***Making Waves*. Bridging theory and practice towards multiple stressor management in freshwater ecosystems**

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Abstract

Despite advances in conceptual understanding, single-stressor abatement approaches remain common in the management of fresh waters, even though they can produce unexpected ecological responses when multiple stressors interact. Here we identify limitations restricting the development of multiple-stressor management strategies and address these, bridging theory and practice, within a novel empirical framework. Those critical limitations include that (i) monitoring schemes fall short of accounting for theory on relationships between multiple-stressor interactions and ecological responses, (ii) current empirical modelling approaches neglect the prevalence and intensity of multiple-stressor interactions, and (iii) mechanisms of stressor interactions are often poorly understood. We offer practical recommendations for the use of empirical models and experiments to predict the effects of freshwater degradation in response to changes in multiple stressors, demonstrating this approach in a case study. Drawing on our framework, we offer practical recommendations to support the development of effective management strategies in three general multiple-stressor scenarios.

1.0 Introduction

1.1 Freshwater ecosystems under stress. Freshwater ecosystems are commonly exposed to multiple anthropogenic stressors, which can interact and produce ecological surprises (Ormerod et al., 2010). While conceptual understanding and experimental demonstration of these interactions is now well established (Schäfer & Piggott, 2018), a major challenge remains to develop approaches to detect, quantify and manage stressor interactions in the real world (Feld et al., 2016). To inform this development, various attempts have been made to assess the frequency of stressor interactions across a broad range of freshwater ecosystems (Birk, 2019). These endeavours have identified issues that limit our capacity to generalise and predict undesirable ecological responses to single stressor reduction strategies. More conspicuously, very few published studies demonstrate the successful management of single or multiple stressors, where interactions and hierarchies have first been quantified.

This inability to generalise poses a problem for ecosystem management, which has historically focussed on abating individual stressors (Schindler et al., 2016). Well-informed multiple-stressor management could offer opportunities to offset effects of large-scale stressors that are hard to manage locally, including anthropogenic warming and changes in precipitation patterns associated with climate change (Moss et al., 2011) or the widespread proliferation of synthetic chemicals (Bernhardt et al., 2017) and toxic substances from industrial and domestic sources (Walters et al., 2020). There is an urgent need to develop methods to diagnose multiple stressor interactions and assess responses of ecological indicators to them across both degradation and

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recovery pathways. These methods must be applicable to data gathered at different scales and resolutions (Blair et al., 2019).

Here, we demonstrate how empirical data on fresh waters can underpin effective management of ecosystems subject to multiple stressors. Specifically, we explore how theory on multiple-stressor interactions and ecological responses is relevant to empirical data, particularly from national monitoring schemes such as those stipulated by the EU Water Framework Directive (WFD; European Commission, 2000) or the USA Federal Water Pollution Control Act (2002, 'The Clean Water Act'). We argue, however, for greater integration of understanding from such monitoring data with outcomes of experiments and modelling. Finally, we build on this understanding to develop practical recommendations for integrating the assessment and management of multiple stressors into future freshwater management and biodiversity protection strategies, highlighting limitations that remain to be addressed.

1.2 The conceptual basis of stressor interactions. Conceptual models describing forms and directions of stressor interactions have predominantly focused on quantifying and classifying deviations from additive effects models (Piggott et al., 2015a). Effects are defined as *additive* when an ecological response is equal to the sum of the effects of the individual stressors. *Synergistic* interactions occur when ecological responses are greater than the sum of the additive effects, and *antagonistic* interactions where ecological responses are less than the sum of the additive effects (Figure 1). Additive effects indicate that stressors act independently of one another, and so control of any one stressor should result in exactly proportional ecological responses. Under such a scenario, gradual changes in ecological response should be

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detected in monitoring data (Hillebrand et al., 2020). Such data may reveal ecological improvements that are greater than expected when stressors producing synergistic interactions are mitigated. In contrast, reduction of an antagonistic stressor could result, counter-intuitively, in the detection of further ecological degradation through monitoring. Piggott et al. (2015b) extended this basic model by considering the cumulative magnitude and direction of effects. This revealed cross-over interactions where combined stressor effects cancel each other and can lead to effects opposite to those of the individual effects. This phenomenon has been called *mitigating synergism* (Piggott et al., 2015b) or *reversal* (Jackson et al., 2016).

2.0 Moving from theory to practice: detection; prediction & management. The prevalence of interactions across scales and ecosystem types is increasingly recognised. An assessment of more than 100,000 water bodies across Europe, reported under the 2nd WFD River Basin Management cycle (2009–2015) showed that 50% of them were affected by two or more stressors, most commonly, hydromorphological modifications and nutrient pollution (EEA, 2018). Likewise, based on 174 pairwise stressor combinations from experiments and surveys across Europe, Birk et al. (2020) report that one-third exhibited detectable interactions and confirmed nutrient pollution as the most common and dominant stressor (i.e. explained the greatest variation in the response variables in the empirical models), although its effects may be moderated by warming and increasing humic content across lakes, with alterations of flow and channel morphology being widespread stressors in rivers. Similar data syntheses across other regions (Rigosi et al., 2014) and ecosystem types can inform large-scale adaptive and mitigative interventions in response to climate

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change. However, these endeavours must be based on a methodology providing robust comparisons across ecosystem types and geographical regions.

2.1 Detection of multiple-stressor interactions. The application of quantitative methodologies to detect multiple-stressor interactions involves a number of key challenges. Firstly, current conceptual frameworks disagree on the null model for expected responses to non-interacting stressors. At least three null models feature in current frameworks (additive, multiplicative and dominance) and the choice affects the classification of interaction type (Côté et al., 2016; Schäfer & Piggott, 2018). Current ecological analyses often employ generalised linear models (GLMs) and their extensions. However, it is not widely appreciated that the null model for the interaction is set by the GLM link function or any transformation of the dependent response variable (e.g. Gaussian, additive null model; Poisson or logarithmic, multiplicative null model; binomial, unspecified null model). Thus, in many cases interactions are statistically tested without reference to current interaction frameworks, while one component of the interaction, *dominan*ce, is not captured by any statistical framework. Greater awareness of how model design influences testing for interactions is needed to avoid statistical pitfalls in informing environmental management.

Secondly, stressors may vary in their intensity of effect and stressor gradient lengths differ among studies and data collections. Both factors can markedly influence the outcome of multiple-stressor analyses where interactions may lurk outside the data range. Notably, large datasets covering wide spatial or temporal scales tend to encompass longer gradients and reveal stronger interactions (Feld et al., 2016; Schinegger et al., 2016).

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Thirdly, paired-stressor interactions may not capture the full complexity of outcomes, yet, are most commonly applied (Gessner & Tlili, 2016), constraining the scope for detection of higher-order interactions (Feld et al., 2016). In addition, stressors can affect multiple ecosystem components, with the predominant types of interactions varying among levels of ecological organisation (individuals, populations, communities) and the specific response variables considered (Côté et al., 2016; Jackson et al., 2016; Gieswein et al., 2017), including functional traits (Schinegger et al., 2016).

Finally, a key factor in determining the detection of stressor interactions is sample size, which will co-vary positively with the statistical power of the interaction term. Thus, more emphasis should be given to identifying interaction forms (e.g. antagonism, synergism, and mutualism) and effect sizes, and to estimating their importance using information-theoretic approaches rather than reporting significance levels (e.g. $p < 0.05$) when interpreting model outputs (Wasserstein et al., 2019).

2.2 Increasing confidence in prediction. There are promising ways forward here. Specifically, to improve understanding of the processes underlying ecosystem responses to stressor interactions, we advocate novel analyses that combine large-scale observations and controlled experiments to take advantage of the strengths of both approaches.

Controlled experiments unravel cause-and-effect relationships by allowing unequivocal comparisons of ecosystem state among levels of anthropogenic stress, and the attribution of ecological responses to theoretically-defined interactions (Richardson et al., 2019). However, experimental settings necessarily simplify real-

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world situations. Moreover, complex (higher-order) interactions can be difficult to assess in controlled experiments, where the number of experimental units is limited, even in outdoor mesocosms (Piggott et al., 2015b; Richardson et al., 2019).

In contrast, assessments based on large-scale datasets are commonly statistically unbalanced, suffer from a multitude of confounding factors that cannot be teased apart, and rarely include controls (Bull et al., 2020). The key strength of this approach, however, is that the assessments reflect real-world responses to stressor gradients, encompassing complex responses of networks of species interacting in natural communities across scales (Bruder et al., 2019). Clearly, an integrated experimental and observational approach is beneficial (Birk et al., 2020), but also potentially expensive and time consuming. However, where complex interactions are detected, and likely to confound recovery, this approach is likely a worthwhile investment to inform costly management interventions.

2.3 Towards a novel multiple-stressor management framework. A general framework for predicting ecological responses to multiple-stressor management is overdue (Côté et al., 2016). In particular, there is a pressing need to move from conceptual diagrams towards real-world context to underpin management decisions (Figure 1). Given the volume and heterogeneity of available data, such a framework needs to be flexible. It should draw on data collected across various scales, both spatial and temporal, from small mesocosm experiments to large river basins and from hours to millennia. Practically, it is essential to understand when controlling stressors at local scales (e.g. reducing local nutrient pollution) can mitigate effects of global stressors not locally-manageable (e.g. climate warming) (Brown et al., 2013).

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We propose a unifying approach that is underpinned by empirical linear models that quantify and visualise multiple-stressor interactions in the context of ecological targets. The first step is to develop a theoretically justified, and well-fitting statistical model to describe multiple-stressor interactions in the given ecosystem (Box 1). The exact model design will depend on both the expertise of the analyst and the data structure. Therefore, we focus here on a generalised linear (mixed) modelling (GL(M)M) framework. GL(M)Ms are widely used and flexible enough to accommodate different data types and implicit grouping structures (e.g. year or site random effects) and have established model selection procedures for optimising the quantification of stressor fixed effects (Box 1).

Once a model has been developed, it can be used to examine stressor-change scenarios relevant to potential management actions (Figure 1). Using the GL(M)M, we can investigate both (i) the expected value of the ecological indicator in response to stressor change, calculated using the fixed effect coefficients and link function, and (ii) the probability of exceeding a critical threshold or meeting a management target, calculated from the fixed effect coefficients and distributions of residual errors and random effect variances.

We have developed this multiple-stressor mitigation approach within a series of conceptual models (Figure 1; Box 1), assuming for simplicity similar individual stressor effect sizes within the interactions. In the additive-stressor scenario, the most effective strategy for ecosystem management would be dual stressor control, with the extent of management intervention depending on the distance between the current ecosystem state and the ecological target on a plane defined by the stressor gradients. The path to recovery can require that longer distances are covered when synergistic interactions occur between stressors, meaning that the stressor abatement required to reach a given ecological target is greater than under the assumption of an additive relationship. In the case of an antagonistic interaction, for example the Romanian Rivers case study in Figure 1, single stressor control (e.g. reduction of NO_3-N at high concentrations of toxic substances) could even be counterproductive, as dampening stressor effects are removed.

3.0 Practical recommendations for multiple-stressor management. The current shortcomings of multiple-stressor management outlined above are global in scope. This represents a clear weakness in ecological assessments underpinning, for example, the European WFD (Carvalho et al., 2019). Indeed, nearly all WFD assessment methods have been developed to be responsive to single stressors (Birk et al., 2012). This raises the question, to what extent the currently limited success in restoring water bodies in Europe is the result of targeting only single stressors? Drawing on our framework, we offer practical recommendations for four general scenarios to support the development of novel multiple-stressor management strategies for fresh waters.

1. **Additive Stressors**. Additive stressors represent the simplest case, where a dominant stressor does not notably interact with other stressors. It is evident that priority must be given here to mitigating impacts of the dominant stressor to achieve improvements (Kath et al., 2018). Where two (or more) stressors act additively and with equal strength, either stressor can be controlled to achieve the same effect. Prioritisation of abatement of one stressor or the other can be

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guided by evaluating cost-effectiveness and expected treatment efficacy as well as opportunities to achieve added benefits (e.g. habitat creation through wetland management to reduce nutrient loading to lakes) beyond the direct abatement effects.

2. **Two interacting stressors**. Where two stressors interact, the type of interaction and the underlying mechanisms need to be considered when selecting measures. If the interaction is antagonistic, the most complex case facing managers, the combined stressor effect can be less than expected. For example, a nutrient enrichment effect on lake phytoplankton biomass, caused by land-use change, might be dampened by an increase in flushing rate associated with increased rainfall, caused by climate change, especially in lakes with short retention times. For lakes with long retention times, an increase in precipitation may have the opposite effect, as it can increase nutrient loading. Thus, it is important to understand the lake and catchment context to assess vulnerability in relation to predicted changes in nutrient loading (non-antagonist) and nutrient losses from the lake due to changes in flushing rate (antagonist). Conversely, when stressors interact synergistically, as observed for phytoplankton and cyanobacteria abundance in relation to nutrient enrichment and warming (Richardson et al., 2019), nutrient control may need to be reinforced to achieve ecological improvements, or warming be restricted, for example through hydrological control, or both.
3. **More than two interacting stressors**. Where three (or more) stressors act to produce higher-order interactions, stressor hierarchies need to be identified to enable prioritisation of mitigation measures. Knowledge on individual effects

and two-way interactions can help inform the potential for higher-order interactions. However, it must be recognised that conclusions derived from such analyses can be misleading especially where higher-order interactions are important. For example, Ryo et al. (2018) report on higher order interactions driving macroinvertebrate diversity in Swiss rivers; diversity increased with terrestrial forest cover (dominant stressor), but this effect was moderated by interactions with both elevation gradient and climatic conditions. Where biotic relationships are complex and dominant stressors are absent, uncertainties in model predictions are likely to be high (Bruder et al., 2019). In this case, experimentation will be vital to managing the risk of undesirable mitigation effects. If the control of three or more stressors is deemed practically impossible to achieve experimentally, managers may have little option but to consider phased mitigation approaches (Dyste & Vallet, 2019) coupled with adaptive management responses (Spears et al., 2016).

4.0 Final Considerations. Three final points need brief mention.

First, in a very recent broad synthesis, Hillebrand et al. (2020) found ecological responses to stressors along the degradation pathway are generally gradual. This finding is highly relevant to water management where notable system changes are expected only when thresholds, at times arbitrary or operational thresholds, are surpassed.

Secondly, our current understanding of multiple stressor effects essentially comes from assessing impacts of increasing stress, that is, the ecosystem degradation pathway (Birk et al., 2020; Spears et al., 2021), whereas there is still much to learn about the

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processes governing recovery, especially where multiple stressor interactions are operating. For example, it remains unknown whether multiple stressor interactions increase the likelihood that recovery trajectories depart from degradation pathways, a phenomenon known as hysteresis, which requires further conceptual, experimental, and empirical attention.

Finally, no study has yet demonstrated the successful management of a freshwater ecosystem in which multiple stressor interactions have been identified and quantified and used to inform interventions. Nevertheless, the freshwater scientific community has an impressive historical resource in long-term monitoring data covering past restoration case studies with which to address this issue. It is important that this resource be utilised to produce systematic evidence (Bernhardt et al., 2005) across a large number of fresh waters for which both ecosystem degradation and recovery data are available (Elosegi et al., 2017); where recovery has been incomplete following single stressor management or has occurred slowly (e.g. Jeppesen et al., 2005; McCrackin, et al., 2016); and for which multiple stressor interactions are operating, but have not yet been tested (Verdonschot et al., 2009). We propose building this evidence base using the approach presented here to retrospectively analyse and report on data from past degradation and restoration case studies.

5.0 Conclusions

1. The lack of consideration of interactions between multiple stressors represent a potential major limitation in achieving ecological restoration of freshwater ecosystems.

2. Conceptual models for multiple stressor interactions can be developed to inform novel management approaches, helping practitioners avoid the many pitfalls associated with the detection of interactions.
3. Outputs from empirical analyses of monitoring data and controlled experiments in realistic settings should be systematically combined to guide multiple stressor management strategies, for example, to support climate change resilience planning.
4. Empirical models can be constructed based on past data covering both stressor increase and decrease to provide novel insights into the effects of interactions on both ecosystem degradation and recovery pathways.

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Figure 1. Conceptual and empirical application of paired-stressor models. **In the upper panel** we demonstrate conceptual situations of common stressor interaction forms as well as paired stressors abatement options relative to an ecological target, for example, as set by the ‘Good-Moderate Boundary’ as defined in the European Water Framework Directive (WFD). The most effective stressor abatement option is coloured green. **In the lower panel** we utilise Romanian National River Monitoring Data to demonstrate the landscape of responses in invertebrate community composition relative to an antagonistic interaction between toxic substances and nutrient enrichment, quantified using the proposed generalised linear modelling approach (GLM) described (Box 1). This analysis is used to estimate the severity of effect of the stressors on the ecological response and also the probability that the ecological indicator will fail management targets for any given stressor combination, within the measured data range. Practically, a manager may wish to explore a range of nutrient abatement scenarios, which are under local control, contrasting with the regional control of toxic substances. However, the manager must proceed cautiously for the model suggests that a reduction of nitrate at high levels of toxic substances may, counter-intuitively, aggravate ecological degradation (e.g. upper left quadrant). Complicating matters further; the most severe interaction effects occur on or beyond the upper limits of the data range for both stressors indicating the need to confirm such effects across stressor gradients using experimental approaches. In general, the most effective stressor management approach in this case would be dual stressor control to ensure the system is maintained within the lower left quadrant.

Case study description. These data represent 62 river monitoring stations between 2013 and 2016 at mountainous and lowland rivers in Romania and are representative of similar monitoring programmes in many other countries. Here, toxic stress is measured as 'multi-substance Potentially Affected Fraction' (msPAF, i.e. composite metric for toxic substances; De Zwart & Posthuma, 2005); nutrient enrichment is measured as nitrate-nitrogen concentration; the ecological response is measured as an Ecological Status Ratio (ESR), i.e. the number of benthic invertebrate families normalised by river type-specific reference values (mean of 0.67). ESR is the observed value of a biological indicator, divided by the expected value under reference conditions. The model output (b) is used here to display the probability that the target threshold of the WFD derived ‘good-moderate’ ecological status (>0.55) is failed across the stressor landscape.

GLM output. The model estimates an antagonistic interaction effect between the dominant stressor ‘nitrate-nitrogen concentration’ and the secondary stressor ‘msPAF’, while controlling for region (R^2adj = 0.31, P<0.001). Circles and triangles show the empirical data, shading and contours the fitted ESR and likelihoods. The 'region' effect in the model adds +0.11 to the plotted expected values for lowland and -0.11 for mountain, depending on which region they are in. The regression formula in R format was normalised number of benthic invertebrate families ~ multi-substance Potentially Affected Fraction * nitrate nitrogen concentration + region.

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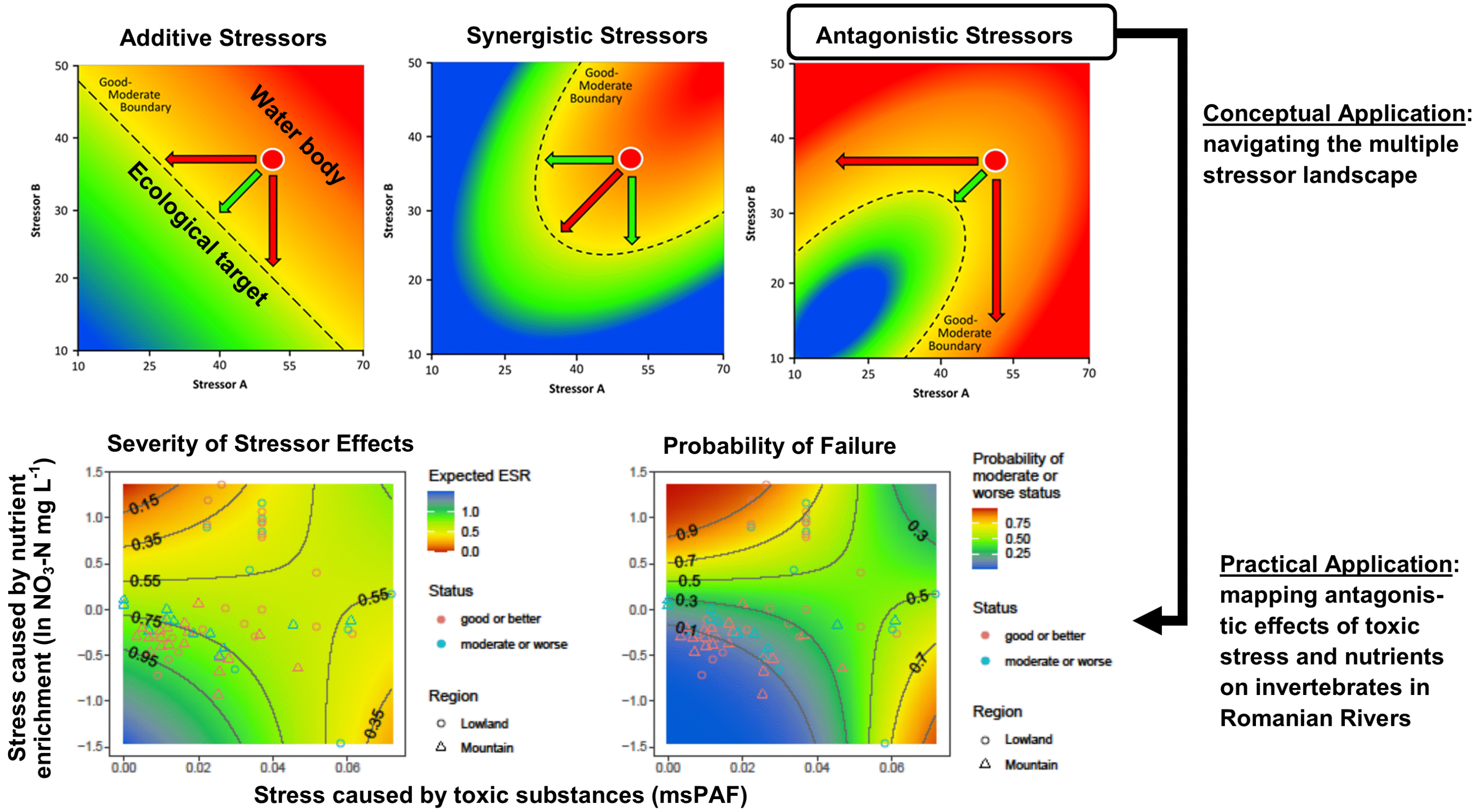
470



471

472

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Box 1.

Proposed approach for estimating multi-stressor interactions from a mixed effect model

A linear mixed effects (LME) model takes the general form: $y = \boldsymbol{\beta x} + \boldsymbol{\nu} + \epsilon$

In which *y* is the ecological response variable, $\boldsymbol{\beta}$ is a vector of fixed effects estimates (including the intercept), $\boldsymbol{x}$ is a vector of explanatory variables (stressors and their interactions), $\boldsymbol{\nu}$ is a vector of normally distributed, independent random effects and ε is the normally distributed residual error.

For two interacting stressors (x_1 and x_2) modelled from data collected in multiple sites and years the LME equation would be rewritten: $y = b_0 + b_1x_1 + b_2x_2 + b_3x_1x_2 + S + Y + \epsilon$

Where *b* are the elements of $\boldsymbol{\beta}$ and *S* and *Y* are the random effects for the site and year. Using this model, the expected value of the ecological response variable *y* for any combination of stressors is $\boldsymbol{\beta x}$. Responses to stressor management scenarios can be estimated easily by changing the values of $\boldsymbol{x}$.

The model can be used to estimate the probability of *y* exceeding a critical threshold (e.g., a management target) for different values of the stressors. This is because the response *y* is normally distributed with a mean of $\bar{y} = \boldsymbol{\beta x}$ and a variance of $\sigma^2 = \sigma_\epsilon^2 + \sum \boldsymbol{\sigma_\nu^2}$, where σ_ϵ^2 is the residual variance and $\boldsymbol{\sigma_\nu^2}$ is a vector of the random effect variances.

From the cumulative distribution function of the normal distribution, the probability of exceeding *y**, a critical value of the response variable, is:

$$P(y > y^*) = 1 - \frac{1}{2}\left[1 + \operatorname{erf}\left(\frac{y^* - \bar{y}}{\sigma\sqrt{2}}\right)\right]$$

And the probability of being under *y** is:

$$P(y < y^*) = \frac{1}{2}\left[1 + \operatorname{erf}\left(\frac{y^* - \bar{y}}{\sigma\sqrt{2}}\right)\right]$$

In both equations, erf is the error function.

Extension to generalised linear mixed models (GLMMs). In some circumstances an ecological response variable cannot be reasonably modelled with an LME, for example because it is a count or binary variable. In these cases GLMMs are an appropriate modelling tool. However, extending the analytical approach proposed above for LMEs to GLMMs is not straightforward because the random effect variances are transformed in the link function. While stressor effects can still be estimated then the link function renders the probability of *y* exceeding a critical threshold difficult to compute directly.

Nevertheless, estimating the likelihood of threshold exceedance by simulation should be relatively simple, using a procedure as follows:

1. Draw random effect coefficients from normal distributions with mean of 0 and variances from $\boldsymbol{\sigma_\nu^2}$.
2. Estimate the expected value of the response variable using these coefficient values and the GLMM link function.
3. Record whether this value exceeds the critical threshold.

Repeat steps 1-3 many times to estimate the exceedance probability.