out}}$ (mol m^{-3}) is the activity of the ion outside of the membrane and $a_{d,\text{in}}$ (mol m^{-3}) is the activity of the ion at the inside of the membrane.

Considering this asymptotic equilibrium and considering the Nernst–Planck equation that extend the Fick's equation to electrolytes, Trapp [47] established an analytical solution for describing the flux of the ion across the membrane:

$$J = P_d \frac{N}{e^N - 1}\left(a_{d,\text{out}} - a_{d,\text{out}}.e^N\right), \quad \text{with} \quad N = \frac{z E_{\text{eq}}\ F}{R\ T} \tag{28}$$

where P_d (m s^{-1}) is the permeability of the membrane for dissociated compounds.

The permeability P_d can be estimated using relationships with octanol-water partition coefficient K_{ow}. Typically, the membrane permeability for dissociated compounds is about 3 times lower than the corresponding permeability for neutral compounds [48].

Ion trapping can also contribute to accumulation of ions within the cell: if pH in soil is low (close to pK_a), weak acids are partially under neutral forms in soil and can diffuse across the membrane according to the processes involved for neutral compounds. As pH inside the cytoplasm is higher, diffused weak acids dissociate

within the cell under anionic forms that diffuse slowly across the biomembrane and are trapped within the cell.

From the flux equation presented above, and combining it with diffusion of neutral form, Trapp [47] and Fu et al. [45] described the way to derive a bioconcentration factor (BCF) describing the partition of the ion between the inner and outer concentration of the ion (C_{in} and C_{out}, respectively), i.e.:

$$\frac{C_{in}}{C_{out}} = \frac{f_{no}.P_n + f_{do}.P_d.N/(e^N - 1)}{f_{ni}.P_n + f_{di}.P_d.e^N.N/(e^N - 1)} \quad (29)$$

where f_{no}, f_{ni}, f_{do} and f_{di} are the fractions of the neutral/dissociated forms outside/inside, respectively (calculated from the Henderson–Hasselbalch equation).

9 Accumulation of Metals

The bioaccumulation concepts developed for neutral hydrophobic substances (based in particular on diffusion across the lipid biomembranes) are not relevant for metals. For these latter compounds, other processes can significantly influence the accumulation of trace elements by plants like sequestration, detoxification, storage and regulation. The accumulation of metals by plants is then generally described by soil-to-plant transfer factors at equilibrium. These factors are defined as the concentration in targeted plant organ (e.g. leaf, fruit, grain or root, expressed in mg kg_{dw}^{-1}) divided by the total concentration in soil (mg kg_{dw}^{-1}). They are generally empirically derived.

A potential source for soil-to-plant transfer factors is a database called BAPPET [49]. Many experimental data of metal concentration in plants and in soil were collected, allowing the calculation of soil-to-plant transfer factors. Concentrations of metal in a plant are given in function of the metal considered, the type of plant and soil, the environmental context (e.g. industrial, rural, urban, and artificial), and experimental conditions (e.g. mode of extraction of metal, i.e. total or semi-total or partial extraction).

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Modelling Bioaccumulation in Aquatic Organisms and in Mammals

Artur Radomyski, Elisa Giubilato, Nicoleta Alina Suciu, Andrea Critto, and Philippe Ciffroy

Abstract The assessment of bioaccumulation processes plays a significant role in the evaluation of chemical risks. The awareness of long-lasting and often irreversible effects of bioaccumulative chemicals on ecological and human targets encouraged the inclusion of bioaccumulation assessment in many national and international legislative frameworks. At the same time, various experimental and modelling approaches have been developed to estimate bioaccumulation metrics such as the bioaccumulation factor (BAF) or the biomagnification factor (BMF). In this chapter, the main processes governing bioaccumulation phenomena in selected aquatic organisms (phytoplankton, invertebrate and fish) and in terrestrial mammals are described, in particular those implemented in the corresponding models available in MERLIN-Expo tool for exposure assessment. The main objective is to describe the development of bioaccumulation models for organic and inorganic contaminants which takes into account recent progresses and which satisfactorily describes bioaccumulation of contaminants along food webs including phytoplankton, invertebrate and fish species for surface waters, and mammals for terrestrial systems, and also allowing dynamic and stochastic assessment according to MERLIN-Expo modelling features. The coupling of different aquatic biota models allows to recreate aquatic food web of different dimensions and complexity, while the coupling of terrestrial mammal model with plant models available in MERLIN-Expo permits to simulate the transfer of contaminants along simplified terrestrial food chains.

Keywords Aquatic food web • Bioaccumulation • Biomagnification • Exposure model • Mammal

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Contents

1 Introduction

The production volumes of hazardous chemicals (i.e. toxic, carcinogenic, mutagenic substances) in the European Union amounted to about 200 million tons per year during the last years [1]. Also natural-occurring substances originating from volcanic emissions and fires or toxin-producing microorganisms contribute to the overall hazardous chemicals present in the environment. Some of these chemicals can enter the food webs and concentrate at higher levels than would otherwise occur [2].

Bioaccumulation of chemicals can be generally described as a phenomenon leading to increase of the concentration of chemicals in a biotic compartment with respect to the surrounding medium [3, 4]. Accumulation processes in living organisms can be classified on the basis of uptake of chemicals: (1) uptake from the environment media together with dietary uptake is described as *bioaccumulation*; (2) *bioconcentration* accounts for accumulated contaminant resulting solely from uptake through respiratory surfaces (body surface, tracheal tubes, gills, lungs); and (3) *biomagnification* is distinguished from other modes because it includes transfer and accumulation of contaminants along trophic levels in a food web [5, 6].

The accumulation of xenobiotics in biota has to be carefully evaluated in ecological risk assessment, because the knowledge of average concentrations in the whole organism or in some specific tissues can help in estimating the likelihood of adverse effects resulting from partitioning between contacting media and food web transfers or in assessing the influence of large masses of biota on overall chemicals fluxes in the environment [7, 8]. The internal concentration level reached in aquatic or terrestrial organisms over long-term exposures may cause adverse effect, either unspecific (e.g. narcosis) or specific (e.g. neurotoxic effects), after reaching a critical threshold, referred to as critical body burden. Since humans consume food originating from both aquatic and terrestrial environment, and they represent the top consumers of food webs, bioaccumulation/biomagnification

processes are relevant also for human health risk assessment [9]. In addition, measurement or modelling of bioaccumulative substances in edible plants and animals has to be performed to complete the assessment of chemical exposure through other routes (e.g. inhalation, dermal contact, soil/dust ingestion).

The awareness that bioaccumulation/biomagnification can be phenomena lasting over decades and inducing effects (often irreversible) long after the environmental release of chemicals encouraged to include bioaccumulation assessment in many national and international legislative frameworks. Stockholm Convention (2004; Annex D and E) [10] requires information on bioaccumulation as one of the screening criteria in identifying persistent organic pollutants and in evaluating chemical risk profile. Bioaccumulation is also listed by Basel Convention among hazardous characteristics of toxic wastes or substances that are subject to transboundary movement, as possible threat to the environment (Basel Convention, Annex III) [11]. In the European Union, the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) regulation (Regulation (EC) No 1907/2006) [12] asks for the identification of chemicals with hazardous properties of concern; in particular substances which are persistent, bioaccumulative and toxic (PBT) or very persistent and very bioaccumulative (vPvB) have to be included in REACH Annex XIV (Authorisation list), meaning that after the 'sunset date', they are banned for all uses except those specifically authorised by the European Commission (EC). REACH indicates that information on bioaccumulation in aquatic species is required for substances manufactured and imported in quantities of 100 tons per year or more [13]. The EU Regulation No 528/2012 [14] on Biocidal Products states that information on bioconcentration is relevant to the assessment of the ecotoxicological profile of the biocidal active substance and that evaluation of aquatic bioconcentration should include an estimate of the bioconcentration factor [15]. The European Food Safety Authority, following the EC Regulation No 1107/2009 [16] on authorisation of Plant Protection Products, recommends in its Guidance Document on Aquatic Ecotoxicology to further elaborate a risk assessment methodology to better address biomagnification in the future and proposes to consider food chain modelling as an option for higher tier assessment [17]. The importance of monitoring bioaccumulation in aquatic organisms is stressed by the European Commission also in the EU Directive 2013/39/EU. It states that for very hydrophobic substances which accumulate in biota and are hardly detectable in water, Environmental Quality Standards (EQS) should be set for biota [18]. For dioxins and dioxin-like compounds, EQS values refer to the concentration in fish, crustaceans and molluscs [19].

Bioaccumulation results from net competing uptake and elimination processes or, more precisely, is the result of absorption, distribution, metabolism and excretion (ADME) of a substance in an organism. The degree to which bioaccumulation occurs can be expressed by different metrics [20], which may also have a regulatory relevance and can be used for priority setting in chemical management. The bioaccumulation factor (BAF) can be expressed as the steady-state (equilibrium) ratio of the substance concentration in an organism to the concentration in the surrounding medium. For sediment-dwelling organisms, the BAF is often

expressed as the ratio of the concentrations in the organism and the sediment, in which case the term is referred to as biota sediment accumulation factor (BSAF). In the absence of dietary exposure, the bioconcentration factor (BCF) can be estimated, while the biomagnification factor (BMF) is the steady-state ratio of chemical concentration between an organism and its food.

Several approaches exist to estimate bioaccumulation metrics. Bioaccumulation data can be obtained from laboratory tests. A number of standardised test guidelines exist for estimating bioconcentration potential of organic compounds using laboratory experiments, such as bioaccumulation in fish – aqueous and dietary exposure (TG 305; [21]), bioaccumulation in sediment-dwelling benthic oligochaetes (TG 305; [22]) and bioaccumulation in terrestrial oligochaetes (TG 317; [23]).

BAF is rarely estimated from laboratory tests; more commonly field data are used for this purpose. The advantage of these measurements is that they include environmentally relevant processes; however field measurements and thus bioaccumulation data are characterised by high variability, which provide challenges to the collection, interpretation and regulatory use of field bioaccumulation data [24].

Bioaccumulation metrics can be also predicted by quantitative structure-activity relationship (QSAR) models. The most common QSAR models are based on the relation between BCF and chemical hydrophobicity (K_{ow}). The relationship can be explained by the analogy between n-octanol and water partitioning to that of tissue lipid-water partitioning. Common BCF/K_{ow} QSARs for non-polar, hydrophobic organic chemicals include models by Veith et al. [25], Mackay and Paterson [26], Meylan et al. [27] and Dimitrov et al. [28]. Linear correlation [25, 26] is a good approximation of the BCF for non-ionic compounds; however this relation fails with more hydrophobic chemicals, overestimating BCF values due to reduced bioavailability of highly hydrophobic compounds, slow membrane transfer of large molecules and processes affecting bioaccumulation such as growth of the organism or metabolism [29]. Higher degree polynomial QSAR models [27, 28, 30] show better performance than linear models in predicting BCF of highly hydrophobic chemicals.

Furthermore, the chemical bioaccumulation process can be simulated by mechanistic mass balance models for specific organisms, based on one or more body compartments [31–34]. In these models, different uptake processes (respiration, dietary uptake) as well as elimination processes (excretion, egestion, metabolism, growth dilution, reproductive losses) can be considered and described, each one characterised by a specific kinetic rate constant [33, 35]. Information on the target chemical and the organism, such as chemical partition coefficients or respiration and feeding rates and absorption efficiencies, are needed by such kind of models [36].

Mass balance models for individual organisms (e.g. fish) can be incorporated into larger descriptions of food webs, to simulate chemical bioaccumulation resulting both from exposure to environmental media (air, water, soil) and diet. Several food web bioaccumulation models are available, both for aquatic (e.g. [33, 37–39]) and terrestrial food webs (e.g. [40, 41]). The great advantage of

these models is that food webs of any dimension can be described, with as many food sources as needed, and concentrations in all species can be calculated simultaneously.

There has been substantial increase in the awareness of key parameters that influence all of the current metrics used to assess chemical bioaccumulation. Metabolic biotransformation rates of organic chemical have been identified as the most important source of uncertainty in modelling bioaccumulation [42, 43]. Complementing human exposure assessment to chemicals through various pathways with food web bioaccumulation process such as bioconcentration, biomagnification and biotransformation will allow better risk management decisions. Some commonly used models, such as EUSES, do not include mechanistic knowledge on uptake and elimination processes in biota; therefore they cannot provide substance- and organism-specific human exposure estimates [44]. Particularly, food web biotransformation is shown to play an important role in human exposure estimation, and neglecting this process in multimedia model calculations is expected to result in substantial errors [45].

In this chapter, the main processes governing bioaccumulation phenomena in aquatic organisms (phytoplankton, invertebrate and fish) and in terrestrial mammals are described, in particular those implemented in the corresponding models available in MERLIN-Expo. Our goal is to give an account on the development of bioaccumulation models which takes into account recent progress and which satisfactorily describes bioaccumulation of contaminants along food chains including phytoplankton, invertebrate and generic fish for surface waters and mammals for terrestrial systems, but also allowing dynamic and stochastic assessment (features available in the MERLIN-Expo software). The coupling of different aquatic biota models allows to recreate aquatic food web of different dimensions and complexity, while the coupling of terrestrial mammal model with plant models available in MERLIN-Expo (see chapter "Modelling the Fate of Chemicals in Plants") permits to simulate transfer of contaminants along simplified terrestrial food chains. All these models can be coupled to human intake model to provide dynamic estimates of human exposure through the diet.

2 Fate of Chemicals in Aquatic Organisms

2.1 General Description of Bioaccumulation Processes in Aquatic Food Webs

A prerequisite for developing a model describing accumulation of chemicals in an aquatic food web is a mechanistic understanding of bioaccumulation phenomena of organics and metals. The model is thus based on the description of the main exchange processes between water and organism compartment, i.e. uptake via respiratory route, uptake via dietary route, elimination via respiratory route (excretion), elimination via gastrointestinal track (egestion), metabolism and growth

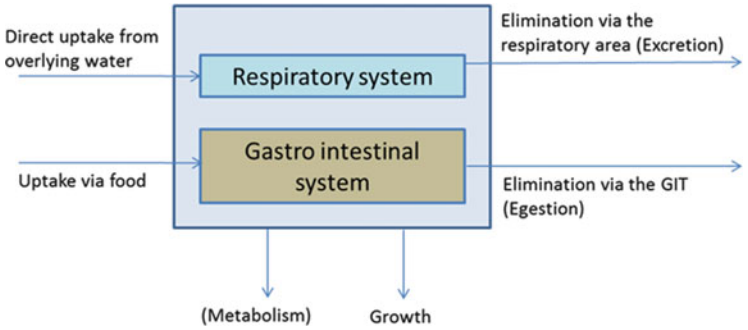

Fig. 1 Main bioaccumulation processes included 'fish' and 'invertebrate' model. Metabolism is not considered for metals

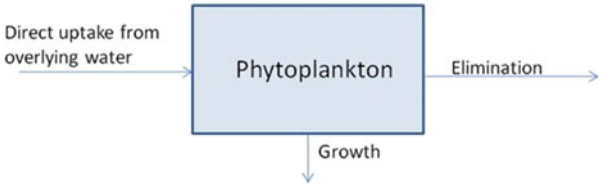

Fig. 2 Main bioaccumulation processes included in 'phytoplankton' model

[6, 46, 47]. The 'fish' and 'invertebrate' models should then include two compartments that correspond to two input/output pathways for chemical accumulation in the organism, i.e. the respiratory system and the gastrointestinal tract (GIT) system. The media considered are represented in Fig. 1.

While processes involved in bioaccumulation may be assumed to be similar for fish and invertebrate species [33], for phytoplankton a simpler assumption can be made. The 'phytoplankton' model can be represented by one compartment, and only uptake from water is considered (Fig. 2) since phytoplankton includes autotrophic species, and dietary uptake can be disregarded [48].

2.2 Respiratory Uptake and Excretion of Chemicals

2.2.1 Process Description

Bioconcentration in invertebrates and fish partially results from chemical uptake via the respiratory surface (fish's gill) of the organism. A variety of models addressing uptake of chemicals via respiratory route exist [33, 37, 49]. All these models can be based on different mathematical formulations and parameter names, but they are actually consistent and consider common assumptions. In particular, they consider that uptake is governed by an assimilation rate that depends on biological attributes of the fish (e.g. water assimilation varies between freshwater and marine organism

as a result of their distinct requirements for osmoregulatory balance), but also on chemical structure of the investigated substance and its affinity with lipids. Assimilation efficiency (AE_{gill}) thus determines the amount of chemicals that fish extracts from the volume of water flowing across the gill membrane. Assimilation efficiency is generally related to the octanol-water partition coefficient (K_{ow}) according to a relationship in the form:

$$AE_{gill} \propto \frac{1}{A + B/K_{ow}} \quad (1)$$

where AE_{gill} (dimensionless) is the assimilation efficiency, K_{ow} (dimensionless) is the octanol-water partition coefficient and A and B (dimensionless) are calibration parameters (see below).

Several parameterisations based on empirical observations were proposed for this relationship [37, 49, 50]. Some of them propose piecewise functions, i.e. different A and B values for several log K_{ow} ranges. For example, Barber [49] observed a positive correlation with K_{ow} for hydrophilic and moderately hydrophobic chemicals and a negative correlation with K_{ow} for extremely hydrophobic chemicals. The decreasing of assimilation efficiency for these latter compounds can be caused by the increasing water phase resistance. The applicability domain of these relationships has also to be checked before application. For example, the solution proposed by Gobas et al. [50] is based on reliable data (i.e. number of observations, confidence intervals), but only chemicals with log $K_{ow} > 4$ were studied.

The Hendrik's model [33] gives a mechanistic interpretation for the A and B coefficients, i.e. they represent resistances in water and lipid membranes, respectively. The resistances for diffusion through water layers can be considered to be the same for different chemicals because molecular weights and volumes are in the same order of magnitude (the use of the constant A derives from this assumption). The resistance during permeation through lipid layers was considered to decrease with the hydrophobicity of the compound ([51, 52]; the use of the expression B/K_{ow} derives from this assumption). In addition to resistances in lipid and water layers, fluxes can also be limited by delays in the flow of water through organisms. However, the delay imposed by the water flow can be ignored for aquatic species because ventilation and filtration are sufficiently fast in these organisms [33].

Uptake of chemicals through the gill membrane also depends on the volume of water flowing across the gill membrane, i.e. on the ventilation rate. In some models, ventilation rates of fish (expressed in $L\ s^{-1}$) are assumed to be directly associated to its needs in oxygen. It is then estimated by the three variables that govern oxygen uptake, i.e. the fish rate of oxygen consumption (expressed in $mgO_2\ s^{-1}$), the fish oxygen assimilation efficiency and the dissolved oxygen concentration of the ambient water (in $mgO_2\ L^{-1}$). Assuming that ventilation rates essentially depend on organism body weight, they can also be estimated by allometric scaling (see Sect. 2.2.2).

In conclusion, Hendrik's model [33] considers that respiratory uptake rate of a chemical depends on K_{ow}, body weight W and resistances ρ_{water_layer} and ρ_{lipid_layer} that substances encounter in lipid and water layers of the organism:

$$k_{uptake\_resp} = \frac{W^{-\kappa}}{\rho_{water\_layer} + \frac{\rho_{lipid\_layer}}{K_{ow}}} \quad (2)$$

where k_{uptake_resp} (L kg^{-1} fw d^{-1}) is the respiratory uptake rate, W (kg fw) is the organism weight, κ (dimensionless) is the allometric factor, ρ_{water_layer} (kg d kg^{-1}) is the water layer diffusion resistance for uptake of chemicals from water, ρ_{lipid_layer} (kg d kg^{-1}) is the lipid layer permeation resistance and K_{ow} (dimensionless) is the octanol-water partition coefficient.

Such model is expected to accurately predict uptake rate, and an uncertainty analysis was already performed by Hauck et al. [32].

QSAR uptake models are another alternative for estimating uptake across gill. Although such empirical models can provide useful conceptual insight, their utility for actual prediction must be carefully evaluated due to limited databases from which they were calculated and also their implicit assumption that biological determinants of uptake are either insignificant or constant across species or body size.

The respiratory pathway includes chemical uptake, as described above, but also chemical excretion. Excretion can be seen as a release of chemicals from fish's water compartment via respiratory route. Chemical uptake via the respiratory surface (fish's gill) of the organism is indeed associated to chemical excretion associated to the outflux of water via the respiratory surface. Both processes are influenced by the same factors connected with respiration. Many experiments were conducted under controlled laboratory conditions where dietary uptake is considered negligible. Under such conditions, equilibrium between concentration of the chemical in fish tissues and surrounding water can be reached. The bioconcentration factor (BCF), defined as the ratio at equilibrium of biota concentration of the substance to water concentration, can then be defined. As equilibrium condition is assumed to be reached, BCF also represents the ratio between respiratory uptake rate and excretion rate. BCF can then be used in combination with the respiratory uptake rate k_{uptake_resp} to estimate the excretion rate $k_{excretion\_resp}$ and to reflect affinity of the substance for staying in the lipid compartment of the organism [36]. The BCF concept was originally developed for hydrophobic organic substances, and several QSAR techniques were proposed to predict BCF from chemical descriptors of hydrophobicity like octanol-water partition coefficients.

2.2.2 Allometric Scaling

As described above, some models simulating uptake rate by respiration are based on allometric scaling. This is also the case for dietary uptake of fish (see Sect. 2.3)

or absorption rate of mammals (see Sect. 3.1). A short introduction to allometric scaling is then proposed here, and it is also valid for other parameters presented in other sections of this chapter.

Allometric relationships provide body-size specific parameters instead of values that are arbitrary or taken from a well-known species. Allometry, or the biology of scaling, is the study of size and its consequences. It has become a useful tool for comparative physiology. There are several empirical allometric equations that relate body size to many parameters, including, for example, ingestion rate, lifespan, inhalation rate, mortality, age at maturity, maximum density, territory size and rate constants. Even if these relationships were originally derived from empirical observations, there is a growing body of evidence that these relationships have their origins in the dynamics of energy transport mechanisms. From a meta-analysis based on 230 relationships, slopes of allometric regressions were shown to be mutually consistent with rate constants and generally decrease with organism mass at a constant exponent [53]. Slope of allometric regression κ is a component of each rate constant used in fish bioaccumulation model. The range of the slope of allometric regression is derived from reviews of empirical studies that have shown that the exponent is usually within the range of 0.25–0.33, theoretically explained by food web networks and surface-volume relationships [33].

2.3 Dietary Uptake and Egestion of Chemicals

The rate at which chemicals are assimilated from the diet via the gastrointestinal tract (GIT) is expressed by the dietary uptake rate constant (kg kg^{-1} d^{-1}), and the rate at which chemicals are eliminated from the organism body via the gastrointestinal tract (GIT) is expressed by the egestion rate constant (kg kg^{-1} d^{-1}). Although direct aqueous uptake is the dominant route of accumulation for moderately hydrophobic chemicals, dietary uptake can be the dominant pathway for extremely hydrophobic chemicals [49]. Due to the fact that water is not a significant contributor to the storage capacity of highly hydrophobic organic chemicals, its value has a negligible impact on the mechanism of biomagnification for these chemicals. Once the dietary exposure pathway becomes dominant, an actual concentration of accumulated chemical can exceed those predicted by thermodynamic partitioning. This is because of fish's decreasing ability to excrete highly hydrophobic chemicals across its gills and also due to its ability to maintain high dietary diffusion gradients [49]. The high diffusion gradient makes assimilation of digestion products more rapid than hydrophobic chemicals, leading to increase concentration of these chemicals in guts.

In complement to what proposed for the respiratory pathway, Hendriks et al. [33] proposed formulations to simulate uptake and egestion of chemicals via diet ingestion. It is assumed that chemical exchanges across the gastrointestinal tract

(GIT) are driven by diffusion gradients, i.e. the concentration differences between phases within the fish and its food/faeces. These exchanges are assumed to be mainly simple molecular diffusions. Although alternative diffusion mechanisms were proposed (e.g. lipid micelle-mediated diffusion model), their role in controlling dietary exchanges of fish is not well established [49].

The distribution of food between digested and undigested fractions, respectively, can be represented by an assimilation fraction AF_{food}. Assimilated food may be allocated to production of somatic or gonadal biomass. Dietary assimilation efficiencies reflect dietary matrix (e.g. organic matter quality and quantity) and digestive physiology of the organism (e.g. feeding rates and gut retention time). As the chemical can be both transported in food water and food lipids, the assimilation fraction of the chemical $AF_{chemical}$ can be different of those applied for food AF_{food}. For this purpose, food is assumed to be composed of lipids and water only, in respective proportions p_{lipid_food} and $(1 - p_{lipid\_food})$. The assimilation fraction of the chemical contained in water is directly related to the assimilation fraction of food AF_{food}; the assimilation fraction of the chemical contained in lipids is assumed to be related to the assimilation fraction of food AF_{food} corrected by the octanol-water partition coefficient K_{ow}.

Similar to what assumed for Hendrik's respiratory uptake model, the dietary uptake is limited by two resistances in series reflecting transport across the water GIT layer and the lipid GIT membrane, respectively. As for respiratory uptake, the resistance for diffusion through the water layer is considered to be the same for different chemicals, while partial resistance from the lipid layer (encountered to and from food) is inversely proportional to K_{ow}. A flow delay of food and faeces, depending on the fraction of undigested chemical contained in lipids, can also be considered. The mathematical formulation respecting these assumptions can be found in Hendriks et al. [33]:

$$k_{uptake\_diet} = \frac{\frac{AF_{food}}{1 - AF_{food}} \cdot \frac{1}{p_{lipid\_food}(K_{ow} - 1) + 1} \cdot W^{-\kappa}}{\rho_{water\_layer\_food} + \frac{\rho_{lipid\_layer}}{K_{ow}} + \frac{1}{p_{lipid\_food} \cdot K_{ow} \cdot (1 - AF_{food}) \cdot \gamma_{food}}} \quad (3)$$

where k_{uptake_diet} (kg fw kg^{-1} fw d^{-1}) is the dietary uptake rate, AF_{food} (dimensionless) is the food assimilation efficiency, p_{lipid_food} (dimensionless) is the proportion of lipids in food, W (kg fw) is the organism weight, κ (dimensionless) is the allometric factor, $\rho_{water\_layer\_food}$ (kg d kg^{-1}) is the water layer diffusion resistance for uptake of chemicals from food, ρ_{lipid_layer} (kg d kg^{-1}) is the lipid layer permeation resistance, K_{ow} (dimensionless) is the octanol-water partition coefficient and γ_{food} (dimensionless) is the food transport coefficient (that represents delay in advective transport of chemical substances through organism due to limited supply of new food).

Alternatively, bioaccumulation models employ dietary uptake formulations based on assimilation efficiencies at equilibrium. Models applying assimilation

implicitly assume that chemical equilibrium assimilation efficiencies describe the net chemical exchange between fish and their food. These models describe a fish's chemical elimination either as a single, lumped parameter process that is independent of the fish's egestion rate or as a process that does not require an explicit faecal egestion term. Chemical assimilation efficiencies via food have often been considered only as functions of K_{ow}, similarly to what is established for respiratory uptake. Moreover, as far as the fish's dietary assimilation efficiencies are concerned, Thomann et al. [54] concluded that a fish's dietary and gill assimilation efficiencies could be estimated with the same empirical function of K_{ow}. These relations are often presented as hyperbolic functions (i.e. $AE_{diet} = (a_0 + a_1 K_{ow})^{-1}$). One example of this approach is described by Gobas et al. [50].

2.4 Metabolic Biotransformation

One of the routes of chemical elimination in fish is metabolic transformation (or biotransformation), defined as a change of the parent substance to another molecule or a conjugated form of the parent substance. Negligible biotransformation rates are often assumed for screening level hazard and risk assessment, thus resulting in overestimates of bioaccumulation, exposure and risk for chemicals that undergo biotransformation processes. Biotransformation can however lead to reduction in bioconcentration of some non-ionic substances due to reactions associated with certain functional groups. Metabolic biotransformation has a larger influence on bioaccumulation factor for more hydrophobic chemicals. This is because the rates of chemical elimination by gill respiration become slower with increasing hydrophobicity of contaminants. Schüürmann et al. [29] states that for predictive BCF assessment, factors such as biotransformation should be taken into account.

Biotransformation results in formation of a more hydrophilic compound which is more easily excreted that a parent compound. The organ that is most commonly involved in the biotransformation of xenobiotics is the liver. The main processes involved in metabolism of chemical in fish body are categorised in three phases [55]: phase I of metabolism involves such process as oxidation, reduction or hydrolysis to unmask or add reactive functional groups to xenobiotic compound; phase II of metabolism involves enzymes catalysing conjugation of the xenobiotic or its metabolite with an endogenous ligand (e.g. glutathione, glucuronic acid), thus facilitating the excretion of chemical; phase III involves enzymes (i.e. peptidases, hydrolases and β-lyase) that catalyse metabolites to form products easily removable from the organism body.

Models that include biotransformation generally assume first-order processes and do not estimate biotransformation rates that may occur under non-first-order conditions, such as enzyme saturation. Biotransformation half-lives and rate constants ($\lambda_{metabolism}$) for organic chemicals in fish can be derived from QSAR models (under applicability domain limitations) [56]. QSAR predictions of metabolic

biotransformation are functions of structural properties and can be presented as normalised values (e.g. to 0.01 kg fish and 15°C). In this latter case, for comparison of models' estimates and use in mass balance models, it is recommended to convert QSAR predicted values to body weight and temperature-specific values. Alternatively, biotransformation rate constant can be calculated as the difference between two quantities, a measured bioconcentration factor or elimination rate constant and a model-derived bioconcentration factor or elimination rate constant estimated assuming no biotransformation.

2.5 *Bioconcentration Factor for Metals*

Bioaccumulation of metals via the respiratory pathway can occur across body surfaces, such as gill, and is generally described by the bioconcentration factor (BCF), defined as the ratio at equilibrium of the substance concentration in fish tissue to water concentration in water. The BCF concept was originally developed for hydrophobic organic substances. Simple passive diffusion across the lipid biomembranes is believed to be the key process for the accumulation of neutral hydrophobic substances in biota, which ensures BCF is independent of exposure concentrations [57]. In the case of metals, however, the assumption of BCF being independent of exposure concentrations is controversial. As a result of complex physiological processes such as sequestration, detoxification, storage and branchial elimination, biota is often actively able to regulate metal bioconcentration via dynamic reaction systems that respond to environmental loading and maintain homeostasis [58, 59]. In addition, Deforest et al. [60] hypothesised the trend in which metal uptake increases at lower exposure concentrations, according to the basis that organisms actively uptake essential metals at low concentrations to satisfy metabolic requirements. Non-essential metals would also be regulated because the mechanisms for regulating essential metals are not metal specific [61].

Based on the factors influencing metal uptake and accumulation described above, it can be assumed that BCF values for metals are not independent of exposure. BCF can then be assumed to be related to the metal concentration in water. Several authors observed an inverse linear relationship between BCF and the total metal concentration in water in log units [33, 57, 60, 62]:

$$\ln(\mathrm{BCF}) = a_{\mathrm{BCF}} + b_{\mathrm{BCF}} \cdot \ln(C_{\mathrm{tot\_water}}) \tag{4}$$

where BCF (L kg^{-1} fw) is the Bioconcentration factor, $C_{\mathrm{tot\_water}}$ (mg L^{-1}) is the total concentration of the chemical in water and a_{BCF} and b_{BCF} (dimensionless) are calibration parameters.

For example, Tanaka et al. [62] built a database containing BCF, as well as concentrations in water, for five metals (Cd, Cu, Zn, Pb and As). Data were extracted from ECETOX and US EPA databases, as well as from data available in McGeer et al. [57] or other more recent papers. Only chronic exposure conditions

(>28 days) were considered for deriving BCFs, because they are assumed to be relevant for equilibrium situations. As a result of the data selection, an estimation of the a_{BCF} and b_{BCF} parameters was thus obtained with confidence intervals. McGeer et al. [57] also fitted BCF-concentration relationships for Ag and Ni.

3 Fate of Chemicals in Mammals

For mammals, bioaccumulation essentially occurs through the dietary route, associated with elimination via gastrointestinal track (egestion), metabolism and growth. Similarly to the 'fish' model previously described, a model simulating the accumulation of chemicals in mammals' organs can include a description of the gastrointestinal tract (GIT) system.

The model described below extends description of ingestion rate constants in bioaccumulation modelling in mammals, by incorporating detailed characteristics of bilayer membrane in intestinal epithelia and varied modes of diffusion resistances. It shares similar assumptions with the approach proposed by Hendriks et al. [33], namely, the use of allometric scaling of rate constants with organism weight, approximation of K_{ow} as the surrogate for cellular apolar membranes, diffusion resistances and flow delays [63].

3.1 Advective Transport and Diffusion of Chemicals In/Across the GIT Membrane

Uptake of chemicals via food highly depends on advective transport along the gastrointestinal tract (GIT) and passive diffusion of digested food across the GIT epithelium membrane towards the blood system. Biological membranes exist as a protein-lipid bilayer. The lipid portion is primarily phospholipid, which have ionic, polar head groups oriented outwards and non-polar lipid chains oriented inwards. Integral membrane proteins may also be transport, receptor or other types of proteins. The driving force for the transport of nutrients and other chemicals is the concentration gradient across the membrane. Passive transport can be further divided into diffusion and facilitated diffusion. Chemicals may simply diffuse across a membrane when they are quite small so as to enter membrane pores and go via the paracellular route or when they are soluble in the lipid membrane. Many lipids or lipophilic compounds are soluble in the lipid bilayer and are transported by simple diffusion. Facilitated diffusion is facilitated by a transport protein, but the driving force is still the concentration gradient. For example, glucose and amino acids use this mechanism. Chemicals can also be transported across the GIT through active transport. Active transport also uses a transport protein, but energy is required in the form of ATP to move nutrients against a concentration gradient.

The best example of this mechanism is the Na^+/K^+ pump that is present in every cell. Transport of glucose and amino acids is also active in the GIT.

Bioaccumulation first depends on the distribution of food between digested and undigested fractions, respectively. Digestion gathers all the mechanical and chemical processes able to break down food; only dissolved nutrients resulting from digestion are thus involved in diffusion across the GIT membrane, while undigested food is egested. Distribution of food between digested and undigested fractions can be represented by the assimilated fraction of food AE_{food}. Assimilated food may be allocated to production of somatic or gonadal biomass. Dietary assimilation efficiencies reflect dietary matrix (e.g. organic matter quality and quantity) and digestive physiology of the organism (e.g. feeding rates and gut retention time). For estimating the assimilation fraction of food, food may be assumed to be composed of lipids and water only, in respective proportions p_{lipid_food} and $(1 - p_{lipid\_food})$. The assimilation fraction of the chemical contained in water is directly related to the assimilation fraction of food water; the assimilation fraction of the chemical contained in lipids is related to the assimilation fraction of food lipids but also to the octanol-water partition coefficient K_{ow}.

The distribution of food between digested and undigested food, respectively, allows quantifying the fraction of chemical able to be transport across the GIT membrane. Most fate models for xenobiotics assume that chemical exchanges across the GIT are driven by diffusion gradients, i.e. the concentration differences between phases within the animal blood and its food/faeces. These exchanges are assumed to be mainly simple and passive molecular diffusions. For the most recent models [63], the lipid membrane separating GIT and the blood system is assumed to be a bilayer structure with an apolar membrane centre and an outer membrane with polar groups. In most bioaccumulation models however, this latter polar layer is neglected, and diffusion in the lipid membrane is only represented by the octanol-water partition coefficient (used as a surrogate for representing substance-lipid affinity). O'Connor et al. [63] instead assumed that membrane phospholipids are ordered creating thus a bilayer structure. They also showed that considering the outer polar membrane allows extending the applicability domain of the model for both hydrophilic and hydrophobic compounds. Active transport across the membrane by carriers was also incorporated in the last version of their model [64].

Considering this background related to the GIT membrane structure, O'Connor's model assumes that ingestion rate constant of chemicals is related to four resistances to diffusion in series or in parallel corresponding to different layers in the membrane (Fig. 3):

- The partial resistance from water layer. Resistance for diffusion through water layer is considered to be the same for different chemicals because molecular weights and volumes are in the same order of magnitude.
- The partial resistance for passive diffusion from outer polar lipid layer, assumed to be inversely proportional to heptane-water partition coefficient K_{hw} (used to describe the polar affinity of chemicals). K_{hw} is calculated as the ratio between octanol-water partition coefficient K_{ow} and octanol-heptane partition coefficient

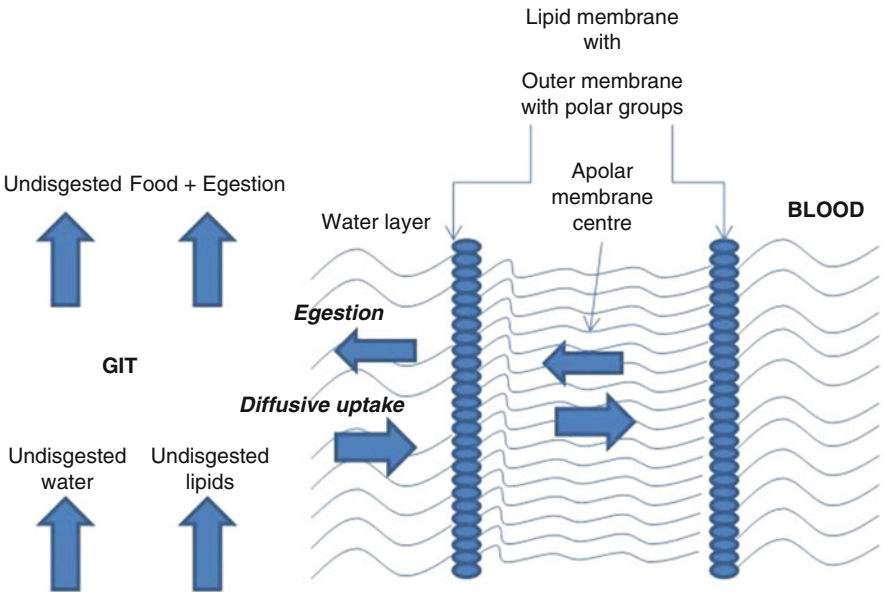

Fig. 3 Exchange processes and resistances taking place across gastrointestinal tract (GIT)

K_{oh}. log K_{oh} is linearly related to the hydrogen bond donor strength of the chemical [65], i.e.:

$$K_{hw} = \frac{K_{ow}}{K_{oh}}, \quad \text{with} \quad K_{oh} = 3.54A + 0.37 \tag{5}$$

where A is the Abrahams hydrogen bond donor strength descriptor.

- The partial resistance for passive diffusion from inner apolar lipid layer, assumed to be inversely proportional to octanol-water partition coefficient K_{ow}.

In addition, a partial resistance for carrier-mediated transport may be considered [64]; this resistance is assumed to be inversely proportional to the transport rate constant that follows Michaelis-Menten kinetics.

Time delay associated to advective transport of food and faeces in the GIT can also be represented by a flow delay, depending on the fraction of undigested chemical contained in water and lipids.

In summary, the total resistance to diffusion ρ_{tot} for the chemical present in digested food is given by the sequence of resistance from water layer, resistance from membrane and time delay for advective transport (if carrier-mediated transport is not considered):

$$\rho_{\text{tot}} = \rho_{\text{water\_layer}} + \frac{\rho_{\text{outer\_membrane}}}{K_{\text{ow}}} + \frac{\rho_{\text{inner\_membrane}}}{K_{\text{hw}}} + \frac{1}{\gamma_{\text{ingestion}}\left(p_{\text{undisgested\_lipid}} + p_{\text{undisgested\_water}}\right)} \quad (6)$$

where $\rho_{\text{water\_layer}}$ (d kg$^{-\kappa}$) is the resistance for diffusion in the water layer, ρ_{membrane} (d kg$^{-\kappa}$) is the resistance for diffusion in the membrane, $\gamma_{\text{ingestion}}$ (kg$^{\kappa}$ d^{-1}) is the food ingestion coefficient, $p_{\text{undigested\_lipid}}$ (dimensionless) is the chemical fraction contained in undigested food lipids and $p_{\text{undigested\_water}}$ (dimensionless) is the chemical fraction contained in undigested food water.

The chemical fractions contained in undigested food lipids $p_{\text{undisgested\_lipid}}$ and in undigested food water $p_{\text{undisgested\_water}}$ are calculated from the lipid and water assimilation efficiencies AE_{lipid} and AE_{water}:

$$p_{\text{undigested\_lipid}} = \left(1 - \text{AE}_{\text{lipid}}\right) \cdot f_{\text{lipid\_food}} \cdot K_{\text{ow}} \quad (7)$$

$$p_{\text{undigested\_water}} = \left(1 - \text{AE}_{\text{water}}\right) \cdot \left(1 - f_{\text{lipid\_food}}\right) \quad (8)$$

where $f_{\text{lipid\_food}}$ (dimensionless) is the fraction of lipids in food.

The rate at which chemicals are assimilated from the diet via the gastrointestinal tract (GIT) can then be expressed by the dietary uptake rate constant $k_{\text{absorption}}$ (kg kg^{-1} d^{-1}) that is assumed to be related to an allometric rate exponent describing the effect of species weight on physiological rate constants:

$$k_{\text{absorption}} = \frac{W^{-\kappa}}{\rho_{\text{tot}}} \cdot \frac{1}{\left(p_{\text{undisgesd\_lipid}} + p_{\text{undisgesd\_water}}\right)} \quad (9)$$

where $k_{\text{absorption}}$ (kg kg^{-1} d^{-1}) is the dietary uptake rate constant, W is the animal weight (kg), κ (dimensionless) is the allometric factor, $\rho_{\text{water\_layer}}$ (d kg$^{-\kappa}$) is the total resistance for diffusion, $p_{\text{undisgested\_lipid}}$ (dimensionless) is the undigested food lipids and $p_{\text{undisgested\_water}}$ (dimensionless) is the undigested food water.

The rate at which chemicals are eliminated from blood to faeces via the GIT can be expressed by the egestion rate constant k_{egestion} (kg kg^{-1} d^{-1}). The combination of absorption and egestion allows calculating the chemical assimilation efficiency $E_{\text{assimilation}}$ [63]:

$$E_{\text{assimilation}} = \frac{1}{\rho_{\text{tot}} \cdot \gamma_{\text{ingestion}}\left(p_{\text{undisgesd\_lipid}} + p_{\text{undisgesd\_water}}\right)} \quad (10)$$

Considering this background, the mass balance equation for estimating the concentration C_{blood} of the chemical in blood is (in case of no metabolism):

$$\frac{dC_{\text{blood}}}{dt} = k_{\text{absorption}} \cdot (C_{\text{diet}} - E_{\text{assimilation}} \cdot C_{\text{blood}}) \quad (11)$$

where C_{blood} (mg L^{-1}) is the concentration of the chemical in blood and C_{diet} (mg kg^{-1}_{ww}) is the concentration of the chemical in diet.

3.2 Circulation of Blood in Tissues and Partition of Chemicals Between Blood and Fat/Tissue

3.2.1 Process Description

Once chemicals have crossed the GIT barrier, their accumulation in animal organs is mainly governed by two processes:

- The circulation of blood fluids through organs, with input from arterial blood and output to venous blood.
- When blood is circulating within the organ, the partition of chemicals between blood and fat contained in the organ. Partition coefficients are usually used for representing such distribution of compounds.

The transport of chemicals from blood to organs first depends on the perfusion rate of the tissues. Blood flow is assumed to be constant and non-pulsatile. The chemical is assumed to distribute evenly and homogeneously throughout the tissue volume. Moreover, the compound distribution into all compartments is assumed to be limited by perfusion, i.e. the tissue membranes present no barrier to diffusion. Perfusion rate of meat tissues (e.g. muscle, liver, kidneys) can be estimated from the cardiac output and the relative blood flow to organs (i.e. the fraction of total blood flow crossing over each organ). For mammal glands, perfusion flow highly depends on lactating stage of the animal, and it is assumed to depend on milk volume production.

Once crossing through the tissue, chemical present in blood is distributed between blood and fat of tissues. Fat-blood or tissue-blood partition coefficients were experimentally determined only for some chemicals, and the collection of experimental data appears unrealistic given the high number of chemicals to be investigated. For this reason, in silico approaches were developed to calculate these partition coefficients for a wide spectrum of chemicals from more easily accessible compound descriptors. Such in silico approaches are based on the fundamental principle that the concentration (or solubility) of a compound in a biological matrix can be expressed as the sum of its concentrations in the respective components of the matrix. For blood and animal organs (like meat and milk), the main components to be considered can be water, neutral lipids, charged phospholipids, haemoglobin and/or plasma proteins. For neutral organic environmental chemicals, models were initially based on hydrophobic interactions with neutral lipids and haemoglobin. Recent predictive models extended their applicability domain for drugs by the

introduction of interactions with charged phospholipids and binding to plasma proteins [66]. Thus, models were developed for neutral compounds, acids and bases and zwitterions. Tissue-blood partition coefficients can be calculated from surrogates for lipophilicity (e.g. octanol-water partition coefficient) and/or binding to proteins (protein-water partition coefficient) and/or phospholipids interactions. Fat-blood partition coefficients can be derived from QSAR models or calculated from the ratio of fat-air and air-blood partition coefficients (especially for VOCs); they are then converted in tissue-blood partition coefficients assuming available fractions of water and lipids in each tissue.

Considering this background, the mass balance equation for estimating the concentration of the chemical in a given organ tissue is (in case of no metabolism):

$$\frac{dC_{\text{tissue\_}i}}{dt} = \text{Flow}_{\text{blood-organ\_}i} \cdot \left(C_{\text{blood}} - \frac{C_{\text{tissue\_}i}}{K_{\text{blood-tissue}}} \right) \tag{12}$$

where C_{blood} (mg L^{-1}) is the concentration of the chemical in blood, $C_{\text{tissue\_}i}$ (mg $\text{kg}^{-1}_{\text{ww}}$) is the concentration of the chemical in tissue i, $\text{Flow}_{\text{blood-organ\_}i}$ (L $\text{kg}^{-1}_{\text{ww}}$ d^{-1}) is the blood flow though organ i and $K_{\text{blood-tissue}}$ (L $\text{kg}^{-1}_{\text{ww}}$) is the blood-tissue partition coefficient.

3.2.2 Organ Weights, Cardiac Output and the Relative Blood Flow to Organs

As previously indicated, the transport of chemicals from blood to organs first depends on the perfusion rate of the tissues. As metabolism needs uptake and delivery of oxygen, cardiac output varies according to a body weight scaling. Lindstedt and Schaeffer [67] collected anatomical and physiological parameters on four mammalian model species (mouse, rat, dog and man) and eventually other mammals if available (e.g. guinea pig, cattle, rabbit). Data available for healthy, resting animals in normal conditions (e.g. normal temperature, no manipulation of blood pressure) were collected. It was observed that organ weights scale as a constant fraction of body weight (i.e. allometric power κ_{weight} close to 1). Some organs can deviate from unity because small animals have a greater surface relative to their volume (e.g. skin) and for neurological control role (e.g. brain). Cardiac output was observed to vary as the allometric factor $\kappa_{\text{cardiac}} = 0.75$. The distribution of cardiac output to the individual organs is roughly constant across species; ordinarily the same fraction of cardiac output perfuses each of the organs. The allometric factor for blood flow κ_{flows} is then close to 0.75 for all the organs. Perfusion of the main organs (contributing to about 90% of total cardiac output) is distributed as follows: muscle 21%, kidneys 16%, liver (splanchnic) 17%, skeleton 14%, skin 7%, heart 6%, liver (hepatic) 4%, lung 3% and brain 2.7%. Perfusion of adipose tissue is about 5% (similar for rats and humans despite the larger contribution that fat makes to the weight of humans (17%) than to rats (5%))

[67]. These values are similar to those proposed by the International Commission on Radiological Protection (ICRP) for humans.

3.3 *Elimination of Chemicals: Growth, Milk Lactation, Urinary Excretion and Metabolism*

The outflux of chemicals from the organism can be evaluated considering the loss rate constants corresponding to losses by milk lactation, urinary excretion, growth (for young animals) and degradation (metabolism).

Elimination via biomass production occurs due to weight increase. If young animals are studied, production of biomass, and as a consequence dilution of chemicals in animal, can be expressed as biomass production rate constant k_{growth} (resulting in a decrease of chemical concentration in animal tissues because of dilution in an increasing volume). Chemical elimination pathways are considered as parallel, the overall removal of chemicals being largely determined by the fastest route. Therefore, production of biomass accounts for elimination of extremely hydrophobic chemicals that are highly retained in animal lipid tissues.

Metabolism (or biotransformation) is defined as a change of the parent substance to another molecule or a conjugated form of the parent substance. In mammals, metabolic pathways have been classified into phase I enzymes (essentially cytochrome P-450), phase II enzymes (e.g. amino acid conjugation, methyl-, sulphotransferases) and phase 0 (transporters). Some models that consider the formation of metabolites assume first-order processes; biotransformation rates that may occur under non-first-order conditions (e.g. enzyme saturation) can also be considered. In this latter case, metabolism is described by a Michaelis-Menten approach, i.e.:

$$\lambda_{\text{metabolism}} = \frac{V_{\max} \cdot CYT \cdot C_{\text{tissue\_}i}}{K_{\text{m}} + C_{\text{tissue\_}i}} \tag{13}$$

where $\lambda_{\text{metabolism}}$ (d^{-1}) is the metabolism rate constant, $C_{\text{tissue\_}i}$ (mg $\text{kg}^{-1}_{\text{ww}}$) is the concentration of the chemical in tissue, CYT (dimensionless) is the activity of the main cytochrome P450 involved in the metabolic reaction, $V_{\max}$ (mg d^{-1}) is the maximum velocity of the metabolic reaction and K_{m} (mg $\text{kg}^{-1}_{\text{ww}}$) is the Michaelis constant of the metabolic reaction.

Metabolic biotransformation is expected to have a larger influence on bioaccumulation factor for more hydrophobic chemicals. This is because the rates of chemical elimination by gut egestion become slower with increasing hydrophobicity of contaminants. Metabolism is specific to each contaminant and to each species. Several approaches were developed to investigate metabolism, i.e. in vitro experiments using tissues of the species of interest (e.g. experiments conducted

with microsomes or hepatocytes), in vivo experiments (when available) or in silico models.

The other loss pathways are renal excretion and milk loss (for lactating mammals). Urinary excretion can be calculated considering the urine volume and the concentration of chemicals in kidneys. For milk compartment, the losses by outflux can be calculated considering the milk cattle lactation as sum of lipids and water in milk.

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Modelling the Fate of Chemicals in Humans Using a Lifetime Physiologically Based Pharmacokinetic (PBPK) Model in MERLIN-Expo

Céline Brochot and Paul Quindroit

Abstract This chapter presents the human model implemented in MERLIN-Expo. This model is a physiologically based pharmacokinetic (PBPK) model that describes the relationship between an external dose and an internal dosimetry using parameters related to the anatomy and physiology of individuals and the physico-chemical properties of the contaminants. The goal of the PBPK model is to simulate the toxicokinetics of contaminants in humans, e.g. the amounts or concentrations of contaminants in different organs/tissues, under various exposure conditions. The generic PBPK model is based on a detailed compartmentalisation of the human body and parameterised with relationships describing the time evolution of the physiology and anatomy of the individuals. In this chapter, we present the detailed description of the human model and the conditions to apply it in MERLIN-Expo. Finally, the model predictability is evaluated by a direct comparison between computational predictions and experimental data on small case studies.

Keywords Childhood • Environmental chemicals • Humans • Lifetime exposure • PBPK model

Contents

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1 Introduction

Humans are constantly exposed to a multitude of compounds including during the in utero life. Numerous monitoring studies in environmental media (outdoor and indoor air, river, soil, sediments, etc.), food and drinking water showed the diversity of the chemical compounds to which humans are exposed daily. The extent of the internal exposure in humans is governed by the external exposure and also the kinetics of the compounds (called toxicokinetics for chemicals and pharmacokinetics for therapeutic compounds) that are the processes of absorption, distribution, metabolism and excretion (ADME). Toxicokinetic models are mathematical tools used to describe the ADME processes in living organisms and aim to link an external exposure to an internal dosimetry in humans (e.g. concentration in blood, in urine or in tissues). A class of toxicokinetic models, the physiologically based pharmacokinetic (PBPK) models, bases the description on the ADME processes on the physiology and the anatomy of individuals and the biochemistry of the compounds [1–4]. A PBPK model subdivides the body in compartments representing organs connected through a fluid, usually blood. Model parameters correspond to physiological and biochemical entities specific to the body and compounds, such as organ volumes, tissue blood flows, affinities of the compounds for the tissues or metabolic clearances. The concept of toxicokinetic modelling based on mass transfers of compounds between compartments having a physiological meaning was first introduced by Teorell in the late 1930s [5]. However, in the absence of adequate integration tools, Teorell had to simplify the model to one or two compartments without physiological significance. The development of PBPK models came with the advent of powerful computing capabilities.

PBPK models can be specific to a compound or a chemical family, but some of them aim to be generic, i.e. applied to a large number of compounds, different individuals or populations, and be applied over long time periods as the lifetime [6–8]. This latter feature is of importance when considering exposure to persistent or semi-persistent compounds that could lead to high body burdens over the years [9]. In such cases, the PBPK model is able to deal the physiological or biochemical variations that arise throughout the growth and the development of a child. Mathematical functions describing the time variations can be assigned to the model parameters and be used to evaluate the influence of these changes on the chemical toxicokinetics [10–12].

PBPK modelling is now a mathematical tool commonly used in toxicological risk assessment [13, 14] and also in pharmaceutical industries for the development of new therapeutic substances [15]. In particular, PBPK models can be applied in two different steps of the risk assessment framework. First, these models can be used to better characterise the relationship between the exposure dose and the adverse effects by modelling the internal exposure in the target tissues (i.e. where the toxic effects arise) [16]. Secondly, PBPK models can be used in the exposure assessment to estimate the external exposure using human biomonitoring data, like the concentrations of chemicals in blood or urine [17, 18]. These predictions can then be compared to existing exposure guidance or reference values such as tolerable daily intakes [19].

In this chapter, we present the generic PBPK model that is implemented in MERLIN-Expo. We start with the description of the model, explain how to use it within MERLIN-Expo and describe some features that can be relevant for building realistic exposure scenarios for risk assessment. Finally we apply the model to simple case studies.

2 Description of the Human PBPK Model

The generic PBPK model provides a detailed description of the human body subdivided into 22 compartments (Fig. 1). The organs/tissues represented as compartments are (the name of the compartment is given in parentheses) the adipose tissues (Adipose), the adrenal glands (Adrenal), the alveolar space (AlveolarSpace), the arterial blood (ArterialBlood), the perfused bones (Bones), the brain (Brain), the breast (Breast), the gut wall (Gut), the gut lumen (Gut_Lumen), the heart (Heart), the kidneys (Kidneys), the liver (Liver), the lungs (Lungs), the bone marrow (Marrow), the muscles (Muscle), the pancreas (Pancreas), the sexual organs (Sexual_Organs), the skin (Skin), the spleen (Spleen), the stomach wall (Stomach), the stomach lumen (Stomach_Lumen), the thyroid (Thyroid), the organs/tissues included in the urinary tract (Urinary_Tract) and the venous blood (VenousBlood). Blood (arterial and venous) links the compartments together (black plain arrows in Fig. 1), but other transfers of contaminants between the compartments can occur (e.g. transfer in stomach and gut lumen, bile excretion) and are represented by black dotted arrows. The loading inputs via inhalation and ingestion are indicated by red arrows and the potential losses of contaminants (metabolism and excretion) by green arrows. The model structure is identical for man and woman.

The generic PBPK model yields to a set of ordinary differential equations that describe the ADME processes. The mathematical equations used to model the anatomical and physiological evolution of the body through lifetime are also integrated for the model parameters. The description of these processes is based on several publications [6, 15, 20]. In the following, the amounts are expressed in mg, the concentrations in mg/L, the volumes in L and the blood flows in L/min.

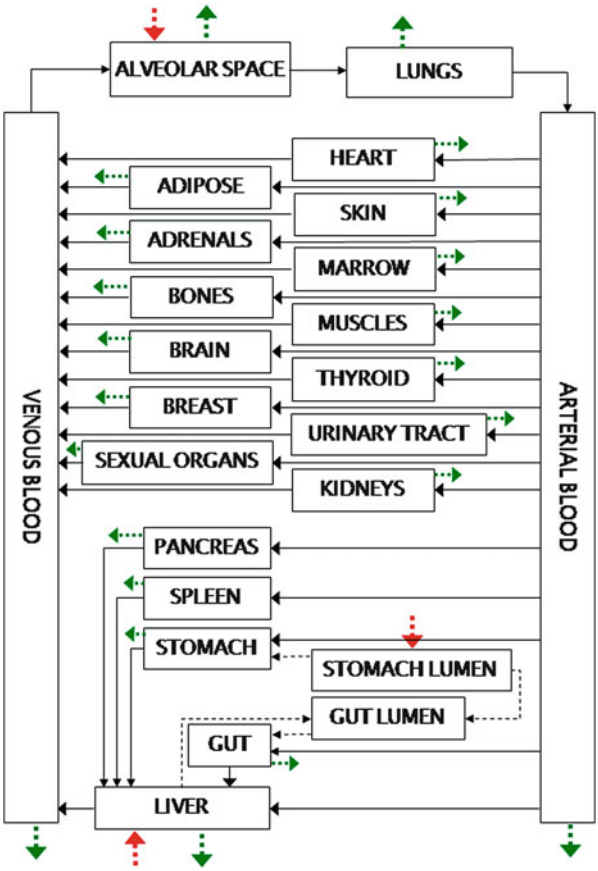

Fig. 1 The human PBPK model in MERLIN-Expo

2.1 Absorption

Two major routes of exposure for environmental contaminants are included in the PBPK model: the inhalation and the ingestion.

2.1.1 Inhalation

Gas exchanges were all assumed to take place in the alveoli at the end of the respiratory tree. We chose to model the gas exchanges in a compartment named alveolar space and to distinguish this from the lungs as an organ (i.e. with distribution, accumulation or elimination processes). In the PBPK model structure, the alveolar space is located between the venous blood and the lungs (Fig. 1). A simple model was selected to describe gas exchanges. A few assumptions were made, as done usually in PBPK models [4]: (1) a one-directional airflow was assumed in the

region of gas exchange (i.e. with air moving through the lungs with a constant flow rate equal to the alveolar ventilation rate), and (2) a rapid equilibrium is reached between the air and blood in the alveoli. The exchanges between air and blood were modelled as follows:

$$\frac{\mathrm{dAlveolarSpace}(t)}{\mathrm{dt}} = Q_C \times (C_{\mathrm{BloodVenous}}(t) - C_{\mathrm{Alveolar}}(t)) + Q_P \times C_{\mathrm{Inhaled}}(t) \times \mathrm{Abs}_{\mathrm{inhalation}} - Q_P \times \frac{C_{\mathrm{Alveolar}}(t)}{\mathrm{PC}_{\mathrm{Blood:Air}}} \quad (1)$$

where AlveolarSpace is the amount in the alveolar space (mg), Q_C is the cardiac output (total blood flow) (L/min), $C_{\mathrm{BloodVenous}}$ is the concentration in the venous blood (mg/L), C_{Alveolar} is the concentration in the alveolar space (mg/L), Q_P is the alveolar ventilation rate (L/min), C_{Inhaled} is the concentration of contaminant in inhaled air (mg/L), $\mathrm{Abs}_{\mathrm{Inhalation}}$ is the fraction of contaminant inhaled (dimensionless) and $\mathrm{PC}_{\mathrm{Blood:Air}}$ is the blood/air partition coefficient (dimensionless). In case of there is no inhalation and exhalation of a contaminant, the venous blood and alveolar space concentrations are similar.

The concentration of contaminants in the alveolar space (C_{Alveolar}) is calculated by dividing the amount of contaminant in the alveolar space over its volume (V_A):

$$C_{\mathrm{Alveolar}}(t) = \frac{\mathrm{AlveolarSpace}(t)}{V_A} \quad (2)$$

In Eq. (1), two compound-specific parameters were introduced: the fraction of contaminant absorbed via inhalation ($\mathrm{Abs}_{\mathrm{inhalation}}$) and the blood/air partition coefficient ($\mathrm{PC}_{\mathrm{BloodAir}}$). The fraction of contaminant absorbed via inhalation ($\mathrm{Abs}_{\mathrm{inhalation}}$) was defined to control the quantity of contaminant that is absorbed by inhalation. This fraction was introduced to take into account mechanisms that may not be well described for some contaminants between an intake and the subsequent concentrations in the body. The blood:air partition coefficient ($\mathrm{PC}_{\mathrm{BloodAir}}$) describes the uptake and the elimination of the contaminant via lungs and is defined as the ratio of the concentration of contaminant in blood over the concentration in air at equilibrium.

2.1.2 Ingestion

Oral absorption refers to the transport of molecules across the enterocytes lining the gastrointestinal tract into the venous capillaries along the gut wall. The majority of compound absorption occurs in the small intestine because of its large absorptive surface area and high blood perfusion rate. Compounds that are not completely absorbed from the small intestine can still be absorbed in the large intestine despite a small absorptive surface area. In our PBPK model, two models were defined for

ingestion: a two-compartmental model for the gastrointestinal tract and a direct input in the liver. The first model consists in separating the gastrointestinal tract into the stomach and the guts. Each of these was divided into two compartments: the lumen (in which the contaminant enters) and the wall (linked to the systemic circulation). The compound first enters in the stomach lumen and either can be absorbed and passed in the stomach wall or can be transferred to the gut lumen. In the gut lumen, the compound can be absorbed (and reach the systemic circulation via the gut wall) or be excreted in the faeces. The exchanges between the lumen and the wall are modelled by a first-order reaction dependent of the concentration of contaminant in the stomach or gut lumen. Alternatively, a direct input can be made in the liver. However, in that case local metabolism in the gut may not be correctly described, but this could be compensated using a fraction of contaminant absorbed lower than 1 (see Eq. (11)).

Differential Equations for Stomach

The stomach is composed by two compartments: the wall and the lumen. The ingested contaminant is introduced in the stomach lumen and can pass to either the stomach wall or the gut lumen. The stomach wall is perfused and then linked to the circulatory system. The equation for the stomach lumen is:

$$\frac{\mathrm{dStomachLumen}(t)}{dt} = \mathrm{Ingestion\_GIT} - \mathrm{Ka_{stomach}} \times \mathrm{StomachLumen}(t) - K_{\mathrm{stom2gut}} \times C_{\mathrm{StomachLumen}}(t) \quad (3)$$

where StomachLumen is the amount in the stomach lumen (mg), $C_{\mathrm{StomachLumen}}$ the concentration in the stomach lumen (mg/L), $\mathrm{Ka_{Stomach}}$ the absorption rate constant in the stomach (min^{-1}), K_{Stom2gut} the rate constant for the transfer to gut lumen (L/min) and Ingestion_GIT the intake of contaminant (mg/min). The first term of Eq. (3) corresponds to the ingestion, the second term to the absorption through the stomach and the last term to the transfer to the gut lumen. The differential equation for the amount in the stomach wall (Stomach) is:

$$\frac{\mathrm{dStomach}(t)}{dt} = \mathrm{Ka_{stomach}} \times \mathrm{StomachLumen}(t) + Q_{\mathrm{Stomach}} \times \left(C_{\mathrm{BloodArterial}}(t) - \frac{C_{\mathrm{Stomach}}(t)}{\mathrm{PC_{Stomach}}} \right) - \mathrm{RoM_{Stomach}}(t) - \mathrm{RoE_{Stomach}}(t) \quad (4)$$

with StomachLumen the amount in the stomach lumen (mg), $\mathrm{Ka_{Stomach}}$ the absorption rate constant in the stomach (min^{-1}), Q_{Stomach} the blood flow entering the stomach wall (L/min), $C_{\mathrm{BloodArterial}}$ the concentration in the arterial blood (mg/L), C_{Stomach} the concentration in the stomach wall (mg/L), $\mathrm{PC_{Stomach}}$ the stomach:blood partition coefficient (dimensionless) and the rates of metabolism and excretion

$\mathrm{RoM}_{\mathrm{Stomach}}$ and $\mathrm{RoE}_{\mathrm{Stomach}}$ in mg/min (see below for the description of metabolism and excretion processes).

Differential Equations for Gut

As stomach, the gut is described by two compartments: the wall and the lumen. The ingested contaminant is introduced in the stomach lumen and can reach the gut lumen. In the lumen, the contaminant can be excreted via faeces or absorbed in the gut wall to reach the blood circulation. The gut wall is perfused and then linked to the circulatory system. The equation for the amount in the gut lumen (GutLumen) is:

$$\frac{\mathrm{dGutLumen}(t)}{dt} = K_{\mathrm{stom2gut}} \times C_{\mathrm{StomachLumen}}(t) + \mathrm{Ke}_{\mathrm{bile}} \times \mathrm{Liver}(t) - \mathrm{K}_{\mathrm{gut2faeces}} \times \mathrm{C}_{\mathrm{GutLumen}}(t) - \mathrm{Ka}_{\mathrm{Gut}} \times \mathrm{GutLumen}(t) \quad (5)$$

The first term of Eq. (5) corresponds to the input from the stomach lumen, the second term to excretion via bile from the liver, the third term to the excretion in the faeces and the last term to the absorption in the gut wall. The notations used in Eq. (5) are GutLumen is the amount in the gut lumen (mg) and Liver is the amount in the liver (mg). C_{GutLumen} is the concentration in the gut lumen (mg/L), $C_{\mathrm{StomachLumen}}$ is the concentration in the stomach lumen (mg/L), K_{stom2gut} is the rate constant for the transfer from stomach lumen to gut lumen (L/min), $K_{\mathrm{gut2faeces}}$ is the rate constant for the excretion in faeces (L/min), $\mathrm{Ke}_{\mathrm{bile}}$ is the biliary excretion rate (min^{-1}) and $\mathrm{Ka}_{\mathrm{Gut}}$ is the absorption rate constant in the gut wall (min^{-1}). The equation for the amount in the gut wall (Gut) is:

$$\frac{\mathrm{dGut}(t)}{dt} = \mathrm{Ka}_{\mathrm{gut}} \times \mathrm{GutLumen}(t) + Q_{\mathrm{Gut}} \times \left(C_{\mathrm{BloodArterial}}(t) - \frac{C_{\mathrm{Gut}}(t)}{\mathrm{PC}_{\mathrm{Gut}}} \right) - \mathrm{RoM}_{\mathrm{Gut}}(t) - \mathrm{RoE}_{\mathrm{Gut}}(t) \quad (6)$$

with GutLumen the amount in the gut lumen (mg), $\mathrm{Ka}_{\mathrm{Gut}}$ the absorption rate constant in the gut (min^{-1}), Q_{Gut} the blood flow entering the gut wall (L/min), $C_{\mathrm{BloodArterial}}$ the concentration in the arterial blood (mg/L), C_{Gut} the concentration in the gut wall (mg/L), $\mathrm{PC}_{\mathrm{Gut}}$ the gut/blood partition coefficient (dimensionless) and the rates of metabolism and excretion $\mathrm{RoM}_{\mathrm{Gut}}$ and $\mathrm{RoE}_{\mathrm{Gut}}$ in mg/min (see below for the description of metabolism and excretion processes).

2.2 Distribution in Compartments

Distribution refers to the reversible partitioning of a compound into the various tissues of the body from the systemic circulation. Each organ or tissue can receive different doses of the compound and the compound can remain in the organs or

tissues for a varying amount of time. The compound can be moved from the blood to the tissue until the equilibrium is established. The distribution in the tissues or organs depends on factors related to the physiology of the individual (e.g. vascular permeability, regional blood flow, cardiac output and perfusion rate of the tissue) and factors related to the compound (e.g. molecular size, lipid solubility, pKa, affinity to bind tissue and plasma proteins). Distribution occurs rapidly into highly perfused tissues such as the liver, heart and kidney. Other tissues with a slower rate of distribution (such as muscle or adipose tissues) will continue to absorb the compound from the plasma over a longer period.

In our model, the blood flow is assumed to be unidirectional, constant and non-pulsatile, and the compound is assumed to distribute evenly and homogeneously throughout the compartment volume. Moreover the compound distribution into all compartments is assumed to be limited by perfusion, i.e. the tissue membranes present no barrier to diffusion. Blood flow is then the limiting factor to distribution in the various organs or tissues. The extent of tissue distribution is determined by a partition coefficient that is a measure of the compound's affinity to the tissue.

2.2.1 Standard Differential Equations

Most of the compartments share the same differential equation to describe the behaviour of the compound. For all the compartments except the compartments involved in the absorption of contaminants (i.e. the gut and stomach lumen for ingestion and the alveolar space, the arterial and venous blood for inhalation) and the liver that has two blood supplies, the amount in the compartment named Cpt is given by:

$$\frac{\mathrm{dCpt}(t)}{dt} = Q_{\mathrm{Cpt}} \times \left(C_{\mathrm{BloodArterial}}(t) - \frac{\mathrm{C}_{\mathrm{Cpt}}(t)}{\mathrm{PC}_{\mathrm{Cpt}}} \right) - \mathrm{RoM}_{\mathrm{Cpt}}(t) - \mathrm{RoE}_{\mathrm{Cpt}}(t) \qquad (7)$$

where Cpt is the amount in the compartment Cpt (mg), $C_{\mathrm{BloodArterial}}$ the concentration in the arterial blood (mg/L), C_{Cpt} the concentration in the compartment Cpt (mg/L), Q_{Cpt} the blood flow entering in the compartment Cpt (L/min), $\mathrm{PC}_{\mathrm{Cpt}}$ the Cpt:blood partition coefficient (dimensionless) and the rates of metabolism and excretion $\mathrm{RoM}_{\mathrm{Cpt}}$ and $\mathrm{RoE}_{\mathrm{Cpt}}$ in mg/min (see below for the description of metabolism and excretion processes). The transfer of contaminants from blood to the tissues is modelled using an equilibrium factor, the partition coefficient ($\mathrm{PC}_{\mathrm{Cpt}}$) that is defined as the ratio of the concentration in a tissue to the concentration in blood. In Eq. (7), the concentration of contaminant leaving the compartment is given by the concentration in the compartment over the partition coefficient. In the cases where the chemical binds to red blood cells (e.g. for lead), Eq. (7) becomes [21]:

$$\frac{\mathrm{dCpt}(t)}{dt} = Q_{\mathrm{Cpt}} \times \left(C_{\mathrm{BloodArterial}}(t) - \frac{\mathrm{C_{Cpt}}(t)}{\mathrm{PC_{Cpt}}} \times \left(0.55 + 0.45 \times \left(1 + \frac{\mathrm{BIND}}{\mathrm{KBIND} + \frac{C_{\mathrm{Cpt}}(t)}{\mathrm{PC_{Cpt}}}} \right) \right) \right) - \mathrm{RoM_{Cpt}}(t) - \mathrm{RoE_{Cpt}}(t) \quad (8)$$

where BIND (in mg/L) is the maximum capacity of erythrocytes to bind the contaminant, and KBIND (in mg/L) is the half-saturation constant.

2.2.2 Differential Equation for Lungs

Because the lungs receive the total blood flow, Eq. (7) should be adapted to:

$$\frac{\mathrm{dLungs}(v)}{dt} = Q_C \times \left(C_{\mathrm{Alveolar}}(t) - \frac{C_{\mathrm{Lungs}}(t)}{\mathrm{PC_{Lungs}}} \right) - \mathrm{RoM_{Lungs}}(t) - \mathrm{RoE_{Lungs}}(t) \quad (9)$$

where Lungs is the amount in the lungs (mg), Q_C the cardiac output (total blood flow) (L/min), C_{Alveolar} the concentration in the alveolar space (mg/L), C_{Lungs} the concentration in the lungs (mg/L), $\mathrm{PC_{Lungs}}$ the lung:blood partition coefficient (dimensionless) and the rates of metabolism and excretion $\mathrm{RoM_{Lungs}}$ and $\mathrm{RoE_{Lungs}}$ (in mg/min).

2.2.3 Differential Equation for Liver

The liver has two blood supplies, the hepatic portal vein and the hepatic artery. The hepatic artery carries blood from the aorta and the portal vein from the gastrointestinal tract, the spleen and the pancreas. The differential equation for the amount in liver is:

$$\begin{aligned}\frac{\mathrm{dLiver}(t)}{dt} = {} & Q_{\mathrm{Liver}} \times C_{\mathrm{BloodArterial}}(t) + Q_{\mathrm{Stomach}} \times \frac{C_{\mathrm{Stomach}}(t)}{\mathrm{PC}_{\mathrm{Stomach}}} \\ & + Q_{\mathrm{Spleen}} \times \frac{C_{\mathrm{Spleen}}(t)}{\mathrm{PC}_{\mathrm{Spleen}}} + Q_{\mathrm{Pancreas}} \times \frac{C_{\mathrm{Pancreas}}(t)}{\mathrm{PC}_{\mathrm{Pancreas}}} + Q_{\mathrm{Gut}} \times \frac{C_{\mathrm{Gut}}(t)}{\mathrm{PC}_{\mathrm{Gut}}} \\ & - \left(Q_{\mathrm{Liver}} + \mathrm{v}_{\mathrm{Stomach}} + Q_{\mathrm{Spleen}} + Q_{\mathrm{Pancreas}} + Q_{\mathrm{Gut}}\right) \times \frac{C_{\mathrm{Liver}}(t)}{\mathrm{PC}_{\mathrm{Liver}}} \\ & - \mathrm{RoM}_{\mathrm{Liver}}(t) - \mathrm{RoE}_{\mathrm{Liver}}(t) - \mathrm{Ke}_{\mathrm{Bile}} \times \mathrm{Liver}(t) + \mathrm{Ingestion\_skipGIT}\end{aligned} \tag{10}$$

The notations used are: Liver is the amount in the liver (mg), $C_{\mathrm{BloodArterial}}$ the concentration in the arterial blood (mg/L), C_{Cpt} the concentration in the compartment Cpt (mg/L), Q_{Cpt} the blood flow entering in the compartment Cpt (L/min), $\mathrm{PC}_{\mathrm{Cpt}}$ the Cpt:blood partition coefficient (dimensionless), $\mathrm{RoM}_{\mathrm{Liver}}$ a transfer describing the metabolism in the compartment (mg/min), $\mathrm{RoE}_{\mathrm{Liver}}$ a transfer describing the excretion in the compartment (mg/min), $\mathrm{Ke}_{\mathrm{bile}}$ is the biliary excretion rate (min^{-1}) and Ingestion_skipGIT an intake of contaminant as a direct input in the liver (mg/min).

The first terms of Eq. (10) correspond to the entry of contaminant in the liver from the arterial blood, the stomach, the spleen, the pancreas and the gut. Last terms correspond to the amount of contaminant that leaves the liver to reach the venous blood. In the liver the contaminant can be metabolised ($\mathrm{RoM}_{\mathrm{Liver}}$), excreted ($\mathrm{RoE}_{\mathrm{Liver}}$) or excreted via bile in the gut lumen. An intake is also modelled directly in the liver in order to skip the description of the absorption through the gastrointestinal tract (Ingestion_skipGIT).

The intake Ingestion_skipGIT is null if the ingestion via the gastrointestinal tract is considered; otherwise it is given by:

$$\mathrm{Ingestion\_skipGIT} = \mathrm{Abs}_{\mathrm{ingestion}} \times Q_{\mathrm{ing,rate}}(t) \tag{11}$$

where $\mathrm{Abs}_{\mathrm{ingestion}}$ is the fraction of contaminant absorbed via ingestion (dimensionless) and $Q_{\mathrm{ing,rate}}$ is the rate at which the contaminant is ingested (mg/min). The fraction of contaminant absorbed via ingestion ($\mathrm{Abs}_{\mathrm{ingestion}}$) was defined to control the quantity of contaminant that is absorbed by ingestion (via the gastrointestinal tract or modelled as a direct input in the liver). This fraction was introduced to take into account mechanisms that may not be well described for some contaminants between an intake and the subsequent concentrations in the body.

2.2.4 Differential Equations for Blood

The blood is represented in the model by two compartments: the arterial and venous blood. Arterial and venous blood are not modelled as compartments for tissues since the whole blood flow passes through these compartments: the arterial blood is

distributed into all tissue compartments, and the venous blood collects blood at the exit of most of the tissue compartments. The equation for arterial blood is then:

$$\frac{d_{\text{ArterialBlood}}(t)}{dt} = Q_C \times \left(\frac{C_{\text{Lungs}}(t)}{\text{PC}_{\text{Lungs}}} - C_{\text{ArterialBlood}}(t)\right) - \text{RoM}_{\text{ArterialBlood}}(t) - \text{RoE}_{\text{ArterialBlood}}(t) \quad (12)$$

where ArterialBlood is the amount in the arterial blood (mg), $C_{\text{ArterialBlood}}$ the concentration in the arterial blood (mg/L), C_{Lungs} the concentration in the lungs (mg/L), Q_C the cardiac output (total blood flow) (L/min), PC_{Lungs} the lung:blood partition coefficient (dimensionless) and the rates of metabolism and excretion $\text{RoM}_{\text{ArterialBlood}}$ and $\text{RoE}_{\text{ArterialBlood}}$ (in mg/min).

The equation for venous blood is:

$$\frac{d_{\text{VenousBlood}}(t)}{dt} = \sum_{\text{Cpt}} Q_{\text{Cpt}} \times \frac{C_{\text{Cpt}}(t)}{\text{PC}_{\text{Cpt}}} + \left(Q_{\text{Liver}} + Q_{\text{Gut}} + Q_{\text{Pancreas}} + Q_{\text{Spleen}} + Q_{\text{Stomach}}\right) \times \frac{\text{C}_{\text{Liver}}(t)}{\text{PC}_{\text{Liver}}} - Q_C \times C_{\text{VenousBlood}}(t) - \text{RoM}_{\text{VenousBlood}}(t) - \text{RoE}_{\text{VenousBlood}}(t) \quad (13)$$

where Cpt designates the compartments adipose, adrenal, bone, brain, breast, heart, kidney, marrow, muscle, sexual organs, skin, thyroid and urinary tract (in mg), VenousBlood the amount in the venous blood (mg), $C_{\text{BloodVenous}}$ the concentration in the venous blood (mg/L), C_{Cpt} the concentration in the compartment Cpt (mg/L), Q_C the cardiac output (total blood flow) (L/min), Q_{Cpt} the blood flow entering in the compartment Cpt (L/min), PC_{Cpt} the Cpt:blood partition coefficient (dimensionless) and the rates of metabolism and excretion $\text{RoM}_{\text{VenousBlood}}$ and $\text{RoE}_{\text{VenousBlood}}$ (in mg/min).

2.3 Metabolism

Xenobiotic metabolism is the irreversible transformation of a parent compound into metabolites by enzymatic reactions. Nearly all metabolic transformations result in more polar products than the parent compound to facilitate the removal from the organism (excretion in bile or urine). Metabolism reactions are generally grouped into two phases. Phase I metabolism includes oxidation, reduction, hydrolysis and hydration reactions. Phase II reactions use an endogenous compound, such as glucuronic acid, glutathione or sulphate, for conjugation to the compound or its phase I-derived metabolite. The liver is the major site of metabolism for most compounds although metabolism can take place in many organs/tissues (gut, lungs,

kidneys, etc.). In our PBPK model, metabolism can occur in all compartments except in the gut and stomach lumen and in the alveolar space. Two equations are proposed to model metabolism either as a saturable (Michaelis–Menten equation) or a linear process (a first-order reaction). The linear model assumes that the rate of metabolism is proportional to the rate of change of the concentration of the contaminant in the organ. The saturable Michaelis–Menten reaction implies that the reaction is essentially first order at low concentrations of the compound, and it approaches zero order after a certain high concentration. The rate of metabolism in the compartment Cpt is given by the sum of these two equations:

$$\begin{aligned} \mathrm{RoM}_{\mathrm{Cpt}}(t) &= \mathrm{CL}_{\mathrm{Cpt}} \times \mathrm{ContentMainCYP} \times C_{\mathrm{Cpt}}(t) \\ &+ \frac{V_{\max_{\mathrm{Cpt}}} \times \mathrm{ContentMainCYP} \times C_{\mathrm{Cpt}}(t)}{K_{m_{\mathrm{Cpt}}} + C_{\mathrm{Cpt}}(t)} \end{aligned} \tag{14}$$

where C_{Cpt} is the concentration in the compartment Cpt (mg/L), $\mathrm{CL}_{\mathrm{Cpt}}$ the clearance of the first-order metabolic reaction (L/min), ContentMainCYP the activity of the main cytochrome P450 involved in the metabolic reaction as a function of the age of the individual (dimensionless), $V_{\max_{\mathrm{CPT}}}$ the maximum velocity of the metabolic reaction in the compartment Cpt (mg/min) and $K_{m_{\mathrm{CPT}}}$ the Michaelis constant of the metabolic reaction in the compartment Cpt (mg/L).

2.3.1 First-Order Reaction

A metabolic clearance is the rate at which a substance is removed from an organ or the body by metabolism. The clearance is specific to each contaminant and species. The clearance (CL in L/min) was assumed to depend on the body weight (BDW) and was calculated as the product of the clearance per kg of BDW ($\mathrm{CL}_{\mathrm{perBDW}}$ in L/min/kg of BDW) by the body weight (BDW).

2.3.2 Michaelis–Menten Reaction

The maximum velocity ($V_{\max}$ in mg/min) and the Michaelis constant (K_m in mg/L) are the parameters of the Michaelis–Menten equation (second term of Eq. (14)). $V_{\max}$ represents the maximum rate achieved by the reaction at maximum (saturating) substrate concentrations and is expressed as amount of product (i.e. metabolites) formed per time (here mg/min). K_m is defined as the substrate concentration at which the reaction rate is half of $V_{\max}$ and is an inverse measure of the affinity of the contaminant for the enzymes (a small K_m indicates a high affinity). In the PBPK model, metabolism was assumed to depend on age and body weight. Then the maximum velocity of the metabolic reaction per kg of body weight ($V_{\max_{\mathrm{perBDW}}}$ in mg/min/kg of BDW) was introduced and used to compute the maximum velocity ($V_{\max}$) together with the body weight (BDW).

The parameters V_{max} and K_m are specific to contaminants and species. Several methods are available to determine them: in vitro experiments using tissues of the species of interest and in vivo experiments or QSAR models. Several in vitro experiments can be used to estimate V_{max} and will provide estimates with different units. The most widely used in vitro experiments for determining V_{max} are cells, subcellular fractions of tissues, tissues slices or recombinant enzymes [22]. For each type of experiments, the extrapolation of the V_{max} estimated in vitro into an in vivo V_{max} value is different. In experiments using microsomes, the in vitro V_{max} values are usually expressed per amount of microsomal proteins. For a tissue, the in vivo V_{max} value is given by:

$$\begin{aligned} V_{max_{vivo}}(\text{nmol/min/kg of BDW}) = {} & V_{max_{micro}}(\text{nmol/min/mg MSP}) \\ & \times \text{MPPGT}(\text{mg MSP/g tissue}) \\ & \times V_{Tissue}(\text{g})/\text{BDW}(\text{kg}) \end{aligned} \tag{15}$$

where $V_{max_{micro}}$ is the maximum velocity estimated using microsomes, MPPGT the content of microsomal protein (MSP) per gram of tissue, V_{Tissue} the volume of the tissue and BDW the body weight. The contents of microsomal proteins in the metabolising tissues can be found in the literature [23]. In case of experiments with hepatocytes, the in vivo V_{max} will be obtained as follows:

$$\begin{aligned} V_{max_{vivo}}(\text{nmol/min/kg of BDW}) = {} & V_{max_{hep}}(\text{nmol/min/\# of cells}) \\ & \times \text{HPGL}(\text{\# of cells/g liver}) \\ & \times V_{Liver}(\text{g})/\text{BDW}(\text{kg}) \end{aligned} \tag{16}$$

where $V_{max_{hep}}$ is the maximum velocity estimated in vitro with hepatocytes, HPGL is the number of hepatocytes per gram of liver, V_{Liver} is the volume of the liver and BDW is the body weight. The number of cells in the metabolising tissues can be found in the literature. For the liver, a value of 99×10^6 cells/g of liver is commonly used (95% CI: 74–131 $\times 10^6$ cells/g of liver) [23]. Usually it will also be necessary to divide by the molar mass to convert the $V_{max_{perBDW}}$ value in mg (and not in mol).

Unlike V_{max}, the units of K_m for in vitro or in vivo experiments are the same (mol/L or mg/L) so scaling is not required (except the molar mass if the in vitro K_m is given in mol/L).

2.4 Excretion

Excretion of a compound refers to the removal of the compound and its metabolites from the body. For most compounds, excretion occurs predominantly *via* the kidneys in urine. Some compounds and their metabolites can also be extensively excreted in the bile and often undergo some degree of reabsorption along the intestine (enterohepatic circulation). Excretion can also happen via saliva, sweat,

lungs and breast milk for nursing mothers. In our PBPK model, excretion can occur in all organs/compartments except in the gut and stomach lumen and in the alveolar space, and is described by a first-order reaction. This model assumes that the rate of excretion is proportional to the rate of change of the amount of the contaminant in the organ. Contaminants excreted by bile enter in the gut lumen and can be reabsorbed. The rate of excretion (in mg/min) is given by:

$$\mathrm{RoE}(t) = \mathrm{Kex}_{\mathrm{Cpt}} \times \mathrm{Cpt}(t) \tag{17}$$

where Cpt is the amount in the compartment Cpt (mg) and $\mathrm{Kex}_{\mathrm{Cpt}}$ the excretion rate in the compartment Cpt (min^{-1}). In kidneys, the excretion is assumed to occur via urine. As for metabolism, the excretion rate $\mathrm{Kex}_{\mathrm{Cpt}}$ is age and body weight-dependent. A parameter corresponding to the excretion rate per kg of body weight ($\mathrm{Kex}_{\mathrm{perBDW}}$) was introduced to compute $\mathrm{Kex}_{\mathrm{Cpt}}$.

Two other excretion routes were modelled: the biliary excretion and the excretion in faeces. The biliary excretion is the transfer of contaminants from the liver to the bile through the hepatocytes and is given by:

$$\frac{\mathrm{dBile}(t)}{dt} = \mathrm{Ke}_{\mathrm{Bile}} \times \mathrm{Liver}(t) \tag{18}$$

with $\mathrm{Ke}_{\mathrm{bile}}$ the biliary excretion rate (min^{-1}) and Liver the amount in the liver (mg). The excretion in the faeces (mg) takes place in the gut lumen and is given by:

$$\frac{\mathrm{dFaeces}(t)}{dt} = K_{\mathrm{gut2faeces}} \times C_{\mathrm{GutLumen}}(t) \tag{19}$$

where C_{GutLumen} is the concentration in the gut lumen (mg/L) and $K_{\mathrm{gut2faeces}}$ the rate constant for the excretion in faeces (L/min).

2.5 Anatomy and Physiology of the Individual

The anatomy and physiology of an individual evolves from birth to elderly. Such evolutions can be integrated in PBPK models using mathematical relationships as function of age for the PBPK parameters. Four types of equations were used to describe the changes related to age: the Preece–Baines model, the von Bertalanffy equation, a sigmoid function and a polynomial function. The Preece–Baines model is a family of curves that conforms to the shape of the human growth curve. It combines two different exponential growth phases to represent the gradual growth of infants followed by a faster growth of adolescents, but becoming rapidly asymptotic. In the von Bertalanffy model, growth is the fastest at the outset, gradually diminishes and finally reaches zero. In the sigmoid or logistic function, the initial stage of growth is approximately exponential, slows and stops (to reach

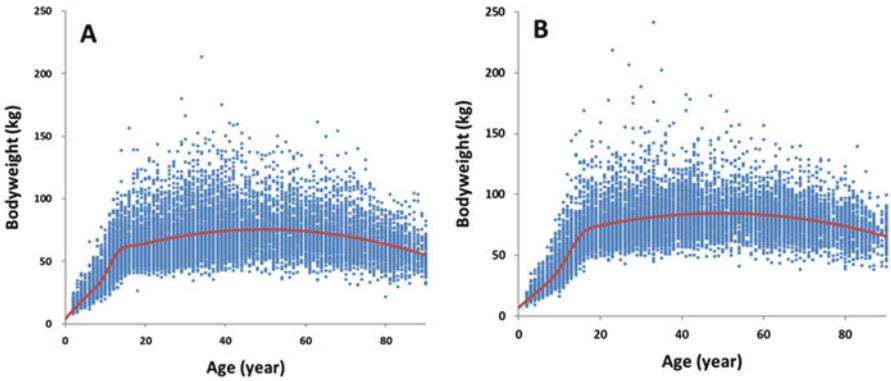

Fig. 2 Time evolution of the body weight in women (**a**) and men (**b**). The *filled circles* are the data and the *curves* the model's prediction

saturation). If none of the von Bertalanffy or the sigmoid models fitted the data correctly, a polynomial function was used. For few parameters, it has not been possible to define a single function for the lifetime, so several functions were used on different time ranges.

2.5.1 Body Weight and Volumes

The body weight model is a combination of the Preece–Baines model during childhood and adolescence and then a polynomial function of order 2 that describes the modifications in adulthood (increase of the adipose tissue volume and skeletal muscle atrophy in elderly people). Ageing atrophy of the muscle begins around 24 years old and thereafter accelerates. The adipose volume starts to increase around age 20. The body weight model was calibrated with the data obtained in the NHANES [24] study by minimising the least squared error (Fig. 2) and is given by for men:

$$\mathrm{BDW}_{\mathrm{Total}} = \begin{cases} 75.2066 - \dfrac{2.0 \times (75.2066 - 55.9612)}{\left(\mathrm{e}^{(0.5524 \times (\mathrm{Age} - 13.0920))} + \mathrm{e}^{(0.0439 \times (\mathrm{Age} - 13.0920))}\right)} & \text{if Age} < 18.5 \\ -0.0116 \times \mathrm{Age}^2 + 1.1510 \times \mathrm{Age} + 56.0646 & \text{if Age} \geq 18.5 \end{cases} \tag{20}$$

and for women:

Table 1 Equations for the relative organ weights (scW) for men

Compartment	Equation	
Adrenals	$2.0 \times 10^{-4} + (0.00171 - 2.0 \times 10^{-4}) \times \exp(-2.02 \times \text{Age})$	
Blood	$-0.0273 \times \text{Age} + 0.0771$ $0.0761 + (0.0289 - 0.0761) \times \exp(-0.5923 \times \text{Age})$	Age <1 Age ≥ 1
Blood arterial	$0.25 \times$ scW [Blood]	
Blood venous	$0.75 \times$ scW [Blood]	
Bones	$0.07492 + (0.05283 - 0.07492) \times \exp(-0.13317 \times \text{Age})$	
Bones NP	$0.0938 - (0.07492 + (0.05283 - 0.07492) \times \exp(-0.13317 \times \text{Age}))$	
Brain	$(1.45 + (0.353 - 1.45) \times \exp(-0.44 \times \text{Age}))/\text{BDW}_{\text{NoVarAdult}}$	
Breast	$0.000342/(1.0 + \exp(-1.42 \times \text{Age} + 20.1))$	
Gut	$-0.000103 \times \text{Age}^2 + 0.00154 \times \text{Age} + 0.0128$ 0.014	Age <14.1 Age ≥ 14.1
Gut lumen	$0.0089 + (0.0276 - 0.0089) \times \exp(-0.574 \times \text{Age})$	
Heart	0.0045	
Kidneys	$0.0042 + (0.00767 - 0.0042) \times \exp(-0.206 \times \text{Age})$	
Liver	$0.0247 + (0.0409 - 0.0247) \times \exp(-0.218 \times \text{Age})$	
Lungs	0.0068	
Marrow	$0.05 + (0.0138 - 0.05) \times \exp(-0.112 \times \text{Age})$	
Muscle	$0.3973 + (0.201 - 0.3973) \times \exp(-0.141 \times \text{Age})$ $(0.3973 + (0.201 - 0.3973) \times \exp(-0.141 \times \text{Age})) \times (-0.000126 \times \text{Age}^2 + 0.00613 \times \text{Age} + 0.926)$	Age <25.9 Age ≥ 25.9
Pancreas	0.00192	
Sexual organs	$-1.52 \times 10^{-7} \times \text{Age}^3 + 9.33 \times 10^{-6} \times \text{Age}^2 - 1.12 \times 10^{-4} \times \text{Age} + 4.80 \times 10^{-4}$ 8.0×10^{-4}	Age <20.4 Age ≥ 20.4
Skin	$-1.17 \times 10^{-5} \times \text{Age}^3 + 5.41 \times 10^{-4} \times \text{Age}^2 - 0.0062 \times \text{Age} + 0.046$ 0.0452	Age <20.0 Age ≥ 20.0
Spleen	0.0021	
Stomach	0.0021	
Stomach lumen	$0.0034 + (0.0105 - 0.0034) \times \exp(-0.522 \times \text{Age})$	
Thyroid	0.000274	
Urinary tract	0.00104	

Table 2 Equations for the relative organ weights (scW) for women

Compartment	Equation	
Adrenals	$2.2 \times 10^{-4} + (0.00171 - 2.2 \times 10^{-4}) \times \exp(-2.02 \times \text{Age})$	
Blood	$-0.0273 \times \text{Age} + 0.0771$ $3.28 \times 10^{-5} \times \text{Age}^3 - 1.21 \times 10^{-3} \times \text{Age}^2 + 1.24 \times 10^{-2} \times \text{Age} + 0.039$ 0.065	Age <1.0 Age ≤14.0 Age >20.0
Blood arterial	0.25 × scW [Blood]	
Blood venous	0.75 × scW [Blood]	
Bones	$0.0679 + (0.0487 - 0.0679) \times \exp(-0.7433 \times \text{Age})$	
Bones NP	$0.085 - (0.0679 + (0.0487 - 0.0679) \times \exp(-0.7433 \times \text{Age}))$	
Brain	$0.0206 + (0.1091 - 0.0206) \times \exp(-0.1644 \times \text{Age})$	
Breast	$0.008329/(1.0 + \exp(-1.69 \times \text{Age} + 25.11))$	
Gut	$-7.421 \times 10^{-5} \times \text{Age}^2 + 1.276 \times 10^{-3} \times \text{Age} + 0.01230$ 0.016	Age <14.4 Age ≥14.4
Gut lumen	$0.0100 + (0.0294 - 0.0100) \times \exp(-0.932 \times \text{Age})$	
Heart	0.0042	
Kidneys	$0.0046 + (0.0071 - 0.0046) \times \exp(-0.221 \times \text{Age})$	
Liver	$0.0231 + (0.0362 - 0.0231) \times \exp(-0.153 \times \text{Age})$	
Lungs	0.0070	
Marrow	$0.045 + (0.0138 - 0.045) \times \exp(-0.136 \times \text{Age})$	
Muscle	$0.2917 + (0.207 - 0.2917) \times \exp(-0.339 \times \text{Age})$ $(0.2917 + (0.207 - 0.2917) \times \exp(-0.339 \times \text{Age})) \times (-0.000126 \times \text{Age}^2 + 0.00613 \times \text{Age} + 0.926)$	Age <25.9 Age ≥25.9
Pancreas	0.0020	
Sexual organs	$-0.0011 \times \text{Age} + 0.0013$ $2.64 \times 10^{-7} \times \text{Age}^3 - 1.79 \times 10^{-6} \times \text{Age}^2 - 5.65 \times 10^{-6} \times \text{Age} + 2.81 \times 10^{-4}$ 0.0015	Age ≤1 Age <20.4 Age ≥20.4
Skin	$-7.89 \times 10^{-6} \times \text{Age}^3 + 4.02 \times 10^{-4} \times \text{Age}^2 - 0.0052 \times \text{Age} + 0.046$ 0.0383	Age <20.0 Age ≥20.0
Spleen	0.0022	
Stomach	0.0023	
Stomach lumen	$0.0038 + (0.013 - 0.0038) \times \exp(-0.882 \times \text{Age})$	
Thyroid	0.00028	
Urinary tract	0.00097	

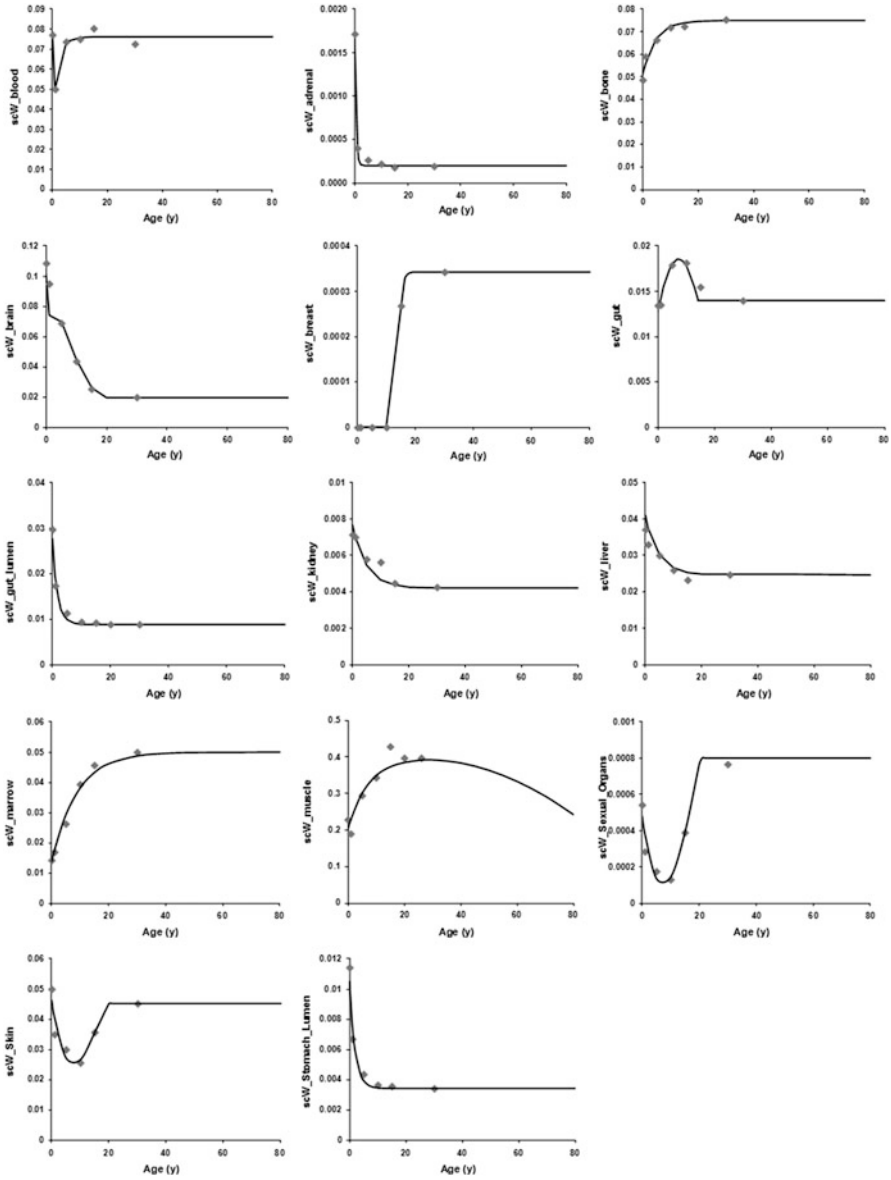

Fig. 3 Fit of the models for the relative weights of organs/tissues to experimental data in men [25–27]

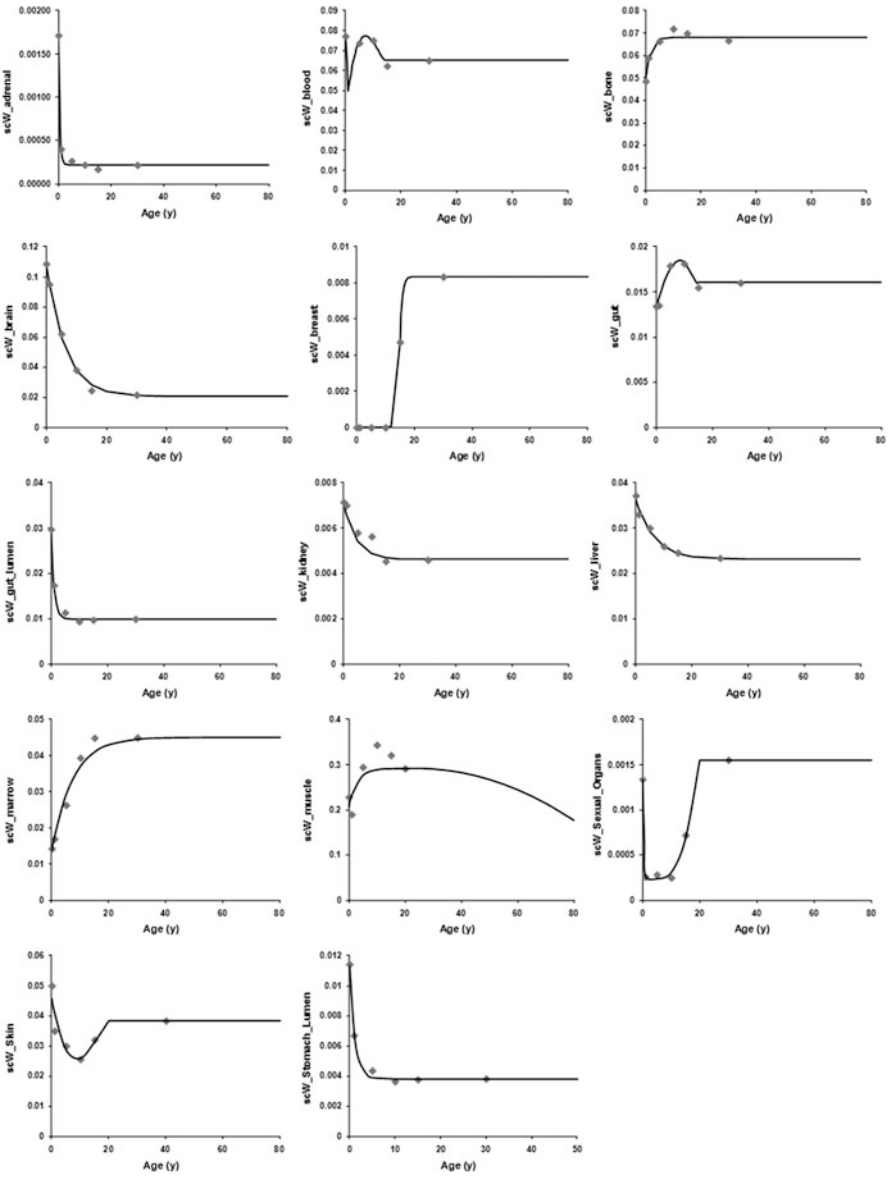

Fig. 4 Fit of the models for the relative weights of organs/tissues to experimental data in women [25–27]

$$\mathrm{BDW}_{\mathrm{Total}} = \begin{cases} 62.9549 - \dfrac{2.0 \times (62.9549 - 49.3657)}{\left(e^{(0.8404 \times (\mathrm{Age} - 11.5669))} + e^{(0.0671 \times (\mathrm{Age} - 11.566))}\right)} & \text{if Age} < 17.9 \\ -0.0126 \times \mathrm{Age}^2 + 1.2503 \times \mathrm{Age} + 44.4459 & \text{if Age} \geq 17.9 \end{cases} \quad (21)$$

The volumes of the compartments (V in L) evolve during lifetime and are calculated as a function of the relative weight of organs as a fraction of the body weight (scW), the body weight of the individual without the adipose volume variations ($\mathrm{BDW}_{\mathrm{NoVarAdult}}$, first terms in Eqs. (20) and (21)) and the organ density. The density of organs was assumed to be 1 kg/L for all organs/tissues except for adipose tissues (0.9 kg/L) and bones (2 kg/L). For all compartments (but adipose tissues), the volume of the compartments (V) was then given by:

$$V = \frac{\mathrm{scW} \times \mathrm{BDW}_{\mathrm{NoVarAdult}}}{\mathrm{DensityOrgan}} \quad (22)$$

For adipose tissues, the equation includes the increase of the weight in adulthood:

$$V_{\mathrm{Adipose}} = \begin{cases} \dfrac{\mathrm{scW} \times \mathrm{BDW}_{\mathrm{NoVarAdult}}}{\mathrm{DensityOrgan}} & \text{if Age} \leq 18.5 \\ \dfrac{(\mathrm{BDW}_{\mathrm{Total}} - \mathrm{BDW}_{\mathrm{NoVarAdult}}) + \mathrm{scW}_{\mathrm{Adipose}} \times \mathrm{BDW}_{\mathrm{NoVarAdult}}}{\mathrm{DensityOrgan}} & \text{if Age} > 18.5 \end{cases} \quad (23)$$

The relative weights (scW) can be constant over the lifetime or can evolve during the growth (e.g. the relative weight of the brain is greater in newborns than in adults). These latter are expressed as a function of age and are presented in Tables 1 and 2 for men and women, respectively. Values reported by several publications were used to derive the equations [25–27]. The adjustment of these equations to the experimental data is displayed in Figs. 3 and 4. To ensure that the sum of the compartment volumes does not exceed the body weight, the relative weight of adipose tissues was calculated as follows:

$$\mathrm{scW}_{\mathrm{Adipose}} = 0.96 - \sum_{i \notin \mathrm{Adipose}} \mathrm{scW}_i \quad (24)$$

4% of the body weight is not included as it corresponds to non-perfused tissues (non-perfused bones are a compartment of the PBPK model).

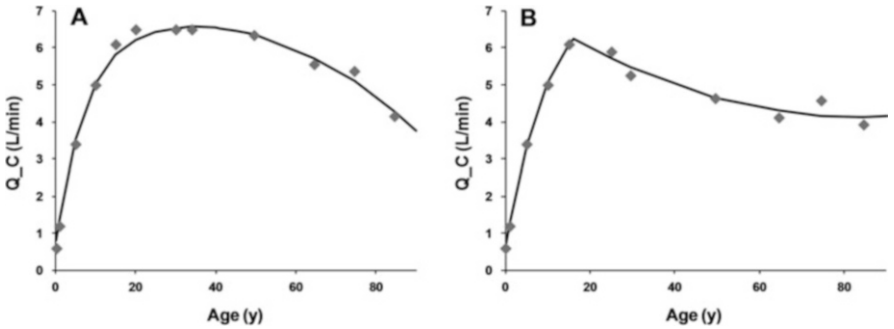

Fig. 5 Fit of the model for the cardiac output to experimental data for men (panel **a**) and for women (panel **b**) [26, 28]

Table 3 Relative blood flows (scQ_{adult}) in adult men and women [26]

Organ	Man	Woman	Organ	Man	Woman	Organ	Man	Woman
Adipose	0.052	0.087	Kidneys	0.196	0.175	Skin	0.052	0.051
Adrenals	0.003	0.003	Liver (arterial)	0.067	0.067	Spleen	0.031	0.031
Bones	0.021	0.021	Lungs	0.026	0.026	Stomach	0.010	0.010
Brain	0.124	0.124	Marrow	0.031	0.031	Thyroid	0.015	0.015
Breast	0.0002	0.004	Muscle	0.175	0.124	Urinary tract	0.001	0.001
Gut	0.144	0.165	Pancreas	0.010	0.010			
Heart	0.041	0.051	Sexual organs	0.001	0.004			

2.5.2 Blood Flows

The evolution of the cardiac output (in L/min) is described by a rapid increase from birth to adulthood and then by a decrease modelling the effects of ageing [26, 28]. The equation for men is:

$$Q_C = \begin{cases} 6.642 + (0.6 - 6.642) \times \exp(-0.1323 \times \text{Age}) & \text{if Age} < 33.4 \\ -8.95 \times 10^{-4} \times \text{Age}^2 + 0.0607 \times \text{Age} + 5.54 & \text{if Age} \geq 33.4 \end{cases} \quad (25)$$

and for women is:

$$Q_C = \begin{cases} 7.734 + (0.6 - 7.734) \times \exp(-0.09747 \times \text{Age}) & \text{if Age} < 16.0 \\ 4.73 \times 10^{-4} \times \text{Age}^2 - 0.0782 \times \text{Age} + 7.37 & \text{if Age} \geq 16.0 \end{cases} \quad (26)$$

The adjustment of these equations to the experimental data is displayed in Fig. 5. The relative blood flows are scaling factors used to compute the blood flow entering in an organ/tissue according to the cardiac output. The scaling factors for the tissular blood flow in adults were computed using the data collected by ICRP

[26]. The values reported here are not exactly the same as proposed in ICRP because the sum of the flows was not equal to 1. Therefore we multiplied the flows by a factor 1.03. Table 3 presents the numerical values for men and women, respectively.

Due to the lack of data on blood flow changes with age, regional blood flows were assumed to change proportionally to tissue volumes, as proposed by Clewell et al. [7]. The scaling factors for the blood flows (scQ) then depend on the ratio of the compartment volume at time t and over the volume during adulthood:

$$\mathrm{scQ} = \frac{\mathrm{scW}}{\mathrm{scW}_{\mathrm{adult}}} \times \mathrm{scQ}_{\mathrm{adult}} \tag{27}$$

A variable corresponding to the sum of the relative blood flows (sum_scQ) was created to ensure that the relative blood flows sum up to 1. The blood flows were given by:

$$Q = \frac{\mathrm{scQ}}{\mathrm{sum\_scQ}} \times Q_C \tag{28}$$

2.5.3 Respiratory Functions

In order to model the gas exchanges throughout the lifetime of the individual, parameters related to the inhalation or exhalation of contaminants were described using time functions. Values reported by the International Commission on Radiological Protection [26] for the activity 'sitting awake' were used to derive these functions. The tidal volume (V_{Tidal} in L) is the volume of air that moves in or out of the lungs in one normal breath. The tidal volume increases with age and is given by for men and women, respectively:

$$V_{\mathrm{Tidal}} = \begin{cases} 0.0337 \times \mathrm{Age} + 0.0407 & \text{if Age} < 21.0 \\ 0.75 & \text{if Age} \geq 21.0 \end{cases} \tag{29}$$

$$V_{\mathrm{Tidal}} = 0.46 + (0.0392 - 0.46) \times \exp(-0.127 \times \mathrm{Age}) \tag{30}$$

In the lungs, the dead space (V_{DS} in L) is the part of the tidal volume that does not participate in gas exchanges and was given for men and women respectively by:

$$\mathrm{V_{DS}} = \begin{cases} 0.0076 \times \mathrm{Age} + 0.0101 & \text{if Age} < 18.4 \\ 0.15 & \text{if Age} \geq 18.4 \end{cases} \tag{31}$$

$$V_{\mathrm{DS}} = \begin{cases} 0.0065 \times \mathrm{Age} + 0.0131 & \text{if Age} < 16.4 \\ 0.12 & \text{if Age} \geq 16.4 \end{cases} \tag{32}$$

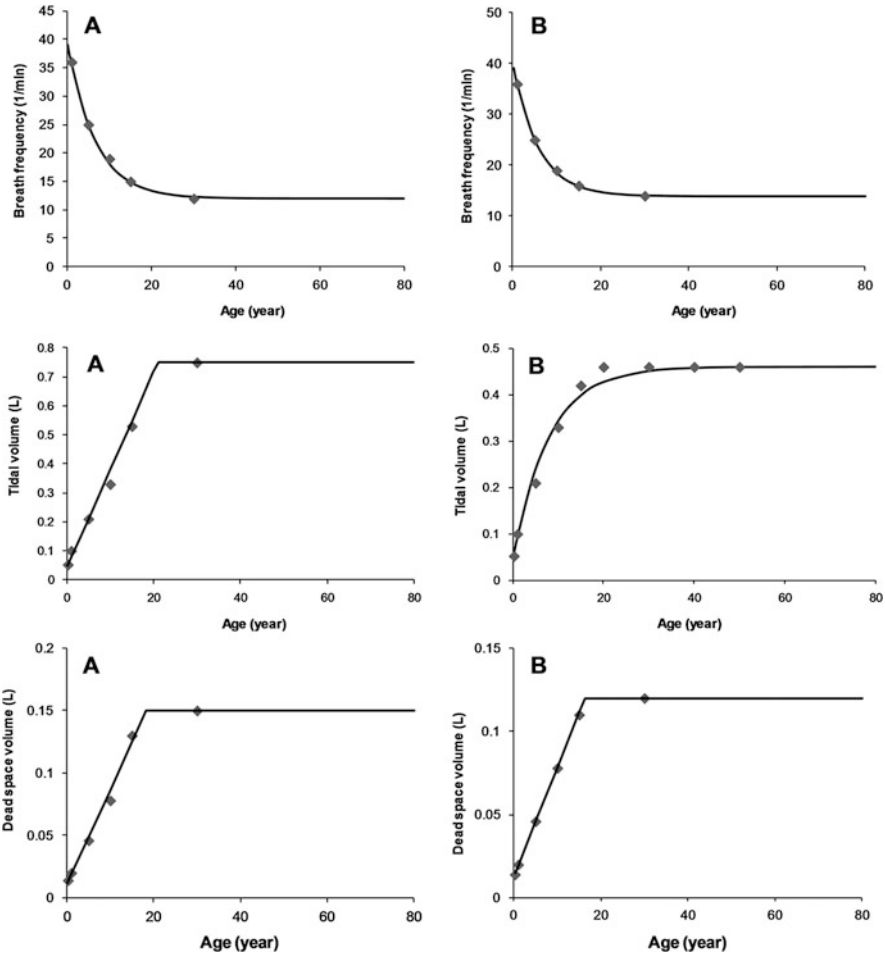

Fig. 6 Fit of the model for the breathing frequency, the tidal volume and the dead space volume to experimental data for men (panel **a**) and for women (panel **b**) [26]

The alveolar volume (V_A in L) is the part of the tidal volume that participates in gas exchanges. The alveolar volume is computed by subtracting the dead space volume to the tidal volume.

The breathing frequency or respiratory rate (BreathFreq) that is the number of breaths taken within a minute also decreases with age and is given by:

$$\text{BreathFreq} = \begin{cases} 12 + (39.94 - 12.00) \times \exp(-0.15 \times \text{Age}) & \text{for men} \\ 14 + (40.2 - 14.0) \times \exp(-0.173 \times \text{Age}) & \text{for women} \end{cases} \quad (33)$$

The adjustments of these equations for the respiratory parameters to the experimental data are displayed in Fig. 6. The breathing frequency is used to compute the

Table 4 Cytochrome P450 activity as a function of the activity in adults [29]

Individual cytochrome P450	Function
CYP1A2	$\min\left(1.0, \frac{\text{Age}^{1.41}}{1.13+\text{Age}^{1.41}}\right)$
CYP2B6	$\min\left(1.0, \frac{1.07\times\text{Age}}{1.31+\text{Age}}\right)$
CYP2C8	$\min\left(1.0, \frac{0.716\times\text{Age}}{0.02+\text{Age}} + 0.3\right)$
CYP2C9	$\min\left(1.0, \frac{0.821\times\text{Age}}{0.01+\text{Age}} + 0.21\right)$
CYP2D6	$\min\left(1.0, \frac{1.01\times\text{Age}}{0.101+\text{Age}} + 0.036\right)$
CYP2E1	$\min\left(1.0, \frac{4.22\times\text{Age}^{0.27}}{7.66+\text{Age}^{0.27}}\right)$
CYP3A	$\min\left(1.0, \frac{0.639\times\text{Age}}{2.36+\text{Age}} + 0.42\right)$
CYP3A4/CYP3A5	$\min\left(1.0, \frac{\text{Age}^{0.83}}{0.31+\text{Age}^{0.83}}\right)$
CYPC18/CYPC19	$\min\left(1.0, \frac{0.857\times\text{Age}}{0.99+\text{Age}} + 0.23\right)$
Others	1.0

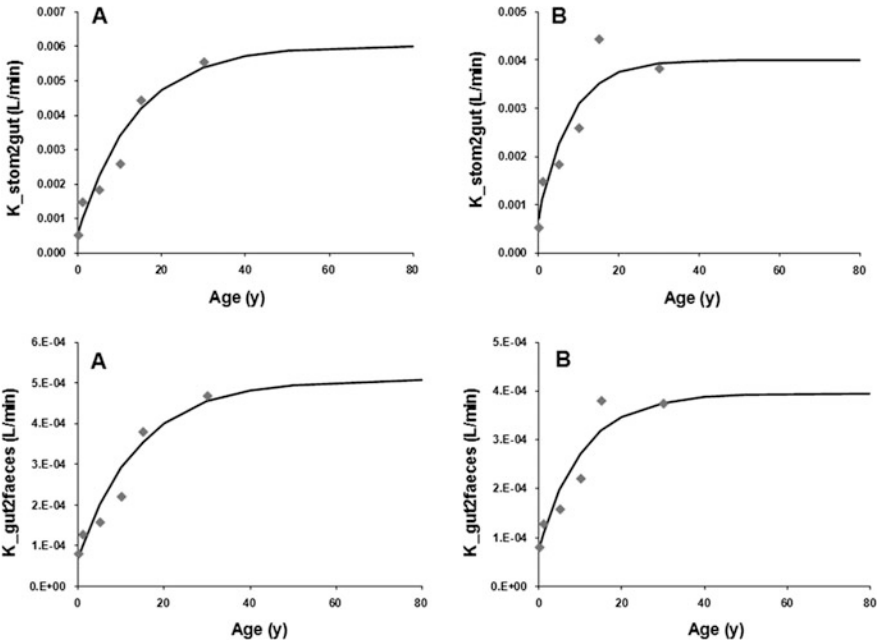

Fig. 7 Fit of the model for the transfer of contaminants from stomach lumen to gut lumen and from gut lumen to faeces to experimental data for men (panel **a**) and for women (panel **b**) [26]

alveolar ventilation rate (Q_P in L/min) that is the rate of air flow that the gas exchange areas of the lungs encounter during normal breathing. This rate is calculated as a function of the breathing frequency and the alveolar volume:

$$Q_P = V_A \times \text{BreathFreq} \tag{34}$$

2.5.4 Enzyme Content in Organs

Metabolism was assumed to be dependent on age but not gender. Data on the ontogeny of cytochrome P450 were integrated in the calculation of the metabolic rates to account for the differences in the enzyme activity between children and adults. The relationships between the age and the enzyme expression and activity of several cytochromes P450 derived by Johnson et al. [29] were used. Table 4 summarises these relationships given as a fraction of adult cytochrome abundance. The fractions could not exceed 1 and are dimensionless.

2.5.5 Intestinal Transit Times

In the PBPK model, the transfer of contaminants in the gastrointestinal tract is governed by two parameters: the transfer of contaminants from the stomach lumen (where the contaminant arrives after ingestion) to the gut lumen (K_{stom2gut}) and the transfer of contaminants from gut to faeces ($K_{\text{gut2faeces}}$). These parameters are age and sex dependent. Values for the stomach and gut contents and transit times were reported by International Commission on Radiological Protection [26] and used to derive the relationships for men and women, respectively:

$$K_{\text{stom2gut}} = \begin{cases} 0.006 + (0.0006 - 0.006) \times \exp(-0.073 \times \text{Age}) & \text{for men} \\ 0.004 + (0.0007 - 0.004) \times \exp(-0.129 \times \text{Age}) & \text{for women} \end{cases} \tag{35}$$

$$K_{\text{gut2faeces}} = \begin{cases} 0.000508 + (0.0000709 - 0.000508) \times \exp(-0.0699 \times \text{Age}) & \text{for men} \\ 0.000394 + (0.0000775 - 0.000394) \times \exp(-0.0095 \times \text{Age}) & \text{for women} \end{cases} \tag{36}$$

The adjustments of these equations to the experimental data are displayed in Fig. 7.

3 Building Exposure Scenarios with the PBPK Model in MERLIN-Expo

The generic PBPK model implemented in MERLIN-Expo can be used alone or together with the multimedia environmental models. This section describes the prerequisites needed to run the model (validity domain, input data) and several features that can be relevant for building realistic exposure scenarios with this model (human variability and links with the environmental models).

3.1 Validity Domain

All models are valid on a defined domain. Usually the assumptions made during model development help in delineating the domain of validity. Here, the validity domain of the PBPK model is defined by the assumptions made to model the ADME processes and the body evolution over lifetime.

The absorption of contaminants is described using simple models that are reasonable in terms of numbers of parameters. For instance, only two compound-specific parameters are needed for the inhalation process, but they can be used only if two conditions are fulfilled: a one-directional airflow and a rapid equilibrium between the air in the lungs and the blood in the alveoli. Very-short exposures (in the order of the minute) cannot be well described with such a modelling approach and more detailed description of the gas exchanges should be preferred [30]. For example, the lungs can be described by several compartments representing different regions of the respiratory tract such as the upper respiratory tract, the dead space, the alveolar space and the pulmonary capillaries. Similarly, more sophisticated models than the ones implemented for oral absorption have been proposed in the literature [31, 32]. These models describe the different sections of the guts and take into account the regional intestinal pH, transit times from one section to another and the presence of active transporters or enzymes in the region. Such models were first developed to describe the oral absorption of therapeutic drugs including the dissolution phase of the drug and to provide reliable predictions of the compound kinetics in the hours or minutes following the administration. These sophisticated models for inhalation and ingestion are however rarely required for environmental contaminants and the related exposure scenarios for the general population. It should also be noted that these models require a high number of physiological and compound-dependent parameters that are difficult to inform.

The PBPK model is based on the assumption that the compound is distributed by blood in the various organs or tissues of the body. Chemicals distributed by another transport (e.g. lymph) are then outside the validity domain. Compartments are supposed to be homogenous and well mixed, and the distribution of the contaminants is assumed to be blood flow limited, i.e. the permeability of the contaminants in the cells of the tissues/organs is much greater than the tissue blood flow rate. The

assumption of perfusion flow-limited kinetics is justified for small lipophilic drugs that are neither too big nor too hydrophilic to distribute into organs. The assumption that a tissue/organ is a single, well-stirred compartment with uniform concentration of the compound within it can fail for compounds whose intracellular concentrations can be different from their extracellular concentrations due to involvements of transporters in their uptake. In this case, the compartment could be divided in several sub-compartments to better describe the physiology of an organ or tissue with a vascular space, an interstitial space and a cellular space [20]. However such a modelling approach is rarely used due to the lack of data to inform the parameters. But the predictions of our model should therefore be taken with caution for such compounds under certain exposure scenarios (short exposures).

The two mathematical function equations used for metabolism (linear model and Michaelis–Menten equation) cover a wide range of contaminants and exposure scenarios (low and high doses). However these functions are not able to deal with contaminants that inhibit or induce their own metabolism. The PBPK model is therefore not suitable under these situations.

Our model for excretion assumes that the excretion is not a saturable process and is only limited by the perfusion of the organ. In some cases (high excretion rate), this could lead to an apparent saturation pattern. But this is quite rare for environmental exposures.

The physiological and anatomical changes related to age are taken into account using mathematical equations for the parameters of the PBPK model. It is therefore possible to simulate exposure over lifetime as well as over short periods. The PBPK model is able to describe the time evolutions of the physiological and anatomical parameters from birth to elderly. The models for the cardiac output and the body weight, two parameters used in the computation of the other physiological and anatomical parameters, were fitted to data obtained in humans aged from 0 to 80 years and 0–90 years, respectively. Outside these time ranges, the model predictions for the cardiac output and the body weight are inaccurate. Hence, the validity time range of the PBPK model is set between 0 and 80 years old.

In the end, the PBPK model is based on a detailed description of the body anatomy and includes a substantial number of tissue compartments. This structure enables the analysis of the toxicokinetics for diverse compounds that induce multiple effects in various target tissues. According to the restrictions presented above, the PBPK model can be used for a majority of environmental contaminants like volatile organic compounds, pesticides, polycyclic aromatic hydrocarbons (PAH) or polychlorinated biphenyls (PCB) and various exposure scenario (short-term, long-term or lifetime exposures).

3.2 Inputs Required to Use the PBPK Model

The parameters related to the exposure scenarios (i.e. populations, contaminants, characteristics of the exposure) have to be informed before running the PBPK

Table 5 PBPK model parameters that have to be informed to run simulations with MERLIN-Expo

Parameter	Abbreviation	Unit	Default value
Age of the individual at the beginning of the simulation	Initial age	Years	0
Interindividual variability of the body weight	$BDW_{Variability}$	Dimensionless	1
Absorption			
Fraction of contaminant absorbed via ingestion	$Abs_{ingestion}$	Dimensionless	1
Absorption from stomach lumen to stomach wall	$Ka_{stomach}$	min^{-1}	0
Absorption from gut lumen to gut wall	Ka_{gut}	min^{-1}	0
Fraction of contaminant absorbed via inhalation	$Abs_{inhalation}$	Dimensionless	0
Blood:air partition coefficient	$PC_{BloodAir}$	Dimensionless	1^{99}
Distribution			
Tissue:blood partition coefficients	PC	Dimensionless	1
Capacity of erythrocytes to bind contaminants	BIND	mg/L	0
Half-saturation constant for blood:plasma partitioning	KBIND	mg/L	1
Metabolism			
Maximum velocity per kg of body weight	$V_{max_{perBDW}}$	mg/min/kg	0
Michaelis constant	Km	mg/L	1
Clearance per kg of body weight	CL_{perBDW}	L/min/kg	0
Main cytochrome P450 involved in metabolism	MainCYP	Dimensionless	0
Excretion			
Excretion rate per kg of body weight	Kex_{perBDW}	min^{-1}/kg	0
Biliary excretion rate	Ke_{bile}	min^{-1}	0

model in MERLIN-Expo. This set of parameters corresponds to individual characteristics and the compound-specific parameters. Because the model was built to be flexible and applied to numerous compounds, two models were proposed for the oral absorption and the distribution of the compound and should be selected.

3.2.1 Modelling Options

As described in the previous section, the PBPK model includes two models for the oral absorption: a simplified model for the gastrointestinal tract and a direct input in the liver. In most cases, the user will select the model according to the available information or experimental data she/he has gathered on the compound absorption. To select the model, a general variable ingestion was created whose possible affectations are the different options: simplified model, direct input in the liver or no absorption.

The second model to be selected concerns the distribution of the compound in blood and its binding capabilities to the red blood cells or erythrocytes. Two

modelling options are possible: the compound binds to the erythrocytes (and Eq. (8) is applied) and the compound does not bind to the erythrocytes or the binding is negligible (and Eq. (7) is applied).

3.2.2 Parameters

Table 5 presents the list of parameters to be set before running simulations with the PBPK model. This list is composed of two parameters related to the individual or population and the others to compound-specific parameters. The individual parameters are the age at the beginning of the exposure or simulation and the human variability for body weight. The compound-specific parameters are used in the mathematical description of the ADME processes. These parameters are usually determined using in vivo controlled studies in humans, in vivo laboratory studies on animals, in vitro testing or in silico tools. It should be noted that the metabolic and excretion rates depend on the body weight.

3.3 Population Scenarios: Interindividual Variability

All the parameters of the PBPK model can possibly be affected by interindividual variability. Numerous factors, as genetic or environmental ones, can explain human variability in toxicokinetics [33–35]. As described in the first section, the PBPK model was parameterised with default values representing an 'average' individual. To apply this model in realistic scenarios including specific individual or sensitive populations, some parameter values can be modified and also be set to probability distribution functions representing the range of possible values in a population or individual.

Body weight is one of the PBPK parameters that can be easily observed and measured in individuals. As most of the anatomical and physiological parameters are related to it, we then chose to create a parameter related to the body weight ($BDW_{Variability}$) to scale the default average value to the observed one or simulate a random population. For example, the default value for a 20-year-old man is about 74 kg. If the body weight of the individual of interest was measured at 80 kg at 20 years old, the user can assign the value of 1.08 to the parameter $BDW_{Variability}$ to adjust the PBPK model parameters to this individual. A default probability distribution function is also proposed for body weight. The interindividual variability for body weight was estimated with the database of the NHANES study gathering the weights of males and females from 2 to 90 years old in the United States [24]. A normal distribution described well these data with mean corresponding to the estimated value of body weight and a standard deviation corresponding to a CV of 15% for men and women. A likelihood-based statistical test was used to assess that the predicted distribution of the body weight at each age (obtained from the 1,000 simulations) does not differ from the observed body weight's distribution of

Table 6 Variability (expressed as coefficients of variation) observed in tissue/plasma partition coefficients from several studies

Tissue	[41]	[42]	[43]	[44]	[45]	[45]	[46]	[47]	[47]	[47]	[48]	Mean
Muscle	27	49	28	29	29	23	16	23	14	10	12	24
Skin	27	–	31	37	–	–	14	–	–	–	–	27
Fat	50	38	18	25	20	14	10	05	52	–	10	24
Liver	07	26	34	–	25	13	09	26	16	11	–	18
Kidneys	38	34	17	13	16	31	10	13	25	37	11	22
Brain	07	22	13	29	17	44	16	08	35	07	–	20
Heart	16	27	16	17	12	34	16	–	–	–	–	20
Lungs	44	33	28	29	16	24	11	–	–	–	–	27
Spleen	–	22	07	–	17	21	10	–	–	–	–	15
Testes	–	28	–	–	18	25	07	–	–	–	–	19
Stomach	–	58	16	–	19	30	–	–	–	–	–	31
Small intestine	–	45	23	–	14	26	17	–	–	–	–	25
Large intestine	–	–	28	–	53	25	–	–	–	–	–	35
Pancreas	–	–	–	–	14	16	13	–	–	–	–	14

the NHANES database. Because the organ weight is a function of body weight, the organ weight variability can be handled by the parameter $BDW_{Variability}$. Moreover the variability in organ weights was observed to be close to 15% (range between 9 and 16%) that is similar to the body weight variability defined above [36, 37]. The interindividual variability related to body weight is the sole source of variability in toxicokinetics implemented in MERLIN-Expo, but the user can enter probability distribution functions for other parameters.

On the contrary to physiological parameters, the human variability of compound-specific parameters is not well characterised with a notable exception for metabolic parameters [38]. This is probably due to the fact that the compound-specific parameters cannot be measured in humans but have to be estimated using statistical analyses [2, 39] or extrapolated from in vitro tests or modelling tools [22, 40]. This generates uncertainty that is added to the natural variation of the parameter values. For instance, we selected several studies and reported the observed variability for the tissue:blood partition coefficients according to the tissue and not the compound (Table 6). We observed that the coefficients of variation vary from 14 to 31%.

3.4 Linking the Human Model to Other MERLIN-Expo Models

To perform simulations, the PBPK model needs to be associated to an exposure scenario defining the duration and the magnitude of the exposure. The magnitude is determined by the contamination of the environment (outdoor or indoor) and the ingested food. In the case that the PBPK model is used alone, the concentration inhaled or the quantity ingested rate has to be informed. The model can also be used in more sophisticated exposure scenarios including multimedia environmental models of the MERLIN-Expo library. Most of the environmental, animal or plant models can provide inputs for the PBPK model. These inputs can be formalised as an inhalation rate of contaminated air or as an ingestion rate for contaminated food. Several models can contribute to the calculation of the dietary intake through food (e.g. fish, fruit or leaf model) or drinking water (e.g. the river model). To integrate several inputs, a module called human intake was developed to sum up the intakes from several sources.

4 Application of the Human PBPK Model Under Different Exposure Scenarios

In this section, the PBPK model of MERLIN-Expo was applied under several exposure scenarios. Two types of assessment were performed: the predictions of MERLIN-Expo were compared either to actual experimental data or to predictions of models published in the scientific literature.

4.1 Lifetime Exposure to Dioxin: A Persistent Compound

Polychlorinated dibenzo-*p*-dioxin (PCDDs) (also called dioxins), including 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), are persistent environmental contaminants. The main current sources of PCDDs in the environment are combustion processes, such as waste incineration, and metal smelting and refining. Among this chemical class, TCDD is one of the most toxic compounds and is classified as a human carcinogen by IARC. Because the persistence of TCDD in the human body is of the order of many years, continuous exposures might lead in the long run to extremely high body burdens [49].

We used the study of Maruyama et al. [50] to benchmark our model for TCDD. In their study, Maruyama et al. [50] applied a PBPK model developed for dioxins to predict the concentrations in several tissues and compared their model predictions to experimental data. The data were measured concentrations in blood, fat, liver and richly perfused tissues of Japanese men whose ages range between 20 and 60 years

Table 7 Parameter values of the PBPK model in MERLIN-Expo used for the testing (dioxin, lead and perfluorinated compounds)

Parameter	Units	TCDD	Lead	PFOS	PFOA
Age of the individual at the beginning of the simulation	Years	*0*	*0*	*0*	*0*
Interindividual variability of the body weight	Dimensionless	0.82	*1*	*1*	*1*
Absorption					
Fraction of contaminant absorbed via ingestion	Dimensionless	0.97	0.11	0.9	0.9
Absorption from stomach lumen to stomach wall	min^{-1}	*0*	*0.*	*0*	*0*
Absorption from gut lumen to gut wall	min^{-1}	*0*	*0*	*0*	*0*
Fraction of contaminant absorbed via inhalation	Dimensionless	*0*	0.5	*0*	*0*
Blood/air partition coefficient	Dimensionless	1^{99}	1^{99}	1^{99}	1^{99}
Distribution					
Tissue/blood partition coefficients	Dimensionless				
Adipose		247	20	0.14	0.04
Adrenal		4.1	100	0.2	0.12
Blood		*1*	*1*	*1*	*1*
Blood_Arterial		*1*	*1*	*1*	*1*
Blood_Venous		*1*	*1*	*1*	*1*
Bones		4.1	1,000	0.2	0.12
Bones_NP		1	1	*1*	1
Brain		4.1	100	0.2	0.12
Breast		17	20	0.2	0.12
Gut		4.1	100	0.57	0.05
Gut_Lumen		*1*	*1*	*1*	*1*
Heart		4.1	100	0.2	0.12
Kidneys		3.1	100	0.8	1.05
Liver		9.8	100	3.72	2.2
Lungs		4.1	100	0.2	0.12
Marrow		4.1	100	0.2	0.12
Muscle		17	20	0.2	0.12
Pancreas		4.1	100	0.2	0.12
Sexual_Organs		4.1	100	0.2	0.12
Skin		2.5	20	0.29	0.1

(continued)

Table 7 (continued)

Parameter	Units	TCDD	Lead	PFOS	PFOA
Spleen		4.1	100	0.2	0.12
Stomach		4.1	100	0.2	0.12
Stomach_Lumen		*1*	*1*	*1*	*1*
Thyroid		4.1	100	0.2	0.12
Urinary_Tract		4.1	100	0.2	0.12
Capacity of erythrocytes to bind contaminants	mg/L	*0*	2.7	*0*	*0*
Half-saturation constant for blood: plasma partitioning	mg/L	*1*	0.0075	*1*	*1*
Metabolism					
Maximum velocity per kg of body weight	mg/min/kg	*0*	*0*	*0*	*0*
Michaelis constant	mg/L	*1*	*1*	*1*	*1*
Clearance per kg of body weight	L/min/kg	*0*	*0*	*0*	*0*
Main cytochrome P450 involved in metabolism	Dimensionless	*0*	*0*	*0*	*0*
Excretion					
Excretion rate per kg of body weight	min^{-1}/kg				
Kidneys		*0*	4.35×10^{-6}	6.9×10^{-7}	2.1×10^{-7}
Liver		4.26×10^{-7}	1.85×10^{-6}	*0*	*0*
Biliary excretion rate	min^{-1}	*0*	*0*	*0*	*0*

Default values are indicated in italic

[51, 52]. Because we were interested in a direct comparison of MERLIN-Expo and this model, we used the same parameter values for the exposure scenario and the PBPK model. Only the excretion rate was set to a value provided by Milbrath et al. [53] to fit with our parameterisation of this process. As the body weight was set to 60 kg for an adult in Maruyama et al. [50], we assigned the value of 0.82 to the parameter body weight variability and defined the probability distribution function as a normal distribution with mean 0.82 and standard deviation 0.12 to perform variability analyses.

The TCDD exposure route was assumed to be solely food ingestion. The daily intake was calculated using concentration data in Japanese food obtained in 1998 and was set to 12.8 pg/day [54]. The values of the PBPK model parameters are reported in Table 7. As in the former study, we assumed that ingested TCDD enters

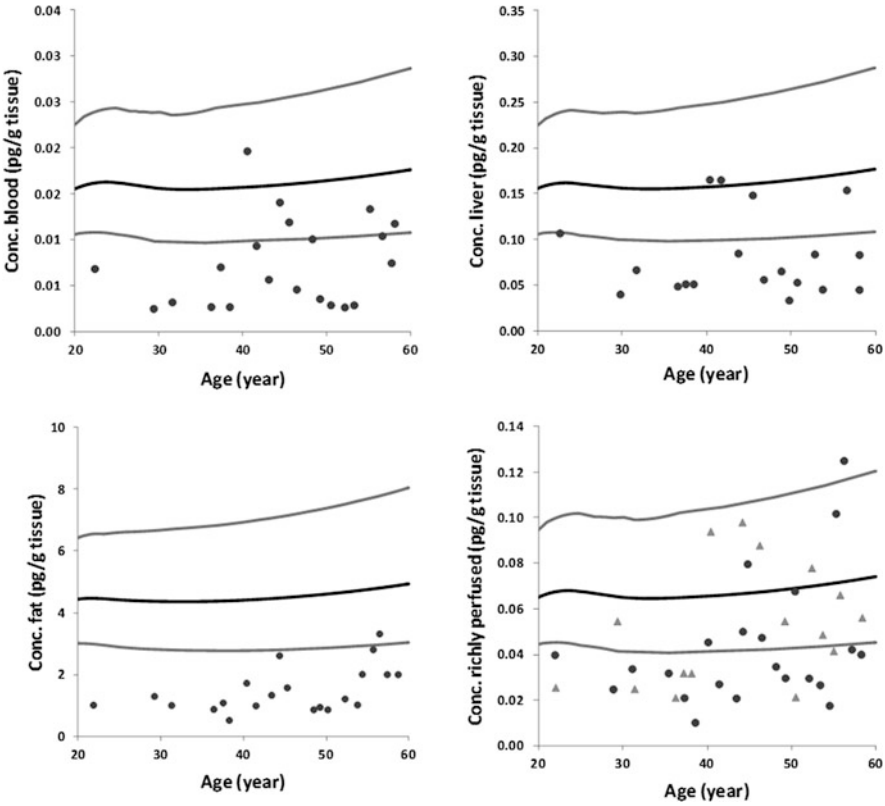

Fig. 8 Simulated (*lines*) and measured (*circles* and *triangles*) TCDD concentrations in blood, liver, fat and richly perfused tissues. The two *grey lines* represent the 95% IC. Measured concentrations represented by *circles* were obtained from the report by Environment Agency [51] and the ones represented by *triangles* were obtained from Iida et al. [52]

Table 8 Predicted and measured average concentrations of TCDD in blood, liver, fat and richly perfused tissue by MERLIN-Expo and a published model [50]

	Concentrations (pg/g tissue)		
Tissue	Measured data (±SD)	MERLIN-Expo (95% IC)	Maruyama et al. [50]
Blood	0.007 ± 0.005	0.016 [0.010; 0.026]	0.048
Liver	0.082 ± 0.045	0.161 [0.102; 0.252]	0.112
Fat	1.51 ± 0.735	4.50 [2.86; 7.05]	6.31
Richly perfused tissues	0.052 ± 0.026	0.067 [0.042; 0.106]	0.197

The mean is given with the standard deviation (SD) for the data and the predictions of MERLIN-Expo with the 95% interval of confidence (IC)

as a direct input in the liver avoiding the first pass effects such as metabolism. The option 'ingestion via the liver' in MERLIN-Expo was then used.

The predicted concentrations in blood, liver, fat and richly perfused tissues (i.e. heart) obtained using MERLIN-Expo are presented in Fig. 8. The average prediction is represented together with the interval of confidence (IC) at 95%. The toxicokinetic profiles were similar in the various organs. Because the concentrations were quite stable over the time period considered, we also calculated the average concentration and compared the predictions with the measurements and the predictions provided by the PBPK model of Maruyama et al. [50] (Table 8). We observed that the predictions provided by both models were close. This result is not surprising because the parameterization of the models was similar. The only difference relied in the values of the initial concentrations in organs in the former PBPK model. So in MERLIN-Expo, we run a lifetime simulation to the same exposure. We also observed that the variability in the experimental data was well reproduced by our model.

4.2 Exposure to Perfluorinated Compounds During Adulthood

Perfluorinated compounds (PFCs) are a group of fluorinated chemicals with surface-active properties, which have been manufactured for over 50 years and widely used in consumer products. Due to their extensive applications, PFCs have been released to the environment and bioaccumulate through the food chain [55, 56]. Recently, a number of studies have reported internal exposures to PFCs in human tissues [57, 58]. Recent investigations have shown that food intake and packaging, water, house dust and indoor air are all potentially significant sources of human exposure [59–61]. Among these sources, water consumption and food (specially, fish) have been identified as the most important routes of human exposure to PFCs.

This scenario focused on two compounds, perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA), the most extensively investigated PFCs, whose half-live are of the order of few years [62]. We used two datasets to benchmark the PBPK implemented in MERLIN-Expo on PFOS and PFOA. The first study reported the measured concentrations of PFOA in blood serum for residents from Little Hocking, Ohio (USA). The data were obtained from the website of the Little Hocking Water Association (LHWA) and from the article by Emmett et al. [63]. The exposure of the population was assumed to occur only via drinking water, and the daily intake was set to 3.55 ppb [63]. The second study was conducted by Ericson et al. [64] and Perez et al. [58]. They measured the PFOS and PFOA concentrations in blood and several tissues (liver, kidneys and lungs) of people living in Catalonia (Spain). To estimate the daily intake for PFOA, we used three studies on food contamination conducted in Spain [59, 65, 66] and

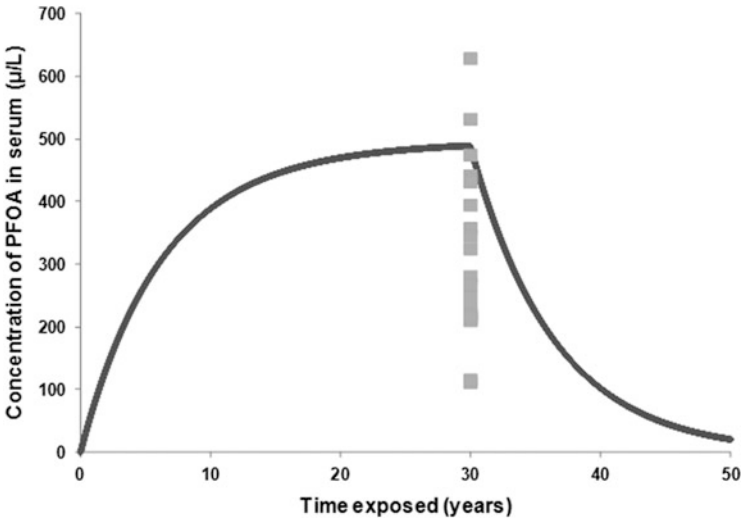

Fig. 9 Comparison of model simulations (*lines*) from MERLIN-Expo (B) with experimental data from Emmett et al. [63] (*squares*) and the Little Hocking Water Association website. The Little Hocking population was exposed to drinking water contaminated with PFOA (3.55 ppb). The simulations were run for an exposure period of 30 years

age-specific food consumption in Spain [67]. The total daily intakes for PFOS and PFOA were set respectively to 204.84 and 33.45 ng/day.

We used the values of a published PBPK model for PFOS and PFOA [68] to parameterise the PBPK model in MERLIN-Expo for the compound-specific parameters (Table 7). The structure of both models slightly differs for the urinary elimination of PFOS and PFOA. Indeed, Loccisano et al. [68] developed a PBPK model that integrates the reabsorption of the two perflurinated compounds in kidneys. Even if this process is not modelled in MERLIN-Expo, we applied our model without modifications.

First we run the scenario for the population of Little Hocking. Because the exposure duration was not known, the model was run until a steady state was reached in blood. The model predictions were then compared to the data (Fig. 9). We observed that the model prediction is included in the range of the observations even it is slightly superior to the mean or median of the measured concentrations. On the same figure, we also observed that 20 years are needed to eliminate PFOA from blood after that type of exposure. Then we run the second scenario for the population in Catalonia. The model predictions are represented together with the data on Fig. 10 for PFOS and on Fig. 11 for PFOA. The predictions of the blood concentration are in good agreement with the data for both compounds. Concentrations in the liver are close to the data for PFOS but are underestimated for PFOA (by a 2-factor). PFOA is detected in only one subject in kidneys, so no conclusion can be drawn, and for PFOS the predictions are underestimated by a factor of 3. Concentrations in lungs are clearly underestimated for both compounds. So the

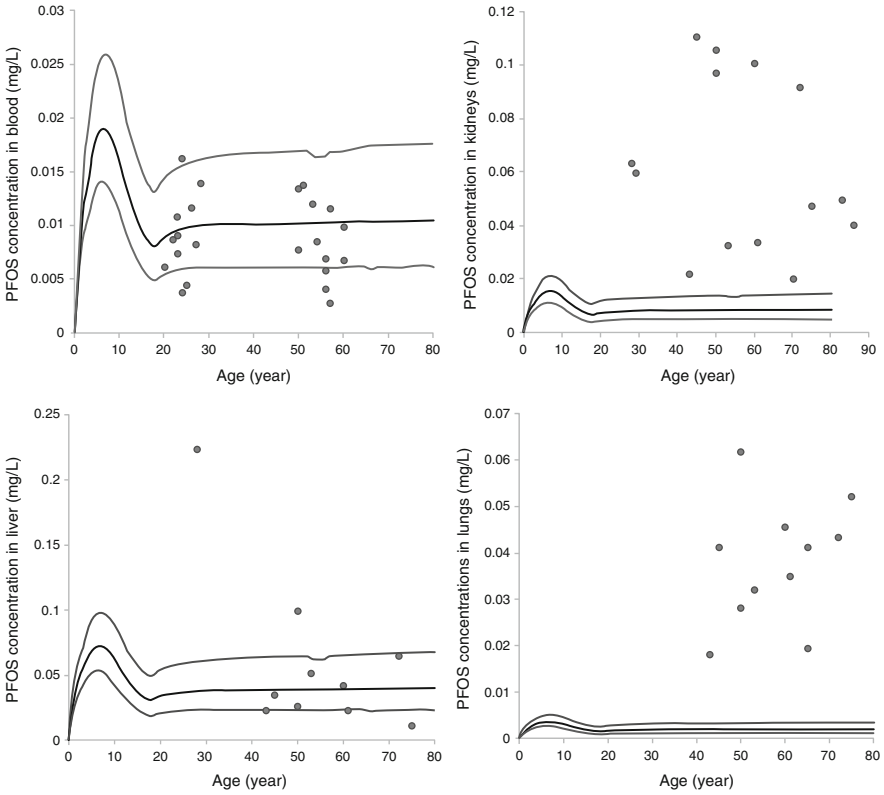

Fig. 10 Simulated (*lines*) and measured (*circles*) PFOS concentrations in blood, kidneys, liver and lungs in a population living in Catalonia, Spain [58, 64]. The two *grey lines* represent the 95% interval of confidence. Simulations were obtained with MERLIN-Expo

predictions are comprised in a 3-factor, except for lungs which value of the partition coefficient used to parameterise MERLIN-Expo is clearly underestimated according to the experimental data.

4.3 Exposure to Lead

Lead is a metal that can be found in all parts of our environment: air, soil, water and indoor environment. Lead compounds have been used in a wide variety of products, including lead-based paints, ceramics, pipes and plumbing materials, solders, gasoline, batteries, ammunition and cosmetics. Long-term exposure to lead can cause toxicity effects as neurotoxicity. The lead blood level is a widely used biomarker to estimate the individual body burden.

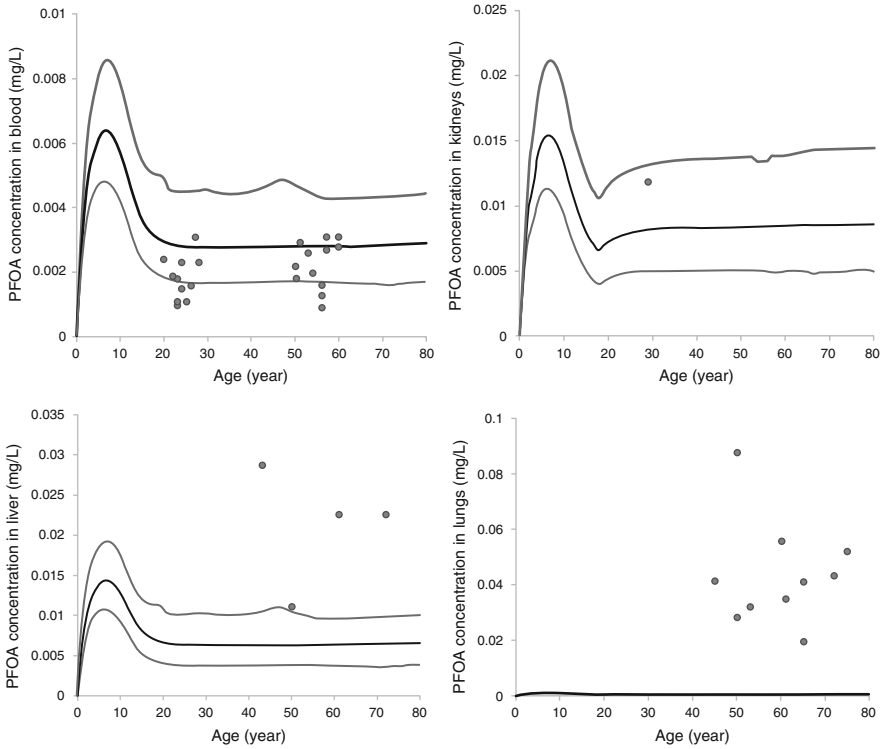

Fig. 11 Simulated (*lines*) and measured (*circles*) PFOA concentrations in blood, kidneys, liver and lungs in a population living in Catalonia, Spain [58, 64]. The two *grey lines* represent the 95% interval of confidence. Simulations were obtained with MERLIN-Expo

We tested the PBPK model in MERLIN-Expo for adult exposure and used experimental data from Azar et al. [69]. In their study, Azar et al. [69] assessed the relationship between exposure to inorganic lead in the atmosphere and indices of lead absorption such as blood lead levels. The air lead exposure of 30 male subjects in five locations in the United States was measured, and blood samples were collected for analyses. Parameter values used for the MERLIN-Expo model are shown in Table 7 and were taken from the article by Sharma et al. [21]. For lead, we used the option 'binding with erythrocytes'.

Figure 12 presents the predictions of the blood lead levels in adults using MERLIN-Expo that reproduced well the measured concentrations. Table 9 also presents the numerical values for the predictions and measurements and highlights the good correspondence between them (differences range between 1 and 20%).

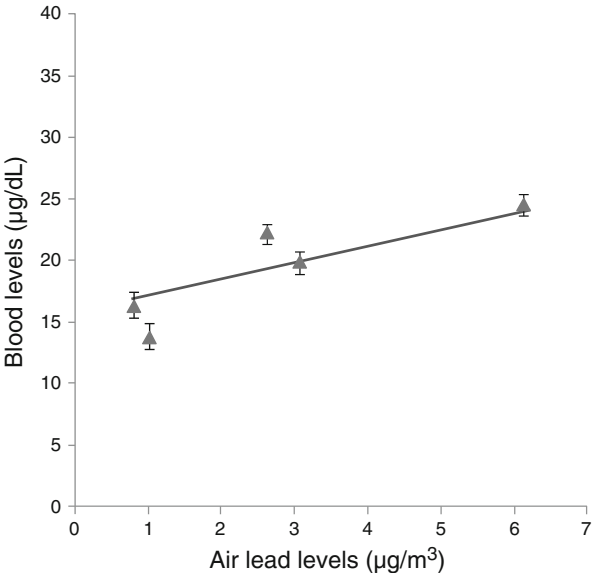

Fig. 12 Comparison of the MERLIN-Expo predictions (*plain curve*) with measured blood levels in adults (*triangles*) [69]

Table 9 Experimental data for the exposure of adults to lead [69] and the blood levels predicted by MERLIN-Expo

Region	Air lead levels (µg/m^3)	Lead concentration in blood (µg/dL)	
		Observed mean	MERLIN-Expo predictions
Philadelphia	2.62	22.4	19.43
Starke, FL	81	16.4	16.99
Barksdale, WI	1.01	13.8	17.27
Los Angeles	6.10	24.6	23.81
Los Angeles	3.06	19.9	201

5 Conclusion

This chapter presented a detailed description of the human PBPK model implemented in MERLIN-Expo including model equations, parameter estimation and domain of validity. The PBPK model can be used either alone or together with multimedia environmental models of the MERLIN-Expo library to build realistic scenarios of exposure. Human variability can be modelled in the form of probability distribution functions to be assigned to the parameters varying within a population. As an illustration, the model was applied to three small case studies to be confronted to actual measurements in humans. Several exposure scenarios were modelled with different characteristics. Our results showed that the PBPK model was able to reproduce the toxicokinetics of the substances of interest within a range (e.g. a factor 3) that is acceptable in toxicokinetics modelling when no optimization was performed and that the human variability was well reproduced. In these case

studies, the parameterization of the model was based on published PBPK models. Our model performance was very similar to the performance of those models. The parameterization is critical for an appropriate use of the PBPK model. Previous published PBPK models (as done in this chapter), toxicological in vivo or in vitro studies or in silico tools (as quantitative structure-activity relationships) can be used for this purpose.

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