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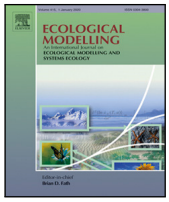

Investigating the effect of pesticides on Daphnia population dynamics by inferring structure and parameters of a stochastic model

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ABSTRACT

Identifying sublethal pesticide effects on aquatic organisms is a challenge for environmental risk assessment. Long-term population experiments can help assessing chronic toxicity. However, population experiments are subject to stochasticity (demographic, environmental, and genetic). Therefore, identifying sublethal chronic effects from "noisy" data can be difficult. Model-based analysis can support this process.

We use stochastic, age-structured population models applied to data from long-term population experiments with *Daphnia galeata* in 1L aquaria with and without chronic pesticide treatments (diazinon and diuron) at sublethal concentrations. Posterior analysis following Bayesian inference of model parameters and states helped choosing an adequate description of life-history characteristics under the specific experimental conditions (a zero-inflated negative binomial distribution for reproduction and mortality without density dependence). For the insecticide treatments, the inferred marginal posterior parameter distributions indicated the need for a mortality rate that increases with time, indicating cumulative chronic toxic effects of diazinon on Daphnia populations. With this study, we demonstrate how stochastic models can be used to infer mechanisms from population data to help identifying sublethal pesticide effects.

1. Introduction

The environmental concentrations of pesticides from agricultural and urban sources raise concerns about their effects on aquatic ecosystems (Liess et al., 2021). Environmental risk assessment for pesticides is challenging (Topping et al., 2020) due to the following reasons: the intermittent nature of many pollution sources, e.g. increased transport during storm events, the large number of compounds and their transformation products, mixture toxicity effects, the large number of potentially affected species and their poorly known biotic interactions, partial knowledge about interacting environmental influence factors, and intrinsic stochasticity of ecosystem dynamics. Therefore, the effects of these pollutants in aquatic ecosystems can primarily be assessed indirectly by statistical analyses (Beketov et al., 2013; Münze et al., 2017; Duong et al., 2021; Belaid and Sbartai, 2021; Silva et al., 2021). Such integrative studies are of high importance, as only investigations of the real systems reflect the full complexity of the environment and the biological communities (Taub, 1997a,b).

Nevertheless, laboratory experiments are important for environmental risk assessment (Taub, 1997a,b). They are essential for prospective hazard assessment and complementary tools to explore the effects of specific pesticides on population or community dynamics of selected organisms. Advantages are the better control of pollutants and environmental conditions, the limited community complexity, and the opportunity of replicating experiments (Taub, 1997b). While short-term bioassays for the assessment of acute (lethal) effects based on single species are routinely used for pesticide registration, experiments with higher ecological realism did not make it into the registration procedures, due to the challenges of standardization and reproducibility (Taub, 1997a; Riedl et al., 2019). However, it is also of particular importance to investigate chronic effects of sublethal concentrations, as pesticide concentrations in the environment are usually well below acute lethal concentrations and may prevail for longer time periods (Moschet et al., 2014; de Souza et al., 2020).

Despite the advantages of laboratory experiments (Taub, 1997a,b), there remain significant challenges, especially for chronic effect studies (Erickson et al., 2014): Maintaining stable communities over a longer time span (e.g. several weeks) can be difficult already in the absence of pesticides; the effect of sublethal concentrations may be

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small (de Souza et al., 2020); perfect replication of experiments is difficult regarding the reproduction of the initial state as well as environmental conditions during the course of the experiment; and demographic stochasticity may be significant for small populations (Shoemaker et al., 2020). These challenges can make the interpretation of the results difficult.

Integrating population modeling into environmental risk assessment can help to address some of the challenges mentioned above (Forbes et al., 2010; Raimondo et al., 2021). A population or community model that makes it possible to consider many of these complicating factors can be a tool to support the interpretation of experimental results. This usually requires a careful model selection process by fitting multiple model versions to the experimental data and the analysis of inferred posterior distributions of model parameters and states to select the most appropriate model and to learn from the corresponding posterior distribution.

Process-based models that can be used for this purpose include (a) deterministic models at the population level, e.g. integral projection models (Ellner et al., 2016) or models that follow the Dynamic Energy Budget approach (Kooijman, 2010; Jager, 2020), that are straightforward to use for model-based inference but do not account for demographic stochasticity, (b) individual based models (IBMs) that describe life history processes at the individual level and can naturally describe demographic stochasticity (Grimm et al., 2005), but are challenging to use for model-based inference (Kattwinkel and Reichert, 2017), (c) age- or stage-structured, stochastic population models (Nisbet and Gurney, 2004; Lande et al., 2003; Chou and Greenman, 2016) that can describe demographic stochasticity while introducing less model complexity than individual based models.

Daphnia is a widely used model organism and many models have been developed to describe its population dynamics. Classical stage structured population models (De Roos et al., 1992; Mccauley et al., 2008; Lamonica et al., 2016) have been extended to include different forms of stochasticity (Preuss et al., 2009; Ananthasubramaniam et al., 2011; Metz and Diekmann, 2014; Erickson et al., 2014). Stochastic population models are particularly relevant when the number of individuals is low and thus demographic stochasticity becomes important (Nisbet and Gurney, 2004).

In this study, we evaluate the chronic effect of sublethal concentrations of the insecticide diazinon and the herbicide diuron on *Daphnia galeata* feeding on algae (*Acutodesmus obliquus*). This is a well known model system for toxicological studies (Brede et al., 2009). We then apply a careful model selection process and calibrate the resulting Daphnia population model to multiple replications of experiments with and without the application of the pesticides. The experimental data includes five replicates of up to 100 day long time series of three different life stages of Daphnia of a control, a treatment with diazinon, a treatment with diuron, and a combined treatment with diazinon and diuron.

We used a stochastic, age-structured, discrete individuals population model to account for demographic stochasticity that was large due to the very small (initial) population size. Our model is similar to the stage-structured model by Erickson et al. (2014) but uses age classes to more easily account for the delays between the transitions to the next life stages. Moreover, we used a different parameterization for (potential) time and density dependence of survival. In the absence of empirical data at different pesticide concentrations, we do not describe the toxic effect explicitly in the model. Instead we calibrate the model to the control and the pesticide treatments separately, and infer the toxic effect from a comparison of the posterior parameter distributions. This helps us to identify empirically the mechanism that best describes the observed toxic effect with the model without the need to decide beforehand, which model parameters may be affected by the pesticides.

The goals of the study are to learn if we can infer chronic effects of diazinon and diuron on the crustacean *Daphnia galeata* from long-term population data with a stochastic model and to gain experience with the model selection and calibration process that could be useful for future studies.

2. Material and methods

A model design and selection process consists of an a priori phase in which reasonable model structures are suggested based on ecological knowledge, the modeling objective, the available data, and on considerations regarding the description of the most important mechanisms in the system (Schuwirth et al., 2019) and an a posteriori phase in which the final model structure is selected by the predictive performance of the model (Roberts et al., 2017; Houlahan et al., 2017), a trade-off between the quality of fit to the data and model complexity (Spiegelhalter et al., 2002; Plummer, 2008; Spiegelhalter et al., 2014; Hooten and Hobbs, 2015), or inference of parameters that characterize potentially relevant processes or that mix different model structures (Robert, 2016; Kamary et al., 2018).

In the following subsections, we therefore first discuss the objectives of the experiment and of the accompanying modeling study, we describe the experimental setup and the resulting data, then we discuss the a priori model design process for this case study, and finally the techniques chosen for a posteriori model structure selection.

2.1. Objectives

The objective of the experiments was to investigate chronic effects of sublethal concentrations of a herbicide and an insecticide on a model community of algae and Daphnia. The model-based analysis should support the identification and quantification of effects on fertility and mortality of Daphnia in the presence of high stochasticity that limits the reproducibility of the experiments. Note that we do not model explicitly the effects of pesticides as only one concentration per treatment was tested. Instead, we calibrate the model separately for each treatment and detect the effects of pesticides by observing the differences in the posterior parameter distributions between the four treatments. Our approach therefore does not require to impose any toxic effect relationship for selected model parameters, but it allows us to identify a posteriori, which parameters may be affected by the pesticides. Experiments at different pesticide concentrations would be needed to infer the response as a function of pesticide concentration.

2.2. Microcosm experiments

We established laboratory communities of the crustacean *Daphnia galeata* and the green alga *Acutodesmus obliquus* in 1 liter microcosms. *Daphnia* genotypes were selected from a living library of *Daphnia galeata* genotypes previously collected from lakes throughout Europe, and maintained in animal care facilities at Eawag, Switzerland. For the experiment presented here, microcosms were innoculated with three *Daphnia* neonates of a single clone from Lake Garlata (IT : 45°49′03″N 9°24′30″E) and with green algae *Acutodesmus obliquus* (3.193mg Carbon - measured by Spectrophotometry @800 nm). We exposed five microcosms to each of four different treatments: control, sublethal concentration of an insecticide (diazinon nominal concentration of 0.6 nM [186 ng/L]), sublethal concentration of a herbicide (diuron nominal concentration of 3.05 nM [711 ng/L]), and the combination of the two pesticides. The microcosms were maintained at 21° with a 16:8 light cycle. Each microcosm was filled with 1 liter of surface water collected from Lake Greifensee (CH : 47°21′16″N 8°40′30″E). Prior to use, media were filtered (pore size 0.45 μm) then autoclaved. After autoclaving media were re-gassed overnight using sterile filtered compressed air. Where appropriate, diazinon and/or diuron was introduced in ethanol (final concentration < 0.0004% - 4 μL ethanol per L). Water was aged prior to use to limit effect of volatile organics (e.g. kairomones) and laboratory conditions maintained at steady state. The microcosms were sampled weekly between June and August, or until the *Daphnia* population declined to extinction. If extinction occurred in the first 2 weeks of the experiment we established new microcosms

to replace them. We followed a protocol from similar population experiments (Beckerman et al., 2010; Dennis et al., 2011). Because the goal was to assess long-term population effects, we chose a natural medium – lake water from a lake close to the lab – and a Daphnia species that naturally occurs in this lake (Keller et al., 2008). The specific clone was originally from another lake but acclimated to the same medium and did well in pre-experiments under similar conditions. The pesticides were chosen based on the following selection criteria: They should be stable under experimental conditions to maintain constant concentrations during the experiments, some knowledge about their effects on Daphnia and algae was already available, and they show measurable sub-lethal effects at environmentally relevant concentrations. The acetylcholinesterase inhibitor diazinon (Kretschmann et al., 2011a,b, 2012) and the photosystem II inhibitor diuron (Nestler et al., 2012a,b) were identified as the most promising candidates (Wittmer et al., 2014). The test concentrations were chosen based on pre-experiments aiming at a roughly 20% reduction of the reproduction rate.

At each sampling event, we filtered (30 μm) populations to census the entire population. *Daphnia* were classified by size (<0.7 mm neonate, juvenile, >1.2 mm adult), and adult reproductive output was assessed by counting the number of eggs in the brood pouch. During each population census a subsample of algae (500 μL) was preserved for algal density assessment. Next, 500 mL of media was transferred to a centrifuge bottle and centrifuged at 5000 rpm and 18° for 5 min. The supernatant was discarded (a subset retained for nutrient analysis) and the algal pellet was resuspended in fresh media before being returned to the microcosm.

Fig. 1 provides an overview of the time series of adult and juvenile Daphnia, of eggs and of the fraction of adults without eggs for all microcosms. Note the high level of demographic noise shown in the time series. In Figure S.9 in the supplementary material we show qualitative time series of relative fluorescence measurements related to algal densities.

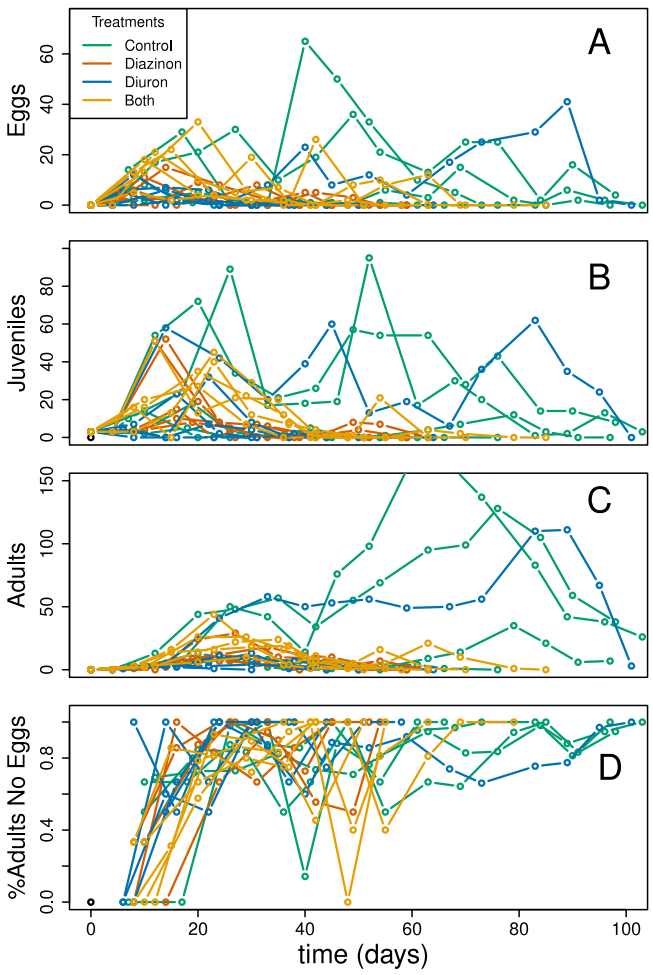

Fig. 1. Overview of experimental data: Time series of eggs (A), juveniles (B), adults (C), and fraction of adults without eggs (D) of *Daphnia galeata* for all treatments (represented by different colors) and all five replicates for each treatment (identical colors). Observations (dots) are connected by lines to clarify the correspondence within each replicate.

2.3. A priori model structure selection

2.3.1. Selection of model class

With "model class" we denote the concept underlying the description of the population or the community, how to deal with stochasticity, and the temporal and spatial resolution of the model. The model class does not describe the detailed equations of the model structure. We select the model class for our specific problem according to the following considerations:

- *Community/populations*: As we only have qualitative data from the algae population (see Figure S.9 in the supplementary material) and do not have indications for food limitation, we focus on the description of the Daphnia population.
- *Individuals*: The small number of individuals (three juveniles) at the beginning of the experiment and the lack of information to distinguish the individuals during the time course of the experiment, suggest using a discrete individuals model that accounts for the discrete nature of the population, but does not distinguish the individuals.
- *Traits*: The resolution of life stages by the model makes it possible to profit from the full information content of the data. Increasing the resolution of the model to age classes allows us to better describe the different residence times in different life stages without additional effort. Life stages are then associated with sets of age classes. As the data does not distinguish other traits, neither does the model.
- *Stochasticity*: Due to the small number of individuals, demographic stochasticity has a large effect on the population. Environmental stochasticity was minimized in the experimental setup. Genetic stochasticity is not relevant, because the populations consist of asexually reproducing clones. We thus consider demographic stochasticity by going for probabilistic descriptions of birth and death processes.
- *Space*: The experiments were carried out in homogeneous microcosms without spatial resolution in observations. We thus choose not to resolve the spatial dimension by the model.
- *Time*: A discrete-time model with the same (daily) resolution for both time and age simplifies the model description, as proceeding one time step increases age by one age class.

The choice of a stochastic, age-structured, discrete population model in discrete time allows us to formulate a mechanistically correct model structure with the processes of reproduction, aging and mortality that naturally contains demographic stochasticity. Using an age- rather than a stage-structured model allows us to consider different retention times in different life stages, avoids numerical diffusion in the aging process, and provides a more detailed description of the population at minor additional costs. On the other hand, this model uses empirical parameterizations of growth, reproduction and mortality processes. Going beyond such an empirical description could not extract more information from the data. Nevertheless, this model allows us to formulate ecological hypotheses by different parameterizations of these processes and to test these with the data.

2.3.2. Formulation of model structure

Model structure formulation within the model class selected in the previous section requires the specification of the number of age

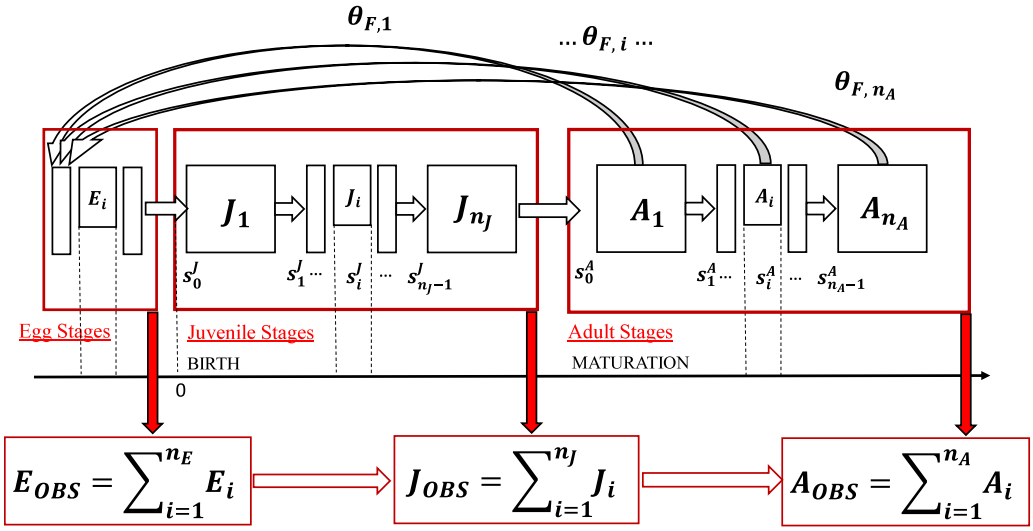

Fig. 2. Schematic representation of a general age-structured model. Transitions between age classes are represented by horizontal arrows and egg production by curved arrows. The observation process is represented in red where individual age classes are divided into the three developmental stages, Eggs (E), Juveniles (J) and Adults (A). $\theta_{F,i}$ are the parameters of the distribution of egg production by a single adult in age class i (see expression (1)) and $s_i^{A/J}$ are the average surviving fractions of adults, A, or juveniles, J, of age class i within one day (see Eqs. (3)–(4)).

classes and how the numbers of individuals in these classes are related through mathematical relations for reproduction (here egg production), aging and mortality (survival). In addition, to relate model output to observations, a description of the observation process is needed. Individuals are distributed into $(n_E + n_J + n_A)$ age classes of length $\Delta t = 1$ day each, where $n_E = 3$, $n_J = 5$ and $n_A = 45$ are the numbers of egg, juvenile and adult age classes respectively, leading to an instar time of $n_E \Delta t = 3$ days, a maturation age of $n_J \Delta t = 5$ days and a maximum age of $(n_J + n_A)\Delta t = 50$ days (see Fig. 2). Note that Δt defines both the time step for the temporal evolution of the model and age class length. We assume every adult produces eggs according to a general fertility distribution F. As each adult only gives birth every n_E days, the distribution of eggs in their different age classes and at time $t + 1\text{d}$ are given by

$$E_1(t + 1\text{d}) \sim \sum_{i=1}^{n_A} \sum_{j=1}^{\left[\frac{A_i(t)}{n_E}\right]} F(\theta_{F,i}) , \quad (1)$$

$$E_i(t + 1\text{d}) = E_{i-1}(t) , \quad i = 2, \dots, n_E . \quad (2)$$

Here, $E_i(t)$ is the number of eggs in egg age class i at time t, $A_i(t)$ is the number of adults in adult age class i at time t, and $\theta_{F,i}$ are the parameters of the fertility distribution for adults in age class i. The square brackets $\left[\frac{A_i(t)}{n_E}\right]$ at the top of the sum represent the number of adults that give birth at this time step, if necessary rounded down to an integer. Note that we ignore mortality of eggs in Eq. (2).

Aging and mortality of individuals across age classes is defined by

$$J_i(t + 1\text{d}) \sim \text{B}\left[J_{i-1}(t); s_i^{\text{J}}(t, J_1, \dots, J_{n_J}, A_1, \dots, A_{n_A})\right] , \quad i = 1, \dots, n_J ; \quad (3)$$

$$A_i(t + 1\text{d}) \sim \text{B}\left[A_{i-1}(t); s_i^{\text{A}}(t, J_1, \dots, J_{n_J}, A_1, \dots, A_{n_A})\right] , \; i = 1, \dots, n_A ; \quad (4)$$

where J_i is the number of juvenile individuals in juvenile age class i, A_i is the number of adult individuals in adult age class i and B is a binomial distribution, whose second argument, s_i^J or s_i^A, define the average surviving fractions of adults, A, or juveniles, J, of age class i within one day, respectively. Note that the number of juveniles in age class 0 is the number of eggs in age class n_E ($J_0 = E_{n_E}$), and that the number of adults in age class 0 is the number of juveniles in age class n_J ($A_0 = J_{n_J}$). The observation process is then defined using the sum of individuals among age classes within stages, given by

$$E_{\text{obs}}(t) = \text{N}\left(\sum_{i=1}^{n_E} E_i(t), \sigma_{\text{obs}}\right) \quad (5)$$

$$J_{\text{obs}}(t) = \text{N}\left(\sum_{i=1}^{n_J} J_i(t), \sigma_{\text{obs}}\right) \quad (6)$$

$$A_{\text{obs}}(t) = \text{N}\left(\sum_{i=1}^{n_A} A_i(t), \sigma_{\text{obs}}\right) \quad (7)$$

where N is a normal distribution with standard deviation $\sigma_{\text{obs}} = 1$, describing complete counting of all individuals in the three developmental stages (Fig. 2). Although this distribution does not represent the results of a count process, it will only be evaluated at non-negative, integer values that represent the observations. This observation model serves primarily the purpose of supporting convergence of the inference algorithm allowing only for small deviations from actual counts that can be assumed to have only minor errors. If the populations would become large in the course of the experiment, we would have to replace this observation model with a model that accounts for larger errors for larger populations. Introducing such an observation process, we make our model hierarchical, in the context of what are typically described as a *State Space Models* in the ecological literature (Auger-Méthé et al., 2021; Newman et al., 2022).

2.3.3. Formulation of hypotheses and associated model versions

We can now formulate different ecological hypotheses to be tested against data, leading to different model versions within the overarching model structure. Note that this has been an iterative process, where identified deficits of models from earlier iterations provided inspiration regarding hypotheses to be tested. During this iterative process, we tested hypotheses regarding the fertility distribution as well as density- and time-dependence of mortality.

Assuming fertility is independent of age in Eq. (1) leads to an egg distribution given by

$$E_1(t) \sim \sum_{j=1}^{\left[\frac{1}{n_E}\sum_{i=1}^{n_A} A_i(t)\right]} F(\theta_F) , \quad (8)$$

where the square brackets $\left[\frac{1}{n_E}\sum_{i=1}^{n_A} A_i(t)\right]$ at the top of the sum represent the total number of adults that give birth at this time step, if necessary rounded down to an integer. Different assumptions can be made for the choice of the distribution F, leading to different model versions. We used four hypotheses for fertility (the labels P, N, PZ and NZ are used to label the model versions):

P: Poisson distribution $F(\theta_F) = \mathrm{P}(f)$: to describe the number of new eggs as a single distribution with the mean equal to the fecundity, f (mean number of eggs per individual).

N: Negative binomial distribution $F(\theta_F) = \mathrm{NB}(f, r)$: often used as an empirical distribution of overdispersed discrete observations (Lindén and Mäntyniemi, 2011), here parameterized with the mean equal to the fecundity, f, and the individual dispersion parameter r.

PZ: Zero-inflated Poisson distribution $F(\theta_F) = \mathrm{PZ}(c, \pi)$: where we assume that there is an excess fraction of adults, π, that does not produce eggs and the other fraction, $(1-\pi)$, produces eggs according to a Poisson distribution with a mean clutch size of $c = f/(1-\pi)$ (where $f = c(1-\pi)$ remains the effective fecundity as above). Note that π is the excess fraction of adults without eggs in addition to the probability for zero eggs described by the Poisson distribution.

NZ: Zero-inflated negative binomial distribution $F(\theta_F) = \mathrm{NBZ}(c, r, \pi)$: where we combine the negative binomial distribution NB with zero-inflation. As for the Poisson distribution, π characterizes the excess fraction of adults without eggs in addition to the probability of zero eggs of the negative binomial distribution.

A large value of the dispersion parameter ($r \to \infty$) reduces the fertility distribution of model version N to that of model version P and analogously for model version NZ to PZ. Setting $\pi = 0$ (leading to $c = f$) reduces model version PZ to P and version NZ to N, respectively. The more complex models thus reduce to the simpler models in a nested design (Fig. 3). See supplementary section S.1 for a detailed description of fertility distributions and their numerical implementation. Note that, despite not being mechanistic, these distributional assumptions are typically used for describing count data, e.g. egg distributions (Lindén and Mäntyniemi, 2011; Brooks et al., 2019).

We then select hypotheses for mortality by parameterizing the mean survival fractions $s^{\mathrm{J/A}}$ in Eqs. (3) and (4), assuming mean survival fractions to be equal among age classes and stages and described by a general, time- and density-dependent expression given by

$$s(t, J_1, \ldots, J_{n_J}, A_1, \ldots, A_{n_A}) = \exp\left[-\left(k_0 + k_1 t\right)\Delta t - k_c\left(\sum_{i=1}^{n_J} J_i(t) + \sum_{i=1}^{n_A} A_i(t)\right)\Delta t\right], \quad (9)$$

where k_0 is the base mortality rate, k_1 is a time-dependent mortality rate coefficient, associated to variation in environmental conditions, while k_c is a coefficient of density-dependent mortality, or crowding (Table 1). Technical details of the implementation of the mortality rate can be found in the supplementary section S.2. Varying the parameters of Eq. (9) leads to a total of four nested hypotheses on the different processes affecting mortality:

Base model: No time and density-dependence ($k_1 = 0$, $k_c = 0$).

Model extensions:

T: Only time-dependent mortality ($k_1 \neq 0$, $k_c = 0$).

C: Only density-dependent mortality ($k_1 = 0$, $k_c \neq 0$).

TC: Time and density-dependent mortality ($k_1 \neq 0$, $k_c \neq 0$).

Again, the simpler model structures can be obtained by setting parameters to specific values (in this case zero). Note that explicit time-dependence of mortality seems to be a strange assumption for an ecological model. This hypothesis entered the model selection process at a later iteration, as the initial increase and fast decline of the populations for some treatments could not be described otherwise. Combining the four hypotheses for fertility and the four hypotheses for mortality, we obtain 16 different nested model versions (Fig. 3) to be fitted to the data with up to six model parameters (Table 1). The priors of the parameters have been chosen to be quite wide and generally for most of the model versions the parameters are identifiable (see Section 3.1.3). These nested model versions will allow us to infer the need for model extensions by the marginal posterior of the corresponding parameters.

2.3.4. Model application strategy

Given $R = 5$ replicated population time series data per treatment and a model version with n_θ parameters, each model version can be fitted to the data, separately for every treatment, using at least two strategies:

J: Joint fit: the model is fitted jointly to the data of all replicas, leading to a total of n_θ parameters.

R: Replica by replica fit: Inference is split into R independent fits of n_θ parameters, leading to a total of $R \cdot n_\theta$ parameters .

Given replicated time series data for the three stages, $\mathbf{y}_{\mathrm{obs}}$, combining model versions and application strategies, we end up with 32 models to make inference with for every treatment. Each model can be represented by the joint probability distribution

$$p(\mathbf{y}_{\mathrm{obs}}, \mathbf{y}, \theta) = p(\mathbf{y}_{\mathrm{obs}} \mid \mathbf{y}, \theta) \cdot p(\mathbf{y} \mid \theta) \cdot p(\theta) \quad (10)$$

where $\mathbf{y}$ are the internal model states (numbers of individuals of each age class at each time step), $p(\mathbf{y}_{\mathrm{obs}} \mid \mathbf{y}, \theta)$ is the observation model, $p(\mathbf{y} \mid \theta)$ is the age-structured population model, $p(\theta)$ is the prior of the model parameters $\theta = (f, r, \pi, k_0, k_1, k_c)$ (Table 1) for the model application strategies J and R.

2.4. A posteriori model structure selection

In this study, we do not have sufficient data to split the time series into a calibration and a validation period for using cross-validation for model selection (Roberts et al., 2017; Houlahan et al., 2017). This would require stable or multiple increase and decline patterns in both of these time periods to have all relevant patterns available for calibration as well as for validation. However, as explained in Section 2.2, our time series typically show an increase in population size followed by a decline with some superimposed fluctuations (see Fig. 1). This does not allow for a sufficiently good model calibration with using only the first part of the time series. In addition, the variation among replicated experiments indicate strong stochasticity, so that the predictive performance of even the best model can only be quite poor (see also Section 4).

The use of information criteria that are based on a trade-off between model fit and model complexity is the most widely applied alternative to cross validation (Spiegelhalter et al., 2002; Johnson and Omland, 2004; Plummer, 2008; Spiegelhalter et al., 2014; Hooten and Hobbs, 2015). However, these criteria have some conceptual problems (O'Hagan, 1995; Tenan et al., 2014; Robert, 2016; Tendeiro and Kiers, 2019), and they do not help to improve the ecological understanding. For this reason, we prefer to primarily base our considerations on a technique that provides more ecological insight. Nevertheless, we include one of these criteria, the deviance information criterion (DIC) in our analysis for comparative purposes (see section S.3 and Figure S.1 in the supplementary material).

As we only have a relatively small number of hypotheses to test, analyzing marginal posterior distributions of model parameters in a nested model structure as outlined in Section 2.3.3, seems to be an adequate model structure selection technique for this study. In this approach, comparing the marginal posteriors of model parameters with their specific values for a simpler structure allows us to assess the need for additional structural elements. If we would have to decide between structurally different models that cannot easily be formulated in a nested structure, mixture model estimation would have been a suitable alternative (Kamary et al., 2018).

In addition to the identification of relevant processes by marginal posterior distributions of individual parameters, we analyze the typical behavior of the model by performing simulations propagating the marginal posterior of all model parameters (marginalizing over the states, but still joint for all parameters). This can be seen as a substitute of cross-validation as it does not consider state information explicitly

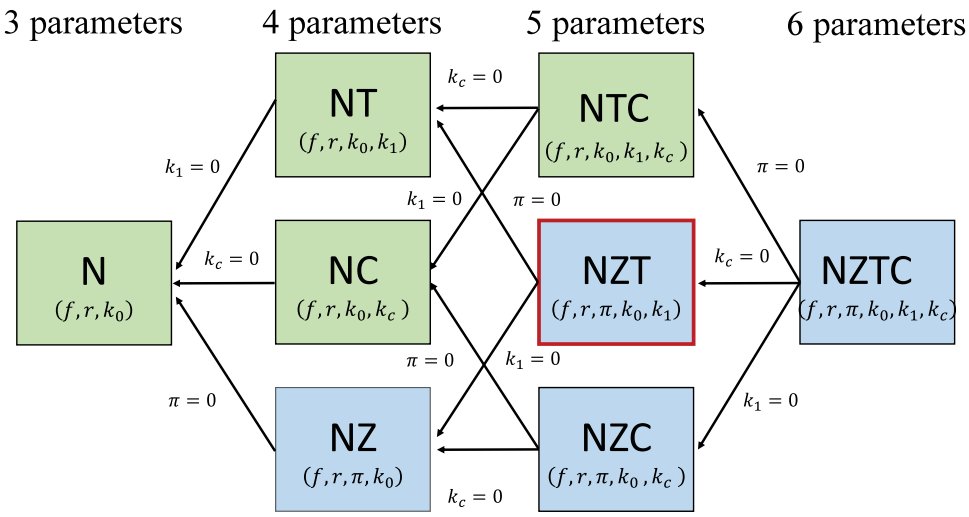

Fig. 3. Schematic representation of eight different model versions. Each box corresponds to a model version and is labeled by the version acronym and the corresponding model parameters. Each arrow shows a transition from a version to another, corresponding also to a decrease in the number of parameters. Each of the eight model versions presented has a negative binomial fertility distribution (N). The corresponding eight model versions with Poisson fertility distributions (P) are obtained in the limit $r \to \infty$. The red box underlines the model version that will turn out the best to fit the experimental data (see Table 2).

Table 1
Six parameters of the model with their corresponding units and prior distributions.

Symbol	Description	Unit	Prior distribution	Prior mean	Prior sd
f	Fecundity	–	Lognormal trunc. at 30	1.5	1.5
π	Excess fract. of adults without eggs	–	Normal trunc. to $[0, 1]$	0.5	0.15
r	Dispersion parameter	–	Lognormal	1	0.25
k_0	Base death rate	day^{-1}	Lognormal	0.1	0.1
k_1	Coefficient of time-dep. mortality	day^{-2}	Normal	0	1
k_c	Coefficient of density-dep. mort.	day^{-1}	Lognormal	0.0001	0.0001

(only implicitly through the posterior of the parameters). Due to the high variability of the replicates that indicates a high stochasticity in the actual microcosms, we expect a high prediction uncertainty for these simulations.

2.5. Numerical methods and implementation

Bayesian inference for each of the model versions was done, separately for each of the four treatments, by Gibbs sampling from the joint posterior of model parameters and states (Gelman et al., 2003). The implementation was based on the software JAGS (Plummer, 2003) that was called from R (R. Core Team, 2021) via its interface `rjags` (http://cran.r-project.org/package=rjags). Five Markov chains with 10^6 iterations were run and for each of them the first half was cut to eliminate burn-in (see also Figure S.2 in the supplementary material). The data considered in Section 3, as well as code to reproduce the results are publicly accessible at https://github.com/Gpalam/Daphnia.

3. Results

To explore the required and identifiable model structure for the data from our experiments, we start the analysis with an a posteriori model selection process for the treatment with diazinon (dz) as this affects Daphnia most directly (Section 3.1). Despite the small amount of data, the model parameters turn out to be identifiable even for the most complex of the investigated model structures. We then proceed with a comparison of all treatments based on the full model to test whether the conclusions regarding the relevance of processes and the need for extended process parameterizations are valid for the other treatments as well (Section 3.2).

3.1. A posteriori model selection

We performed a model selection process as described in Section 2.4 for the experiments with diazinon treatment, testing the 16 model versions described in Fig. 3 and both application strategies J and R (Section 2.3.4).

3.1.1. Convergence

We fitted all the model versions to the time series data and checked for convergence of the Markov chains. The models with Poisson fertility and zero-inflation (PZ) clearly did not converge (see log posterior chains in Figure S.2 in the supplementary material). The fraction of zero-inflation, π, tended to approach unity whereas the clutch size, c, became large to keep a reasonable fecundity, $f = c(1-\pi)$. The inference algorithm appeared to widen the fertility distribution by increasing zero-inflation, indicating that the negative binomial distribution with its dispersion parameter is better suited to describe fertility. The PZ model versions were thus discarded from further analysis for poor convergence due to structural deficits. None of the other model versions showed severe convergence problems.

3.1.2. Model output and predictions

Next, we qualitatively discuss the posterior model predictions and rely on the posterior marginals of the parameters for model selection (see Section 3.1.3 below). The predictions based on the posterior marginal of the parameters (still joint for all parameters, but marginalized over the states), are used as a replacement for cross-validation (see Section 2.4). In principle, this is a sensitive test for stochastic models because in contrast to the inferred time-series of the states, the parameters do not contain detailed information about the time series of the data and thus represent typical model behavior. However, as already mentioned in Section 2.4, replication of the data is very poor, indicating high stochasticity. As the supplementary Figures S.3

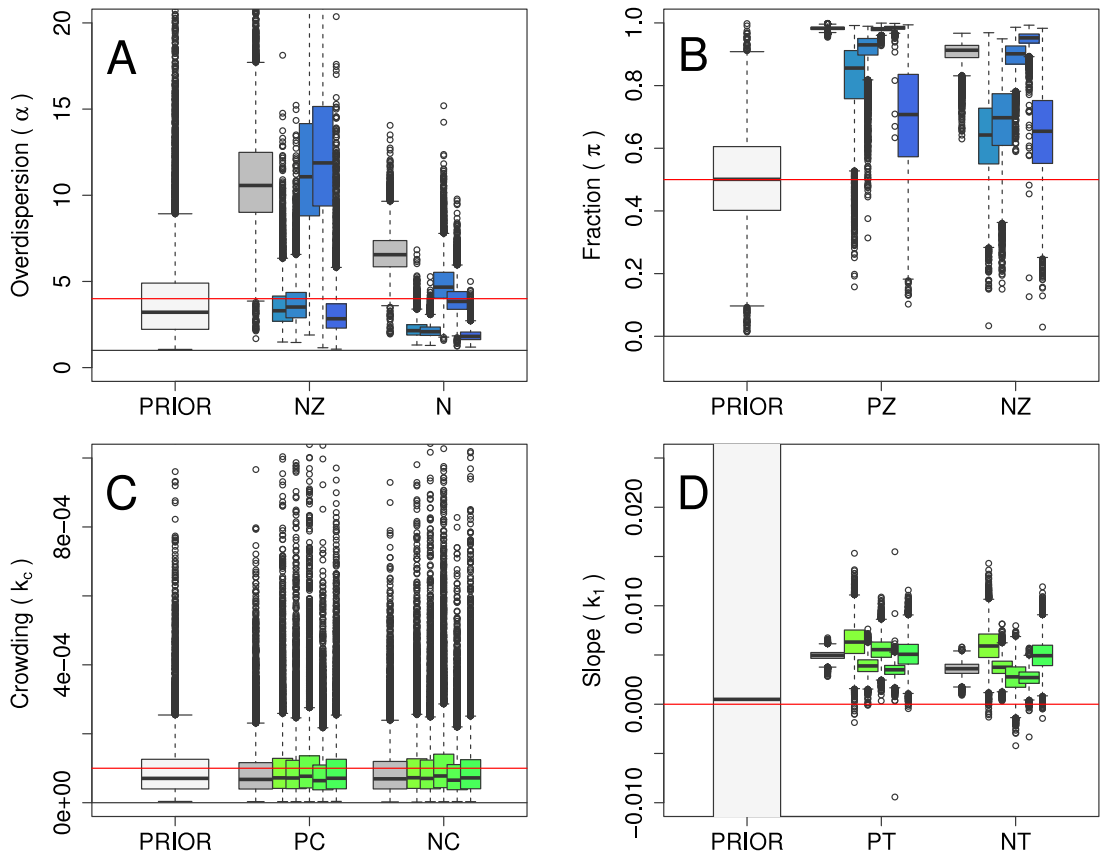

Fig. 4. Box plot of fertility (blue) and mortality (green) parameters for models in the joint fit (J: gray) and replica by replica fit (R: colored), priors are displayed in light gray. In the upper panels we show the marginal posterior distribution of the overdispersion parameter ($\alpha = 1 + f/r$) for model versions N and NZ (panel A) and of the zero-inflation parameter (π) for model versions PZ and NZ (panel B). In the lower panels we show marginal posterior of coefficients of density-dependent mortality (k_c) for model versions PC and NC (panel C) and of coefficients of time-dependent mortality (k_1) for model versions PT and NT (panel D). The red horizontal lines show the mean of the priors.

and S.5 and to a lesser extent the supplementary Figures S.4 and S.6 demonstrate, this leads to a high uncertainty in predictions, induced by the high stochasticity of the model. Model versions N, NZ, NZT show a general improvement of model predictions, compared to the corresponding Poisson model versions, allowing more variability in the egg time series. However, predictions obtained using models N and NZ show unrealistic population growth. In fact, all models without time-dependent mortality do not show the typical extinction of the populations in the experiments. This can be corrected using models with time-dependent mortality (e.g. NZT), which are able to capture population decline and lead to a better fit of the states.

3.1.3. Marginal posterior model parameter distributions

All marginal parameter distributions except the one for k_c are either shifted from or narrower than their priors indicating good identifiability despite the small number of data points (see Fig. 4 and supplementary Figures S.7–S.8). This also indicates a minor dependence of the results on the prior parameter distributions. Over-dispersion and zero-inflation are important for a realistic description of the empirical egg distributions. All model fits, especially for replicas three and four, show a significant over-dispersion quantified by the parameter α equal to the variance divided by the mean ($\alpha > 1$), compared to Poisson ($\alpha = 1$) (Fig. 4 A). All models with zero-inflation led to zero-inflation of 60 to 90% (Fig. 4 B; note that results for model PZ are not reliable for convergence reasons, see Section 3.1.1).

Marginal posterior analysis shows no significant effect of crowding, as the posterior coefficient of density-dependent mortality (k_c) remains with the prior and leads to a very small contribution to the mortality rate when multiplied with typical population sizes (Fig. 4 C). On the other hand, we observe a significant effect of time-dependent mortality on population dynamics as the marginal posteriors of the coefficients of time-dependent mortality, k_1, are always significantly larger than zero (Fig. 4 D). This effect can be an indication of cumulative effects of diazinon unless the other treatments would show this effect also. To stress the importance of the single mechanisms associated to the relevant parameters, in Fig. 4 we show a subset of the (simplest) model versions. See supplementary Figures S.7 and S.8 for a complete comparison of all the parameters for all the model versions.

The two-dimensional marginals plots of the posterior parameter distribution (see Fig. 5) show strong negative correlation between the mortality parameters k_0 and k_1 and positive correlation between the parameters c, π and r. All these results have a clear ecological interpretation: k_0 and k_1 both affect mortality positively, which results in a negative posterior correlation. The clutch size, c, and the fraction of adults without eggs, π, lead to a mean fecundity of $f = c(1-\pi)$. As the model results are sensitive to the mean fecundity, this leads to a positive correlation of c and π. Overdispersion can either be increased by decreasing values of r or increasing values of π which leads to a positive correlation of these parameters. Finally, c and r are positively correlated because of their positive correlation with π.

3.1.4. Model selection

The results outlined in the previous section are the basis for our reasoning for model selection for nested stochastic ecological model versions (Table 2). The Poisson fertility distribution P clearly demonstrates the difficulty of model structure selection for stochastic models. Despite the small variance of this distribution, a model fit is always possible with low probability due to the stochastic nature of the model. Only the extensions to negative binomial fertility distributions and

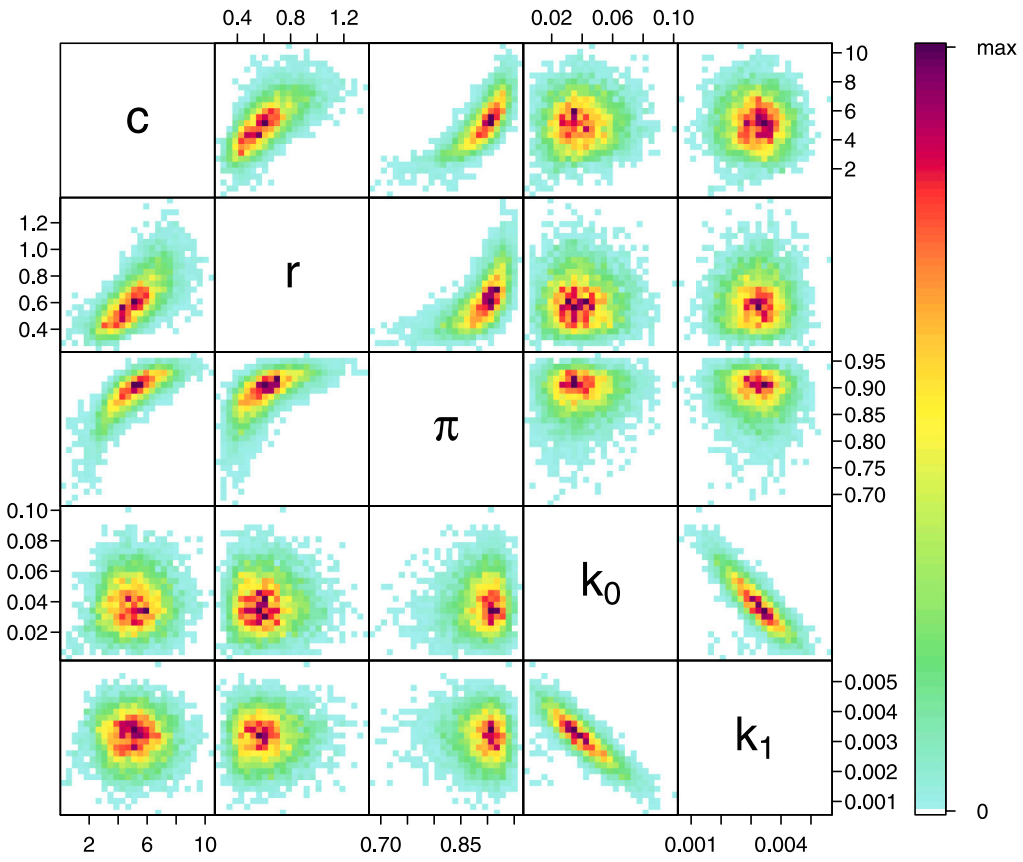

Fig. 5. Plot of two-dimensional marginals of the posterior parameter distribution for the model NZTJ. The color scale encodes the density of the points in the scatter plot. See Table 1 for the units of measure of the parameters.

to zero-inflation demonstrate the weakness of the Poisson assumption (Lindén and Mäntyniemi, 2011; Brooks et al., 2019), with strong evidence for the need of these extensions with the models N and NZ. This need is clearly seen by the marginal posteriors of the parameters α and π in Fig. 4, which indicate values significantly different from 1 and 0 respectively. The result that the joint fit for the model N requires a higher overdispersion than any of the replica fits for this model may be an indication of a structural weakness of this model. Numerically, the need of overdispersion and zero-inflation is quantified by the means and standard deviations of the associated parameters given in Table 2 (second column) which demonstrate a significant deviation from the values associated to a Poisson fertility distribution. Note that in this case lack of convergence reveals a structural deficit of the model PZ: it does not converge as zero-inflation tends towards unity, and clutch size tends to very large values (to keep effective fecundity $f = c(1-\pi)$ at a reasonable level). Finally, both marginal posterior analysis and predictions with posterior parameters clearly indicate the need for an increase in mortality over time in the microcosms with diazinon treatment. In fact, total mortality in models with time-dependent mortality ($k_0 + 20k_1 = 0.23 \pm 0.02d^{-1}$) becomes three times higher at the end of the experiment ($k_0 + 60k_1 = 0.34 \pm 0.05d^{-1}$), compared to the total mortality of models without time-dependent mortality ($k_0 = 0.11 \pm 0.008d^{-1}$). Similarly, we found that density-dependence seems not to be relevant for these microcosms. In fact, the mortality due to crowding ($k_c \left(\sum_{i=1}^{n_J} J_i(t) + \sum_{i=1}^{n_A} A_i(t)\right)$), computed when the population reaches its maximum size, is at least one order of magnitude smaller than the average total mortality.

These arguments were formulated in an iterative process of testing and discarding model versions leading to the selection of the model NZTJ with a zero-inflated negative binomial distribution for fertility and an increasing mortality rate with time for the treatments with diazinon. Model NZTJ clearly has the correct behavior with finally leading to extinction of the population. In this model version, all parameters are identifiable, and π and k_1 are clearly different from zero (indicating strong evidence for zero-inflation and increasing mortality with time) and r indicating strong overdispersion of the negative binomial fertility distribution compared to the Poisson distribution. This choice is confirmed by classical model selection metrics (see Figure S.1 in supplementary section S.3). The nested model structures made it possible to assess the importance of model extensions by Bayesian inference and analysis of marginal posterior parameter distributions, giving results that are much easier to explain and communicate than abstract numbers that represent information criteria or Bayes factors.

3.2. Comparison of treatments

The careful model structure selection process for the diazinon treatments summarized in Table 2 prepares us for the comparative analysis of the different treatments. For this analysis, we have to consider the zero-inflated negative binomial distribution for fertility, a potential increase in mortality during the experiment, and we will focus on the joint evaluation of all replica for each treatment, keeping the replica-specific treatments to visualize the variability among replicated experiments. Although this model, NZT, is the most parsimonious model for the diazinon treatment, as all parameters are identifiable, we choose the model NZTC, that considers a potential density-dependence of Daphnia mortality, for the comparison to check whether density-dependence could be an issue for one of the other treatments. Fig. 6 shows the marginal posterior densities of some combinations of the six model parameters for all four treatments.

These results show a clear separation of average mortality between the treatments with and without the insecticide diazinon (Fig. 6, panel I). As the marginals for the parameter of time-dependence of the mortality rate demonstrates (parameter k_1 in Fig. 6, panel E), the increase

Table 2
Reasoning for selecting the model NZTJ. See Sections 2.3.3 and 2.3.4 for explanation of abbreviations. Gray rows indicate the best choices for fertility, mortality and application strategy.

	Version	Statistics	Conclusion
Fertility	P		Fit seems ok; but see below for improvements.
	PZ	$\pi \sim 1$	No convergence; overdispersion seems to be mapped to zero-inflation.
	N	$\alpha = 6.7 \pm 1.2$	Dispersion parameter clearly indicates overdispersion compared to P.
	NZ	$\alpha = 10.9 \pm 2.7$ $\pi = 0.9 \pm 0.03$	**Strong evidence for overdispersion and zero-inflation.**
Mortality	(const.)		Posterior predictions indicate incorrect predictions (low probability of extinction).
	C		Small posterior value indicates irrelevance of density-dependence in this case.
	T	$k_1 = 0.003$ $\pm 0.0007 d^{-2}$	**Strong evidence for positive value of the parameter k_1.**
	CT		Small posterior value indicates irrelevance of density-dependence in this case.
Application Strategy	R		Good fit (except PZ); small deviations between replicas indicates low systematic variability between replicas.
	J		**Good fit (except PZ); good summary of information from data, as there is no evidence for different conditions among replica.**

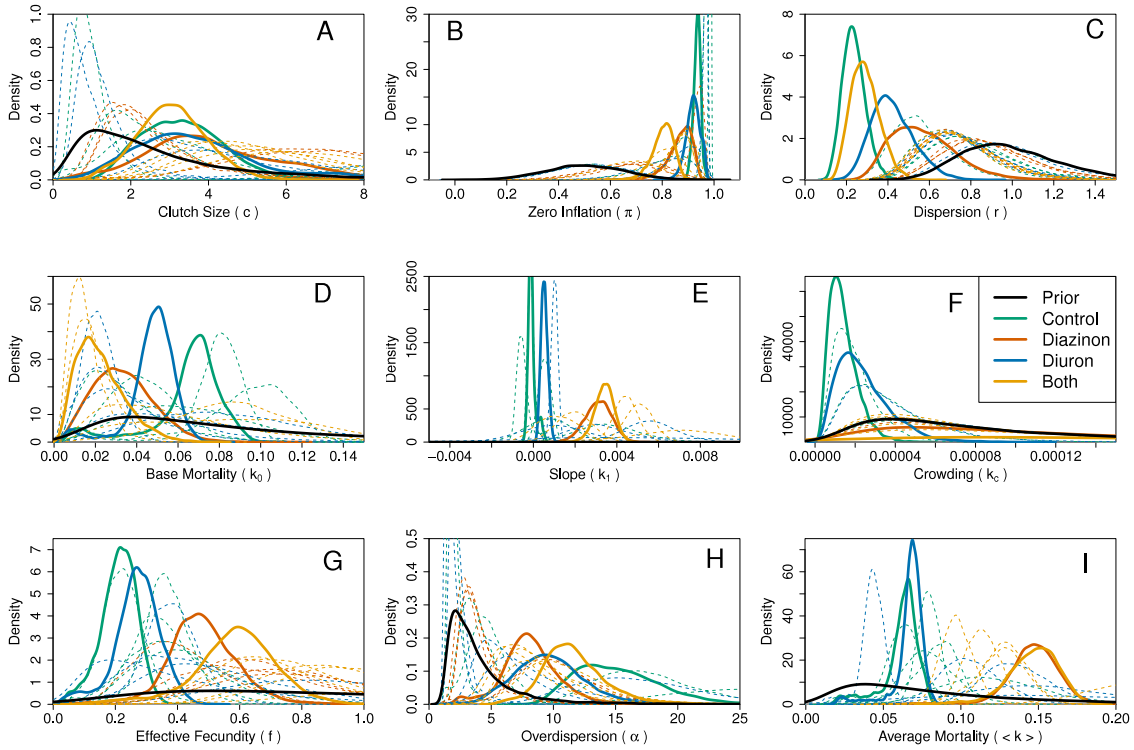

Fig. 6. Plots of marginal posterior densities of parameters for treatments control (green), herbicide (blue), insecticide (red), and both pesticides (orange) for model NZTC for the joint fit (J: continuous lines) and replica by replica fit (R: dashed lines); priors are displayed in black. In the upper panels we show clutch size (c) (panel A), Zero-inflation (π) (panel B), dispersion parameter (r) (panel C), in the middle plots we show base mortality (k_0) (panel D), slope of time-dependent mortality (k_1) (panel E), crowding parameter (k_c) (panel F) and in the lower panel we show the composed parameters: effective fecundity $c(1-\pi)$ (panel G), overdispersion ($\alpha = 1 + f/r$) (panel H) and average mortality $< k >= k_0 + \overline{T}k_1/2$ (panel I) (where $\overline{T}$ is the duration of the experiment averaged across the five replicates).

in mortality over time identified in Section 3.1.3 for the diazinon treatment seems to be a consequence of diazinon and not of generally deteriorating conditions in the microcosms. For the treatments that do not contain diazinon, the values of this parameter are compatible with zero. Effective fecundity seems also to increase for the diazinon treatments (Fig. 6, panel I), although this increase is less significant than the one we observe for mortality and mortality slope. This difference is mostly caused by an increase in the fraction of adults without eggs, i.e. by a decrease in zero-inflation parameter π (Fig. 6, panel B), and not by the average clutch size, that remains around 3 eggs per individual in all treatments (Fig. 6, panel A). The differences in the density-dependence parameter, k_c (Fig. 6, panel F) may be caused by the better identifiability of this parameter for the treatments without diazinon due to the larger numbers of individuals reached for some treatments (see Fig. 1). In all cases, the order of magnitude of the crowding parameter makes its effect negligible for all treatments, so that these differences are not relevant for the model outcomes.

Fig. 7 shows the time series of posterior knowledge of the number of adult individuals for all the treatments and replicates as obtained by

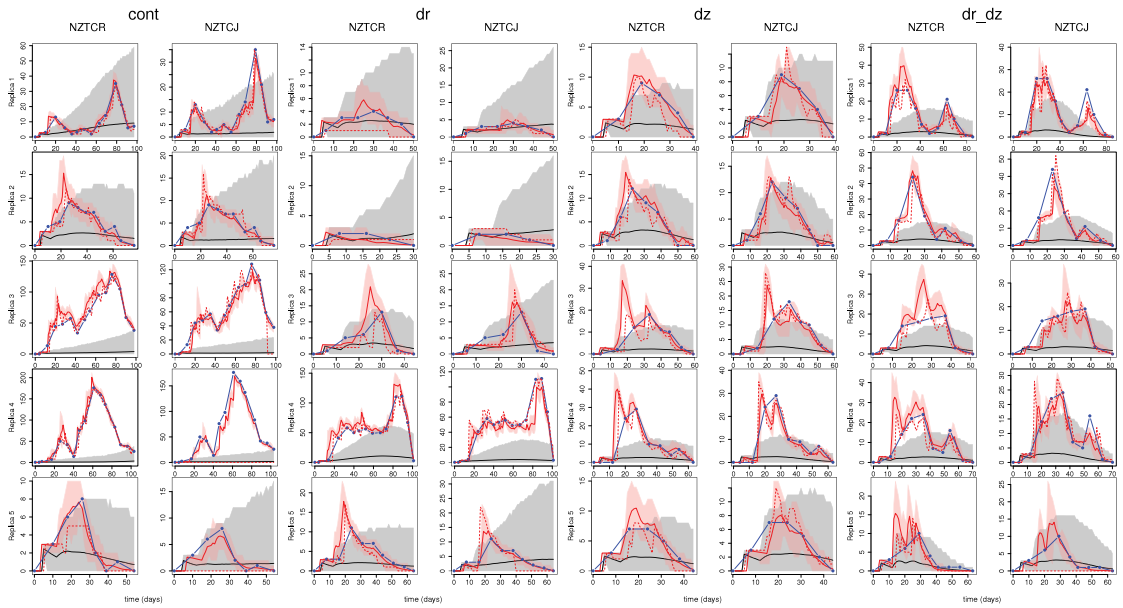

Fig. 7. Time series of adults of *Daphnia galeata* obtained from fitting models NZTC to all 5 replicas (rows) for the four different treatments (Control: cont; diazinon: dz; diuron: dr; Both Pesticides: dr_dz), using application strategies R and J (columns). The black line and the gray shaded area refers to the mean and 95% quantiles of the predictions obtained by forward simulating the model with the inferred parameters, while the red lines and red shaded area refers to the mean and 95% quantiles of the posterior of the states. The red dotted line shows the maximum posterior trajectory. The blue dots represent the observations.

the model (red areas) as well as the posterior predictions for potential future experiments (gray areas).

An apparent feature of the unconditioned predictions are the large uncertainties resulting from the high demographic stochasticity of the model, which reflects the high stochasticity in the data. As already the poor replicability of the data demonstrates (see Fig. 1), we cannot expect small prediction uncertainties by the model. See also supplementary Figures S.10–S.11 for the time series of posterior knowledge of the number of individuals in all developmental stages, for all the treatments and replicates, and supplementary Figures S.12–S.15 for all plots of two-dimensional marginals of the posterior parameter distribution for the four treatments.

4. Discussion

To analyze the Daphnia population dynamics in our experiments, we chose to use an age-structured, discrete individuals model to consider the observed life stages and to account for demographic stochasticity of the (initially) small populations. The model structure was formulated as a discrete-time model with the processes of reproduction, aging and mortality. This structure was extended to different model versions based on different distributional assumptions for fertility and different parameterizations of the mortality rate. Bayesian inference was performed for a joint description of replicated experiments and for a replica-specific description for each treatment separately. With this population-based approach we expect to be able to extract as much information as possible from the data (Forbes et al., 2009, 2011), as it allows us to investigate shifts in inferred parameter values that characterize different processes across different treatments. The high variability between replicated experiments with the same treatment was a strong indication for the need of using a stochastic model. Our approach is similar to the one by Erickson et al. (2014), except that we use an age- instead of a stage-structured model and a different parameterization for potential density dependence of survival. Also, as we only have experimental data for one concentration of each pesticide (and their combination) we do not formulate a model for the toxic effect (Erickson et al., 2014). By fitting all parameters for each treatment separately and interpreting the resulting shifts in the marginal posterior parameter distribution relative to the control, we do not have to make any assumptions about the shape of the response-curve nor on the processes that are affected by the pesticide. This gives more flexibility in identifying potential treatment effects, but also implies that we cannot use the model to make predictions for other pesticide concentrations. For this purpose a different experimental design that covers the range of relevant concentrations (Kreyling et al., 2018) would be necessary.

The high variability among the observations for different replica of the same treatment led to corresponding differences in posterior parameter distributions for replica-specific inference. As all daphnid individuals were of the same clone and the environmental conditions were kept identical to the degree possible, these results can best be explained by remaining, mainly demographic stochasticity. For this reason, joint calibration of all data from replicated experiments using a model that accounts for demographic stochasticity seemed to be the most adequate model application strategy. Model selection based on the marginal posterior parameter distributions that characterize the different model versions and based on the joint calibration approach led to the conclusions that (i) modeling fertility with a zero-inflated negative binomial distribution leads to a better fit than without zero-inflation or with a Poisson distribution; (ii) there was no significant effect of density-dependence on mortality; (iii) variability resulted primarily from stochasticity in fertility and mortality; (iv) treatments with sublethal concentrations of the insecticide diazinon showed a significant increase in mortality over time as well as in average mortality over the duration of the experiment. The same experiments also showed a less significant increase in effective fecundity caused by an increase of the number of adults without eggs.

The need to account for overdispersion compared to a Poisson distribution to appropriately describe variability of the number of eggs across individuals in Daphnia populations has been found in many other studies also, and in many of those it was also described by a negative binomial distribution (Delignette-Muller et al., 2014). The increase in mortality is very clear and is an expected result for insecticide treatments that has been reported in other studies also (Erickson et al., 2014). Increased fertility has been reported as a possible stress response of Daphnia, for example in response to kairomones (Liu and Steiner, 2014), or presence of fish (Boersma et al., 1999). But also

reduced fertility has been observed in response to diazinon (Fernandez-Casalderrey et al., 1995). As our results regarding fertility are less significant than the effects in mortality, it remains unclear whether this result is a true response of the individuals or just an artifact of the high stochasticity in the experiments that would decrease with a larger sample size. This would need further investigation.

Our results indicate both the potential of model-based analysis of data that are difficult to interpret directly due to high (in this case primarily demographic) stochasticity as well as the difficulties of drawing final conclusions from such data even with the use of a model that considers the dominant cause of stochasticity. The limited amount of replicates, given the high demographic stochasticity, constrains the complexity of the model structures that still leads to identifiable parameters. Interesting extensions to be further investigated include adding variability in residence times in different life stages (instar period and maturation age are assumed to be constant) and adding age-dependence to fertility and mortality parameters (although we observed little difference in the results when using different survival rates for adults and juveniles).

A further advantage of the model-based analysis of the results is the potential to learn for the design of future experiments. The potential gain of information by increasing the number of individuals at the start of the experiment to reduce demographic stochasticity or to increase the number of replications could be investigated to find an optimal compromise between experimental effort and gain of information.

5. Conclusion

In this paper, we formulate a set of stochastic age-structured discrete population models to analyze experimental data with clonal populations of *Daphnia galeata* that were exposed to sub-lethal concentrations of two different pesticides. We use a nested multi-model approach to make inference with, and select among model versions, in a way that simplifies model comparison. The development of model versions has been performed in an iterative way, combining quantitative ecological hypothesis formulation and Bayesian inference, to provide improved insights into the effects of pesticides on *Daphnia* population dynamics.

The developed pipeline enables us to identify the main processes affecting population dynamics of *Daphnia* despite the high level of demographic stochasticity observed in the experiments. A zero-inflated negative binomial distribution provides the best description of fertility for all pesticide treatments, while, in the treatments with the insecticide diazinon, the marginal posterior of the slope of time dependent mortality is significantly greater than zero showing a significant chronic effects of the insecticide on the populations. In sum, our approach turned out to be adequate for identifying relevant ecological processes affecting reproduction and mortality of *Daphnia*, using computationally cheap techniques that complement classical model selection metrics. Moreover, the models we presented can be easily generalized to describe different ecological systems and extended to include different ecological processes.

CRediT authorship contribution statement

Gian Marco Palamara: Conceived ideas and methodology, analyzed the data, led writing of the manuscript, performed coding and simulations. **Stuart R. Dennis:** Performed the experiment and collected the data, analyzed the data, contributed to writing. **Corinne Haenggi:** Performed the experiment and collected the data. **Nele Schuwirth:** Conceived ideas and methodology, analyzed the data, contributed to writing. **Peter Reichert:** Conceived ideas and methodology, analyzed the data, led writing of the manuscript, coding and simulations.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: None

Data availability

We have shared the data/code at https://github.com/Gpalam/Daphnia.

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Appendix A. Supplementary material

Supplementary material related to this article can be found online at https://doi.org/10.1016/j.ecolmodel.2022.110076.

References

Ananthasubramaniam, B., Nisbet, R.M., Nelson, W.A., McCauley, E., Gurney, W.S.C., 2011. Stochastic growth reduces population fluctuations in daphnia–algal systems. Ecology 92 (2), 362–372. http://dx.doi.org/10.1890/09-2346.1.

Auger-Méthé, M., Newman, K., Cole, D., Empacher, F., Gryba, R., King, A.A., Leos-Barajas, V., Mills Flemming, J., Nielsen, A., Petris, G., Thomas, L., 2021. A guide to state–space modeling of ecological time series. Ecol. Monograph 91 (4), e01470. http://dx.doi.org/10.1002/ecm.1470.

Beckerman, A.P., Rodgers, G.M., Dennis, S.R., 2010. The reaction norm of size and age at maturity under multiple predator risk. J. Anim. Ecol. 79 (5), 1069–1076. http://dx.doi.org/10.1111/j.1365-2656.2010.01703.x.

Beketov, M.A., Kefford, B.J., Schäfer, R.B., Liess, M., 2013. Pesticides reduce regional biodiversity of stream invertebrates. Proc. Natl. Acad. Sci. 110 (27), 11039–11043. http://dx.doi.org/10.1073/pnas.1305618110.

Belaid, C., Sbartai, I., 2021. Assessing the effects of thiram to oxidative stress responses in a freshwater bioindicator cladoceran *(Daphnia magna)*. Chemosphere 268, 128808. http://dx.doi.org/10.1016/j.chemosphere.2020.128808.

Boersma, M., De Meester, L., Spaak, P., 1999. Environmental stress and local adaptation in *Daphnia magna*. Limnol. Oceanogr. 44 (2), 393–402.

Brede, N., Sandrock, C., Straile, D., Spaak, P., Jankowski, T., Streit, B., Schwenk, K., 2009. The impact of human-made ecological changes on the genetic architecture of daphnia species. Proc. Natl. Acad. Sci. 106 (12), 4758–4763. http://dx.doi.org/10.1073/pnas.0807187106.

Brooks, M.E., Kristensen, K., Darrigo, M.R., Rubim, P., Uriarte, M., Bruna, E., Bolker, B.M., 2019. Statistical modeling of patterns in annual reproductive rates. Ecology 100 (7), e02706. http://dx.doi.org/10.1002/ecy.2706.

Chou, T., Greenman, C.D., 2016. A hierarchical kinetic theory of birth, death and fission in age-structured interacting populations. J. Stat. Phys. 164 (1), 49–76. http://dx.doi.org/10.1007/s10955-016-1524-x.

De Roos, A.M., Diekmann, O., Metz, J.A.J., 1992. Studying the dynamics of structured population models: A versatile technique and its application to Daphnia. Amer. Nat. 139 (1), 123–147. http://dx.doi.org/10.1086/285316.

de Souza, R.M., Seibert, D., Quesada, H.B., de Jesus Bassetti, F., Fagundes-Klen, M.R., Bergamasco, R., 2020. Occurrence, impacts and general aspects of pesticides in surface water: A review. Process Saf. Environ. Prot. 135, 22–37. http://dx.doi.org/10.1016/j.psep.2019.12.035.

Delignette-Muller, M.L., Lopes, C., Veber, P., Charles, S., 2014. Statistical handling of reproduction data for exposure-response modeling. Environ. Sci. Technol. 48, 7544–7551. http://dx.doi.org/10.1021/es502009r.

Dennis, S., Carter, M.J., Hentley, W., Beckerman, A., 2011. Phenotypic convergence along a gradient of predation risk. Proc. Royal Soc. B 278 (1712), 1687–1696. http://dx.doi.org/10.1098/rspb.2010.1989.

Duong, T.-B., Odhiambo, B., Oldham, D., Hoffman, M., Frankel, T.E., 2021. Acute exposure to an organochlorine pesticide alters locomotor behavior and cardiac function in the freshwater invertebrate *Daphnia magna*. Mar. Freshwater Behav. Physiol. 54 (2), 51–64. http://dx.doi.org/10.1080/10236244.2021.1918551.

Ellner, S., Childs, D., Rees, M., 2016. Data-Driven Modelling of Structured Populations: a Practical Guide to the Integral Projection Models. In: Lecture Notes on Mathematical Modelling in the Life Sciences, Springer International Publishing.

Erickson, R.A., Cox, S.B., Oates, J.L., Anderson, T.A., Salice, C.J., Long, K.R., 2014. A daphnia population model that considers pesticide exposure and demographic stochasticity. Ecol. Model. 275 (1), 37–47. http://dx.doi.org/10.1016/j.ecolmodel.2013.12.015.

Fernandez-Casalderrey, A., Ferrando, M.D., Andreu-Moliner, E., 1995. Chronic toxicity of diazinon to *Daphnia magna*: effects on survival, reproduction and growth. Toxicol. Environ. Chem. 49, 25–32. http://dx.doi.org/10.1080/02772249509358173.

Forbes, V.E., Calow, P., Grimm, V., Hayashi, T.I., Jager, T., Katholm, A., Palmqvist, A., Pastorok, R., Salvito, D., Sibly, R., Spromberg, J., Stark, J., Stillman, R.A., 2011. Adding value to ecological risk assessment with population modeling. Hum. Ecol. Risk Assess. Int. J. 17 (2), 287–299. http://dx.doi.org/10.1080/10807039.2011.552391.

Forbes, V.E., Calow, P., Grimmz, V., Hayashi, T., Jager, T., Palmqvisty, A., Pastorok, R., Salvitoy, D., Siblyzz, R., Spromberg, J., Stark, J., Stillman, R.A., 2010. Integrating population modeling into ecological risk assessment. Integr. Environ. Assess. Manag. 6 (1), 191–193. http://dx.doi.org/10.1002/ieam.25.

Forbes, V.E., Hommen, U., Thorbek, P., Heimbach, F., Van den Brink, J., Thulke, H.H., Grimm, V., 2009. Ecological models in support of regulatory risk assessments of pesticides: developing a strategy for the future. Integr. Environ. Assess. Manag. 2 (1), 167–172. http://dx.doi.org/10.1897/IEAM_2008-029.1.

Gelman, A., Carlin, J., Stern, H., Rubin, D., 2003. Bayesian Data Analysis. In: Chapman & Hall/CRC Texts in Statistical Science, Chapman & Hall/CRC.

Grimm, V., Revilla, E., Berger, U., Jeltsch, F., Mooij, W.M., Railsback, S.F., Thulke, H.-H., Weiner, J., Wiegand, T., DeAngelis, D.L., 2005. Pattern-oriented modeling of agent-based complex systems: Lessons from ecology. Science 310 (5750), 987–991. http://dx.doi.org/10.1126/science.1116681.

Hooten, M.B., Hobbs, N.T., 2015. A guide to Bayesian model selection for ecologists. Ecol. Monograph 85 (1), 3–28. http://dx.doi.org/10.1890/14-0661.1.

Houlahan, J.E., McKinney, S.T., Anderson, T.M., McGill, B.J., 2017. The priority of prediction in ecological understanding. Oikos 126 (1), 1–7. http://dx.doi.org/10.1111/oik.03726.

Jager, T., 2020. Revisiting simplified DEBtox models for analysing ecotoxicity data. Ecol. Model. 416, 108904. http://dx.doi.org/10.1016/j.ecolmodel.2019.108904.

Johnson, J.B., Omland, K.S., 2004. Model selection in ecology and evolution. Trends Ecol. Evol. 19 (2), 101–108. http://dx.doi.org/10.1016/j.tree.2003.10.013.

Kamary, K., Mengersen, K.K., Robert, C., Rousseau, J.J., 2018. Testing hypotheses via a mixture estimation model. arxiv preprint, https://arXiv:1412.2044.

Kattwinkel, M., Reichert, P., 2017. BayesIan parameter inference for individual-based models using a particle Markov chain Monte Carlo method. Environ. Model. Softw. 87, 110–119. http://dx.doi.org/10.1016/j.envsoft.2016.11.001.

Keller, B., Wolinska, J., Manca, M., Spaak, P., 2008. Spatial, environmental and anthropogenic effects on the taxon composition of hybridizing daphnia. Philos. Trans. R. Soc. B 363 (1505), 2943–2952. http://dx.doi.org/10.1098/rstb.2008.0044.

Kooijman, S.A.L.M., 2010. Dynamic Energy Budget Theory for Metabolic Organisation. Cambridge University Press.

Kretschmann, A., Ashauer, R., Hitzfeld, K., Spaak, P., Hollender, J., Escher, B.I., 2011a. Mechanistic toxicodynamic model for receptor-mediated toxicity of diazoxon, the active metabolite of Diazinon, in *Daphnia magna*. Environ. Sci. Technol. 45 (11), 4980–4987. http://dx.doi.org/10.1021/es1042386.

Kretschmann, A., Ashauer, R., Hollender, J., Escher, B.I., 2012. Toxicokinetic and toxicodynamic model for diazinon toxicity—mechanistic explanation of differences in the sensitivity of *Daphnia magna* and Gammarus pulex. Environ. Toxicol. Chem. 31 (9), 2014–2022. http://dx.doi.org/10.1002/etc.1905.

Kretschmann, A., Ashauer, R., Preuss, T.G., Spaak, P., Escher, B.I., Hollender, J., 2011b. Toxicokinetic model describing bioconcentration and Biotransformation of diazinon in *Daphnia magna*. Environ. Sci. Technol. 45 (11), 4995–5002. http://dx.doi.org/10.1021/es104324v.

Kreyling, J., Schweiger, A.H., Bahn, M., Ineson, P., Migliavacca, M., Morel-Journel, T., Christiansen, J.R., Schtickzelle, N., Larsen, K.S., 2018. To replicate, or not to replicate – that is the question: how to tackle nonlinear responses in ecological experiments. Ecol. Lett. 21 (11), 1629–1638. http://dx.doi.org/10.1111/ele.13134.

Lamonica, D., Herbach, U., Orias, F., Clément, B., Charles, S., Lopes, C., 2016. Mechanistic modelling of daphnid-algae dynamics within a laboratory microcosm. Ecol. Model. 320, 213–230. http://dx.doi.org/10.1016/j.ecolmodel.2015.09.020.

Lande, R., Engen, S., Sæther, B., 2003. Stochastic Population Dynamics in Ecology and Conservation. In: Oxford Series in Ecology and Evolution, Oxford University Press.

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. 201, 117262. http://dx.doi.org/10.1016/j.watres.2021.117262.

Lindén, A., Mäntyniemi, S., 2011. Using the negative binomial distribution to model overdispersion in ecological count data. Ecology 92 (7), 1414–1421. http://dx.doi.org/10.1890/10-1831.1.

Liu, X., Steiner, C.F., 2014. Ecotoxicology of salinity tolerance in daphnia pulex: interactive effects of clonal variation, salinity stress and predation. J. Plankton Res. 39 (4), 687–697. http://dx.doi.org/10.1093/plankt/fbx027.

Mccauley, E., Nelson, W.A., Nisbet, R.M., 2008. Small-amplitude cycles emerge from stage- structured interactions in daphnia – algal systems. Nature 455, 1240–1243. http://dx.doi.org/10.1038/nature07220.

Metz, J.A., Diekmann, O., 2014. The Dynamics of Physiologically Structured Populations, Vol. 68. Springer.

Moschet, C., Wittmer, I., Simovic, J., Junghans, M., Piazzoli, A., Singer, H., Stamm, C., Leu, C., Hollender, J., 2014. How a complete pesticide screening changes the assessment of surface water quality. Environ. Sci. Technol. 48 (10), 5423–5432. http://dx.doi.org/10.1021/es500371t.

Münze, R., Hannemann, C., Orlinskiy, P., Gunold, R., Paschke, A., Foit, K., Becker, J., Kaske, O., Paulsson, E., Peterson, M., Jernstedt, H., Kreuger, J., Schüürmann, G., Liess, M., 2017. Pesticides from wastewater treatment plant effluents affect invertebrate communities. Sci. Total Environ. 599–600, 387–399. http://dx.doi.org/10.1016/j.scitotenv.2017.03.008.

Nestler, H., Groh, K.J., Schönenberger, R., Behra, R., Schirmer, K., Eggen, R.I.L., Suter, M.J.F., 2012a. Multiple-endpoint assay provides a detailed mechanistic view of responses to herbicide exposure in chlamydomonas reinhardtii. Aquat. Toxicol. 110–111, 214–224. http://dx.doi.org/10.1016/j.aquatox.2012.01.014.

Nestler, H., Groh, K.J., Schönenberger, R., Eggen, R.I.L., Suter, M.J.F., 2012b. Linking proteome responses with physiological and biochemical effects in herbicide-exposed chlamydomonas reinhardtii. J. Proteomics 75 (17), 5370–5385. http://dx.doi.org/10.1016/j.jprot.2012.06.017.

Newman, K., King, R., Elvira, V., de Valpine, P., McCrea, R.S., Morgan, B.J., 2022. State-space models for ecological time-series data: Practical model-fitting. Methods Ecol. Evol. 00, 1–17. http://dx.doi.org/10.1111/2041-210X.13833.

Nisbet, R., Gurney, W., 2004. Modelling Fluctuating Populations. Blackburn Press.

O'Hagan, A., 1995. Fractional Bayes factors for model comparison. J. R. Stat. Soc. Ser. B Stat. Methodol. 57 (1), 99–118. http://dx.doi.org/10.1111/j.2517-6161.1995.tb02017.x.

Plummer, M., 2003. JAGS: A program for analysis of Bayesian graphical models using gibbs sampling. In: Proceedings of the 3rd International Workshop on Distributed Statistical Computing, Vol. 124, no. 125.10. Vienna, Austria, pp. 1–10.

Plummer, M., 2008. Penalized loss functions for Bayesian model comparison. Biostatistics 9 (3), 523–539. http://dx.doi.org/10.1093/biostatistics/kxm049.

Preuss, T.G., Hammers-Wirtz, M., Hommen, U., Rubach, M.N., Ratte, H.T., 2009. Development and validation of an individual based *Daphnia magna* population model: The influence of crowding on population dynamics. Ecol. Model. 220 (3), 310–329. http://dx.doi.org/10.1016/j.ecolmodel.2008.09.018.

R. Core Team, 2021. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria.

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. http://dx.doi.org/10.1002/ieam.4377.

Riedl, V., Agatz, A., Benstead, R., Ashauer, R., 2019. Factors affecting the growth of pseudokirchneriella subcapitata in single-species tests: Lessons for the experimental design and the reproducibility of a multitrophic laboratory microcosm. Environ. Toxicol. Chem. 38 (5), 1120–1131. http://dx.doi.org/10.1002/etc.4393.

Robert, C.P., 2016. The expected demise of the Bayes factor. J. Math. Psych. 72 (1), 33–37. http://dx.doi.org/10.1016/j.jmp.2015.08.002.

Roberts, D.R., Bahn, V., Ciuti, S., Boyce, M.S., Elith, J., Guillera-Arroita, G., Hauenstein, S., Lahoz-Monfort, J.J., Schröder, B., Thuiller, W., Warton, D.I., Wintle, B.A., Hartig, F., Dormann, C.F., 2017. Cross-validation strategies for data with temporal, spatial, hierarchical, or phylogenetic structure. Ecography 40 (8), 913–929. http://dx.doi.org/10.1111/ecog.02881.

Schuwirth, N., Borgwardt, F., Domisch, S., Friedrichs, M., Kattwinkel, M., Kneis, D., Kuemmerlen, M., Langhans, S.D., Martínez-López, J., Vermeiren, P., 2019. How to make ecological models useful for environmental management. Ecol. Model. 411 (1), 108784. http://dx.doi.org/10.1016/j.ecolmodel.2019.108784.

Shoemaker, L.G., Sullivan, L.L., Donohue, I., Cabral, J.S., Williams, R.J., Mayfield, M.M., Chase, J.M., Chu, C., Harpole, W.S., Huth, A., HilleRisLambers, J., James, A.R.M., Kraft, N.J.B., May, F., Muthukrishnan, R., Satterlee, S., Taubert, F., Wang, X., Wiegand, T., Yang, Q., Abbott, K.C., 2020. Integrating the underlying structure of stochasticity into community ecology. Ecology 101 (2), e02922. http://dx.doi.org/10.1002/ecy.2922.

Silva, L.C., Moreira, R.A., Pinto, T.J., Vanderlei, M.R., Athayde, D.B., Lopes, L.F., Ogura, A.P., Yoshii, M.P., Freitas, J.S., Montagner, C.C., et al., 2021. Lethal and sublethal toxicity of pesticides and vinasse used in sugarcane cultivation to ceriodaphnia silvestrii (Crustacea: Cladocera). Aquat. Toxicol. 241, 106017. http://dx.doi.org/10.1016/j.aquatox.2021.106017.

Spiegelhalter, D.J., Best, N.G., Carlin, B.P., van der Linde, A., 2014. The deviance information criterion: 12 years on. J. R. Stat. Soc. Ser. B Stat. Methodol. 76 (3), 485–493. http://dx.doi.org/10.1111/rssb.12062.

Spiegelhalter, D.J., Best, N.G., Carlin, B.P., Van Der Linde, A., 2002. BayesIan measures of model complexity and fit. J. R. Stat. Soc. Ser. B Stat. Methodol. 64 (4), 583–639. http://dx.doi.org/10.1111/1467-9868.00353.

Taub, F.B., 1997a. Are ecological studies relevant to pesticide registration decisions? Ecol. Appl. 7 (4), 1083–1085. http://dx.doi.org/10.1890/1051-0761(1997)007[1083:AESRTP]2.0.CO;2.

Taub, F.B., 1997b. Unique information contributed by multispecies systems: examples from the standardized aquatic microcosm. Ecol. Appl. 7 (4), 1103–1110. http://dx.doi.org/10.1890/1051-0761(1997)007[1103:UICBMS]2.0.CO;2.

Tenan, S., O'Hara, R.B., Hendriks, I., Tavecchia, G., 2014. BayesIan model selection: The steepest mountain to climb. Ecol. Model. 283, 62–69. http://dx.doi.org/10.1016/j.ecolmodel.2014.03.017.

Tendeiro, J.N., Kiers, H.A., 2019. A review of issues about null hypothesis Bayesian testing. Psychol. Methods 24 (6), 774–795. http://dx.doi.org/10.1037/met0000221.

Topping, C.J., Aldrich, A., Berny, P., 2020. Overhaul environmental risk assessment for pesticides. Science 367 (6476), 360–363, https://10.1126/science.aay1144.

Wittmer, I., Moschet, C., Simovic, J., Stamm, C., Hollender, J., Junghans, M., Leu, C., 2014. Ueber 100 pestizide in fliessgewaessern. Programm NAWA spez zeigt die Pestizidbelastung der Schweizer Fliessgewaesser auf. Aqua Gas 94, 32–43, https://www.aquaetgas.ch/.