Towards a general framework for the assessment of interactive effects of multiple stressors on aquatic ecosystems:

Results from the Making Aquatic Ecosystems Great Again (MAEGA) workshop

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Abstract

A workshop was held in Wageningen, The Netherlands, in September 2017 to collate data and literature on three aquatic ecosystem types (agricultural drainage ditches, urban floodplains, and urban estuaries), and develop a general framework for the assessment of multiple stressors on the structure and functioning of these systems. An assessment framework considering multiple stressors is crucial for our understanding of ecosystem responses within a multiply stressed environment, and to inform appropriate environmental management strategies. The framework consists of two components: (i) problem identification and (ii) impact assessment. Both assessments together proceed through the following steps: 1) ecosystem selection; 2) identification of stressors and quantification of their intensity; 3) identification of receptors or sensitive groups for each stressor; 4) identification of stressor-response relationships and their potential interactions; 5) construction of an ecological model that includes relevant functional groups and endpoints; 6) prediction of impacts of multiple stressors, 7) confirmation of these predictions with experimental and monitoring data, and 8) potential adjustment of the ecological model. Steps 7 and 8 allow the assessment to be adaptive and can be repeated until a satisfactory match between model predictions and experimental and monitoring data has been obtained. This paper is the preface of the MAEGA (Making Aquatic Ecosystems Great Again) special section that includes three associated papers which are also published in this volume, which present applications of the framework for each of the three aquatic systems.

Keywords: multiple stressors, aquatic ecosystems, workshop, ecological models, ecological risk assessment framework

1. Introduction

Decision makers generally focus on single-stressors, even though multiple stressor impacts are the norm rather than the exception as causes of observed ecosystem degradation. For example, Schinegger et al. (2012) analysed human pressures on fish and benthic invertebrate communities at 9330 river sites in Europe, indicating 31% of the communities were affected by one of the four evaluated stressors (water quality, hydrology, morphology or connectivity) and 47% by two or more. Similarly, Schäfer et al. (2016) evaluated monitoring data of large streams and rivers in Germany and found that all sites were at risk of effects by at least one stressor, with 97% of the sites exposed to two stressors or more. In marine systems, Halpern et al. (2015) ruled out a single stressor approach for situations where management efforts need to be prioritised, instead focusing on the cumulative human impact of twenty identified stressors over time.

A major obstacle to any discussion of the interactive effects of multiple stressors is the lack of a clear terminology, e.g. stressors', 'additivity', 'synergism' and 'antagonism'. As defined by Schäfer and Piggott (2018), a stressor is "a natural or anthropogenic environmental factor that can affect an individual", and synergism and antagonism are "the interactions between stressors that result in a stronger and weaker combined effect of stressors, respectively, than that predicted by a null model". Although synergism has received the most attention in the scientific literature, more complex types of interaction categories may be required to appropriately capture the joint response (for an overview see Piggott et al., 2015a). Further, the prevalence of the different types of interactions varied strongly across meta-analyses (Côté et al., 2016). The level of biological organisation studied may partly explain this variability, given that antagonism was rarely observed in physiological responses, whereas synergism was rarely associated with the community and ecosystem level. However, the assessment of which types of interactions are prevalent across studies varied with the null model used, which is often overlooked by authors (Griffen et al., 2016; Schäfer and Piggott, 2018), and may also contribute to the high variability, e.g. Coté et al. (2016). Schäfer and Piggott (2018) presented a range of null models and guidance on their selection based on the underlying mechanistic assumptions and their applicability in predicting effects of multiple stressors. In contrast to commonly used statistical null models, such as simple addition based on the linear model, several authors (Schäfer and Piggott, 2018; De Laender, 2018; Thompson et al., 2018) urged the development of mechanistic models for the prediction of interactions that explicitly incorporate ecological processes. De Laender (2018) illustrated that mechanistic inferences from statistical null models are hampered when the same mechanisms of interaction lead to different deviations from a null model and that different mechanisms can lead to the same deviations. In light of the observation that interaction mechanisms depend on the level of biological organisation (Côté et al., 2016), we suggest that different mechanistic models are required for different levels of biological organisation. Depending on the expected interaction of effects, at the individual level a toxicokinetic-toxicodynamic (TK-TD) model predicting the interactive effects of chemicals (e.g. Ashauer et al., 2007) may be most appropriate, whereas at the community level, models based on simpler predator-prey relationships (e.g. Peace et al., 2016) or resource competition (De Laender, 2018) may be more appropriate. At the ecosystem level, models including a simple (e.g. De Laender et al., 2015) or complex (i.e. non-spatial (Traas et al., 2004) or spatial (e.g. Topping et al., 2016)) food-web structure could be more appropriate. However, guidance for incorporating models into the assessment of the ecological consequences of multiple stressors is lacking. In light of this, the horizon scanning exercise executed by the Society of Environmental Toxicology and Chemistry (SETAC) identified multiple stressors of chemicals in the environment as a top question for European and Latin American environmental science communities (Van den Brink et al., 2018; Furley et al., 2018).

We aim to develop an approach, supporting model incorporation within an assessment framework of ecological consequences from multiple stressors, and apply this framework to three aquatic ecosystem types facing increasing pressure due to anthropogenic activities: agricultural drainage ditches, urban floodplains, and urban estuaries. The Making Aquatic Ecosystems Great Again (MAEGA) workshop was held in Wageningen, The Netherlands, in September 2017, and resulted in a proposed framework on how modelling can be used to assess interactions among stressors. Moreover, we collated data and literature on the three ecosystem types. This information was then used for assessing multiple stressor effects on the structure and functioning of these systems. The current paper is the preface of the MAEGA (Making Aquatic Ecosystems Great Again) special section of STOTEN that presents the framework. The following papers present the application of the framework in each of the three ecosystems (O'Brien et al., this volume; Monk et al., this volume; Bracewell et al., this volume).

2. General framework

The proposed framework builds on the approach from a previous workshop held in Sydney, Australia in 2014. The outcomes from the first workshop are presented in Baird et al. (2016), Dafforn et al. (2016), Chariton et al. (2016) and Van den Brink et al. (2016). The proposed framework consists of two components, (i) problem identification and (ii) impact assessment. This framework is based on practical steps formulated by Van den Brink et al. (2016) for the future ecological risk assessment of multiple stressors (Fig. 1). Applying both components of the framework consists of the following steps: 1) ecosystem selection; 2) identification of stressors and quantification of their intensity; 3) identification of receptors or sensitive groups for each stressor; 4) identification of stressor-response relationships and their potential interactions; 5) construction of an ecological model that includes relevant functional groups and endpoints; 6) prediction of the impact of multiple stressors, 7) confronting these predictions with experimental and monitoring data, and 8) potential adjustment of the ecological model. Steps 7 and 8 can be repeated until a satisfactory match between model predictions and observations is obtained.

2.1. Problem identification process

The problem identification component of the framework has many analogies with the construction of environmental scenarios for ecological risk assessment of chemicals (Rico et al., 2016). In both cases, the ecosystem of concern has to be identified and data on its physico-chemical characteristics, as well as its biological communities, have to be collected. The focus of the data collection (step 1) will depend on the stressor identity, stressor intensity, and related sensitive biological endpoints (step 2 and 3), rendering this identification process an iterative process. For instance, if a photosynthesis inhibiting herbicide is one of the stressors, then local data collection should focus on primary producers or photosynthesis inhibition (Van den Brink et al., 2006), whereas when deposited sediment is one of the stressors, data on the sedimentation-sensitive benthic invertebrates (e.g. determined based on traits, Piggott et al., 2015b) are needed. Conversely, the selection of stressors will require an assessment of their relevance for the organisms in the chosen ecosystem. This typically requires data on how the intensity of each stressor varies in space and time. If available, the data collection should extend its focus from classical monitoring data on communities and stressor intensity (e.g. concentrations in water) to new forms of evidence, including ecogenomics information, remote sensing data, and other 'big data' sets, to provide a broader view on the biodiversity and types of stressor modes of action present in the chosen environment (Brack et al., 2018; Chariton et al., 2016; Dafforn et al., 2016). All data on the ecosystem and stressor of concern should be integrated (sensu Rico et al., 2016) into an environmental scenario, including a description of both the stressor and the ecosystem of consideration, though this data will overlap in certain parameters or variables (e.g. temperature, invasive species).

Once environmental and stressor data are collected and integrated (steps 1 and 2), the next step is to identify the biological endpoints that are most sensitive to the stressors (step 3). If the stressor is a toxicant, knowledge on the chemical mode of action (Barron et al., 2015; Napierska et al., 2018), ecotoxicological modes of action (Barata et al., 2012), classical sensitivity data (e.g. at https://cfpub.epa.gov/ecotox/), or data from models that can predict sensitivity (e.g. Rico and Van den Brink, 2015; Raimondo et al., 2015; Toropov et al., 2017) can be used to assess sensitive groups. When the stressor is not a toxicant, a literature search on previously conducted experiments performed with these stressors, using single and multi-species test systems, will be a good starting point (e.g. Jackson et al., 2016; Crain et al., 2008). If experimental information is lacking, knowledge of the stressor mode of action (for classifications see e.g. Martin et al., 2014; Schäfer and Piggott, 2018) can be used to draw hypotheses on the relative sensitivity of biological endpoints related to the chosen ecosystem and level of biological organisation. Such data can also be used to derive stressor-response relationships for the identified sensitive endpoint or endpoints (step 4). For instance, classical species sensitivity distributions incorporating only species from sensitive groups (sensu Maltby et al., 2005) can be used for chemicals, if the aim is to establish community level stressor-response relationships. For other stressors, these stressor-response relationships can either be derived from the results of controlled experiments (e.g. Wagenhoff et al., 2012) or estimated using available evidence and expert knowledge, including environmental preferences or species occurrence data (Schmidt-Kloiber and Hering, 2015). Next, determining how the different stressors interact with each other given the biological scenario (step 4) needs to be carefully considered. For this, a simple, conceptual model of the ecosystem of concern should be developed (step 5) that at least includes the expected sensitive endpoints to the stressors (step 3) and their physico-chemical and biological stressor-response pathways (Van den Brink et al., 2016). These models can vary in their level of complexity and focus on different levels of biological organisation, as necessary.

2.2. Impact assessment of multiple stressors

From the conceptual model developed in step 5, predictions of interactive effects should be derived to generate hypotheses (step 6). These predictions should indicate, at minimum, the qualitative response of endpoints (e.g. increase or decrease in population size or receptor activity) and thus evaluate predictions in the context of observations (step 7). Observations refer to a) experimental data on the stressors of concern using relevant species or species assemblages, preferentially acquired under natural conditions, and b) monitoring data from the ecosystem of concern that evaluate the stressors of concern. If deviations are found between prediction and observation, the conceptual model may be adjusted until a satisfactory fit is obtained (Grimm et al., 2014). When no satisfactory fit can be obtained, the observed deviations should be translated into research questions and more experimental, monitoring or modelling work should be performed. The same data used for the construction of the model and stressor-response relationships may be partly needed for the evaluation of the model outcome. Therefore, it may not always be possible to complete a full validation or "evaludation" of the model using independent data (sensu Augusiak et al., 2014).

3. Case studies

3.1. Agricultural drainage ditches

Drainage ditches are ubiquitous features of agricultural landscapes and can be havens for biodiversity when properly managed (Verdonschot et al., 2011). Using the framework presented here, Bracewell et al. (this volume) developed a conceptual food web model using functional groups to assess the effects of selected stressors on ditch communities. Nutrients, pesticides, management practices (dredging and mowing), salinisation, and siltation were identified as the most common and important stressors for this ecosystem type. Bracewell et al. (this volume) performed a literature review of each stressor-functional group combination to determine the relative effects of individual stressors on each functional group. Due to limited published experimental results for most of the stressors, they took a qualitative approach to assess the impact of each stressor on the food web structure of ditches. A series of conceptual null models were then developed to illustrate this qualitative assessment of the direct effects of single stressors and selected paired-stressor combinations. Such a qualitative approach proved to be useful in identifying potential stressor interactions within these data-poor systems and as a first-step to considering multiple stressor scenarios in drainage ditch management.

3.2. Urban floodplains

Freshwater floodplains are highly complex, dynamic, and diverse ecosystems. Key drivers of change (e.g. urbanisation) cause direct and indirect pressures (e.g. altered inundation period) acting to create complex stress regimes. In the third paper of this special section, Monk et al. (this volume) applied a conceptual iterative model that incorporated stressor-based environmental filtering of biota within urban floodplains. Evidence was obtained from scientific literature using standardised search terms focusing on urbanisation as the driver of key pressures and stressors and their subsequent impacts on the biotic response of composition (i.e. species presence-absence) and function (i.e. biomass). The strength of direct and indirect effects of both individual and multiple pathways was quantified using two literature-based analyses: a weight-of-evidence approach and a network meta-analysis. The weight-of-evidence approach demonstrated the strength of incorporating study quality alongside data sufficiency, while the network meta-analysis highlighted the significance of indirect pathways within multiple pressure and stressor environments. Indeed, the importance of indirect effects in the analysis suggests that we are often missing key mechanistic evidence by which urbanisation pressures influence key biological receptors. The two approaches highlight that combining multiple spatio-temporal scales is critical for our understanding of direct and indirect ecological responses within multiple pressure and stressor environments.

3.3. Urban estuaries

Urban estuaries are highly diverse and among the most productive and valuable ecosystems in the world (e.g. Costanza et al 2014), but they are also among the most degraded (Crain et al 2009). Given that three-quarters of all large cities and more than 40% of the global population lives within 100 km of the coast, urbanised estuarine ecosystems are particularly vulnerable to compounding impacts from several anthropogenic stressors (Crain et al 2008). Urban estuaries, including ports and harbours are commonly exposed to chemical (e.g. contaminants), physical (e.g. built infrastructure), and biological (non-indigenous species) stressors. It is important to understand the interactive threats posed by these stressors so management efforts can be prioritised relative to the severity of the threats. In the fourth and last paper of this special section, O'Brien et al. (this volume) explored selected urban stressors and their potential interactions, linking interactive effects to responses in community structure and key ecological functions, including productivity and metabolism. They highlighted the potential for stressor combinations to change the nature of urban estuarine environments, creating new impacts that could not be predicted by studying only single stressors. Structural and functional endpoints were assessed in a meta-analysis approach that revealed unexpected trends in the magnitude of responses to multiple stressors. This allowed them to go beyond comparisons relying on community structural responses to single stressors, and to propose a new idea of how multiple stressor impacts should be measured at locally relevant scales. Importantly, the authors highlighted significant gaps in the literature, which are hindering our understanding of the effects of multiple stressors on urban estuarine ecosystems.

4. Next steps

Each of the three workshop groups worked independently to explore the application of the proposed general framework outlined above. The groups used different methods dictated by the different availabilities of formal evidence, and explored the use of different meta-analysis methods. The next workshop will focus on an evaluation of the relative pros and cons of each approach, and the development and application of the consensus methodology on specific data-rich ecosystem case studies.

References

Ashauer, R., Boxall, A.B.A., Brown, C.D., 2007. Modelling combined effects of pulsed exposure to carbaryl and chlorpyrifos on *Gammarus pulex*. Environ. Sci. Technol. 41, 5535-5541.

Augusiak, J., Van den Brink, P.J., Grimm, V., 2014. Merging validation and evaluation of ecological models to 'evaludation': A review of terminology and a practical approach. Ecol. Model. 280, 117–128.

Baird, D.J., Van den Brink, P.J., Chariton, A.A., Dafforn, K.A., Johnston, E.L., 2016. New diagnostics for multiply stressed marine and freshwater ecosystems: integrating models, ecoinformatics and big data. Mar. Freshwater. Res. 67, 391-392.

Barata, C., San Juan, M.F., Feo, M.L., Eljarrat, E., Soares, A.M.V.M., Barcelo, D., Baird, D.J., 2012. Population growth rate responses of *Ceriodaphnia dubia* to ternary mixtures of specific-acting chemicals: pharmacological versus ecotoxicological modes of action. Environ. Sci. Technol. 46, 9663-9672.

Barron, M.G., Lilavois, C.R., Martin, T.M., 2015. MOAtox: A comprehensive mode of action and acute aquatic toxicity database for predictive model development. Aquat. Toxicol. 161, 102-107.

Bracewell, S., Verdonschot, R.C.M., Schäfer, R.B., Bush, A., Lapen, D.R., Van den Brink, P.J., This volume. Predicting the response of drainage ditch ecosystems to multiple stressors. Sci. Total Environ.

Brack, W., Escher, B.I., Müller, E., Schmitt‒Jansen, M., Schulze, T., Slobodnik, J., Hollert, H., 2018. Towards a holistic and solution‒oriented monitoring of chemical status of European water bodies: how to support the EU strategy for a non‒toxic environment? Environmental Sciences Europe 30, 33.

Chariton, A.A., Sun, M., Gibson, J., Webb, J.A., Leung, K.M.Y., Hickey, C.W., Hose, G.C., 2016. Emergent Technologies and analytical approaches for understanding the effects of multiple stressors in aquatic environments. Mar. Freshwater. Res. 67, 414-428.

Côté, I.M., Darling, E.S., Brown, C.J., 2016. Interactions among ecosystem stressors and their importance in conservation. Proc. R. Soc. Lond. B. Biol. Sci. 283, 20152592.

Crain, C.M., Kroeker, K., Halpern, B.S., 2008. Interactive and cumulative effects of multiple human stressors in marine systems. Ecol. Lett. 11, 1304–1315.

Dafforn, K.A., Johnston, E.L., Ferguson, A., Humphrey, C.L., Monk, W., Nichols, S.J., Simpson, S.L., Tulbure, M.G., Baird, D.J., 2016. Big data opportunities and challenges for assessing multiple stressors across scales in aquatic ecosystems. Mar. Freshwater. Res. 67, 393-413.

De Laender, F., 2018. Community- and ecosystem-level effects of multiple environmental change drivers: beyond null model testing. Glob. Change Biol. 24, 5021-5030.

De Laender, F., Morselli, M., Baveco, H., Van den Brink, P.J., Di Guardo, A. 2015. Theoretically exploring direct and indirect chemical effects across ecological and exposure scenarios using mechanistic fate and effects modelling. Environ. Int. 74, 181-190.

Furley, T.H., Brodeur, J., Silva de Assis, H.C., Carriquiriborde, P., Chagas, K.R., Corrales, J., Denadai, M., Fuchs, J., Mascarenhas, R., Miglioranza, K.S., Miguez Caramés, D.M., Navas, J.M., Nugegoda, D., Planes, E., Rodriguez-Jorquera, I.A., Orozco-Medina, M., Boxall, A.B.A., Rudd, M.A., Brooks, B.W., 2018. Toward sustainable environmental quality: Identifying priority research questions for Latin America. Integr. Environ. Assess. Manag. 14, 344–357.

Griffen B., Belgrad B., Cannizzo Z., Knotts E., Hancock E., 2016. Rethinking our approach to multiple stressor studies in marine environments. Mar. Ecol. Prog. Ser. 543, 273–281.

Grimm, V., Augusiak, J., Focks, A., Frank, B.M., Gabsi, F., Johnston, A.S.A., Liu, C., Martin, B.T., Meli, M., Radchuk, V., Thorbek, P., Railsback, S.F., 2014. Towards better modelling and decision support: Documenting model development, testing, and analysis using TRACE. Ecol. Model. 280, 129–139.

Halpern, B.S., Walbridge, S., Selkoe, K.A., Kappel, C.V., Micheli, F., D'Agrosa,C., Bruno, J.F., Casey, K.S., Ebert, C., Fox, H.E., Fujita, R., Heinemann, D., Lenihan, H.S., Madin, E.M.P., Perry, M.T., Selig, E.R., Spalding, M., Steneck, R., Watson, R., 2008. A global map of human impact on marine ecosystems. Science 319, 948–52.

Jackson, M.C., Loewen, C.J.G., Vinebrooke, R.D., Chimimba, C.T., 2016. Net effects of multiple stressors in freshwater ecosystems: A meta-analysis. Glob. Change Biol. 22, 180–189.

Maltby, L., Blake, N., Brock, T.C.M., Van den Brink, P.J., 2005. Insecticide species sensitivity distributions: the importance of test species selection and relevance to aquatic ecosystems. Environ. Toxicol. Chem. 24, 379-388.

Martin B., Jager T., Nisbet R.M., Preuss T.G., Grimm V., 2014. Limitations of extrapolating toxic effects on reproduction to the population level. Ecol. Appl. 24, 1972–1983.

Monk, W.A., Compson, Z.G., Bo Choung, C., Korbel, K., Rideout, N., Baird, D.J., This volume. Urbanisation of floodplain ecosystems: weight-of-evidence and network meta-analysis elucidate multiple stressor pathways. Sci. Total Environ.

Napierska, D., Sanseverino, I., Loos, R., Gómez Cortés, L., Niegowska, M., Lettieri, T., 2018. Modes of action of the current Priority Substances list under the Water Framework Directive and other substances of interest. EUR 29008 EN, JRC110117, Publications Office of the European Union, Luxembourg, Luxembourg.

O'Brien, A.L., Dafforn, K.A., Chariton, A.A., Johnston, E.L., Mayer-Pinto, M.M., This volume. After decades of stressor research in coastal marine ecosystems the focus is still on single stressors: a meta-analysis. Sci. Total Environ.

Peace, A., Poteat, M.D., Wang, H., 2016. Somatic Growth Dilution of a toxicant in a predator–prey model under stoichiometric constraints. J. Theor. Biol. 407, 198-211.

Piggott J.J., Townsend C.R., Matthaei C.D., 2015a. Reconceptualizing synergism and antagonism among multiple stressors. Ecol. Evol. 5, 1538–1547.

Piggott, J.J., Salis, R.K., Lear, G., Townsend, C.R., Matthaei, C.D., 2015b. Climate warming and agricultural stressors interact to determine stream periphyton community composition. Glob. Change Biol. 21, 206–222.

Raimondo, S., Lilavois, C.R., Barron, M.G., 2015. Web-based Interspecies Correlation Estimation (Web-ICE) for Acute Toxicity: User Manual. Version 3.3, EPA/600/R-15/192 (https://www3.epa.gov/webice/). U.S. Environmental Protection Agency, Office of Research and Development, Gulf Ecology Division. Gulf Breeze, FL. USA.

Rico, A., Van den Brink, P.J., 2015. Evaluating aquatic invertebrate vulnerability to insecticides based on intrinsic sensitivity, biological traits and toxic mode-of-action. Environ. Toxicol. Chem. 34, 1907–1917.

Rico, A., Van den Brink, P.J., Gylstra, R., Focks, A., Brock, T.C.M., 2016. Developing ecological scenarios for the prospective aquatic risk assessment of pesticides. Integr. Environ. Asses. 12, 510-521.

Schäfer, R. B., Kühn, B., Malaj, E., König, A., Gergs, R., 2016. Contribution of organic toxicants to multiple stress in river ecosystems. Freshwater Biol. 61, 2116–2128.

Schäfer, R.B., Piggott, J.J., 2018. Advancing understanding and prediction in multiple stressor research through a mechanistic basis for null models. Glob. Change Biol. 24, 1817-1826.

Schinegger, R., Trautwein, C., Melcher, A., Schmutz, S., 2012. Multiple human pressures and their spatial patterns in European running waters. Water Environ. J. 26, 261–273.

Schmidt-Kloiber, A., Hering D., 2015. www.freshwaterecology.info - an online tool that unifies, standardises and codifies more than 20,000 European freshwater organisms and their ecological preferences. Ecol. Indic. 53, 271-282.

Thompson P.L., MacLennan M.M., Vinebrooke R.D., 2018. An improved null model for assessing the net effects of multiple stressors on communities. Glob. Change Biol. 24, 517–525.

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.

Toropov, A.A., Toropova, A.P., Marzo, M., Dorne, J-L., Georgiadis, N., Benfenati, E., 2017. QSAR models for predicting acute toxicity of pesticides in rainbow trout using the CORAL software and EFSA's OpenFoodTox database. Environ. Toxicol. Phar. 53, 158-163.

Traas, T.P., Janse, J.H., Van den Brink, P.J., Brock, T.C.M., Aldenberg, T., 2004. A freshwater food web model for the combined effects of nutrients and insecticide stress and subsequent recovery. Environ. Toxicol. Chem.23, 521-529.

Van den Brink, P.J., Blake, N., Brock, T.C.M., Maltby L., 2006. Predictive value of Species Sensitivity Distributions for effects of herbicides in freshwater ecosystems. Hum. Ecol. Risk Assess. 12: 645-674.

Van den Brink, P.J., Bo Choung, C., Landis, W., Mayer-Pinto, M., Pettigrove, V., Scanes, P., Smith, R., Stauber, J., 2016. New approaches to the risk assessment of multiple stressors. Mar. Freshwater. Res. 67, 429-439.

Van den Brink, P.J., Boxall, A.B.A., Maltby, L., Brooks, B.W., Rudd, M.A., Backhaus, T., Spurgeon, D., Verougstraete, V., Ajao, C., Ankley, G.T., Apitz, S.E., Arnold, K., Brodin, T., Canedo-Arguelles, M., Chapman, J., Corrales, J., Coutellec, M-A., Fernandes, T.F., Fick, J., Ford, A., Gimenez Papiol, G., Groh, K.J., Hutchinson, T.H., Kruger, H., Kukkonen, J.V.K., Loutset, S., Marshall, S., Muir, D., Ortiz-Santaliestra, M.E., Paul, K.B., Rico, A., Rodea-Palomares, I., Rombke, J., Rydberg, T., Segner, H., Smit, M., van Gestel, C.A.M., Vighi, M., Werner, I., Zimmer, E.I., van Wensem, J., 2018. Towards sustainable environmental quality: priority research questions for Europe. Environ. Toxicol. Chem. 37, 2281-2295.

Verdonschot R.C.M., Keizer-Vlek H.E., Verdonschot P.F.M., 2011. Biodiversity value of agricultural drainage ditches: a comparative analysis of the aquatic invertebrate fauna of ditches and small lakes. Aquat. Conserv. 21, 715-727.

Wagenhoff, A., Townsend, C.R., Matthaei, C.D., 2012. Macroinvertebrate responses along broad stressor gradients of deposited fine sediment and dissolved nutrients: a stream mesocosm experiment. J. Appl. Ecol. 49, 892–902.

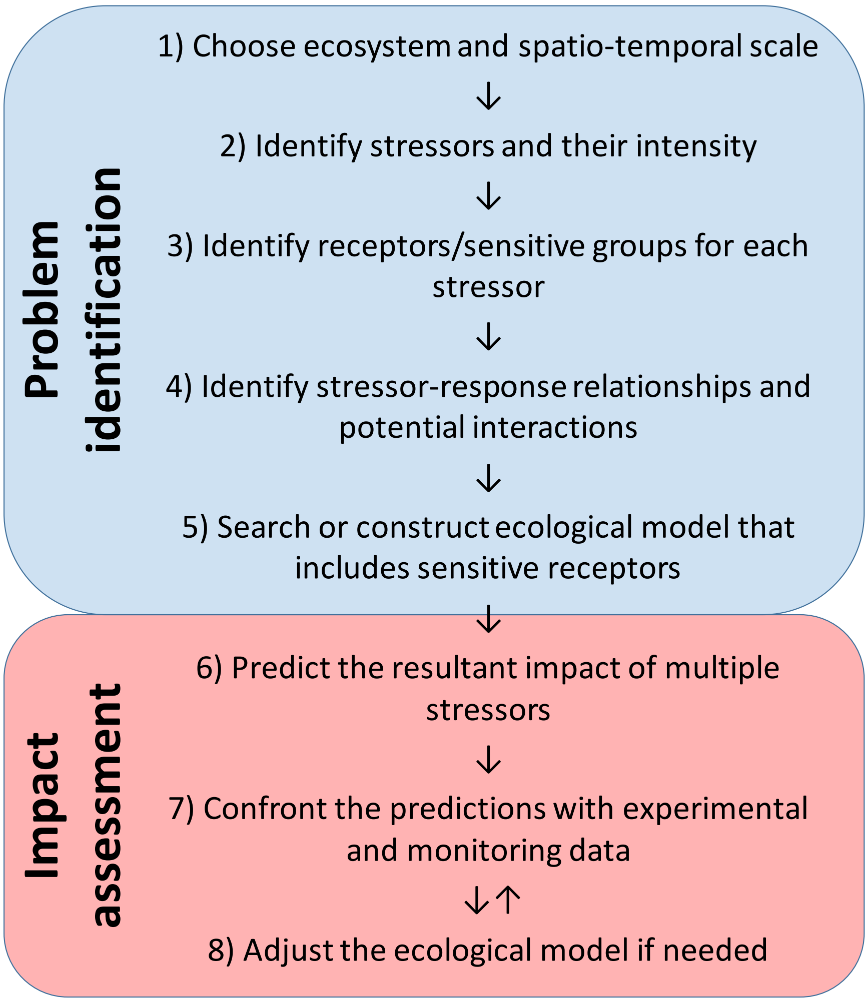

Figure 1. General framework showing how models can be incorporated into the assessment of the interactive ecological consequences of multiple stressors.