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ABSTRACT

While pesticide use is subject to strict regulatory oversight worldwide, it remains a main concern for environmental protection, including biodiversity conservation. This is partly due to the current regulatory approach that relies on separate assessments for each single pesticide, crop use, and non-target organism group at local scales. Such assessments tend to overlook the combined effects of overall pesticide usage at larger spatial scales. Integrative landscape-based approaches are emerging, enabling the consideration of agricultural management, the environmental characteristics, and the combined effects of pesticides applied in a same or in different crops within an area. These developments offer the opportunity to deliver informative risk predictions relevant for different decision contexts including their connection to larger spatial scales and to combine environmental risks

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of pesticides, with those from other environmental stressors. We discuss the needs, challenges, opportunities and available tools for implementing landscape-based approaches for prospective and retrospective pesticide Environmental Risk Assessments (ERA). A set of "building blocks" that emerged from the discussions have been integrated into a conceptual framework. The framework includes elements to facilitate its implementation, in particular: flexibility to address the needs of relevant users and stakeholders; means to address the inherent complexity of environmental systems; connections to make use of and integrate data derived from monitoring programs; and options for validation and approaches to facilitate future use in a regulatory context. The conceptual model can be applied to existing ERA methodologies, facilitating its comparability, and highlighting interoperability drivers at landscape level. The benefits of landscape-based pesticide ERA extend beyond regulation. Linking and validating risk predictions with relevant environmental impacts under a solid science-based approach will support the setting of protection goals and the formulation of sustainable agricultural strategies. Moreover, landscape ERA offers a communication tool on realistic pesticide impacts in a multistressors environment for stakeholders and citizens.

1. Introduction

The use of plant protection products (PPPs) is subject to a prospective environmental risk assessment (ERA), covering the pesticidal active substance and the marketed product, and regulatory approval in most jurisdictions worldwide, with some differences among jurisdictions (van der Vegt et al., 2022). Typically, in this process, risk assessors provide scientific advice to risk managers on risks that the use of the pesticide may pose to human, animal, and environmental health. The ERA process is widely used for prospective/predictive evaluations (i.e., pre-market registration assessments) and in retrospective evaluations (i.e., post-market monitoring programs). Depending on the substance and legislative regime, the endpoints selected for environmental assessments cover specific non-target organism groups, or selected indicators of impacts on biodiversity and/or ecosystem functions and services. In the EU, the responsibility for conducting ERA for pesticides is shared by the European Food Safety Authority (EFSA) and national agencies of the Member States. EFSA is involved in the assessment of pesticide active substances, while the ERA for PPPs is conducted at zonal and national level. In the ERA process, risks are characterized by testing specific hypotheses on predicted exposure levels and the probability and severity for potential environmental harm.

Over the past several decades, the development and implementation of prospective methods for assessing the environmental risks of pesticides led to a plethora of ERA guidance documents tailored to the needs of specific sectors and jurisdictions. While the complexity of data requirements, models, scenarios, approaches, and other tools in support of ERA increased substantially in time, today's ERAs do still rely on the traditional risk assessment and risk management paradigm that has been the basis of environmental protection (e.g., Burke et al., 2017). This paradigm relies on compartmentalized and pollutant-specific, risk-based approaches. For pesticides, this implies individualized assessments for each substance, each use, and each recognized non-target group. Currently, this approach does not enable comparison of risk assessments for different substances within the same framework. It does not directly address the complexity of the environmental reality that includes ecological interactions and processes at individual and population-relevant landscape scales. The need for more integrative approaches for the ERA of pesticides has been highlighted by academics (i.e., Topping et al., 2020; Sousa et al., 2022, Leenhardt et al., 2023), regulatory scientists (i.e., Streissl et al., 2018; Devos et al., 2022a, b) and institutions (EFSA, 2018, EFSA 2021, 2022a, b; EFSA Scientific Committee, 2021; EEA, 2023).

Pesticide use remains a major concern for biodiversity conservation in agricultural and non-agricultural areas. Despite the implementation of ERA in the regulatory context, issues have been identified for most taxonomic groups, including pollinators (Rundlöf et al., 2015; 2022), aquatic invertebrates (Beketov et al., 2013; Liess et al., 2021), terrestrial invertebrates (Sanchez-Bayo et al., 2019; Forister et al., 2019; Sanchez-Bayo and Wyckhuys, 2021), and birds (Li et al., 2020; Rigal et al., 2023; Mineau and Kern, 2023). Recently, for example, EASAC (2023) and Morrissey et al. (2023) argued that current ERA methodologies do not sufficiently consider ecological and practical realities to achieve the desired level of environmental protection.

To further advance ERA methodologies for pesticides, it has been suggested that they must integrate the assessment of: (1) aggregated effects of all intended uses of the pesticide active substance (e.g., Tarazona et al., 2021); (2) combined effects of all pesticides used in an area (e.g., Tarazona et al., 2021); (3) interactions with other environmental stress factors (such as climate change) (e.g., Liess et al., 2016); (4) population recovery, including recolonization, following harmful effects (e.g., Kattwinkel et al., 2015); and (5) adaptation to pesticide stress (e.g., Siddique et al., 2021). An essential element in this process is the consideration of the landscape characteristics as they influence biodiversity and species distribution (e.g., Tscharntke et al., 2022), exposure patterns and ecological consequences. From these considerations, the landscape context emerges as the key modifier of pesticide exposure and associated risks. Since the current regulatory framework provides limited considerations for landscape aspects, the need for further development has been highlighted (Schäfer et al., 2019; Topping et al., 2020; Sousa et al., 2022). Indeed, it has been demonstrated that the environmental impact of pesticide use is drastically influenced by aspects such as: the composition and configuration of the agricultural land; past usage of pesticides; crop density; connectivity to semi-natural habitats and to the water basin; and agricultural management (other farming practices such as fertilizer uses or soil tillage) (Knillmann et al., 2018; Andersson et al. 2021; Lindström et al., 2021). While some relevant ecological aspects (e.g. the ecological recovery option (ERO)) are considered in the ERA of pesticides, there is growing scientific evidence that the impact of ecosystem stressors exceeds the resilience of ecosystems (IPBES, 2019). In the EU, EFSA is developing proposals for addressing landscape aspects in pesticide ERA. Additionally, the EU Green Deal introduced new policy targets to further reduce the impact of pesticides on ecosystems. The ambition to improve the ecological realism of pesticide ERA through the consideration of landscape aspects may not primarily be applicable to pre-market registration dossiers of individual pesticidal active substances, but rather to inform decision makers responsible for PPP authorization and post-marketing surveillance on necessary measures to reduce ecosystem impact of pesticides, e.g., by restrictions in their use following the identification of vulnerable areas linked to landscape characteristics, as well as the implementation of improved landscape management measures such as compensation areas.

The explicit consideration of the spatial and temporal variability of agro-ecosystems in pesticide ERA would facilitate the linkage of ecological assessments performed under other legislative regimes such as the Water Framework Directive, and integration of pesticide monitoring data in prospective ERA. Since the landscape conceptualization and model development also intend to consider agricultural management and the role of other environmental stress factors, it will help to increase the ERA capacity to address environmental complexity and the capacity for evaluating relevant environmental impacts on biodiversity and ecosystem services, in agricultural and associated areas. Such an integrative approach requires the exploration of new conceptualizations and strategies. Furthermore, it requires a constructive dialogue between risk assessors and risk managers, involving all relevant stakeholders, at the problem formulation phase to achieve "fit-for-purpose" ERA (Devos et al., 2019, 2022).

A series of workshops were held in November-December 2022 to explore the key elements required for developing a conceptual framework for landscape-based ERA of pesticides, under the EU Partnership PARC (Marx-Stoelting et al., 2023). The workshops included a set of presentations from experts covering the different elements required for assessing environmental risks at the landscape level and structured discussions. Here, we present the main outcomes of the workshops, propose a conceptual framework for implementing landscape-based approaches for ERA, discuss challenges and possible solutions, and introduce the next steps under PARC 6.4.4 (See Section A under Supplementary materials for additional information on the project) for materializing these concepts as a landscape-based ERA methodology.

2. Conceptualization method

The conceptualization process was based on structured expert discussions, including three main steps: (1) definition of the research questions; (2) four on-line workshops held between November and December 2022 involving over thirty experts from academia and regulatory agencies; and (3) integration of the identified elements into a landscape-based ERA framework.

The overall research question was defined as "*What is the combined environmental impact (*i.e.*, relative impact in relation to other environmental stress factors) of the overall use of pesticides in a certain agro-ecosystem and its associated freshwater ecosystems?*" Subsequently, the overall question was divided into sub-questions that cover the four successive phases of the ERA process, i.e., the problem formulation or hazard identification, dose–response characterization or hazard assessment, exposure assessment, and risk characterization. The sub-questions included considerations of spatial and temporal variability. The discussions considered the available information sources, i.e., ecotoxicity data, models, scenarios, monitoring information and other tools already available, as well as those that could be developed during the project time frame. Organizational issues such as the implementation of complex tools in regulatory assessments, the risk assessment/management dialogue, or the identification of relevant stakeholders and potential users of the risk characterization results, were also discussed.

The workshop discussions were supported by a targeted literature collection. The outcomes of the workshops (including discussions and preparatory materials) were reported in internal workshop minutes, and structured around five complementary ERA areas, serving as organizing framework for the building blocks identified during the expert discussions. Each area covered prospective and retrospective assessments including the use of monitoring data.

- ERA area 1: Framing issues, scope, and problem formulation
- ERA area 2: Exposure-related issues, including environmental fate processes
- ERA area 3: Effect-related issues
- ERA area 4: Specific considerations about other environmental stress factors
- ERA area 5: Risk characterization issues, policy needs and translation of risks into environmental impacts

3. Building blocks for landscape-based ERA

The main discussion elements derived from the series of workshops, extracted as building blocks, and classified into the five abovementioned areas are summarized in Section B of Supplementary Materials. Building blocks were diverse in nature, and considered a broad spectrum of elements, including, among other aspects, the available data and tools, specificities of agroecosystems, differences in landscape assessments between aquatic and terrestrial systems, regulatory needs for different decision-making processes, geographical scales, and stakeholders and potential users. The main cross-cutting complementary elements are summarized below.

3.1. Ontologies and vocabularies

An essential element for providing flexibility while ensuring coherence, transparency and interoperability is the selection and use of harmonized ontologies and vocabularies. Under the PARC initiative, it has been proposed to use EnvThes vocabularies for ecological terms (see https://vocabs.lter-europe.net/envthes/en/index).

The proposed definition for landscape "[*GEMET] The traits, patterns, and structure of a specific geographic area, including its biological composition, its physical environment, and its anthropogenic or social patterns. An area where interacting ecosystems are grouped and repeated in similar form.*" is applicable to landscape-based ERA of pesticides and the conceptual model description.

It is important to highlight the interdependency between landscape-based ERA and systems-based ERA. The conceptual approach of PARC 6.4.4 is framed by the systems-based ERA proposed by Sousa et al. (2022) in the PERA Roadmap report "Building a European partnership for next generation, systems-based ERA". The systems-based ERA is defined more broadly than landscape-based ERA, but involves and integrates, landscape considerations. In line with the abovementioned GEMET definition, a landscape approach for pesticide ERA requires spatially-explicit considerations of the physical, biological, and anthropogenic characteristics of the agro-ecosystems.

Specifically for pesticides ERA, a landscape approach requires considerations on the spatial distribution of land uses, and spatial and temporal considerations of agricultural management, linked to local or regional environmental and ecological characteristics. The combination of landcover (mainly distribution of crops, field margins, non-crop areas, and watershed structure including runoff and drainage for aquatic organisms) with ecological traits and agricultural management defines the exposure potential of each individual as a function of its location. The approach allows a more realistic risk estimations, as the for the same non-target organism group, the risks, including expected impacts and potential for recovery, may be differ significantly depending on the landscape characteristics. Nevertheless, the main advantage of pesticide landscape ERA is the possibility for addressing the aggregated and combined risks of all pesticide applications within an area, as the sum of effects assumed to be acceptable for each application, may lead to unacceptable impacts on populations and ecosystem functions.

Landscape consideration should support different regulatory needs for prospective and retrospective assessments, and be implementable as tools to assess i) the overall risk of all uses proposed for an individual pesticide (aggregated exposure), ii) the combined risk of different pesticides on a particular non-target species or taxa; and iii) the overall environmental impact of pesticide usage and, or in comparison with, other stressors. Including landscape considerations in ERA is a challenge as the scope expands and the overall complexity of the assessed system increases. To avoid unnecessary complexity, ERA tools should be suitable for different decision contexts (as exemplified below) and adaptable for example in terms of appropriate specificity and level of detail. Additionally, to avoid regulatory silos, a system-based approach should include a holistic perspective that addresses the connectivity of agro-ecosystem elements, as well as the political, economic and social contexts (Sousa et al., 2022).

3.2. Landscape models

Landscape considerations play a key role in enabling the transitioning to next generation ERA, with spatially explicit models constituting the most relevant enabling tool to understand how complex systems, such non-targed populations in agricultural environments, work (Focks et al., 2014), if they are appropriately parametrized and validated. Such models may enable a more realistic and context-specific assessment of risks at the landscape scale, which includes the aggregated exposure to the same pesticide from different locations and routes as well as the combined exposure to multiple pesticides, on a routine basis. At the same time the use of a context-specific model requires ensuring that the context is representative and covers the scope and applicability domain in which the model is intended to be used, which for landscape models is linked to the decision scope to be supported by the model. Decision scopes on pesticide use and associated risks may range from a single field to regional, national and EU levels. In addition, landscape models could be used to support other relevant aspects within the ERA process, such as the definition of specific protection goals, the design of monitoring strategies, and the evaluation of the efficacy of different farm management practices including risk mitigation measures. Therefore, a challenge for landscape-based ERA is the necessity to accommodate for the different needs of risk managers or "users" regarding the risk characterization results. This includes the development of a new framework for "fit-for-purpose" and protective regulatory ERA of individual pesticides. Several landscape-based ERA models, which follow different approaches, have been proposed by different authors. The conceptual framework presented here will facilitate the comparison of approaches and integration of results from different models reported in the scientific literature.

The main features of a landscape-based ERA model for pesticides are the consideration of: (1) the spatial distribution of the crops and associated systems (such as watersheds) in the exposure assessment; (2) the spatial and temporal distribution of the non-target organisms in the area; and (3) the cropping and farm management practices and their spatial and temporal distribution. The development and implementation of a landscape-based ERA will require substantial efforts as landscape structures and associated characteristics are heterogeneous, as well as spatially and temporally challenging. Landscape models should connect exposure and effects by coupling pesticides fate in air, soil, water and biota, with the presence, movements, relevant exposure routes and resulting effects on non-target organisms in the landscape mosaic.

The integration of landscape ERA in the regulatory context should consider the decision context and focus on the specific needs, avoiding unnecessary complexity. An exploratory phase is needed for the identification of the processes to include and boundaries to set for supporting the specific decision making. The models may be used at different levels of the assessment process, and not primarily linked to the assessment of a specific pesticide. Typical examples are for screening as an introductory level prior to ERA, for benchmarking and focussing the ERA on specific aspects, for defining protection goals or management options, etc. Transparency is a critical element for all users, the interface should facilitate the use, but keep the traceability regarding the selection for the input parameters, the model considerations including the level of validation, and the uncertainty assessment of the results.

As an initial first step, landscape considerations may be applied to exposure models, but should ideally be extended to the effect models. Some models, such as ALMaSS (Topping et al., 2003), allow exposure and risk estimations using geographical information from real landscapes, this approach could be combined with local monitoring programs enabling the comparison of model predictions with monitoring results at the local level. More generic spatial approaches, using representative scenarios, are relevant for identifying the most significant factors serving as drivers of exposure and effects of PPP on biodiversity, which, in turn, can support the identification of generic risk mitigation approaches. Spatially explicit models can: a) integrate multiple sources and exposure routes, b) consider scenarios for exposure of several terrestrial and aquatic taxa, and c) predict the combined exposure to multiple pesticides present at different periods in various landscape elements. The inclusion of temporal trends offers the possibility to consider the trends in weather and land use scenarios in prospective ways, and if extended to multiple years, would address long-term consequences of moderated but repeated impacts as well as the influence of climate change. Landscape composition and configuration can include both semi-natural habitats and cultivated fields, as well as diversity in cropping and farm management practices including risk mitigation measures (Vasseur et al, 2013). Developing spatially explicit exposure models is a promising avenue to increase realism in predictions dependent on the landscape and local ecological characteristics. The association of climatic conditions to geographical regions is also very relevant and has become a new challenge due to anthropogenic climate alterations. For pesticide ERA in addition to organism traits, the landscape context metrics (landscape configuration and composition, farmer interventions, etc.) can maximize or mitigate pesticide exposure and/or effects and affect the potential biodiversity recovery from the surrounding non-impacted areas. In addition, indirect effects, which occur widely in ecosystems when considering communities and food webs, must be considered and, if possible, differentiated from direct effects. The main current limitation of models addressing indirect effects is the very partial knowledge of key processes and species interactions for most ecosystems (Fleeger, 2020).

3.3. *Monitoring*

The application of pesticides, including their quantity, frequency, timing location and co-occurrences, is linked to specific spatial areas and timeframes. Therefore, a landscape approach is essential for linking realistic pesticide usage and chemical monitoring data. Information on when, where, and how pesticides are applied is the first step to quantify exposure levels, and co-exposure to multiple pesticides, for non-target organisms. Yet, monitoring pesticide occurrence in the environment and monitoring their possible effects on biodiversity require different approaches, tools, and expertise. The tools may include chemical, biological and ecological indicators and must connect spatial and temporal frames to assess the impact of pesticides on specific populations/communities and overall biodiversity. The interoperability must be extended to other aspects, i.e., for linking pesticide levels with actual use and fate processes, or for considering the impact of other cropping and farm management practices and environmental stress factors than pesticides in biomonitoring schemes. Landscape ecotoxicology approaches provide the basis for integrating all these aspects through retrospective landscape-based ERA (Focks, 2014). In the EU actual pesticide use data, at field level, is expected from the implementation of national plans under the Sustainable Use Directive; if actual use data is available, landscape exposure models are a key tool for connecting actual uses with monitoring results, in order to confirm or refine model estimations. In addition, chemical and biological monitoring are essential for calibrating and assessing the suitability of prospective models and approaches (Centanni et al., 2023).

Monitoring performed to assess pesticide presence, including transformation products, or pesticide effects, using biological and ecological indicators, is, by definition, temporally and spatially explicit. Data derived through such monitoring are available typically as "post-market registration", hampering their inclusion in prospective ERA. To circumvent this issue, it has been suggested to establish pre-market registration monitoring farm-catchment networks with realistic pesticide application patterns. Monitoring data may be overlooked during the renewal of market approval (in general every 10 years in the EU system) of registered pesticides, as this information may not be included in the pre-registration data aggregation process (Schäfer, et al., 2019). Additional considerations are needed for substances with natural or historical backgrounds, and EFSA has developed specific recommendations on the use of monitoring data for metals used as pesticides (EFSA PPR Panel et al., 2021).

3.4. Implementation

The implementation of landscape ERA in regulatory assessments should consider that these approaches are conceptually more complex than current single-substance regulatory ERA, requiring more effort and specific expertise. Yet, the implementation in integrated platforms will increase efficiency and is likely to be more effective for supporting decisions than currently used in in-field *vs.* off-field simplifications, enabling more realistic context-specific ERA predictions. Landscape models may include the assessment of the combined exposure to multiple pesticides and their potential adverse effects on the environment within an area, offering the possibility for comparing environmental impacts of different management scenarios (e.g., crop protection strategies, structural and/or compositional characteristics of landscapes).

A two-fold connection with chemical monitoring was identified: measured environmental concentrations would support spatially and temporally explicit landscape-based exposure assessments, while prospective landscape ERA models would support the design and implementation of chemical and ecological monitoring programs. The models are also essential for incorporating spatio-temporal distribution, activity patterns and population dynamics of non-target organisms (e.g., niche models) in the landscape mosaic (e.g., between treated and non-treated area). Following a trait-based (diet, body characteristics, mobility, …) approach (Knapp, et al., 2023), which are strong drivers of exposure and effects, would be ecologically relevant and an important issue for current ERA. For pragmatic reasons, ERA has always differentiated aquatic and terrestrial systems, but we need to consider pesticide transfer and ecological connectivity (e.g., amphibian species, insectivorous organisms that depend on the emergence from aquatic systems; mixed trophic chains) during the implementation and final integration of risks into environmental impacts (Schulz et al., 2015).

While pesticides are considered “data-rich” chemicals, effect assessments are limited by the available information, which mostly focuses on direct toxic effects. Therefore, effect modelling must use the existing information that mostly derive from laboratory studies that are conducted with pre-selected “model species” and under controlled exposure conditions. The currently applied tiered approach creates heterogeneity in the information available for different pesticides (Morrissey et al., 2023). In practice, only lower tier information is available for most pesticides, while additional risk assessment information is gathered among higher tiers for the more hazardous pesticides to refine the risk. Consequently, the landscape-based ERA should account for the different levels of information available for the different pesticide-NTO combinations, usually with more information available in cases where there is higher potential for effects. This situation affects both prospective and retrospective assessments.

New Approach Methodologies (NAMs) are an emerging set of *in silico* (computational), *in chemico,* and *in vitro* methods that can replace, reduce and refine traditional animal-based testing in chemical risk assessment. The utility of NAMs has mostly been explored for human health risk assessment, but their value to ecotoxicological hazard assessment and ERA has been increasingly acknowledged for some time (Bean et al., 2023; Di Nicola et al., 2023; Rattner et al., 2023). For example, *in silico* methods include effect modelling at the organism level; ecological models for estimating effects from the laboratory to the field, from individuals to populations, and for extrapolating effects across untested species and different levels of biological organisation; and landscape modelling (Astuto et al., 2022). *In chemico* and *in vitro,* including *omics*, can provide improved mechanistic knowledge of toxic effects on biological systems and should be investigated as options for the early identification of effect drivers, targeted traits and vulnerable species based on molecular and sub-organismal level data. High-throughput screening methods may facilitate gathering empirical information on combined effects on biological systems; provide quantitative dose-responses relationships for different pesticide combinations; and help to identify synergistic effects. However, the relationships between responses of such biomarkers and the fitness of organism (survival and reproduction parameters) should be unraveled in order to allow for the assessment of population outcomes. This approach could be facilitated through the consideration of Adverse Outcome Pathway (AOP) approaches (Lee et al., 2015; Camp and Lehmann, 2021).

3.5. Validation

While validation is essential for the regulatory acceptance and uptake of models, the complexity and intrinsic variability of ecological responses makes conventional validation (comparison of predictions with real observations) challenging for landscape ERA models. Effects at the landscape scale are context dependent. Models covering all relevant environmental stress factors, and validation over large timescale would probably not be feasible with the current level of knowledge. Alternative approaches are needed, however the key element regarding the validation of landscape models needs to be met: the representation of the fundamental behavior of the populations under consideration within its ecological context. This requires expert knowledge of ecological interactions, as it will allow to identify the meaningful levels of interaction to be included in a model and the essential data to gather for the verification of the model capabilities.

Validation of the next stages, including differentiating contributions (i.e., role of pesticides, other farming practices, and climate change), is challenging, as it requires sufficient knowledge and data on each stressor to compare independent prospective predictions with observed combined effects. Landscape level evaluation should be feasible at the local scale but is rarely done. This is first due to the difficulty to get extensive databases required to implement the models with input data and/or parameterizations as well as to assess their performance with observed data. Second, this requires a high resource demand.

Improving the knowledge on the interactions between farming practices and impact of pesticides is a priority, as this will support the development of more sustainable practices. Concepts such as integration of larger amounts of data from multiple studies could be explored as a complementing approach in combination with simpler models based on key impact drivers over larger scales. It is advisable to identify representative landscape scenarios and use citizen science as complementary data collection sources to validate model predictions over short to medium time scales. Specific elements of the model can be validated through the conventional comparison of predictions and observations, in particular exposure predictions and some direct short-term effects following pesticide applications. One critical aspect that would gain of a landscape level approach is to predict the co-occurrence of the organism and pesticide exposure in space and time. The model may identify the main determinant, the risk-driver, of the impact, allowing the use of the model for testing mitigation measures.

Another possible route could be to validate some of the most crucial building blocks of the model composed of several modules. For example, individual building blocks could be validated at individual levels for an individual-based model where individuals are represented by dynamic energy budget theory and toxicokinetic-toxicodynamic processes. Nevertheless, validation of individual-based models and other landscape approaches at large scales appear unfeasible currently as indicated above. Where a conventional comprehensive validation is unfeasible, case studies may provide the basis for “fit-for-purpose” qualifications, in the sense that model predictions, including the variability and uncertainty estimations, provide reliable information for supporting the decision-making process. Thus, the feasibility of using higher-tier field studies in combination with landscape scale models in regulatory ERA, as suggested in the EFSA guidance on pesticide risk assessment for bees (EFSA, 2023a), could be evaluated. In addition, models provide the possibility to calculate margins of safety for risks. In the context of the uncertainty about the model quality that emerges with complex landscape models, the use of margins of safety, similar to the concept of the LPx/EPx introduced for the use of TKTD models by EFSA could allow to use models according to the quality to which they could be validated/tested, and relative to the experience with the specific model (EFSA PPR Panel et al., 2018a). Using landscape scenarios for the quantification of the margin of safety have recently also been suggested for a complex, landscape scaled model such as the ApisRAM for honey bees (EFSA, 2023b), and could be considered for other organisms.

The required level of "reliability" and acceptable uncertainty for model estimations must consider the specific needs of each stakeholder (which is defined here as the final user of the model predictions). A proper problem formulation is essential. In addition to uncertainties and modelling capacities, quantitative estimations may be highly variable due to different landscape, ecological and environmental characteristics. This high variability affects the feasibility of validation approaches, requiring the selection of representative landscape scenarios. Sensitivity analysis tools, such as those offered through Monte Carlo analysis, should support this process, and may facility a reduction of model complexity while guaranteeing the reliability of the model estimates in line with the user needs. In some cases, the most relevant information to extract from landscape-based ERAs are: (1) possible trends in the ERA estimation due to specific landscape characteristics, including landscape management; and (2) the identification of the taxa/traits driving the risk in different agricultural systems. This type of "fit-for-purpose" qualification approach should specifically consider the users' needs. For example, in the case of regulatory ERAs, the qualification can be based on the model capacity to properly identify differences in the relative risk among agricultural conditions representing a gradient of agricultural intensiveness, based on factors related to land management (distribution/percentage of in-field/off-field areas; percentage of in-field buffer areas) and pesticide use (distribution/percentage of conventional/organic farming, in-crop buffer areas).

4. Conceptual framework for landscape-based ERA

The proposed conceptual framework for landscape-based ERA is flexible and compatible with different existing modelling approaches, including options to extrapolate toxicological effects from the laboratory to field; adapt the different levels of resolution to the available information and data gathering capacities; and tailor the assessment to the user's needs. The conceptual framework can be represented as a 3-D structure where the landscape structure is defined by the horizontal plane (XY dimension in Fig. 1), and the biological organization is built in the vertical dimension (dimension Z in Fig. 1), which includes individuals nested within populations and communities associated to the landscape horizontal plane. In this approach, each biological entity has a value in the Z dimension defining its typology, and an associated spatial distribution defined in the XY dimension (representing the habitat and defined as path, probability distribution or density distribution). The framework is based on iterations to consider the temporal dimension, and assumes that the biological entity and the associated XY component may change with time. Cropping and farm management practices, including pesticide application, environmental and other external factors are incorporated as iterations. Within this conceptual framework (see Fig. 1), pesticide environmental fate and the direct and indirect exposure patterns are linked to the structures defined in the horizontal dimension. The effects are estimated for the different biological entities in the vertical dimension. The outer line, circles, represent individuals, which are grouped into populations and represented as pentagons in a second line. Populations are further integrated in a single structure, the

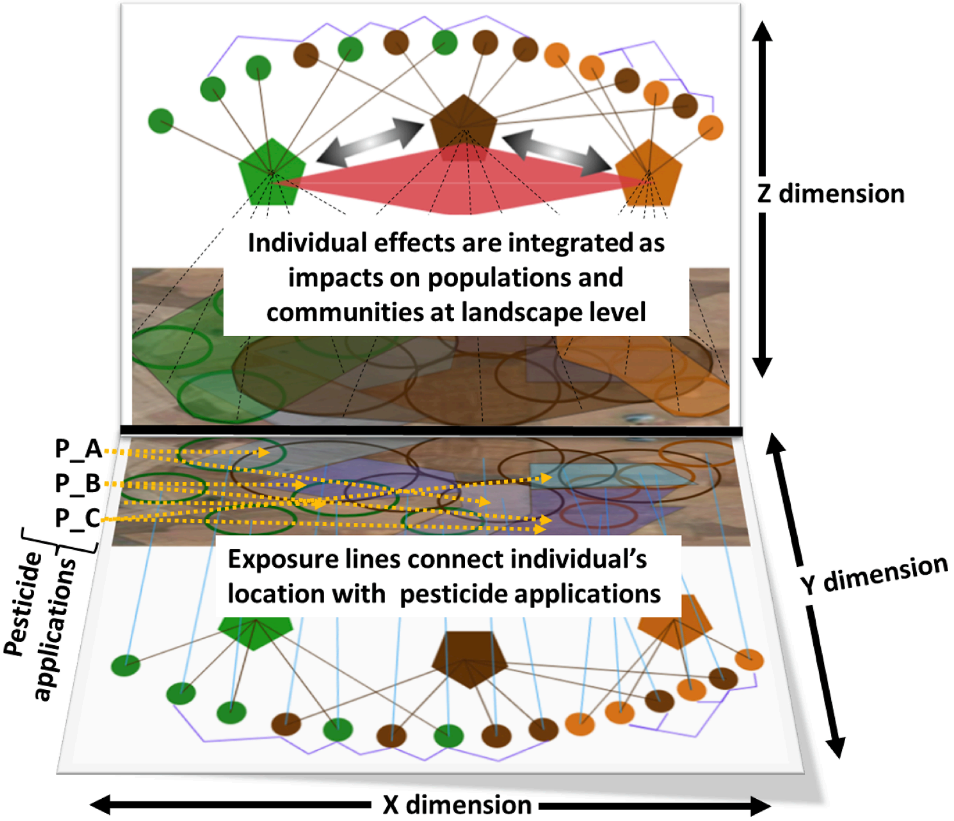

Fig. 1. Graphical representation of the conceptual framework proposed for landscape-based environmental risk assessment, with application of different pesticides (P_A to C) in different fields. For simplification, only the terrestrial compartment is presented, the aquatic compartment follows a similar approach associated to the catchment areas and river-basin structure. Circles represent individuals and each has an associated territory used for the exposure assessment. Lines connecting individuals represent ecological interactions. Pentagons represent populations, the population distribution area is the sum of those of their individuals. The effect assessment considers the interactions between populations sharing the same territory. The biological entities are projected in the horizontal plane to represent the exposure paths, including bioaccumulation and predation.

closest to the planes' intersection, the community, which is represented as a diamond. Ecological dependencies can be defined at different vertical levels. These are relevant only for biological entities that share at least part of the horizontal dimension, or are connected through indirect factors, e.g., two prey species not sharing the same area may be connected by a common predator.

As further refinement, models covering both terrestrial and aquatic systems can use positive Z values for terrestrial organisms and negative values for aquatic organisms. Therefore, Z=|3| defines individuals, Z=|2| define populations, and Z=|1| define communities, with values negative for aquatic and positive for terrestrial systems. The order reflects the aspirations of system-based approaches, i.e., a level 1 model offers a higher level of ecological integration than a level 2 or level 3 model and will allow the incorporation of Adverse Outcome Pathway approaches based on effects measured at sub-individual level ($|Z| > 3$).

A graphical representation of the conceptual model is presented in Fig. 2.

To facilitate a wide applicability of the conceptual approach, the framework proposes principles and naming conventions based on the set theory, which can be applied retrospectively to any landscape model to assist the comparison/integration of different models.

Individuals of the species “j”, I_iS_j, are defined as Z=|3| elements belonging to a Species set “S_j”; where

$$S_j = \{I_1S_j, \ldots, I_nS_j\}$$

Each individual “I_x” has an associated spatial location in the XY dimension associated to its biological characteristics, which triggers the exposure assessment and the identification of relevant interspecies interactions. The location of each individual at the time of and after pesticide applications, the traits, and the landcover (mainly distribution of crops, field margins, non-crop areas, and watershed structure including runoff and drainage for aquatic organisms) define the exposure potential of each individual. The location also defines inter-individual links, e.g., predators are exposed through preys sharing their spatial location. Depending on the model, the spatial location can be defined as a fixed area, a probability distribution, a pathway indicating the movement of the individual through the territory, or any other function. The modelled territory is defined in the XY plane, migration and recolonization, if included in the model, is represented as individuals leaving or entering the XY limits. Individuals from species “i” sharing at least partly their spatial location are considered a Population set “P_kS_j” of the Species set.

$$P_kS_i = \{I_1S_j, \ldots, I_nS_j\} for I_iS_j with similar/shared spatial locations, i.e., f(x,y) for I_iS_j \approx f(x,y) for I_{ii}S_j$$

If all organisms share the territory there is a single population $S_j = PS_j$; if there are different groups, each group represents a Population of S_i and

$S_j = \{P_1S_i, \ldots, P_kS_i\}$ where f(x,y) for S_j includes all geographical areas with presence of individuals from species S_j.

Populations are defined as Z=|2| elements. The spatial distribution

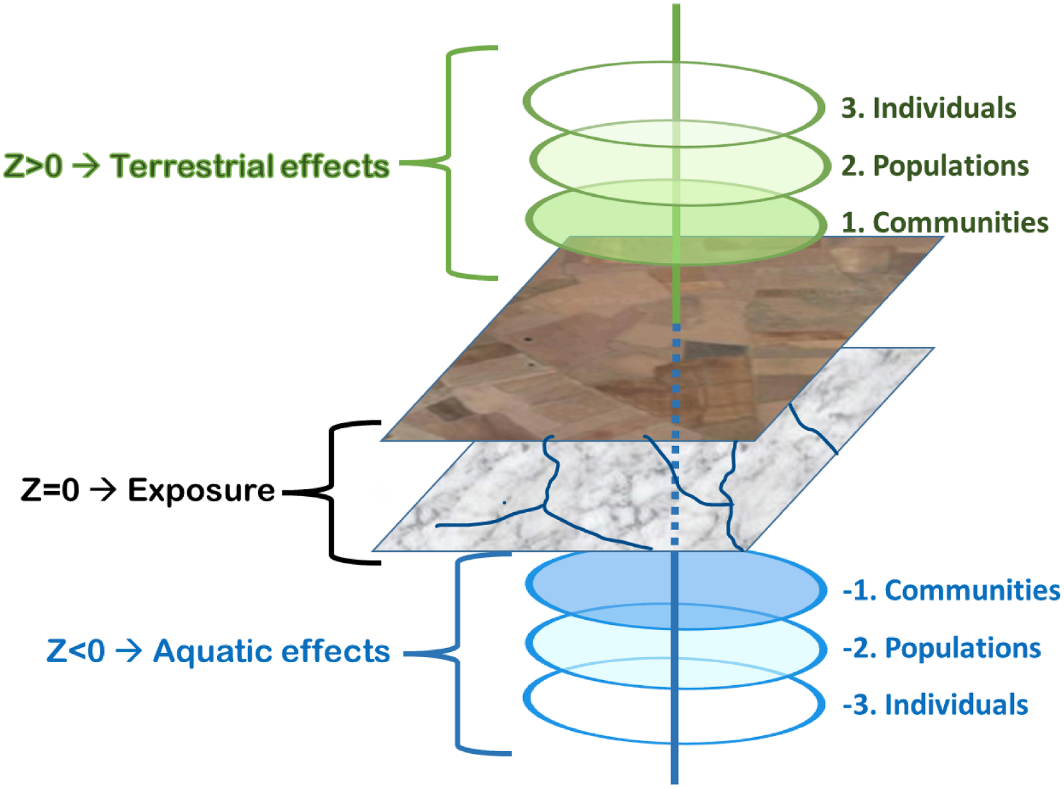

Fig. 2. Graphical representation of the proposed approach for describing landscape-based ERA models. Typically, effect models estimate direct effects on individuals or populations, and forecast the impacts at higher levels of biological organisation. When the direct effects produce significant changes in the ecological dynamics indirect effects should be considered. A spatially explicit exposure model/tool would provide information at the XY plane level, and can be complement with effect assessment models/tools to cover the Z dimension.

of the population is built through the integration of the spatial distribution for each individual belonging to the population, i.e., as a fixed area, a joint probability distribution or the combination of individual pathways. When building the spatial distribution for the population, it is possible to use a different approach compared to the one used for individuals, i.e., fixed individual areas or individual pathways can be integrated as probably distributions for the population.

Most model estimations focus on individuals or populations, but it is possible to also consider communities as a higher ecological hierarchical level. In this case, populations of different species sharing the same geographical area are integrated in a Community, “C”, where:

$C_l = \{P_1S_1, \ldots, P_kS_{j,} \ldots, P_nS_m\}$ for P_kS_j with similar/shared spatial locations, i.e., f(x,y) for $P_kS_j \approx$ f(x,y) for $P_{kk}S_{jj}$.

Communities are defined as $Z=|1|$ elements. The spatial location function for the negative Z values must be linked to the identified aquatic areas. This approach facilitates biological considerations and allows to address separately different exposure pathways. For example, amphibians use both terrestrial and aquatic habitat depending on their life-stage and seasonality. This means the same individual may have part of its spatial distribution function, f(x,y), associated to terrestrial habitats ($Z=3$) and part associated to aquatic habitat ($Z=-3$). Depending on the species biology, the same individual may therefore be associated to Z equal to 3 and to -3 for parts of the same day, or change the sign with the developmental stage, i.e., aquatic insect larvae have $Z=-3$ and the individual moves to $Z=+3$ when emerging as adult. In this way, the terrestrial and aquatic exposure pathways can be differentiated and combined as needed. In the traditional set theory, each object is either a member or not of a set, meaning $Z=|3|$ individuals are part or not of a | $Z=|2|$ population, and $Z=|2|$ populations are part or not of a $Z=|1|$ community; although the allocation may change with time, i.e., due to dispersal processes, emergence of aquatic individuals, etc. If additional flexibility is needed, the fuzzy set theory relaxes this condition, and each object is associated with a “degree of membership” for the next level sets.

The temporal component sets the dynamics of fate processes and those of the biological entities. The dynamics of each individual is established as a combination of biological parameters from specific stages of the life cycle (e.g., reproduction that may be limited to specific seasons), background factors (those not related to stressors covered by the model) and impacts of the stressors (pesticide exposure in this case). Default parameters or functions can cover biology and background factors to fix the timing for the different developmental stages, background mortality, and reproduction rate. The level of information is limited for most species, requiring parametrization based on a set of assumptions derived from trait-based approaches anchored in existing knowledge. These limitations should be presented in the uncertainty assessment model. The information availability and the user’s needs should be considered for selecting the optimal model resolution. The temporal dynamics may be done at the individual level, $Z=\pm3$, and then integrated for each population set at level $Z=\pm2$, or directly at the population level. When the model includes several populations for the same species associated to different spatial locations, the overall evolution of the species dynamics is represented by the evolution of the Species set, still at level $Z=\pm2$. When the model includes interspecies linkages, such as predation, competition, or coevolution, the links are limited to individuals and populations within the same community. Depending on the model design, individuals can be aggregated in nests or populations, and species can be aggregated by traits or other conditions. In addition, the links can be established as functions at different levels. The lower resolution is for level $Z=|1|$, the full community, and the higher resolution levels, $Z=|2|$ for populations or $Z=|3|$ for individuals, may have intermediate values, $|1|<Z<|2|$ represents groups of species and $|2|<Z<|3|$ represents groups of individuals from the same species.

Regarding the exposure assessment, a key element for a landscape model is associating exposure with the spatial and temporal dimensions. Spatialized multi-compartment models allow integrating multiple sources and exposure routes for several taxa, terrestrial, and aquatic, offering the possibility to consider climate and land use scenarios in prospective ways to estimate concentrations of a mixture of pesticides present at different periods and landscape elements. For pesticides, at least three exposure paths should be considered: direct exposure during the application, indirect exposure related to the environmental fate of the pesticide following each application, and secondary exposure from food items; taking into account relevant transformation products. Direct and indirect exposure paths should be associated with the spatial distribution defined horizontal plane, with associated XY dimensions and $Z=0$. For prospective models linked to regulatory assessments, direct exposure is defined according to the agricultural land-use pattern. For each patch, usually represented by the agricultural fields, a temporal agricultural timeline should be defined (i.e., as steps linked to soil preparation, sowing, crop development, harvesting, post-harvest preparation); for arable crops, crop rotation may be considered and require multiannual assessments. Pesticide applications are defined for each agricultural patch and connected to specific dates, pesticides, and application rates and conditions. Indirect exposure paths should consider the relevant fate processes during and after application, i.e., deposition on the crop, transfer to the ground, leaching, spray drift (both downwind deposition and airborne contamination), runoff, drainage, volatilisation, atmospheric transport, degradation, etc. Regulatory agencies such as EFSA in the EU and EPA in the USA have developed detailed environmental fate guidance documents for pesticides. Landscape pesticide ERA models may be based on these processes and scenarios, but the implementation should be spatially explicit, i.e., linked to the landform and including ecological infrastructures such as hedges, ditches, environmental characteristics, and agricultural practices that modify the pesticide environmental fate. For example, it may be considered as part of the agricultural practices that tillage may reduce runoff or that ditches may affect pesticide transfer from the fields to aquatic bodies (Dollinger et al., 2015). Accordingly, landscape-based ERA models need to represent in both the exposure and effect assessments, the main structures and processes that provide connectivity between landscape patches and compartments (air, soil, water). Secondary exposure from the diet requires first the definition of the diet of the organisms and then quantitative estimations of the concentration in each food item, including its variability and temporal evolution. When the “food items” are individuals from other species included in the model, organisms are exposed to those belonging to the same community and in line with the hierarchical allocation within the food chain. For models with estimation at the individual level, quantification for $Z=|3|$, the exposure can be limited to those individuals within the community sharing at least partly the spatial location, i.e, f(x,y) for $I_iS_j \approx$ f(x,y) for I_iS_{jj}, and in the case of models with the XY dimension presented as individualized paths, the exposure is estimated for each individual according to the expected exposure from each XY plane point and the time expended or the percentage of food consumed at that point.

The impact of pesticides is defined based on the existing (eco)toxicological information, generally covering mortality and reproduction, and may be extended with other effects such as growth, behaviour, or susceptibility to pathogens. Several options for representing this impact include exceeding threshold levels, full dose–response curves, toxicokinetic-toxicodynamic (TKTD) models, or population dynamics approaches; all can be used in spatially explicit effect models. Although pesticides are considered “data rich” chemicals, limitations in the (publicly) available ecotoxicological information for non-standard test species represent a major challenge for implementing landscape ERA models. In general, the available (eco)toxicological information covers laboratory studies on a set of selected experimental species, measuring survival and effects on reproduction, mostly with continuous exposure to the pesticide during different timelines defined in the test guidelines. The results of the laboratory studies are used for estimating the expected effects in the field, requiring extrapolations from acute to chronic effects, from the lab to the field, to other species, and from the effects on individuals to the expected consequences on populations and communities. The (eco)toxicity tests provide information on the direct effects of pesticides at some exposure levels, defined by the combination of dose/concentration and exposure time, and may also include the impact of abiotic factors such as temperature. The use of TKTD models can, given that sufficient ecotoxicological information is available, resolve the time dependency of the effects and reduce uncertainties for example concerning size dependency or the influence of temperature or multiple stressors on pesticide effects (EFSA PPR Panel et al., 2018a; Mangold-Döring et al., 2022).

The assessment of indirect effects requires the integration of ecological dynamic responses in the landscape ERA model. Basically, the results of laboratory studies should be translated into expected direct effects on individuals at level Z=|3|, then these effects should be translated into direct effects on populations at level Z=|2|. The consequences of direct Z=|3| effects at the population level, Z=|2|, and then at the community level Z=|1|, may indirectly affect populations and individuals linked through food chains and other ecological relationships, including competition. These effects may be integrated into the successional community dynamics, considering, for example, the background mortality, dispersion, and reproduction rates of individuals at level Z=|3|, which may be affected by changes in the abundance (density and prevalence) of individuals from the same and other species, modelled at level Z=|2|.

An additional complexity for pesticide ERA is that exposures are discontinuous, linked to the pattern of pesticide uses and their environmental fate; therefore, it is essential to consider the temporal and spatial scales of the fate and ecological processes related to the exposure patterns to different pesticides applied during the season by different farmers in the modelled area. In fact, the models should consider that the same direct effect on individuals may have different consequences on level Z=|2| outcomes depending on at which point of the population cycle the exposure occurs. The combined toxicity assessment should include individuals simultaneously exposed to different pesticides and additional options, such as individuals successively exposed to different pesticides or individuals from the same population exposed at different times to different pesticides.

5. Linking the conceptual framework to existing models and approaches

There are several models and approaches for estimating the environmental impact of pesticides at a landscape level. Ideally, these models and approaches should meet the needs of different users and be adapted/tailored to the available information. Consequently, a battery of landscape-based models and approaches addressing different (regulatory) needs should be developed, tested under different conditions, and complemented with guidance that clarifies the supported domains with clear indications of their advantages and limitations. The proposed conceptual model is expected to facilitate the integration and interoperability of different tools/models, and the comparison of results obtained from different approaches; guiding the selection of those most adequate to the data and users' needs during the problem formulation. As proof of concept, this section applies the proposed conceptual framework to a non-exhaustive selection of landscape models identified during the workshops based on the participants' experience focusing on those developed by the partners. The selection of the models and integration tools to be used in a specific landscape ERA will depend on factors such as user's needs, data availability and time/cost constrains. A set of case studies are being conducted in this PARC project and will provide recommendations on model selection and integration.

5.1. *Landscape pesticide exposure models (focus on XY plane)*

Landscape modelling of pesticide fate is complex due to the intricacy of involved processes, their non-linearity, coupling and variability in time and space (Leenhart et al., 2023). Existing models usually address specific processes such as hydrological transfers (e.g., SWAT, Neitsch et al., 2005) or spatial scales (i.e., soil profile, plot, or catchments). Most of them simulate the transport of water and pesticides in the soil and their transfer to the different environmental compartments (groundwater, surface water, plants and air) (e.g., PEARL (Van den Berg et al.,2016), MACRO, (Larsbo et al., 2005)); few ones consider ecological infrastructures at local scale such as ditches (e.g., TOXSWA (Adriaanse, 2009), PITCH (Dagès et al., 2023)) or grassed strips (e.g., VFSMOD (Muñoz-Carpena et al., 2010)). At the catchment scale, modeling strategies go from GIS-based multilocal approach (e.g., GeoPEARL (Tiktak et al., 2003)) to more complex ones such as the one developed, for example, in SWAT, widely used at the international level. A new integrative pesticide landscape exposure model MIPP (Modélisation Intégrée du devenir des Pesticides dans les Paysages agricoles) (Voltz et al., 2019) is currently being developed by several groups at INRAE in France, and PARC 6.4.4. partners. A main improvement offered by this tool is that it considers the horizontal hydrological and atmospheric transfers within the landscape. It is based on a spatially explicit mechanistic approach that couples the fate of pesticides in soil, water, and air as influenced by the spatial and temporal organization of farming practices and landscape properties (land use distribution, ditches). Main simulated processes are drift, soil and plant volatilization, atmospheric dispersion, diffuse and concentrated overland flow, coupled air, water and energy transfer in soil, root uptake, degradation, and sorption. It is planned to link the model with exposure models for non-target organisms likely to be exposed to pesticides by different pathways depending on their habitat. The model is currently applied to study the exposure of earthworms in a typical vineyard landscape submitted to various plant protection and soil management strategies. Given its complexity and requirements in computing time, the MIPP model is not intended for regulatory applications, but it can be used for identifying the main processes driving exposure at the landscape scale that need to be considered in more synthetic modelling approaches or for designing the most important features to be considered in landscape scenarios for exposure/effect assessments.

5.2. *Approaches for linking risks with actual environmental impacts (focus on Z)*

A challenge for the ERA of pesticides is to extrapolate effects from standard test conditions to real world conditions. However, several actions can be taken to transition to field-supported ERA: (1) rely on innovative approaches, including modelling and NAMs, as well as strengthened integration of ERA components (i.e. existing and new environmental monitoring data into model and method development); (2) consider indirect, chronic and sublethal effects better; (3) review test species and test protocols; (4) consider landscape aspects as presented in the previous sections, including spatial and temporal dynamics of pesticides and non-target organisms; (5) integrate environmental monitoring/surveillance data (including those gathered through post-registration monitoring); and (6) consider simultaneous exposure to multiple chemicals (including co-formulants and adjuvants), transformation products, and various environmental stress factors (i.e. climate change, invasive species, resources reduction).

Despite the limitations and remaining uncertainties, as it is not feasible to simulate reality, several tools and approaches are moving towards assessments closer to real-world conditions. For example, SPEAR identification of insecticidal pesticide effects in streams (Liess and Ohe, 2005) is a trait-based biological indicator system. SPEAR will be integrated within the indicator systems and German Plant Protection Index in a forthcoming iteration.

A multipartite working group under the SETAC umbrella depicted a comprehensive summary of the state of art of mechanistic effect models (MEMs) (Focks et al., under review). Seven book chapters cover relevant topics for the regulatory use of mechanistic effect models. They touch on aspects of the general use of MEMs, and provide considerations about criteria for model evaluation. This book delivers relevant and a possibly very useful collection of knowledge and approaches, including considerations for the formulation of regulatory questions; scenario development for the use of MEMs in regulatory ERA; and the evaluation of data underlying MEMs. It also provides specific perspectives of modular model evaluation, model calibration and validation, and uncertainty and sensitivity analyses. In all chapters, the general aim is to provide the scientific grounds for future regulatory discussions. All chapters also support both model developers and model evaluators with their tasks.

5.3. Individual-based risk assessment models ($Z=|3|$)

An example of landscape-based ERA approach focusing on individuals are the ALMaSS-based models (Topping, 2022; Topping et al., 2003); linking detailed individual-based models of animals and people ($Z=3$) through a richly simulated spatial environment (XY plane defined by site specific real conditions). Landscape size is limited by computing power only, and although typical landscapes are 10x10 km, sizes up to 50x50 km have been used. Most recently, the entire German states Lower Saxony and Brandenburg were simulated to evaluate landscape effects on ERA (UBA report in prep). XY plane resolution was 1 m^2, and details included pesticide fate, daily crop management and simulation of off-crop areas. Animal population models available included models for European Brown Hare (*Lepus europaeus*) (i.e. Topping et al., 2016), Field Vole (*Microtus agrestis*) (i.e. Dalkvist et al., 2009), Skylark (*Alauda arvensis*) (i.e. Topping and Odderskaer, 2004), Roe Deer (Capreolus capreolus) (Jepsen & Topping, 2004), non-target arthropods (*Ergione atra* and *Bembidion lampros*), Great Crested Newt (*Triturus cristatus*) (EFSA PPR Panel et al., 2018b), the honey bee (Apis mellifera) (Duan et al., 2022), and models in the final stages of development for *Osmia bicornis*, *Bombus terrestris*, *Poecilus cupreus*, and *Coccinella septempunctata*, as well as major European aphid pests. ALMaSS pesticide handling now includes spray (with drift), granule and seed coating application with fate in vegetation, soil, and plant component compartments and the capability of including body-burden and internal pesticide elimination rates (Poulsen et al, submitted). Population responses are typically described in terms of changes in local occupancy and abundance ($Z=2$), allowing effects that change density and range to be described (Hoye et al., 2012). ALMaSS outputs can be used to evaluate the impacts of indirect effects, spatial and temporal effects (Topping and Odderskaer, 2004; Topping et al., 2014, 2015) and can be used to derive simpler functions used in regulatory procedures such as deriving a benchmark dose (i.e., Topping and Luttik, 2017).

5.4. Population-based risk assessment models ($Z=|2|$)

A spatially explicit *meta*-population model for a dragonfly (Streib et al., 2020, 2022) has been implemented in Python and currently includes $Z=2$ elements, though extensions to community dynamics are currently ongoing. The model integrates generated landscapes of different configurations but could also be used with real landscapes. The simulation of population dynamics accounts for various factors, such as the insect's movement capabilities, landscape-type dependent dispersal, and environmental variables and stressors affecting habitat quality. The latter is linked to agriculture and could reflect pesticide effects on survival, growth, and reproduction. The model has been used to simulate and analyze the effects of habitat connectivity on the colonization success by the aquatic insect and to study the effects of multiple stressors, including agrochemicals, on the persistence of the population.

For vertebrates, a simplified terrestrial model (Tarazona et al., 2021) is available. It is basically a $Z=2$ model implemented in Python, which includes some $Z=3$ elements for modelling the population dynamics. The agricultural landscape, horizontal plane, is defined by the user as polygons and may be generic or reproduce an actual place in terms of both size and field distribution. Pesticide applications (active substance, application rate, day of application) are defined for each polygon. Individuals are grouped in nests, each associated with a feeding area. Exposure and effects are estimated daily and presented in graphical form with the option for downloading the raw data. Exposure is estimated for each species, nest, and age group according to the EFSA guidance available at that moment (EFSA, 2009), but can be adapted according to the updated guidance (EFSA et al., 2023c). The nest location and the pesticides applied in the associated feeding area represent the exposure drivers. Population dynamics are based on survival and reproduction rates defined for each age group, and the user may select the details of the reproductive period for each species, which can be adapted to specific regional and ecological characteristics. The drivers for effects are acute lethality, morbidity associated mortality and impact on reproduction rate, and are estimated as quantitative equations following a *meta*-analysis of the available laboratory studies, considering the timing of occurrence for the selected effects. Combined probability theory is used for estimating the combined effects of different pesticides on the survival and reproduction rates. Estimations are conducted for each nest and can be grouped according to the user's needs.

5.5. Integrative system-based approaches (moving towards $Z=|1|$) and next steps under PARC

For the moment, in general the available landscape effect models focus on a single species, may include interactions with other species and even integrate several models covering several species, but at the best of our knowledge there are no fully integrated landscape models estimating the evolution on the full ecological community following pesticide applications. As an alternative approach, ecosystem services have been proposed by EFSA as the basis for setting specific protection goals (Nienstedt et al., 2012; EFSA, 2016), and in areas such as the EU have been mapped covering the full territory (Maes et al., 2020). Some exploratory activities have linked the risk assessment results with the impact on specific services (Urionabarrenetxea et al., 2023), but further work is needed for moving towards landscape ERA integrating the pesticide risks at community or service level. Currently, the EFSA-funded AENEAS project is working on the development of protocols for linking effects and impacts on ecosystem services and their implementation in case studies for non-target arthropods.

The next step under PARC 6.6.4 is implementing this conceptual approach to a set of actual case studies in Europe. The definition of each case study includes the location, specific research questions, and the relevant regional stakeholders. Different tools and approaches, including those mentioned above, will be used and benchmarked against each other for each case study, and the results will be integrated into the continued collaborations between projects in PARC 6.4.4 as well as in specific recommendations, complementing related activities conducted in other jurisdictions such as the US Pop-Guide (Raimondo et al., 2021).

The main aims of a case study based on aquatic monitoring data are (1) to understand the predictive power of the exposure-activity ratios (EAR) approach and (2) to check for established AOPs being evidenced by the data for further investigation to evaluate the benefit of using these concepts in landscape model-based risk assessment. In particular, EAR will be calculated based on chemical monitoring data from a monitoring campaign in Switzerland (water, sediment, fish) and biotest data for agricultural sites, that will then be compared with biological monitoring data. Where meaningful, measured concentrations of individual chemicals from chemical monitoring data will be compared to biological activities determined in high-throughput *in vitro* assays (U.S. EPA ToxCast).

A second case study will be based on a Danish dataset (Rasmussen et al., 2015) aiming to (1) understand ecological effects (benthic macroinvertebrates) of multiple sequential pesticide exposures occurring in agricultural streams through the main pesticide application season and (2) evaluate the potential for factoring in multiple significant pesticide exposures in effect predictions of the landscape ERA. The case study will focus on biological and ecological traits to describe functional community structures before, during, and after the main pesticide application season and compared to measured pesticide exposure peaks during heavy precipitation events.

A set of terrestrial case studies has been designed using vineyards as a common crop while addressing the landscape variability for European vineyard landscapes. They include an exposure modelling based on accurate definition of transfer processes of PPP across landscape components linked to organism trait matrices in order to rank their potential exposure based on their ecological traits, as well as predictions and monitoring of environmental impacts at landscape level for different non-target organisms.

All case studies will consider the needs of local stakeholders to implement science-based proposals for assessing the sustainability of agricultural practices and improving biodiversity conservation in agricultural environments. In this sense, special contributions are expected from the most recently incorporated case, located in a farm in UK managed by an organization which has been testing landscape mitigation strategies to produce food cost effectively while also benefiting wildlife conservation. Additional cases may be incorporated in the future.

6. Conclusions

The conceptualization and implementation of landscape-based modelling approaches for the ERA of pesticides is an essential step to further advance the current ERA for pesticides and transition towards a systems-based ERA advocated by the scientific community (i.e., SAM, 2018; Streissl et al., 2018; Topping et al., 2020; Devos et al., 2022a, b; Sousa et al., 2022; Leenhardt et al., 2023; Williams et al., 2023), including EFSA (EFSA Scientific Committee, 2021; EFSA, 2018, 2021, 2022a, b) and other EU agencies (EEA, 2023).

It is essential to move towards more informative risk characterizations that connect risks with environmental impacts (Streissl et al., 2018). This is expected to solve some of the current limitations (de Luca Peña et al., 2022) when coupling ERA to life cycle assessments (LCA) and ecosystem services assessments (ESA). Scientific developments should be implemented in a stepwise manner. In this stepwise approach, the integration of landscape considerations in pesticide ERA is an essential step to foster the transition towards systems-based ERA (EFSA, 2022, Sousa et al., 2022). Following a stepwise approach would enable to implement different incremental and tangible steps (that would serve as steppingstones), and reach agreement on medium and long-term strategic priorities for the full implementation of landscape ERA.

Aggregating exposures from all different sources and merging hazard assessments would represent a first step in the implementation process of landscape-based ERA. This first step may be easier to take in jurisdictions with centralized assessment bodies. In the EU, this would require coordination and political endorsement, which could be achieved through the One Substance – One Assessment (OS-OA) approach under the EU Chemicals Strategy for Sustainability (van Dijk et al., 2021). Linking more realistic and context-specific ERA predictions with relevant environmental impacts would help to improve the dialogue between risk assessors and risk managers for setting protection goals and formulating sustainable agricultural strategies. It is therefore important that the different applications and stakeholders' needs are considered as part of the development and implementation process.

Environmental chemical, biological, and ecological monitoring are essential elements for the calibration and validation of landscape models. Currently, there are several initiatives from regulatory bodies and research projects, such as EESE, SYBERAC, TerraChem, PollinERA, among others, developing landscape ERA approaches, but such efforts are fragmented. Ideally, a large-scale monitoring scheme harmonized at the EU level should be envisaged. This will require political willingness and the prioritization of resources.

Despite the European focus of PARC, the developments presented here are relevant at an international level, and further international collaboration is envisaged. The impact of pesticides on biodiversity is a worldwide concern, and the use of landscape ERA for connecting the identified risks with actual environmental impacts, at prospective and retrospective levels, is emerging as a key tool for supporting agricultural sustainability and biodiversity conservation, particularly considering the challenges of climate change and the exponential increase of human population and their food needs.

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CRediT authorship contribution statement

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2024.108999.

References

Adriaanse, P.I., Beltman, W.H.J., 2009. Transient Water Flow in the TOXSWA Model (FOCUS Versions): Concepts and Mathematical Description. SC-DLO, Wageningen. https://www.wur.nl/en/publication-details.htm?publicationId=80af96b3-c389-4e22-b599-f120859dac79.

Andersson et al., 2021 KEMI. PM 7/21: Resilience of biodiversity to plant protection product use – the modifying influence of landscape and interventions" https://www.kemi.se/en/publications/pms/2021/pm-7-21-resilience-of-biodiversity-to-plant-protection-product-use—the-modifying-influence-of-landscape-and-interventions.

Astuto, M.C., Di Nicola, M.R., Tarazona, J.V., Rortais, A., Devos, Y., Liem, A.K.D., Kass, G.E.N., Bastaki, M., Schoonjans, R., Maggiore, A., Charles, S., Ratier, A., Lopes, C., Gestin, O., Robinson, T., Williams, A., Kramer, N., Carnesecchi, E., Dorne, J.L.C.M., 2022. In silico methods for environmental risk assessment: Principles, tiered approaches, applications, and future perspectives. Methods Mol. Biol. 2425, 589–636. https://doi.org/10.1007/978-1-0716-1960-5_23.

Beketov MA, Kefford BJ, Schäfer RB, Liess M. 2013. Pesticides reduce regional biodiversity of stream invertebrates. Proceedings of the National Academy of Sciences 110:11039-11043. 10.1073/pnas.1305618110.

Burke, T.A., Cascio, W.E., Costa, D.L., Deener, K., Fontaine, T.D., Fulk, F.A., Zartarian, V. G., 2017. Rethinking environmental protection: Meeting the challenges of a changing world. Environ. Health Perspect. 125 (3), A43–A49. https://doi.org/10.1289/EHP1465.

Camp, A.A., Lehmann, D.M., 2021. Impacts of neonicotinoids on the bumble bees bombus terrestris and bombus impatiens examined through the lens of an adverse outcome pathway framework. Environ. Toxicol. Chem. 40, 309–322. https://doi.org/10.1002/etc.4939.

Centanni, M., Ricci, G.F., De Girolamo, A.M., Romano, G., Gentile, F., 2023. A review of modeling pesticides in freshwaters: Current status, progress achieved and desirable improvements. Environ. Pollut. 316, 120553 https://doi.org/10.1016/j.envpol.2022.120553.

Dagès, C., Voltz, M., Bailly, J.-S., Crevoisier, D., Dollinger, J., Margoum, C., 2023. PITCH: A model simulating the transfer and retention of pesticides in infiltrating ditches and channel networks for management design purposes. Sci. Total Environ. 891, 164602 https://doi.org/10.1016/j.scitotenv.2023.164602.

Dalkvist, T., Topping, C.J., Forbes, V.E., 2009. Population-level impacts of pesticide-induced chronic effects on individuals depend more on ecology than toxicology. Ecotoxicol. Environ. Saf. 72 (6), 1663–1672. https://doi.org/10.1016/j.ecoenv.2008.10.002.

de Luca Peña, L.V., Taelman, S.E., Préat, N., Boone, L., van der Biest, K., Custódio, M., Hernandez Lucas, S., Everaert, G., Dewulf, J., 2022. Towards a comprehensive sustainability methodology to assess anthropogenic impacts on ecosystems: Review of the integration of Life Cycle Assessment, Environmental Risk Assessment and Ecosystem Services Assessment. Sci. Total Environ. 808, 152125 https://doi.org/10.1016/j.scitotenv.2021.152125.

Devos, Y., Craig, W., Devlin, R.H., Ippolito, A., Leggatt, R.A., Romeis, J., Shaw, R., Svendsen, C., Topping, C.J., 2019. Using problem formulation for fit-for-purpose pre-market environmental risk assessments of regulated stressors. EFSA J. Eur. Food Saf. Authority 17 (Suppl 1), e170708. https://doi.org/10.2903/j.efsa.2019.e170708.

Devos, Y., Arena, M., Ashe, S., Blanck, M., Bray, E., Broglia, A., Bronzwaer, S., Cafaro, A., Corsini, E., Dujardin, B., Fernandez Dumont, A., Gomez Garcia, M., Gardi, C., Guerra, B., Kass, G.E.N., Maggiore, A., Martino, L., Merten, C., Percivaldi, C., Szoradi, A., Valtueña Martinez, S., Ververis, S., Vrbos, D., Hugas, M., 2022. Addressing the need for safe, nutritious and sustainable food: Outcomes of the "ONE – Health, Environment & Society – Conference 2022″. Trends Food Sci. Technol. 129, 164–178. https://doi.org/10.1016/j.tifs.2022.09.014.

Di Nicola, M.R., Cattaneo, I., Nathanail, A.V., Carnesecchi, E., Astuto, M.C., Steinbach, M., Williams, A.J., Charles, S., Gestin, O., Lopes, C., Lamonica, D., Tarazona, J.V., Dorne, J.L.C.M., 2023. The use of new approach methodologies for the environmental risk assessment of food and feed chemicals. Curr. Opin. Environ. Sci. Health 31, 100416. https://doi.org/10.1016/j.coesh.2022.100416.

Duan, X., Wallis, D., Hatjina, F., Simon-Delso, N., Bruun Jensen, A., Topping, C.J., 2022. ApisRAM formal model description. EFSA Supporting Publications 19 (2), 7184E. https://doi.org/10.2903/sp.efsa.2022.EN-7184.

EEA, 2023. How pesticides impact human health and ecosystems in Europe. *EEA Journal*. DOI : https://www.eea.europa.eu/publications/how-pesticides-impact-human-health/.

EFSA PPR Panel, Ockleford, C, Adriaanse, P, Berny, P, Brock, T, Duquesne, S, Grilli, S, Hernandez-Jerez, AF, Bennekou, SH, Klein, M, Kuhl, T, Laskowski, R, Machera, K, Pelkonen, O, Pieper, S, Smith, RH, Stemmer, M, Sundh, I, Tiktak, A, Topping, CJ, Wolterink, G, Cedergreen, N, Charles, S, Focks, A, Reed, M, Arena, M, Ippolito, A, Byers, H and Teodorovic, I, 2018a. Scientific Opinion on the state of the art of Toxicokinetic/Toxicodynamic (TKTD) effect models for regulatory risk assessment of pesticides for aquatic organisms. EFSA Journal 2018;16(8):5377, 188 pp. 10.2903/j.efsa.2018.5377.

EFSA PPR Panel, Ockleford, C., Adriaanse, P., Berny, P., Brock, T., Duquesne, S., Grilli, S., Hernandez-Jerez, A. F., Bennekou, S. H., Klein, M., Kuhl, T., Laskowski, R., Machera, K., Pelkonen, O., Pieper, S., Stemmer, M., Sundh, I., Teodorovic, I., Tiktak, A., . . . Smith, R. H., 2018b. Scientific Opinion on the state of the science on pesticide risk assessment for amphibians and reptiles. *EFSA Journal*, *16*(2), e05125. 10.2903/j.efsa.2018.5125.

EFSA PPR Panel, Hernandez-Jerez A, Adriaanse P, Aldrich A, Berny P, Coja T, Duquesne S, Focks A, Marinovich M, Millet M, Pelkonen O, Tiktak A, Topping C, Widenfalk A, Wilks M, Wolterink G, Conrad A and Pieper S, 2021. Statement of the PPR Panel on a framework for conducting the environmental exposure and risk assessment for transition metals when used as active substances in plant protection products (PPP). EFSA Journal 2021;19(3):6498, 88 pp. 10.2903/j.efsa.2021.6498.

EFSA Scientific Committee, More, S., Bampidis, V., Benford, D., Bragard, C., Halldorsson, T., Hernández-Jerez, A., Hougaard Bennekou, S., Koutsoumanis, K., Machera, K., Naegeli, H., Saxmose Nielsen, S., Schlatter, J., Schrenk, D., Silano, V., Turck, D., Younes, M., Arnold, G., Dorne, JL., Maggiore, A., Pagani, S., Szentes, C., Terry, S., Tosi, S., Vrbos, D., Zamariola, G., Rortais, A... (2021). A Systems-Based Approach to the Environmental Risk Assessment of Multiple Stressors in Honey Bees. *EFSA Journal*, 19(5). 10.2903/j.efsa.2021.6607.

EFSA, 2009. Guidance Document on Risk Assessment for Birds & Mammals on request from EFSA. *EFSA Journal* 2009; 7(12):1438. 10.2903/j.efsa.2009.1438.

EFSA, 2018. Scientific risk assessment of pesticides in the European Union (EU): EFSA contribution to on-going reflections by the EC. *EFSA Supporting Publications*, *15*(1), 1367E. 10.2903/sp.efsa.2018.EN-1367.

EFSA, 2021. EFSA Strategy 2027 - Science Safe Food Sustainability Adopted at the Management Board Meeting. *EFSA journal*. https://www.efsa.europa.eu/sites/default/files/2021-07/efsa-strategy-2027.pdf.

EFSA, Auteri, D., Devos, Y., Fabrega, J., Pagani, S., Rortais, A., de Seze, G., Heppner, C., Hugas, M. (2022). Theme (Concept) Paper – Advancing the Environmental Risk Assessment of Chemicals to Better Protect Insect Pollinators (IPol-ERA). *EFSA Supporting Publications, 19(5).* 10.2903/sp.efsa.2022.e200505.

EFSA, Devos, Y., Auteri, D., de Seze, G., Fabrega, J., Heppner, C., Rortais, A., & Hugas, M. (2022). Theme (concept) paper – Building a European Partnership for next generation, systems-based Environmental Risk Assessment (PERA). *EFSA Supporting Publications*, *19*(5), E200503E. 10.2903/sp.efsa.2022.e200503.

EFSA, Adriaanse P, Arce A, Focks A, Ingels B,J¨olli D, Lambin S, Rundlof M, Süßenbach D, Del Aguila M, Ercolano V, Ferilli F, Ippolito A, Szentes Cs,Neri FM, Padovani L, Rortais A, Wassenberg J and Auteri D, 2023a. Revised guidance on the risk assessment of plant protection products on bees (Apis mellifera, Bombus spp. and solitary bees). EFSA Journal 2023;21(5):7989, 133 pp. 10.2903/j.efsa.2023.7989.

EFSA, Rortais A, Alaux C, Crall J, Duan X, Focks A, Linguadoca A, Topping C and More S, 2023b. Environmental scenarios for ApisRAM version 3, a honey bee colony model for pesticides risk assessment. EFSA supporting publication 2023:EN-8535. 35pp. 10.2903/sp.efsa.2023.EN-8535.

EFSA, Aagaard, A, Berny, P, Chaton, PF, Antia, AL, McVey, E, Arena, M, Fait, G, Ippolito, A, Linguadoca, A, Sharp, R, Theobald, A and Brock, T., 2023c. Guidance on the risk assessment for Birds and Mammals. *EFSA Journal*; 21(2):7790, 300 pp. 10.2903/j.efsa.2023.7790.

Fleeger, J.W., 2020. How do indirect effects of contaminants inform ecotoxicology? A Review. Processes 8, 1659. https://doi.org/10.3390/pr8121659.

Focks, A., 2014. The challenge: Landscape ecotoxicology and spatially explicit risk assessment. Environ. Toxicol. Chem. 33, 1193. https://doi.org/10.1002/etc.2568.

Focks, A., ter Horst, M., van den Berg, E., Baveco, H., van den Brink, P.J., 2014. Integrating chemical fate and population-level effect models for pesticides at landscape scale: New options for risk assessment. Ecol. Model. 280, 102–116. https://doi.org/10.1016/j.ecolmodel.2013.09.023.

Forister, M.L., Pelton, E.M., Black, S.H., 2019. Declines in insect abundance and diversity: We know enough to act now. Conserv. Sci. Pract. 1 (8) https://doi.org/10.1111/csp2.80.

Hoye, T.T., Skov, F., Topping, C.J., 2012. Interpreting outputs of agent-based models using abundance-occupancy relationships. Ecol. Ind. 20, 221–227. https://doi.org/10.1016/j.ecolind.2012.01.017.

IPBES (2019): Global assessment report on biodiversity and ecosystem services of the Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services. E. S. Brondizio, J. Settele, S. Díaz, and H. T. Ngo (editors). IPBES secretariat, Bonn, Germany. 1148 pages. 10.5281/zenodo.3831673.

Jepsen, J.U., Topping, C.J., 2004. Modelling roe deer (Capreolus capreolus) in a gradient of forest fragmentation: Behavioural plasticity and choice of cover. Can. J. Zool.-Rev. Can. Zool. 82 (9), 1528–1541. https://doi.org/10.1139/Z04-131.

Kattwinkel, M., Liess, M., Arena, M., Bopp, S., Streissl, F., Römbke, J., 2015. Recovery of aquatic and terrestrial populations in the context of European pesticide risk assessment. Environ. Rev. 23, 382–394. https://doi.org/10.1139/er-2015-0013.

Knapp, J.L., Nicholson, C.C., Jonsson, O., de Miranda, J.R., Rundlöf, M., 2023. Ecological traits interact with landscape context to determine bees' pesticide risk. Nat. Ecol. Evol. 7 (4), 547–556. https://doi.org/10.1038/s41559-023-01990-5.

Knillmann, S., Orlinskiy, P., Kaske, O., Foit, K., Liess, M., 2018. Indication of pesticide effects and recolonization in streams. Sci. Total Environ. 630, 1619–1627. https://doi.org/10.1016/j.scitotenv.2018.02.056.

Larsbo, M., Roulier, S., Stenemo, F., Kasteel, and R., Jarvis, N., 2005. An improved dual-permeability model of water flow and solute transport in the vadose zone. *Vadose Zone Journal*, 4, 398–406. 10.2136/vzj2004.0137.

Lee, J.W., Won, E.-J., Raisuddin, S., Lee, J.-S., 2015. Significance of adverse outcome pathways in biomarker-based environmental risk assessment in aquatic organisms. J. Environ. Sci. 35, 115–127. https://doi.org/10.1016/j.jes.2015.05.002.

Leenhardt S., Mamy L., Pesce S., Sanchez W., 2023. Impacts of plant protection products on biodiversity and ecosystem services, Versailles, Éditions Quæ, 174 p. 10.35690/978-2-7592-3749-4.

Li, Y., Miao, R., Khanna, M., 2020. Neonicotinoids and decline in bird biodiversity in the United States. Nat. Sustain. 3, 1027–1035. https://doi.org/10.1038/s41893-020-0582-x.

Liess, M., von der Ohe, P.C., 2005. Analyzing effects of pesticides on invertebrate communities in streams. Environ. Toxicol. Chem. 24 (4), 954–965. https://doi.org/10.1897/03-652.1.

Liess, M., Foit, K., Knillmann, S., Schäfer, R.B., Liess, H.-D., 2016. Predicting the synergy of multiple stress effects. Scientific Re-Ports 6, 32965. https://doi.org/10.1038/srep32965.

Liess, M., Liebmann, L., Vormeier, P., Weisner, O., Altenburger, R., Borchardt, D., Brack, W., Chatzinotas, A., Escher, B., Foit, K., Gunold, R., Henz, S., Hitzfeld, K.L., Schmitt-Jansen, M., Kamjunke, N., Kaske, O., Knillmann, S., Krauss, M., Küster, E., Link, M., Lück, M., Möder, M., Müller, A., Paschke, A., Schäfer, R.B., Schneeweiss, A., Schreiner, V.C., Schulze, T., Schüürmann, G., von Tümpling, W., Weitere, M., Wogram, J., Reemtsma, T., 2021. Pesticides are the dominant stressors for vulnerable insects in lowland streams. Water Res., 117262 https://doi.org/10.1016/j.watres.2021.117262.

Lindström et al., 2021; KEMI PM 2/21: Methods for assessing the effects of plant protection products on biodiversity". https://www.kemi.se/en/publications/pms/2021/pm-2-21-methods-for-assessing-the-effects-of-plant-protection-products-on-biodiversity.

Maes, J., Teller, A., Erhard, M., Condé, S., Vallecillo, S., Barredo, J.I., Paracchini, M.L., Abdul Malak, D., Trombetti, M., Vigiak, O., Zulian, G., Addamo, A.M., Grizzetti, B., Somma, F., Hagyo, A., Vogt, P., Polce, C., Jones, A., Marin, A.I., Ivits, E., Mauri, A., Rega, C., Czúcz, B., Ceccherini, G., Pisoni, E., Ceglar, A., De Palma, P., Cerrani, I., Meroni, M., Caudullo, G., Lugato, E., Vogt, J.V., Spinoni, J., Cammalleri, C., Bastrup-Birk, A., San Miguel, J., San Román, S., Kristensen, P., Christiansen, T., Zal, N., de Roo, A., Cardoso, A.C., Pistocchi, A., Del Barrio Alvarellos, I., Tsiamis, K., Gervasini, E., Deriu, I., La Notte, A., Abad Viñas, R., Vizzarri, M., Camia, A., Robert, N., Kakoulaki, G., Garcia Bendito, E., Panagos, P., Ballabio, C., Scarpa, S., Montanarella, L., Orgiazzi, A., Fernandez Ugalde, O., Santos-Martín, F., *Mapping and Assessment of Ecosystems and their Services: An EU ecosystem assessment*, EUR 30161 EN, Publications Office of the European Union, Ispra, 2020, ISBN 978-92-76-17833-0. https://publications.jrc.ec.europa.eu/repository/handle/JRC120383.

Mangold-Döring, A., Huang, A., van Nes, E.H., Focks, A., van den Brink, P.J., 2022. Explicit consideration of temperature improves predictions of toxicokinetic–toxicodynamic models for flupyradifurone and imidacloprid in gammarus pulex. Environ. Sci. Tech. 56, 15920–15929. https://doi.org/10.1021/acs.est.2c04085.

Marx-Stoelting, P., Rivière, G., Luijten, M., et al., 2023. A walk in the PARC: Developing and implementing 21st century chemical risk assessment in Europe. Arch Toxicol 97, 893–908. https://doi.org/10.1007/s00204-022-03435-7.

Mineau P, Kern H. 2023. Neonicotinoid insecticides: Failing to come to grips with a predictable environmental disaster. American Bird Conservancy, pp 121. https://abcbirds.org/wp-content/uploads/2023/07/2023-Neonic-Report.pdf.

Morrissey, C., Fritsch, C., Fremlin, K., Adams, W., Borgå, K., Brinkmann, M., et al., 2023. Advancing exposure assessment approaches to improve wildlife risk assessment. Integr. Environ. Assess. Manag. https://doi.org/10.1002/ieam.4743.

Muñoz-Carpena, R., Fox, G.A., Sabbagh, G.J., 2010. Parameter importance and uncertainty in predicting runoff pesticide reduction with filter strips. J. Environ. Qual. 39 (2), 630–641. https://doi.org/10.2134/jeq2009.0300.

Neitsch, S.L., Arnold, J.G., Kiniry, J.R., Williams, J.R., 2005. Soil and Water Assessment Tool Theoretical Documentation, Version 2005. Agricultural Research Service and Blackland Research Centre. Texas A&M University, College Station, TX. https://swat.tamu.edu/media/1292/SWAT2005theory.pdf.

Nienstedt, K.M., Brock, T.C., van Wensem, J., Montforts, M., Hart, A., Aagaard, A., et al., 2012. Development of a framework based on an ecosystem services approach for deriving specific protection goals for environmental risk assessment of pesticides. Sci. Total Environ. 415, 31–38. https://doi.org/10.1016/j.scitotenv.2011.05.057.

Raimondo, S., Schmolke, A., Pollesch, N., Accolla, C., Galic, N., Moore, A., Vaugeois, M., Rueda-Cediel, P., Kanarek, A., Awkerman, J., Forbes, V., 2021. Pop-guide: Population modeling guidance, use, interpretation, and development for ecological risk assessment. Integr. Environ. Assess. Manag. 17 (4), 767–784. https://doi.org/10.1002/ieam.4377.

Rasmussen, J.J., Wiberg-Larsen, P., Baattrup-Pedersen, A., Cedergreen, N., McKnight, U. S., Kreuger, J., Jacobsen, D., Kristensen, E.A., Friberg, N., 2015. The legacy of pesticide pollution: An overlooked factor in current risk assessments of freshwater systems. Water Res. 84, 25–32. https://doi.org/10.1016/j.watres.2015.07.021.

Rigal S, Dakos V, Alonso H, Auniņš A, Benkő Z, Brotons L, et al. 2023. Farmland practices are driving bird population decline across europe. Proceedings of the National Academy of Sciences 120:e2216573120. 10.1073/pnas.221657312.

Rundlof, M., Andersson, G.K.S., Bommarco, R., Fries, I., Hederstrom, V., Herbertsson, L., Jonsson, O., Klatt, B.K., Pedersen, T.R., Yourstone, J., Smith, H.G., 2015. Seed coating with a neonicotinoid insecticide negatively affects wild bees. Nature 521. https://doi.org/10.1038/nature14420.

Rundlöf, M., Stuligross, C., Lindh, A., Malfi, R.L., Burns, K., Mola, J.M., Cibotti, S., Williams, N.M., 2022. Flower plantings support wild bee reproduction and may also mitigate pesticide exposure effects. J. Appl. Ecol. 59, 2117–2127. https://doi.org/10.1111/1365-2664.14223.

Sánchez-Bayo, F., Wyckhuys, K.A.G., 2019. Worldwide decline of the entomofauna: A review of its drivers. Biol. Conserv. 232, 8–27. https://doi.org/10.1016/j.biocon.2019.01.020.

Schäfer, R.B., Liess, M., Altenburger, R., Filser, J., Hollert, H., Roß-Nickoll, M., Schäffer, A., Scheringer, M., 2019. Future pesticide risk assessment – narrowing the gap between intention and reality. Environ. Sci. Eur. 31 (21) https://doi.org/10.1186/s12302-019-0203-3.

Schulz, R., Bundschuh, M., Gergs, R., Brühl, C.A., Diehl, D., Entling, M.H., Fahse, L., Frör, O., Jungkunst, H.F., Lorke, A., Schäfer, R.B., Schaumann, G.E., Schwenk, K., 2015. Review on environmental alterations propagating from aquatic to terrestrial ecosystems. Sci. Total Environ. 538, 246–261. https://doi.org/10.1016/j.scitotenv.2015.08.038.

Siddique, A., Shahid, N., Liess, M., 2021. Multiple stress reduces the advantage of pesticide adaptation. Environ. Sci. Technol. https://doi.org/10.1021/acs.est.1c02669.

Sousa, J.P., Aldrich, A., Axelman, J., Backhaus, T., Brendel, S., Dorronsoro, B., Duquesne, S., Focks, A., Holz, S., Knillmann, S., Pieper, S., Schmied-Tobies, M., Silva, E., Topping, C., Wipfler, L., Williams, J., 2022. Building a European Partnership for next generation, systems-based Environmental Risk Assessment (PERA). EFSA Supporting Publications 19 (8), 7546E. https://doi.org/10.2903/sp.efsa.2022.EN-7546.

Streib, L., Kattwinkel, M., Heer, H., Ruzika, S., Schäfer, R.B., 2020. How does habitat connectivity influence the colonization success of a hemimetabolous aquatic insect? - A modeling approach. Ecol. Model. 416, 108909 https://doi.org/10.1016/j.ecolmodel.2019.108909.

Streib, L., Juvigny-Khenafou, N., Heer, H., Kattwinkel, M., Schäfer, R.B., 2022. Spatiotemporal dynamics drive synergism of land use and climatic extreme events in insect meta-populations. Sci. Total Environ. 814, 152602 https://doi.org/10.1016/j.scitotenv.2021.152602.

Streissl, F., Egsmose, M., & Tarazona, J. v. (2018). Linking pesticide marketing authorisations with environmental impact assessments through realistic landscape risk assessment paradigms. *Ecotoxicology*, *27*(7). 10.1007/s10646-018-1962-0.

Tiktak, Aaldrik & van der Linden, Ton & JJTI, Boesten. (2003). The GeoPEARL model. Description, applications and manual. https://www.pbl.nl/sites/default/files/downloads/716601007_0.pdf.

Topping, C.J., 2022. The Animal Landscape and Man Simulation System (ALMaSS): A history, design, and philosophy. Res. Ideas Outcomes 8. https://doi.org/10.3897/rio.8.e89919.

Topping, C.J., Hansen, T.S., Jensen, T.S., Jepsen, J.U., Nikolajsen, F., Odderskaer, P., 2003. ALMaSS, an agent-based model for animals in temperate European landscapes. Ecol. Model. 167 (1–2), 65–82. https://doi.org/10.1016/S0304-3800(03)00173-X.

Topping, C.J., Hansen, T.S., Jensen, T.S., Jepsen, J.U., Nikolajsen, F., Odderskær, P., 2003. ALMaSS, an agent-based model for animals in temperate European landscapes. Ecol. Model. 167, 65–82. https://doi.org/10.1016/S0304-3800(03)00173-X.

Topping, C.J., Kjaer, L.J., Hommen, U., Hoye, T.T., Preuss, T.G., Sibly, R.M., van Vliet, P., 2014. Recovery based on plot experiments is a poor predictor of landscape-level population impacts of agricultural pesticides. Environ. Toxicol. Chem. 33 (7), 1499–1507. https://doi.org/10.1002/etc.2388.

Topping, C.J., Craig, P.S., de Jong, F., Klein, M., Laskowski, R., Manachini, B., Pieper, S., Smith, R., Sousa, J.P., Streissl, F., Swarowsky, K., Tiktak, A., van der Linden, T., 2015. Towards a landscape scale management of pesticides: ERA using changes in modelled occupancy and abundance to assess long-term population impacts of pesticides. Sci. Total Environ. 537, 159–169. https://doi.org/10.1016/j.scitotenv.2015.07.152.

Topping, C.J., Dalby, L., Skov, F., 2016. Landscape structure and management alter the outcome of a pesticide ERA: Evaluating impacts of endocrine disruption using the ALMaSS European Brown Hare model. Sci. Total Environ. 541, 1477–1488. https://doi.org/10.1016/j.scitotenv.2015.10.042.

Topping, C. J., Aldrich, A., & Berny, P. (2020). Overhaul environmental risk assessment for pesticides. In *Science* (Vol. 367, Issue 6476). 10.1126/science.aay1144.

Topping, C.J., Luttik, R., 2017. Simulation to aid in interpreting biological relevance and setting of population-level protection goals for risk assessment of pesticides. Regul. Toxicol. Pharm. 89, 40–49. https://doi.org/10.1016/j.yrtph.2017.07.011.

Topping, C., Odderskaer, P., 2004. Modeling the influence of temporal and spatial factors on the assessment of impacts of pesticides on skylarks. Environ. Toxicol. Chem. 23 (2), 509–520. https://doi.org/10.1897/02-524a.

Tscharntke, T., Grass, I., Wanger, T.C., Westphal, C., Batáry, P., 2022. Spatiotemporal land-use diversification for biodiversity. Trends in Ecology & Evolution S0169534722001355. 10.1016/j.tree.2022.06.002.

Urionabarrenetxea, E., Casás, C., Garcia-Velasco, N., Santos, M.J.G., Tarazona, J.V., Soto, M., 2023. Environmental risk assessment of ppp application in European soils and potential ecosystem service losses considering impacts on non-target organisms. Ecotoxicol. Environ. Saf. 266, 115577 https://doi.org/10.1016/j.ecoenv.2023.115577.

Van den Berg, F., Tiktak, A., Boesten, J.J.T.I. and Linden, A.M.A. van der, 2016. PEARL model for pesticide behaviour and emissions in soil-plant systems. Wot-technical 41report, No. 61. Statutory Research Tasks Unit for Nature and the Environment. https://edepot.wur.nl/377664.

Van der Vegt, R.G., Maguire, S., Crump, D., Hecker, M., Basu, N., Hickey, G.M., 2022. Chemical risk governance: Exploring stakeholder participation in Canada, the USA, and the EU. Ambio 51 (7), 1698–1710. https://doi.org/10.1007/s13280-021-01671-2.

Van Dijk, J., Gustavsson, M., Dekker, S.C., van Wezel, A.P., 2021. Towards 'one substance – one assessment': An analysis of EU chemical registration and aquatic risk assessment frameworks. J. Environ. Manage. 280, 111692 https://doi.org/10.1016/j.jenvman.2020.111692.

Vasseur, C., Joannon, A., Aviron, S., Burel, F., Meynard, J.M., Baudry, J., 2013. The cropping systems mosaic: how does the hidden heterogeneity of agricultural landscapes drive arthropod populations? Agr. Ecosyst. Environ. 166, 3–14. https://doi.org/10.1016/j.agee.2012.08.013.

Voltz M., Bedos C., Crevoisier, D., Dagès C., Fabre J.C., Lafolie F., Loubet B., Personne E., Casellas E., Chabrier P., Chataigner M., Chambon C., Nouguier C., Bankwal P., Barriuso E., Benoit P., Brunet Y., Douzals J.P., Drouet J.L., Mamy L., Moitrier N., Pot V., Raynal H., Ruelle B., Samouelian A., Saudreau M. (2019). Integrated modelling of pesticide fate in agricultural landscapes. 21st International Fresenius AGRO Conference "Behaviour of Pesticides in Air, Soil and Water", 25-26 june 2019, Mainz, Germany.

Williams, J. H., Bordoni, A., Bednarska, A., Pinto, A., Martins, C. A., Henriques, D., Sgolastra, F., Knapp, J., Loureiro, J., Sousa, J. P., Gócs, K., Marcussen, L. K., Rundlöf, M., von Post, M., Castro, M., Mølgaard, N., Simon, N., Capela, N., Thomsen, P., … Topping, C. J. (2023). Roadmap for action on the environmental risk assessment of chemicals for insect pollinators (IPol-ERA). EFSA Supporting Publications, 20(11). 10.2903/sp.efsa.2023.en-8431.