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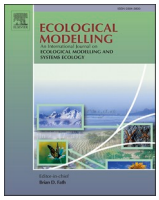

How relevant are temperature corrections of toxicity parameters in population models for environmental risk assessment of chemicals?

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ABSTRACT

Population models provide insights into population dynamics under diverse and untested chemical exposure scenarios, supporting their environmental risk assessment (ERA). In this study, we investigate the interplay of temperature and imidacloprid exposure on population dynamics using an Individual-Based Model (IBM) incorporating a dynamic energy budget (DEB) model for population dynamics and toxicokinetic-toxicodynamic models of the General Unified Threshold model for Survival (GUTS) framework to predict toxicity effects. For this, we tested different model configurations, where i) only the DEB parameters are corrected for temperature, as is common practice, and ii) also the TKTD parameters of the GUTS model are corrected for temperature. In doing so, we aim to evaluate the importance of temperature corrections in the GUTS model within an IBM framework. As expected, increased temperature amplitudes increase the range of simulated population sizes, and chemical exposure reduces the maximum population size. The combined effect of correcting both the DEB and TKTD parameters, however, yield an overall strongly negative effect on population sizes, particularly at lower temperatures. These results highlight the necessity of temperature-sensitive parameterization in population models for a protective risk assessment under the projected future climate conditions with increased temperatures and variability. Future considerations include incorporating local adaptations and acclimatization, particularly in different climate zones, to accurately interpret population model outcomes in the context of evolving environmental conditions. Such insights contribute to the refinement of ecological realism in ERA, enhancing the robustness of chemical risk management strategies.

1. Introduction

Ecological models can help us to study, formulate, and understand the fundamental processes of the real-life systems they represent by integrating the basic building blocks of the system of interest. In environmental risk assessment (ERA) of chemicals, population models are powerful tools (Forbes et al., 2009; Schmolke et al., 2017), especially as the protection goals are often defined at the population level (EFSA Panel on Plant Protection Products and their Residues (PPR), 2010), while testing is done at the individual level. Population models provide robust and traceable insights into population dynamics under a wide range of exposure scenarios that would otherwise be associated with too high costs and time demand to be evaluated in (semi-)field experiments. With their demographic endpoints (e.g., intrinsic population growth rates, equilibrium densities), they are primarily used in the "higher tier" ERA (EFSA Panel on Plant Protection Products and their Residues (PPR) et al., 2018; Larras et al., 2022). Briefly, the "tiered approach" in ERA separates different levels of complexity regarding the experimental system used for the assessment. While always starting at Tier 1, it can thus be possible to refine the biotic and abiotic factors in pursuit of a more realistic assessment scenario in higher tiers (EFSA Panel on Plant Protection Products and their Residues (PPR), 2013).

Frequently used types of population models are individual-based models (IBMs) making up half of the population models used in the ERA of plant protection products (Larras et al., 2022). In IBMs, the population is constructed from many individual organisms that can have specific attributes. The life histories of individuals are tracked, and they interact with each other and with their local environment. From these interactions population dynamics emerge, that might be influenced by environmental changes or stressors. As the variety of processes that can

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be implemented in IBMs is manifold, experts see a high potential to use them in ERA (Accolla et al., 2021; EFSA Panel on Plant Protection Products and their Residues (PPR), 2014; Forbes et al., 2016).

Temperature is an important abiotic factor, especially in seasonal environments, influencing basic organismal processes like aging, growth, and reproduction (Kooijman, 2010) and also the toxicokinetics and toxicodynamics (TKTD) of chemicals in individuals (Huang et al., 2023; Mangold-Döring et al., 2022; Raths et al., 2023). These influences are generally considered through the Arrhenius equation (Arrhenius, 1889), correcting all rate parameters. Considering the future prediction of increasing temperature extremes due to climate change, there is a rising concern about temperature effects on organisms' health, especially regarding temperature induced increased sensitivity to chemical stressors (Hermann et al., 2023; Polazzo et al., 2022). Recent investigations have highlighted the importance of temperature's influence on TKTD processes on the individual level (Mangold-Döring et al., 2022; Raths et al., 2023). In IBM's, the individual growth and development is often based on the dynamic energy budget (DEB) model (Kooijman, 2010) frequently coupled with a TKTD model for chemical effects, like the General Unified Threshold model for Survival (GUTS) (Jager and Ashauer, 2018). There are thus, at least two modules within an IBM where temperature should be considered (i.e., the GUTS and the DEB module) when assessing the effects of chemicals on population dynamics in different exposure scenarios. Yet, while in practice the DEB model parameters are commonly corrected for temperature, the parameters for the TKTD model are not (thus assuming toxicant effects under constant laboratory conditions).

In this study, we examine the relevance of including temperature corrections in the GUTS models within the IBM framework.

For this, we are assessing the impacts of chemical exposure on *Gammarus pulex*, a frequently studied freshwater crustacean, contributing to organic matter decomposition (Maltby et al., 2002) and representing a good model organism for ecotoxicological studies (Kunz et al., 2010). Specifically, we will focus on the insecticide imidacloprid and its effects under different temperature and exposure scenarios. While being banned for outdoor use in Europe since 2018 (European Commission, 2018), the neonicotinoid imidacloprid is often used in modeling studies, owing to the existing knowledge of its toxicity and good availability of data from acute and chronic effect studies. Lethal and sublethal effects of imidacloprid on *G. pulex* have been studied extensively (Agatz et al., 2013; Huang et al., 2022b, 2021; Nyman et al., 2013), and these range from feeding inhibition over immobility to mortality. There are a few studies on the influence of temperature on the toxicity of imidacloprid (Huang et al., 2023; Mangold-Döring et al., 2022). Hence, building on those studies, we chose imidacloprid as the pesticide for our simulation exercises. In this study, we focused on lethal effects only. In future steps, temperature effects on sublethal effects such as feeding inhibition could be implemented. As a proof-of-concept approach, we seek to compare and evaluate the performance of two different model configurations: i) the standard DEB-GUTS where only the DEB parameters are corrected for temperature, as is common practice, and ii) the DEB-GUTS-T, where also the TKTD parameters of the GUTS model are corrected for temperature.

By testing these different model configurations, we aim to evaluate the importance of temperature corrections in the GUTS model within an IBM framework. The study will provide insights into the effects of accounting for temperature in the GUTS model for population-level responses to imidacloprid exposure under constant and pulsed exposure conditions and varying temperature scenarios. Ultimately, this research has the potential to contribute to the advancement of the use of IBM models in ERA, through increased realism in population models and process-based understanding of effect mechanisms, herewith aiding in developing more robust chemical risk assessment and risk management strategies.

2. Methods

In the individual-based population model (IBM), each individual incorporates a dynamic-energy-budget (DEB) model and a reduced version of the General Unified Threshold model of Survival (GUTS-RED). As a toxicokinetic-toxicodynamic (TKTD) model, GUTS-RED describes the internal damage depending on the external exposure concentration over time (i.e., TK part) and quantifies the daily survival probability (i.e., TD part) (Jager and Ashauer, 2018). No feedbacks between the DEB and the GUTS model (e.g., growth dilution) were implemented due to the proof-of-concept character of this study, but they should be considered in future developments (Jager, 2020a; Jager et al., 2023).

Including temperature in a population model for a seasonal environmental risk assessment implies the presence of temperature-dependent processes. Indeed, for the DEB module these temperature dependent processes are growth and development, where development determines when reproduction starts. For the pesticide impact on survival (i.e., simulated by the GUTS-RED module), we compare the standard GUTS to the temperature corrected GUTS-T (Mangold-Döring et al., 2022). To explore the net impact of these temperature modulated processes on population dynamics in a seasonal environment, we implemented different IBM configurations, i.e., with DEB-GUTS modules or DEB-GUTS-T modules (Fig. 1). Note that we will refer to the DEB-GUTS, and DEB-GUTS-T to keep it short, while in fact using the GUTS-RED versions in both configurations.

Starting from the NetLogo implementation described in Martin et al. 2012 (Martin et al., 2012), the scaled standard DEB model (Kooijman et al., 2008) was implemented and verified in the software Smalltalk (Squeak 5.3) using the open-source Squeak integrated programming environment (www.squeak.org). The standard DEB model was parameterised on the entry in the Add-my-Pet (AmP) species collection (https://www.bio.vu.nl/thb/deb/deblab/add_my_pet/species_list.html) for *G. pulex* (Zimmer et al., ("Add-my-Pet," 2021) parameter estimated based on version 20210703). Model equations and parameters can be found in appendix B. Furthermore, to guarantee the reproducibility and transparency of all results in accordance with the FAIR guiding principles (Wilkinson et al., 2016), we uploaded the simulation raw data (Mangold-Döring et al., 2024) along with the model and data analysis scripts (https://github.com/NikaGoldring/GammarusPulex_DEB-GUTS-T.git) to publicly accessible repositories.

The GUTS-T model was developed by Mangold-Döring et al. (2022) and calibrated for *G. pulex* exposed to imidacloprid at three different temperatures, using experimental data previously published (Huang et al., 2023, 2022a). Briefly, we extended the standard GUTS model scripts available within the Bring Your Own Model (BYOM) modeling platform (https://debtox.info/byom.html, version 6.2), with the Arrhenius temperature correction based on previously applied approaches (Gergs et al., 2019; Mangold-Döring et al., 2022). Based on the reasoning discussed in Mangold-Döring et al. (2022), parameters describing a rate (i.e., with time in their unit) were corrected with the Arrhenius equation, i.e., the dominant rate k_d and the killing rate b_w (Mangold-Döring et al., 2022). Briefly, we know that chemical reactions accelerate with increasing temperature, a process which is commonly described by the Arrhenius equation. Therefore, we assume that temperature influences the rate parameters by increasing or decreasing their value, i.e., speeding up or slowing down the respective process. Hence, we assume that rates scale with temperature in the GUTS-T configuration, while the median (m_w, for SD model) and the spread factor (F_s, for IT model) of the threshold distribution were kept constant. For the standard GUTS, the parameters at reference temperature (20 °C) were applied and not corrected for the actual temperature scenario. GUTS(-T) model equations and parameters can be found in appendix B, 7.5.

The experimental data used for the calibration comprised survival recordings of field-caught *G. pulex* from the Heelsumse brook (coordinates: 51.973400, 5.748697). During the 28 days exposure to a full

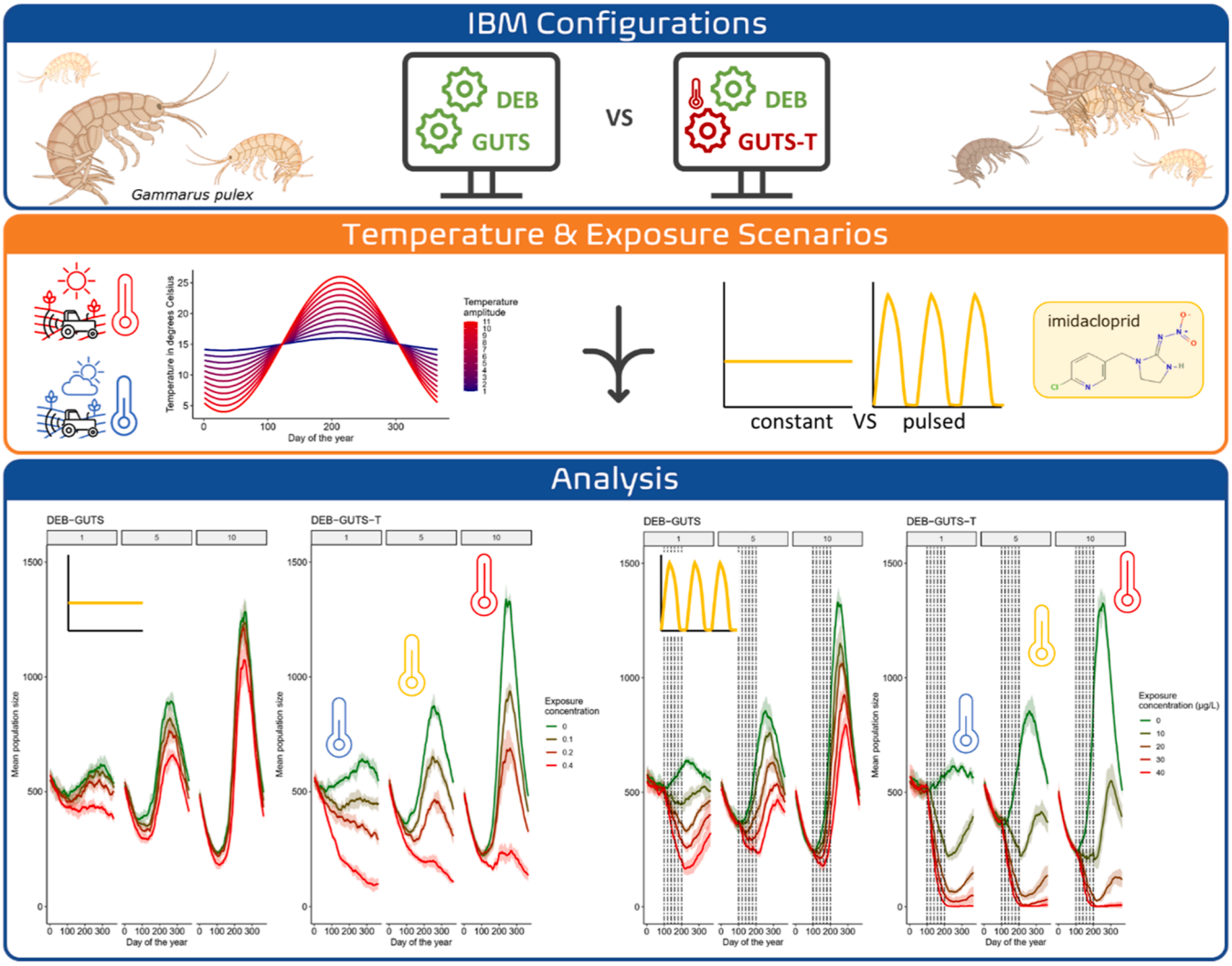

Fig. 1. Conceptual figure of the study workflow. Two model configurations of the individual based (IBM) population model for Gammarus pulex were compared: the DEB-GUTS and the DEB-GUTS-T configuration. These model configurations were used to simulate population dynamics in different temperature and imidacloprid exposure scenarios (i.e., constant and pulsed exposure). The simulation results were compared between the model configuration and scenarios in the final analysis step.

factorial exposure to different imidacloprid concentrations (i.e., 0, 0.3, 1, 3, 10, and 30 µg • L^{-1}) and temperatures (i.e., 7, 11, and 15 °C), the effects on mortality were assessed. The organisms (length: 5.23 mm, sd:1.09 mm) were fed with *Populus* leaves (Huang et al., 2023). We calibrated both the stochastic death (SD) and individual tolerance (IT) model versions in both configurations. GUTS model parameters were estimated based on the Nelder-Mead simplex algorithm provided in the BYOM platform. Their 95% confidence intervals were estimated through the likelihood region method. The best fitting value for the parameter estimates were subsequently used in the IBM.

The different IBM configurations (i.e., DEB-GUTS and DEB-GUTS-T) were used to simulate *G. pulex* populations at different environmental scenarios, i.e., various temperatures and static or pulsed exposure conditions. The different scenarios were simulated over 18 years. Each simulation started with an initialization period of three years without exposure, followed by a period of 10 years with either a constant exposure to imidacloprid (i.e., 0.0 to 1.0 µg L^{-1} with an interval of 0.1 µg L^{-1}) or pulsed exposure scenarios. These concentration ranges were selected to get a range of effect intensities, from control and effect free exposure scenarios to severe mortality. In line with the proof-of-concept character of this study, the intention was not simulate realistic worse case exposure scenarios for the purposes of a risk assessment, but to look at effects of exposure in general.

The initialization period was included as a warm-up period to obtain stable population dynamics within a simulation before the exposure period started. We further selected 10 years of exposure to have a sufficient number of years with effects such that population dynamics can stabilize over time. The final five-year period was simulated to enable a check if population dynamics return to stable pre-exposure dynamics. However, the assessment of recovery potential was not a part of this study.

Pulsed exposure scenarios consisted of six consecutive concentration peaks, starting at day number 100, with a 20-day interval between each peak (i.e., at day-in-year numbers 100, 120, 140, 160, 180 and 200). The duration of these peaks was 24 h, with a constant peak concentration ranging from 10 to 100 µg L^{-1} with an interval of 10 µg L^{-1}.

The seasonal water temperature was simulated using a forcing function with time, with a maximum at the end of July. The temperature was simulated to be fluctuating around the average temperature T_{av} (15 °C), in a cosine curve (eq.2). The average temperature of 15 °C was chosen as a realistic value for shallow Dutch water bodies, derived from the personal observation of the Heelsumse brook with measured temperatures between 4 and 17° (Huang et al., 2023).

The different temperature scenarios were added as a range of tem-

perature amplitudes T_{amp} of 1 to 11 °C with an interval of 1 °C (Fig. 2).

$$T(t) = T_{av} - T_{amp} \cdot \cos\left(\frac{t - shift}{365} \cdot 2\pi\right) \quad (1)$$

The value of the parameter *shift* sets the timing of the day with annual minimum temperature after January 1st and the day with maximum temperature after July 1st. Here, we chose a value of 31 to shift the day with minimum temperature from January 1st to 31st and with the maximum temperature from July 1st to 31st. In this study, we chose to apply oscillating temperature scenarios as they were easy to implement and their fixed dynamic promotes an easier interpretation of the simulation results. The temperature amplitudes were selected to cover a range of temperature scenarios from limited oscillation (i.e., $T_{amp} = 1$), to a very strong oscillation ($T_{amp} = 11$). A T_{amp} of 0 would mean a fixed temperature, which was not considered here. Furthermore, the high amplitude scenarios allowed us to gain insight into the effects of very high and very low temperatures, indicative for expected extreme weather events (i.e., colder and hotter) in future climate projections (IPCC, 2019; Johnson et al., 2018; Woolway et al., 2021).

Model simulation results were further processed in R studio (version 2023.3.1.446 and R version 4.3.0 (R Core Team, 2024) and packages *tidyverse* (Wickham et al., 2019), *patchwork* (Pedersen, 2024), and *ggpubr* (Kassambara, 2023)) to analyze the mean population size of simulation replicates ($n = 5$) with the described scenario settings. A time series analysis of the first year of imidacloprid application was performed, followed by a cumulative frequency distribution analysis to cover the whole exposure period, i.e., mean daily population sizes during the 10 years of exposure. The two model configurations were then also compared directly through a visual analysis of the 1:1 equality line, plotting different quantiles of the mean population size.

3. Results and discussion

During the evaluation of the model simulations for the different exposure and temperature scenarios, we observed that some scenarios led to the extinction of the population. Those scenarios (i.e., for constant exposures higher than 0.4 µg • L^{-1}, for pulsed higher than 40 µg • L^{-1}, and the temperature amplitude 11 °C or higher) were thus excluded for further analysis.

Although both SD and IT calibrations resulted in a good visual fit (Appendix B, Figs. B3 and B5), when looking at the likelihood-based joint-confidence regions for the model parameter (Appendix B, Figs. B4 and B6), we see identifiability problems as previously described for this dataset (Mangold-Döring et al., 2022). Briefly, as the experimental data does not hold enough information (i.e., too little differences in effects observed between concentrations), the model parameter and/or its lower and upper boundary may not be defined conclusively. Hence, we do not have enough information to know the exact value for the parameter of k_d, for instance. Due to the lack of a better-suited dataset (i.e., including both chemical and temperature scenarios) and the proof-of-concept character of this study, we decided to use the calibrated best-fitting values as presented (Appendix B, Tables B4 and B5). Alternatively, one or more model parameters could have been fixed in the estimation process, e.g., based on literature knowledge, to allow a better parameter estimation with defined parameter boundaries for the remaining parameters. Nevertheless, we must provide a fixed value as input for the IBM, and here, we chose the best-fitting estimates based on experimental data as described. Further implications of this will be outlined in the following.

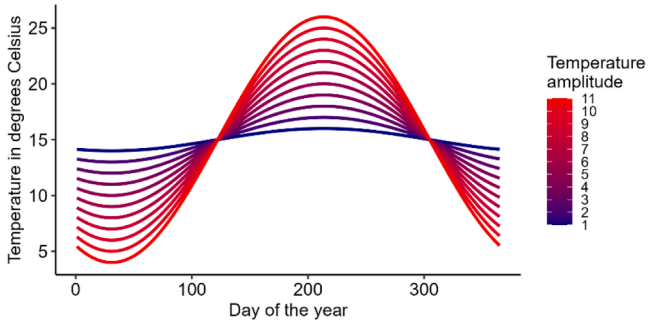

Fig. 2. Applied temperature scenarios. The temperature over one year of simulation is plotted for different temperature amplitudes.

For use in a risk assessment dossier the official guidance of using GUTS models in ERA (EFSA Panel on Plant Protection Products and their Residues (PPR) et al., 2018) suggests running and comparing both GUTS-SD and GUTS-IT versions to be able to choose the most conservative model (i.e., here, the DEB-GUTS-T, SD model version). Therefore the paper will focus on results for the SD model. For completeness the IT model results are provided in the appendix A.

3.1. Comparing model simulation over the first year of application

When evaluating the model simulations of the first year of imidacloprid application, we observed considerable differences between the used model configurations in both the constant and pulsed exposure scenarios for the SD model (Figs. 3 and 4). For the standard DEB-GUTS, where no temperature correction is done on the TKTD parameters, the range of the mean population size at control conditions over the first year increased with increasing temperature amplitudes from a maximum population size of roughly 600 at 1 °C to 1300 at 10 °C amplitude (Figs. 3 and 4, 1–3, green lines). The same trend was observed in the model simulations with the DEB-GUTS-T configuration (Figs. 3 and 4, 4–6, green lines). Thus, as expected, temperature amplitude drives the population dynamics, with mean population sizes following the same pattern as the applied temperature amplitude scenario (Fig. 2), with a minor phase-shift in timing, i.e., the model curves follow the shape of the yearly temperature scenario, simply shifted on the time-axis (Figs. 3 and 4, green lines). This pattern matches well with the seasonal dynamics observed for *G. pulex* (Hynes, 1955; Welton, 1979).

3.1.1. Constant exposure scenarios

Imidacloprid affects the population size maxima and minima in a dose-dependent manner, i.e., increasing adverse effects with increasing exposure concentration (Fig. 3, 1). This effect is amplified in the DEB-GUTS-T model configuration (Figs. 3 and 4). However, we did not observe the same difference in population sizes between the model configurations using the IT version of the GUTS model (Appendix A, Figs. A1 and A2). To explain this, in the following, we want to discuss two different aspects of the model.

Firstly, we postulated that the chemical effect on population dynamics depends on the chosen death mechanism. Conceptually, the GUTS-IT model version relates to the idea that individuals differ in their sensitivity, while in GUTS-SD, the death of the organisms is a stochastic process (Jager and Ashauer, 2018). Thus, in the SD version, all organisms have the same sensitivity towards the chemical, and the chance of dying increases with increasing concentration. Contrastingly, in the IT version, the organisms differ in their sensitivity, and the chance to die is 100% once their individual threshold concentration is reached. Consequently, these different model approaches result in different outcomes in long-term settings, especially in constant exposure conditions (Jager and Ashauer, 2018, Chapter 1.4). Specifically, the SD mechanisms will lead to an ongoing decline of the population over time with continuous exposure, while for the IT mechanism, the sensitive individuals will be dead once the internal concentration reaches its equilibrium, while the less-sensitive ones will survive no matter how long the exposure lasts. We can see these differences when comparing the SD and IT models of the DEB-GUTS configurations without temperature correction. Here, we already observe a stronger dose response relationship in the SD model, showing higher effects (Figs. 3, 1–3 and A1, 1–3).

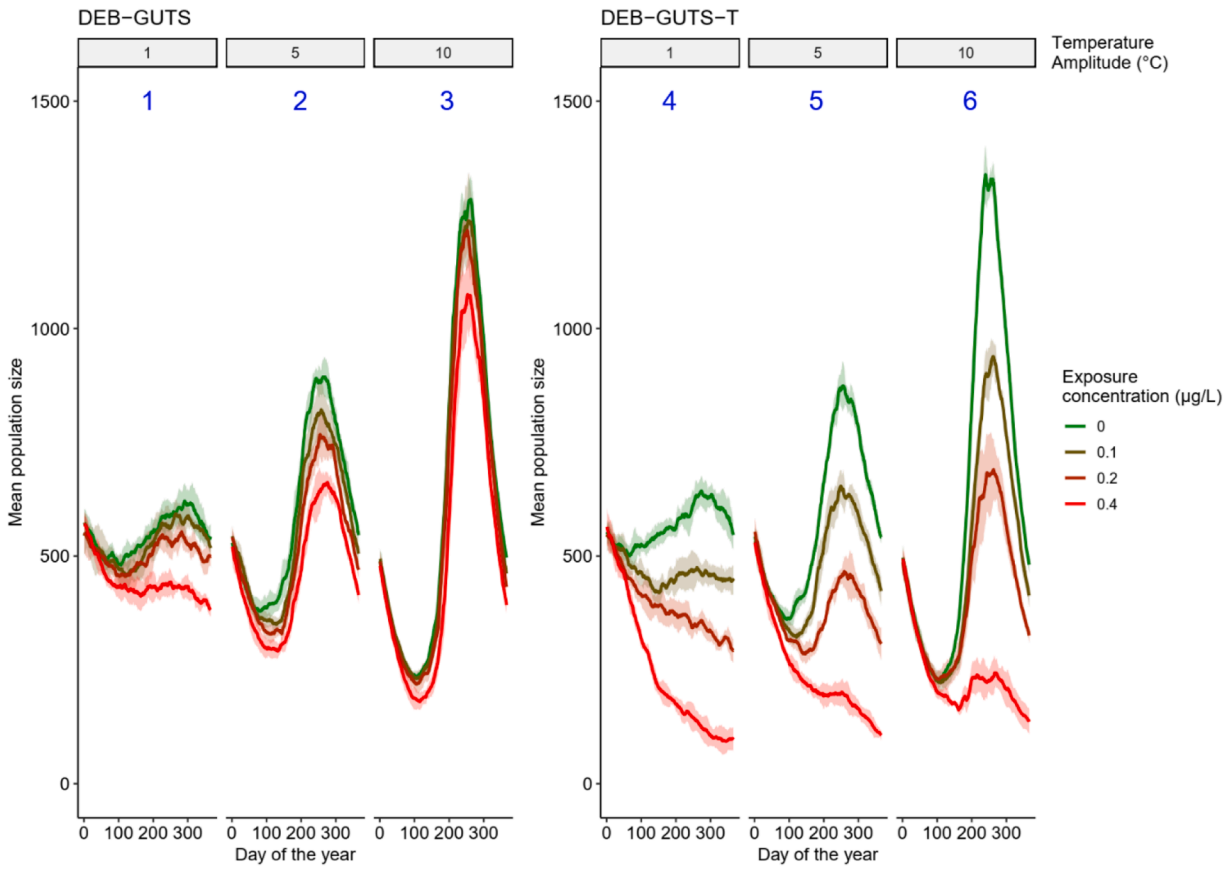

Fig. 3. Simulation results of the mean population size of Gammarus pulex in the first year of constant imidacloprid application at different exposure concentrations and temperature scenarios for both model configurations (SD). The mean of the population size of $n = 5$ model simulations for each configuration and scenario is plotted over the year of the first application, in days of the year, starting on January 1st. The plots on the left side of the figure (1–3) show the results of the simulation with the DEB-GUTS configuration, and the right side (4–6) displays the DEB-GUTS-T configuration results. The different environmental scenarios encompass different exposure concentrations, displayed in different colors ranging from 0 to 0.4 µg • L^{-1}, and the different temperature amplitudes are shown in the different panels for each configuration, i.e., 1 and 4 show the temperature scenario with the amplitude of 1 °C, 2 and 5 for 5 °C and 3 and 6 for 10 °C (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.).

Secondly, we also looked at the calibrated values for the GUTS-RED models in the context of the applied temperature correction (Appendix B, Tables B.4 and B.5). For the GUTS-RED version used in this study, the parameter corrected for temperature includes the dominant rate k_d for both IT and SD versions and the killing rate b_w for SD only. Note that the background hazard rate is accounted for in the DEB model. Thus, to avoid accounting for this twice, it is not considered in the GUTS models of either configuration. The calibrated values were significantly different, with $k_d \approx 0.03\ d^{-1}$ for the SD version and $k_d = 1e^{-6}\ d^{-1}$ for the IT version; both values correspond to the reference temperature of 20 °C. Considering the applied temperature correction, this resulted in a higher impact on the bigger k_d value of the SD model. Therefore, we see an amplified dose-response curve for the SD model (Fig. 3, 1–3 and 4–6) while the temperature correction on the parameters in the IT model has a negligible impact (Fig. A1, 1–3 and 4–6). Furthermore, the additional temperature modulation of the killing rate (b_w) in the SD model version in the DEB-GUTS-T approach might add to the discussed differences between the IT and SD versions.

To further explore the importance of k_d for the observed differences in mean population sizes, we artificially set the k_d of the SD model version to $1e^{-6}d^{-1}$ and repeated the simulations. While accepting the fact that the resulting parameter set is not calibrated to real data, we could show that the value of k_d was responsible for the observed differences in the population dynamics of the modeled exposure scenarios, as they were absent in these additional simulations (Appendix A, Figs. A7 and A8).

Particularly noteworthy is the significant influence of the temperature correction in the low 1 °C temperature amplitude scenario of the SD model (Figs. 3 and 4). While the DEB-GUTS configuration uses the reference values for k_d and b_w at 20 °C, these values are corrected to lower temperatures in the DEB-GUTS-T model, i.e., to temperatures below the reference temperature ranging from 14 to 16 °C in the 1 °C amplitude scenario (Fig. 2). This results in the parameter being lower than in the uncorrected DEB-GUTS configuration throughout the simulation period (shown for k_d as an example in Appendix A, Fig. A11). While a smaller value for the killing rate b_w should intuitively result in less mortality, a small value for the dominant rate constant k_d represents so-called "slow kinetics" and leads to a linear accumulation of internal concentration at constant exposure, and practically no elimination (discussed in Jager, 2020b, section 4.4 Slow kinetics). Under these circumstances, the slow kinetics (i.e., low value for k_d) determines the high mortality through the building up of the internal exposure concentration in the 1 °C amplitude scenario of the DEB-GUTS-T configuration.

Furthermore, in the summer period of the simulation (between day 160 and 280) the value for k_d is bigger than the reference value for the 10 °C temperature amplitude scenario (Appendix A, Fig. A11). This is likely the explanation for the small increase in the mean population size that is visible in the 0.4 µg/L scenario (Figs. 3 and 6). In this period, k_d is big enough to allow faster kinetics and thus the elimination of the compound to a level that is beneath the threshold concentration, resulting in less mortality. Finally, even though the value is bigger than the reference value in the summer period of the simulation for the 10 °C

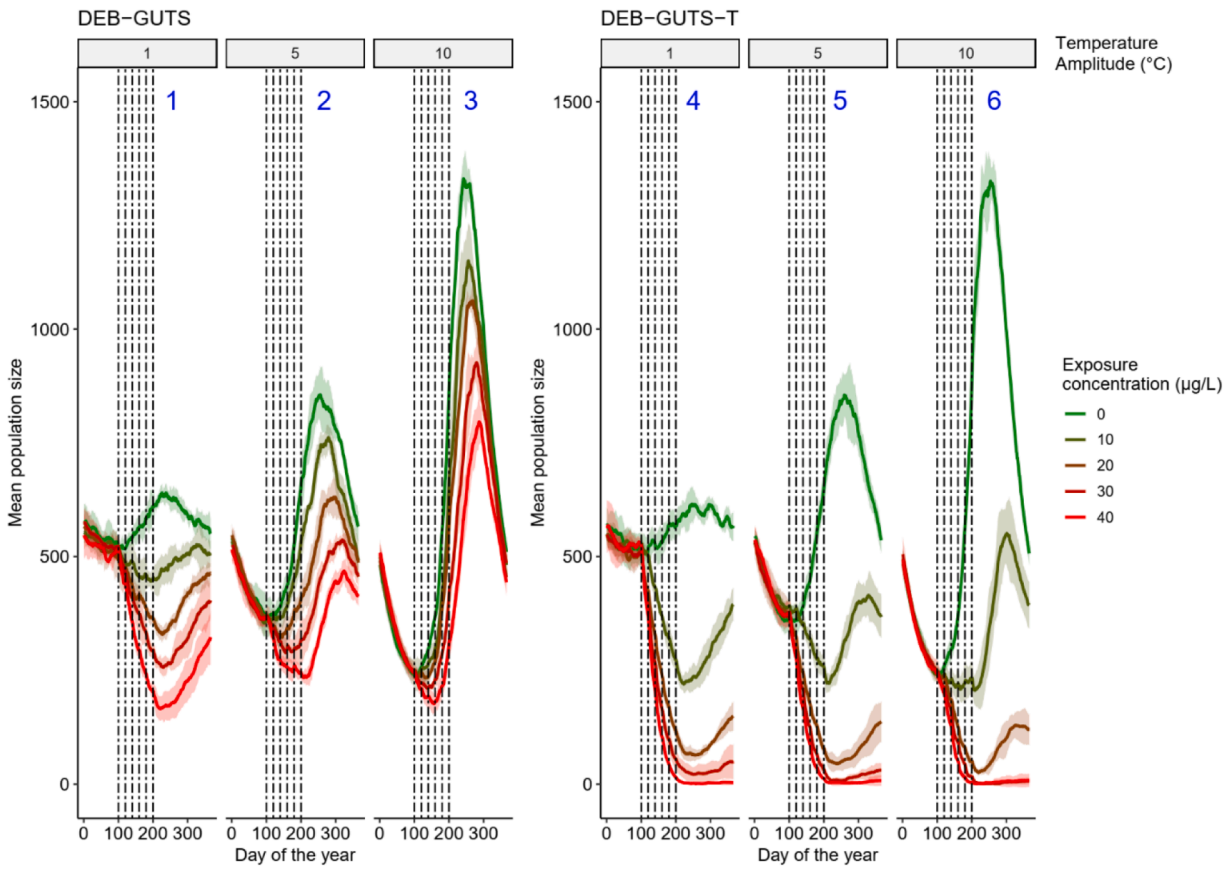

Fig. 4. Simulation results of the mean population size of Gammarus pulex in the first year of pulsed imidacloprid application at different exposure concentrations and temperature scenarios for both model configurations (SD). The mean of the population size of $n = 5$ model simulations for each configuration and scenario is plotted over the year of the first application, in days of the year, starting on January 1st. The plots on the left side of the figure (1–3) show the results of the simulation with the DEB-GUTS configuration, and the right side (4–6) displays the DEB-GUTS-T configuration results. The vertical dotted lines indicate the exposure pulses of imidacloprid concentrations ranging from 0 to 40 µg • L^{-1} (i.e., displayed in different colors) were applied for 1 day at days 100, 120, 140, 160, 180, and 200. The different temperature amplitudes are shown in the different panels for each configuration, i.e., 1 and 4 show the temperature scenario with the amplitude of 1 °C, 2 and 5 for 5 °C, and 3 and 6 for 10 °C, respectively (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.).

temperature amplitude scenario, the driving factor for the observed increased population decline in the DEB-GUTS-T configuration compared to the DEB-GUTS configuration, are the periods where k_d is corrected below the reference value resulting in slow kinetics.

3.1.2. *Pulsed exposure scenarios*

Looking at the results for the pulsed exposure scenarios for the SD model (Fig. 4), we observed similar trends as described for the constant exposure settings. However, the concentration effect on the population size is greater in the pulsed scenarios for the DEB-GUTS (Fig. 4, 1) than in the constant exposure scenario (Fig. 3, 1), due to the higher exposure levels. For the DEB-GUTS-T model simulations, we observed a significant decrease in population size for concentration pulses above and including 10 µg • L^{-1} (Fig. 4, 4–6). Furthermore, in the 40 µg • L^{-1} exposure treatment, the population got extinct in all temperature amplitude scenarios in the temperature corrected simulations (Fig. 4, 4–6, light red lines), while this is not the case when the toxicity is not corrected for temperature (Fig. 4, 1–3, light red lines). Thus, in the pulsed exposure scenarios, the temperature correction of the DEB-GUTS-T impacts the chemical effect quite substantially at all levels of exposure. This is again associated to the calibrated value for k_d in the SD model and the discussed implications of its temperature correction towards slow kinetics in low temperature scenarios.

Furthermore, all the pulses occur in the period with rising temperature (9 April up till 18 July). While in the constant scenarios, the populations are still showing a reproduction peak in the summer month, just at a lower level compared to the control (Fig. 3, 4-6), the three highest concentrations in the pulsed exposure, either die out or increase in size after the summer period (i.e., when temperature declines and exposure has stopped) at a slower rate (Figs. 4–6). To get a bit more insight in the influence of the start of the pulse application, we briefly looked at the 20 µg • L^{-1} scenario at temperature amplitude 10 and ran simulations with different pesticide application start times (Appendix A, Fig. A9). When evaluating the relative population size simulated by the two different model configurations (Appendix A, Fig. A10), we can conclude that an earlier application start (and therefore an earlier application stop) resulted in the highest relative population size at the end of the year. Likewise, a population disturbed by pulsed chemical exposure in the field will be impacted by the application start relative to the temperature influencing their reproduction potential. These considerations are important for the populations recovery potential as this is mainly driven by the reproductive summer period (Galic et al., 2012).

Interestingly, we observed that when correcting the TKTD parameter for temperature, the IT model exhibits even smaller changes than the SD model across the applied imidacloprid concentrations, particularly in the 1 °C amplitude group (Appendix A, Fig. A1, 4–6 and A2, 4–6). This result is in contrast with the observed increased concentration effect in the SD version of DEB-GUTS-T as previously discussed. However, as discussed earlier, for the IT version the only temperature corrected parameter was k_d, the dominant rate constant, which was calibrated to

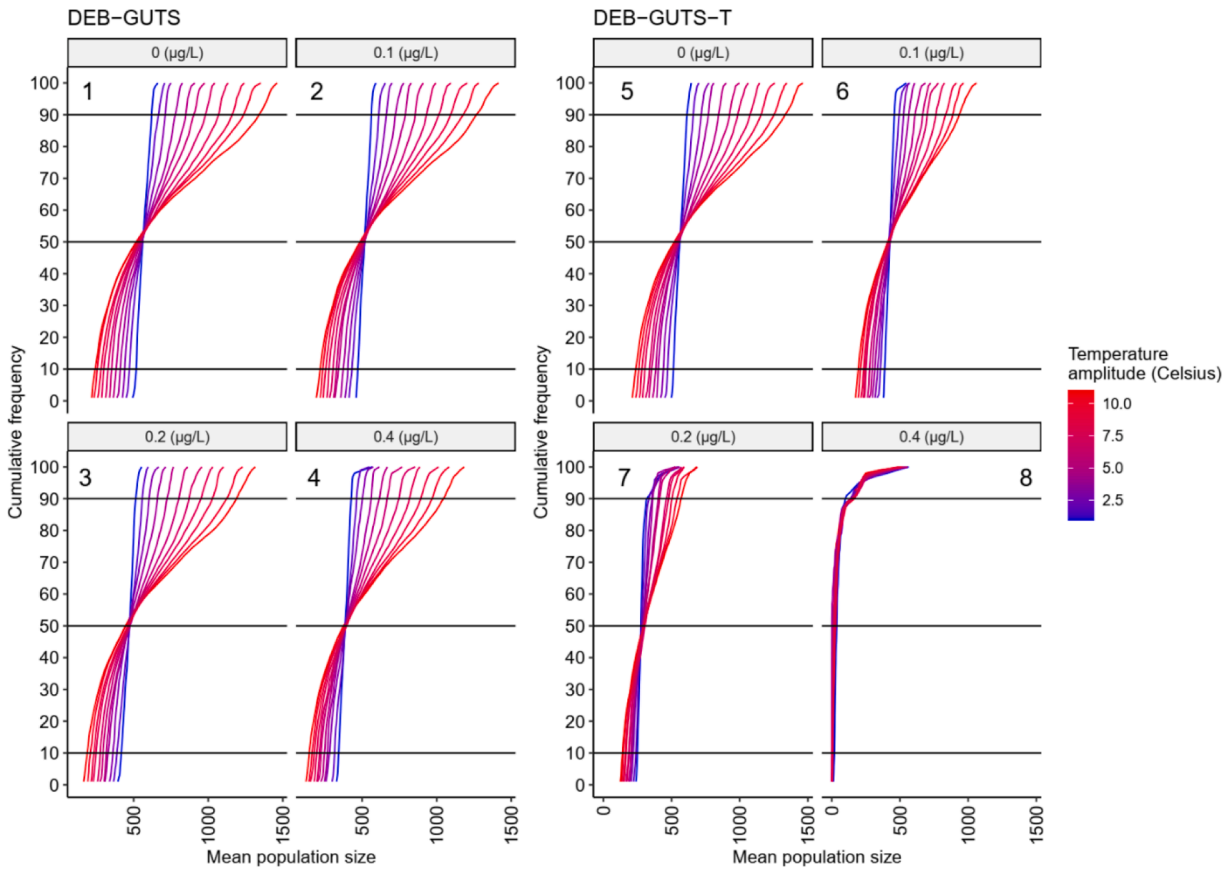

Fig. 5. Cumulative frequency distribution of mean Gammarus pulex population sizes exposed to constant concentrations of imidacloprid at different temperature scenarios (SD). The cumulative frequencies of mean daily population sizes ($n = 5$) over the 10 year exposure period are plotted for each temperature amplitude (1–10 °C) represented in the color scale from blue to red at different constant exposure concentrations, i.e., 0, 0.1, 0.2, and 0.4 µg • L^{-1}. The left panel (1–4) shows the results of the DEB-GUTS model, and the same scenario combinations for the DEB-GUTS-T model are displayed in the right panel (5–8), both for the SD model version. Horizontal lines mark the cumulative frequency distribution's 10th, 50th, and 90th quantiles (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.).

$1e^{-6}d^{-1}$ at reference temperature. Thus, this value got even smaller when corrected for the applied temperatures in this scenario and we correct only from slow kinetics to slower kinetics, making stochastic artefacts the most likely explanation for the observed differences.

3.2. Comparing model simulation over the whole simulation period

When plotting the mean population sizes of each day for the five model simulation replicates and over the 10 year exposure period in a cumulative frequency distribution, the different temperature scenarios show different shapes, i.e., from almost straight vertical for the lowest temperature amplitude (Fig. 5, 1 blue line) to a nearly convex line for the highest temperature amplitude (Fig. 5, 1 red line). A vertical line indicates a relatively constant mean population size throughout the whole simulation period, as the mean population size does not differ in its frequency between the days. In general, the steeper the slope of the curve in the beginning, the more observations were made in the lower ranges of population sizes. For the different temperature scenarios, the trend is that the observed population size range increases with increasing temperature amplitude. For example, under control conditions, the range of population sizes is the biggest in the 10 °C temperature amplitude scenario, with the lowest value around 150 and the highest value at 1500 (Fig. 5, 1 red line). For the other temperature scenarios the mean population size range is smaller, with a general trend of Q10 values decreasing and Q90 values increasing with increasing temperature amplitude. The Q50 values are marking the intersection of all temperature scenarios, which is observed across chemical exposure scenarios. With increasing exposure concentration, the range of population sizes decreased.

In these cumulative frequency figures, the steeper the slope, the less variation there is in population size over time. Thus we can conclude, that there are less profound seasonal density fluctuations in the low temperature amplitudes than in the high ones, which is also reflected in the quantiles plots (Fig. 6, green dots) and the results of a single year as shown previously (Fig. 3). The same trend is observed in the DEB-GUTS-T configuration (Fig. 5, 5–7), however, more pronounced, with the 0.4 µg • L^{-1} treatment showing the same cumulative frequency with mostly low population sizes observed throughout all temperature scenarios (Fig. 5, 8), due to extinction.

Primarily, we can see that an increased temperature amplitude widens the range of observed population sizes during the simulated period (Fig. 5, 1–4). This effect is, however, countered by the exposure scenarios, decreasing the observed maximum and minimum population sizes with increasing imidacloprid concentrations (Fig. 5, 1–4). Effectively, on the upper end of the temperature spectrum, the trend of the combined effect is offsetting, i.e., increased temperature amplitudes increases the population size gradient while increased concentration decreases the population size gradient. At lower temperature extremes, the combined effect results in an overall negative trend, reducing the population size gradient. The same trend is observed for the DEB-GUTS-T configuration, although the combined effect is predominantly negative (Fig. 5, 5–8). This can be explained by the increasing population dynamic under increasing temperature amplitudes (i.e., the mean population size gradient increases), while the changing temperature causes

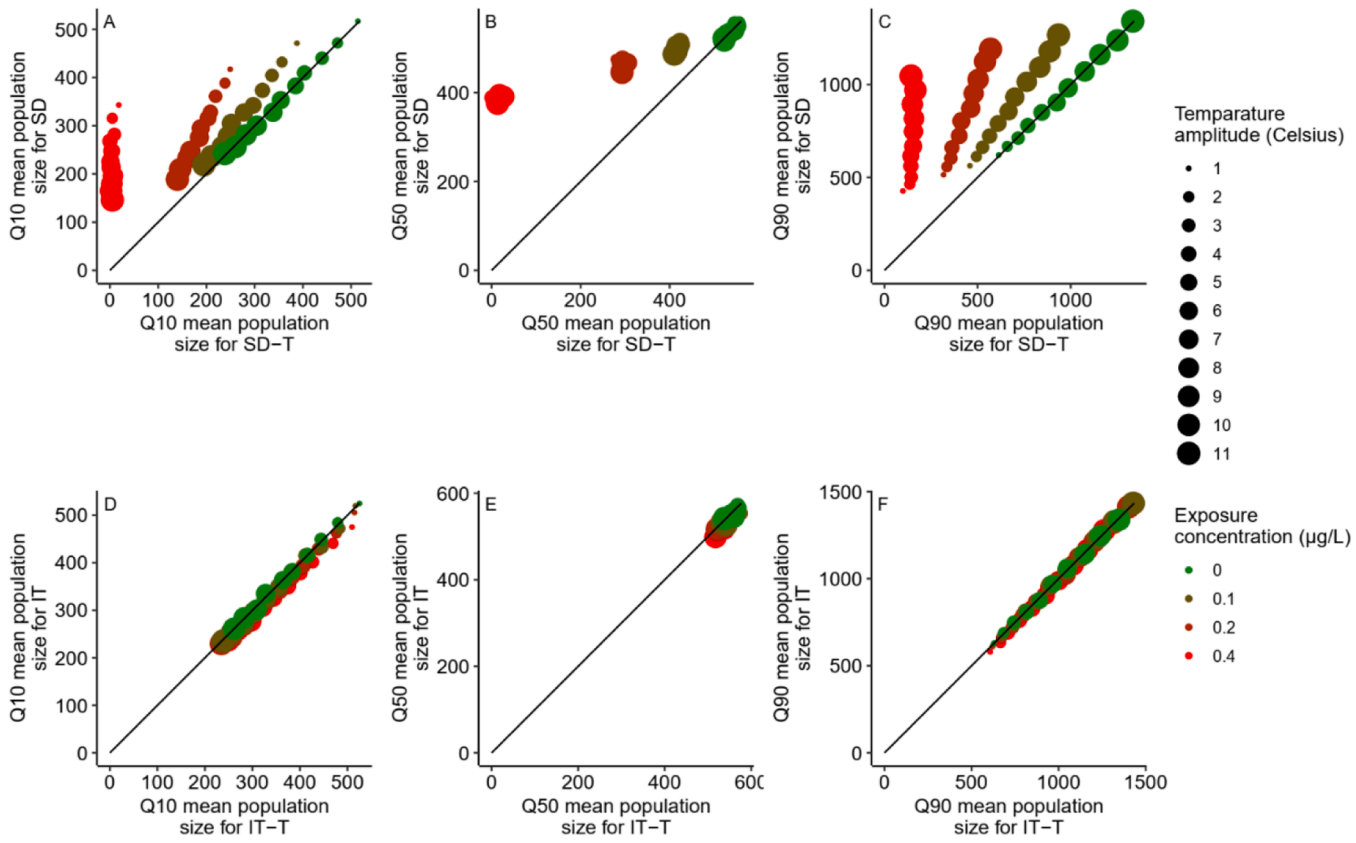

Fig. 6. Mean Gammarus pulex population size quantiles and line of equality comparing the different model configurations for constant exposure to imidacloprid. The top panel (A-C) shows the results for the SD model versions and the lower panel (D-F) display the results for the IT models. The black diagonal line represents the 1:1 line, or line of equality, indicating when both model configurations produced the same results. The 10th, 50th, and 90th quantiles of the mean population size for the different environmental scenarios were plotted for DEB-GUTS against those of the DEB-GUTS-T model configuration. While the size of the dots indicates the temperature amplitude (1–11 °C), the colors refer to the exposure concentration of imidacloprid in µg • L^{-1} (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.).

TKTD parameter changes resulting in the discussed slow kinetics effect leading to a lower population size over time (Section 3.1).

Bringing these results into perspective of future climate scenarios, where more frequent extreme temperatures are predicted (IPCC, 2019; Johnson et al., 2018; Woolway et al., 2021), we can expect higher population density fluctuations in the future. However, locally adapted populations in different climate zones, i.e., Scandinavia, central Europe and the Mediterranean (Foucreau et al., 2014) already experience different magnitudes of temperature fluctuations at present. Thus, it will be important to interpret population model results considering the local populations and potential acclimatization (Pörtner and Farrell, 2008) or evolutionary adaptions of their thermal window (Stoks et al., 2017; Verheyen and Stoks, 2019).

Looking at the same data displayed as quantiles (i.e., data points on the horizontal lines in Fig. 5), we can compare the results of the DEB-GUTS and DEB-GUTS-T versions based on the 1:1 equality line, representing the agreement of the two model configurations (Fig. 6). Thus, we observe the control exposure scenarios (i.e., green dots) align with this 1:1 line for all quantiles across temperature amplitudes in SD (Fig. 6, A–C) and IT (Fig. 6, D–F) model versions. Furthermore, in the Q10 plot, the highest temperature amplitude results in the lowest population size (Fig. 6, A and D), while for the Q90 plot, we see the opposite orientation of those scenarios (Fig. 6, C and F). For the Q50, there was no clear trend observed (Fig. 6, B and E). Looking across exposure concentrations, the DEB-GUTS-T model shows lower population sizes with increasing concentration throughout the simulation period, i.e., in all quantiles (Fig. 6, A–C), represented by the increasingly vertical orientation of the dots. This indicates that the influence of temperature amplitude on population dynamics decreases with increasing concentrations. This contrasts with the DEB-GUTS model, where temperature amplitude remains an important factor driving populations dynamics, regardless of concentration level, which would be indicated by the presence of horizontal dots. An exception to this is seen for the medians (Fig. 6, B and E), where there is very little variation between temperature amplitudes in both models and dots appear clumped. This is because the median is similar across temperature amplitudes, after all the average temperature is the same for all temperature scenarios which on average evens out differences between scenarios. For the IT model versions, the results of both model configurations are similar (i.e., in line with the equality line) across the different temperature and concentration settings (Fig. 6, D–F). Similar results were observed in the pulsed exposure scenarios (Appendix A, Fig. A6).

These results highlight the importance of considering temperature influences on TKTD parameters in IBMs. For example, the Q90 mean population size for the DEB-GUTS-T decreases significantly with increasing imidacloprid concentration, i.e., Q90 values shift to the left of the x-axis with an almost vertical line for 0.4 µg • L^{-1}. At the same time, the DEB-GUTS models still show a wide range of population sizes over the y-axis (Fig. 6, C). Therefore, evaluating the population size range of an population model that does not account for a temperature effect on the TKTD parameter, underestimates the combined effect of temperature and chemical exposure to the population dynamics.

3.3. Implications for scenario development in environmental risk assessment

While these result are explainable by the nature of the model and how temperature is implemented (i.e., increasing the temperature speeds up all biological processes implemented in the IBM, i.e., growth and reproduction)(Kooijman, 2010), our simulated results remain theoretic. For instance, temperature can also act as an additional stressor (Mangold-Döring et al., 2023),which was not implemented here. Furthermore, the current IBM does not account for different temperature sensitivity at different life stages (Madeira et al., 2020), that might be integrated in the field observations. To investigate how this aspect influences population dynamics, it would need to be modeled explicitly in the standard DEB model. Therefore, we cannot compare them directly to data observed in laboratory or field (semi-)studies.

Nevertheless, individual-based population models are powerful tools for evaluating the effect of chemicals on freshwater species. The simulation results presented in this study showed that considering temperature influences on the TKTD model parameter of a DEB-GUTS model combination is essential when evaluating different temperature scenarios. Due to the effect of temperature on the speed of toxicokinetic and physiological processes, both field or lab experiments need to be performed through longer periods when performed at lower environmental temperatures. Alternatively, if the relationship between the pesticide effect with temperature is known, experiments might be performed at higher temperatures to reduce the experimental period and thus, associated costs. Ideally however, we should continue to pursuit a mechanistic understanding of the influence of temperature on the toxicity of chemicals, to extrapolate to realistic field scenarios though in silico simulations, minimizing the extend of expensive and ethically concerning lab or field studies.

It should be highlighted, that simulations with FOCUS scenarios (temperature and concentration) or real time concentration time series are possible as performed previously in higher tier risk assessments (Authority (EFSA) et al., 2020). To explore the seasonal effect of pesticide application, model simulations with exposures during different times of the year, i.e., late autumn or early spring, should be considered. Furthermore, other climate change scenarios, like increased mean temperatures (instead of the raised amplitude applied in this study) or heatwave scenarios could be tested. Finally, local population's adaptation to different climate zones with different temperature extremes should be considered, facilitating zone specific registration of pesticides.

4. Conclusion

This study presents a proof-of-concept for the implementation of temperature corrected GUTS models in an individual-based population model for *G. pulex*. The results of this study offer valuable insights in the relevance of the temperature correction in population models for risk assessment of chemicals. By comparing the two different model configurations, we could highlight the importance of using a temperature corrected GUTS module to avoid an underestimation of the population risks in temperature variable environments. While the DEB-GUTS-T approach offers a first step towards the use of realistic temperature scenarios in the assessment of chemical effects on populations, we discussed further advancements and emphasize the benefit of confirming the simulation results with field data.

CRediT authorship contribution statement

Annika Mangold-Döring: Writing – review & editing, Writing – original draft, Visualization, Software, Methodology, Investigation, Formal analysis, Conceptualization. **Willem B. Buddendorf:** Writing – review & editing, Writing – original draft, Visualization, Software, Methodology, Investigation, Formal analysis, Conceptualization. **Paul J. van den Brink:** Writing – review & editing, Resources, Conceptualization. **Johannes M. Baveco:** Writing – review & editing, Writing – original draft, Visualization, Software, Methodology, Investigation, Formal analysis, Conceptualization.

Declaration of competing interest

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

Data availability

The simulation raw data as well as the model code, and code for analysis are uploaded to publicly accessible repositories as discribed in the method section.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ecolmodel.2024.110880.

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