META-ANALYSIS OF INTRINSIC RATES OF INCREASE AND CARRYING CAPACITY OF POPULATIONS AFFECTED BY TOXIC AND OTHER STRESSORS

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Abstract—Most of the thousands of substances and species that are of concern for environmental management will not be investigated empirically at ecologically relevant levels because of financial, practical, and ethical constraints. To allow risk assessment for these less well-known categories, we have developed a mechanistic model with classical equations from toxicology and ecology. The parameters are linked to well-known properties, such as the octanol–water partition ratio $K_{ow}$, acute lethal (body) concentrations, and organism size. This allows estimation of intrinsic rates of increase $r$ and carrying capacity $K$ over a wide range of substances and species. The model was calibrated with parameter values ($\mu \pm 95\%$ confidence interval) obtained in reviews and validated by a meta-analysis with largely independent data from 200 laboratory experiments. For single substances, the 5 to 95% interval of the observations on intrinsic rates of increase overlapped with the range predicted by the model. Model and experiments independently indicated that population growth ceased below 1% of the acute median lethal concentration in about 5% of the cases. Exceptional values and possible explanations were identified. The reduction of the carrying capacity $K$ was nearly proportional to the inhibition of the population growth $r$. Population-level effects of mixtures as estimated by concentration addition were confirmed by observations in the experiments. The impact of a toxicant and another stressor could generally be described by response multiplication, with the exception of cases with extreme stress. Data sets on population laboratory experiments are biased to metals and crustaceans. This field will benefit from empirical studies on chemicals, conditions, and species, identified as risky by the model. Other implications of the model for environmental management and research are discussed.

Keywords—Rate of increase Carrying capacity Multistress Ecotoxicology Meta-analysis

INTRODUCTION

Over the past two decades, several chemicals have been tested in laboratory population studies. Yet most of the thousands of substances and species that are of concern for environmental management will not be investigated empirically at ecologically relevant levels because of financial, practical, and ethical constraints. So far, discussions on chronic toxicity focused on the correct endpoint to be measured. Mortality, reproduction, extinction probability, and recovery time have been put forward as important under density-dependent or density-independent conditions [1–6]. In addition, mechanistic models have been developed for population development under toxic stress [7–11]. Unfortunately, these models have only been tested on a few substances and species because of the large number of parameters values that has to be determined. Alternatively, empirical relationships have been derived [12]. Here, extrapolation is restricted by the lack of a mechanistic basis.

To allow risk assessment for many substances and species, we have developed a model in which parameters of traditional equations are linked to well-known properties such as the octanol–water partition ratio $K_{ow}$, acute lethal (body) concentrations, and organism size [13,14]. In a previous modeling study, the model was equipped with tentative parameter values and preliminarily tested on single-toxicant experiments carried out in our laboratory [13,15,16]. In the present study, the parameters are set to more accurate values taken from previous calibration studies [17,18]. To validate the model for other toxicants and species, data obtained from literature reviews on laboratory experiments are used [13,19, present study]. The model is also tested on related types of contamination, that is, toxins and irradiation. In addition, the approach was extended with exposure to a toxicant in combination with other toxicants or other environmental stressors such as temperature and food. Finally, application to environmental monitoring and implications for risk assessment are considered.

The aim is to extrapolate single-substance acute mortality tests to population development with and without the presence of other toxicant and nontoxicant stressors. The model should be parameter sparse to allow application to many substances and species, as needed in environmental management. The approach should allow prediction of population density in single-species experiments, where food, temperature, and other conditions are constant. We do not intend to cover the detailed dynamics of fluctuating populations in variable multispecies field systems.

METHODS

Data collection

Intrinsic rates of increase $r$ and carrying capacities $K$ were obtained by combining and extending previous reviews
with the acute–chronic ratio $q_{ac}$ obtained from the reviews. These few validation data are thus not completely independent from the calibration set. For algae, LC50 values cannot be determined, and concentrations were standardized to the highest exposure level to allow some comparison to animal tests. For toxins and irradiation, the time to 50% mortality (LT50) and the median lethal dose (LD50) were used for standardization, respectively. Combined exposure to toxicants and different food (starvation) or temperature levels was standardized to one LC50 for all food and temperature levels. Level-specific values were not measured (acute assays are always carried out without food) or scarce (temperature).

For the overall analysis, single toxicant studies were included only. Standardized intrinsic rates of increase $r(C)/r(0)$ were linearly correlated to standardized concentrations $C/LC50$. Since $r(C)/r(0)$ equals $r(0)/r(0)$ at $C/LC50 = 0$ by definition, the y-intercept was set equal to one. For each study, the slope of each correlation was calculated by ordinary linear regression, a common procedure [2,8]. Next, the fifth, 50th, and 95th percentiles of all slopes were determined.

For analyses of specific substances or species, data were plotted individually on logarithmic concentrations scales to accentuate differences at low concentrations. Concentrations of less than 0.001 times the acute lethal level were plotted as 0.001/LC50. Negative standardized rates of increase $r(C)/r(0) \to -\infty$ were graphed as $r(C)/r(0) = -1$ if below $-1$.

**Specification of equations**

Population density $N(t)$ [kg·km$^{-2}$, ind·L$^{-1}$] is often considered to be a logistic function of time $t$ as

$$\frac{dN}{dt} = N(t) \cdot r \cdot \left[1 - \frac{N(t)}{K}\right]$$  

(1)

with the intrinsic rate of increase $r$ [ind·ind$^{-1}$·d$^{-1}$, kg·kg$^{-1}$·d$^{-1}$] and the carrying capacity $K$ [kg·km$^{-2}$, ind·L$^{-1}$]; ind represents the number of individuals. The rate of population increase per individual $\frac{dN}{dt}/N(t)$ is thus considered to be a linear function of population size $N(t)$. Equation 1 requires individuals to be equivalent and to respond immediately to changes in density. In addition, the intrinsic rate of increase $r$, the carrying capacity $K$, the environment, and the age distribution are constant over time. The intrinsic rate of increase $r$ is a function of the
generation time \( \tau_g \) [d] and the total number of young per surviving adult, here abbreviated as lifetime fecundity or net reproduction \( R_0 \) [ind], as \([20–23]\)

\[
r = \frac{\ln(R_0)}{\tau_g}
\]

Equation 2

If age-specific data are available, the intrinsic rate of increase \( r \), generation time \( \tau_g \), and lifetime fecundity \( R_0 \) can be computed exactly. If age-specific data are not available and population development is dominated by initial reproduction, lifetime fecundity \( R_0 \) and generation time \( \tau \) can be approximated by the first clutch or litter size \( \min(R_0) \) and the age at maturity \( \tau_m \), respectively \([24]\).

Environmental stressors, including chemicals, may affect population size \( N \) by reducing the intrinsic rate of increase \( r(C) \) as a function of the exposure concentration \( C \). For some toxicants and species, the intrinsic rate of increase \( r(C) \) has been determined from age-specific reproduction and survival in chronic experiments with cohorts \([25]\). For most toxicants and species, only acute mortality concentrations LC50 are available. However, acute lethal concentrations can be translated to chronic sublethal levels with so-called extrapolation or safety factors. The acute–chronic ratio \( q_{ac} \) represents the median lethal concentration after short-term (\( \leq 5 \) d) versus long-term (>5 d) exposure. The lethal–sublethal ratio \( q_r \) reflects the difference between concentrations with 50% survival and reproduction reduction. If we assume that a toxicant affects survival and reproduction of each age class by the same fraction, we can now write the lifetime fecundity in exposed \( R_0(C) \) versus nonexposed \( R_0(0) \) populations as a traditional logistic concentration–response function (see \([13]\) for detailed derivation).

\[
\frac{R_0(C)}{R_0(0)} = \text{reproduction reduction \cdot survival reduction}
\]

\[
= 1 + \left( q_{ac} \cdot C/\text{LC50} \right)^{-\frac{1}{\beta}} \quad \text{and} \quad 1 + \left( q_{ac} \cdot C/\text{LC50} \right)^{-\frac{1}{\beta}}
\]

Equation 3

where the exponent \( \beta \) represents the slope of the concentration–response function. Equation 3 holds if the generation time \( \tau \) is not affected by contaminants and within the same order as the duration of the cohort assay. A preliminary analysis of laboratory assays indicated that the generation time remains fairly constant up to about a concentration of 0.1 to 1 times the acute LC50 (data not shown). Following our objective to keep the model as simple as possible, we did not include a variable generation time in the present version. Obviously, it can be incorporated in the future for cases where this assumption does not hold. Filling in Equation 3 into Equation 2 yields the intrinsic rate of increase of exposed \( r(C) \) versus nonexposed \( r(0) \) populations as (see \([13]\) for detailed derivation)

\[
r(C) = 1 - \{\ln[1 + (q_{ac} \cdot C/\text{LC50})^{-1/\beta}] \]

\[
+ \ln[1 + (q_{ac} \cdot C/\text{LC50})^{-1/\beta}]/[\ln(R_0(0))] \}
\]

Equation 4

to combinations of toxicants, the standardized concentration \( C/\text{LC50} \) can simply be replaced by the sum of the standardized concentrations \( \Sigma(C/\text{LC50}) \) of each substance \( i \) in the mixture. The term \( \Sigma(C/\text{LC50}) \) reflects mixture toxicity by concentration addition, a common and valid approximation for substances with similar modes of action (for details, see \([17]\)).

In addition to an inhibition of the intrinsic rate of increase \( r \), toxic and other stress may also reduce the carrying capacity \( K \). To allow for a first approximation of this impact, Equation 1 on logistic population increase may be rewritten to \([22]\)

\[
\frac{dN}{dt} = N(t) \cdot [r - q_K \cdot N(t)]
\]

Equation 5

where the coefficient for intraspecific competition \( q_K \) represents the ratio of \( r \) and \( K \) \([13]\). If one assumes that the crowding coefficient is constant, that is, \( q_K = r(0)/K(0) = r(C)/K(C) \), stressors affect population increase rates and carrying capacity proportionally, that is, \( K(C)/K(0) = r(C)/r(0) \).

RESULTS

Calibration

Equation 4 has four parameters to be calibrated. Their values were derived from independent data obtained from earlier studies. Since rate and time constants scale to species mass with exponents of \(-\frac{1}{4}\) and \(\frac{1}{4}\), respectively, the lifetime fecundity \( R_0 = e^{\tau r} \) is expected to be independent of size \([26]\). Potentially, the lifetime fecundity \( R_0 \) varies between 2 for unicellular and \(10^6\) for some multicellular organisms, indeed without a relationship to size \([27]\). This range applies to conditions that are more or less met in laboratory experiments. Lower values are achieved under suboptimal field conditions. The number of eggs per clutch \( \min(R_0) \) increases with size for some cold-blooded species groups but has a constant value of about 4 and 2.5 for birds and mammals, respectively \([28]\). From these data, one may obtain the range of possible values for the lifetime fecundity \( R_0 \). These general patterns, however, may be overridden by the impact of prevailing conditions. For instance, \textit{Daphnia magna} invests in many small young if food is abundant, while its brood consisted of a few large individuals if sources are scarce \([29]\). In our simulations, we therefore used the average measured in the controls of the experiments, both for all species together and for specific taxa (Table 2).

The concentration–response slope \( \beta \) depended on the species group and, not unequivocally, the exposure period \([18]\) (Table 2). Slopes for organic substances were significantly steeper than those for metals, but no relationship was observed with the mode of action of subgroups. The average slope of \(-0.36\) corresponds to an EC50/EC5 ratio of \(2.6\). Variability was low for organic compounds, algae, or crustaceans and high for metals, mollusks, or fish. On average, chronic exposure levels for lethal and sublethal (i.e., ingestion, growth, offspring) response differed by a factor \( q_{ac} \) of 2.5 \([17]\) (Table 2). Although acute–chronic ratios \( q_{ac} \) can be related to the \( K_{in} \) of the chemical and the size \( m \) of the species, we used a constant value of \(3.2\) here for the sake of simplicity \([14,17,30]\). The data used to calibrate these toxicological parameters were biased toward toxicants and species that are tested most. However, the values were generally in accordance with safety factors reported in other studies, as collected in the reviews or published afterward \([17,18,31–34]\).

Following these reviews, parameters were set at the unfavorable \( R_0 = 7.6, \beta = -0.092, q_{ac} = 4.9, q_{ac} = 4.7\), average
Table 2. Factors used in the equations with typical or default values

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
<th>Unit</th>
<th>Typical or default value with 95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\beta$</td>
<td>Concentration–response slope</td>
<td>-</td>
<td>$-0.36 (-0.092$ to $-1.4)$, $-0.51 (-0.63$ to $-0.42)$, $-0.33 (-0.40$ to $-0.27)$</td>
</tr>
<tr>
<td>$C$</td>
<td>Exposure concentration</td>
<td>$\mu g L^{-1}$, $\mu g kg^{-1}$</td>
<td>Variable</td>
</tr>
<tr>
<td>LC50</td>
<td>Acute lethal concentration</td>
<td>$\mu g L^{-1}$, $\mu g kg^{-1}$</td>
<td>Variable</td>
</tr>
<tr>
<td>$m$</td>
<td>Individual mass</td>
<td>kg</td>
<td>Variable</td>
</tr>
<tr>
<td>$N$</td>
<td>Population number or mass</td>
<td>ind, kg</td>
<td>Variable</td>
</tr>
<tr>
<td>$K$</td>
<td>Carrying capacity number or mass</td>
<td>ind, kg</td>
<td>Variable</td>
</tr>
<tr>
<td>$r$</td>
<td>Intrinsic rate of increase</td>
<td>$d^{-1}$</td>
<td>Variable</td>
</tr>
<tr>
<td>$R_o$</td>
<td>Total number of young per adult in a lifetime</td>
<td>eggs·adult$^{-1}$</td>
<td>92 (7.6±1,100), 57 (38±87)</td>
</tr>
<tr>
<td>$q_{ac}$</td>
<td>Lethal–sublethal concentration ratio</td>
<td>/</td>
<td>3.2 (2.1±4.7), 3.5 (2.5±5.0)</td>
</tr>
<tr>
<td>$q_{ls}$</td>
<td>Acute–chronic concentration ratio</td>
<td>/</td>
<td>2.5 (1.3±4.9), 2.5 (1.4±4.2)</td>
</tr>
<tr>
<td>$q$</td>
<td>Competition coefficient</td>
<td>$km^2 kg^{-1} d^{-1}$</td>
<td>Variable</td>
</tr>
<tr>
<td>$\tau_s$</td>
<td>Generation time</td>
<td>d</td>
<td>Variable</td>
</tr>
</tbody>
</table>

*Specific values for $^a$ metals, $^b$ organics, $^d$ arthropods, mainly crustaceans. ind = individuals. Sources [17, 18].

$(R_o = 92, \beta = -0.36, q_v = 2.5, q_m = 3.2)$, and favorable $(R_o = 1,100, \beta = -1.4, q_v = 1.3, q_m = 2.1)$ values of the 95% confidence interval (CI) (Table 2). A full quantitative sensitivity analysis is beyond the purpose of the present paper. Tentative calculations (not shown) indicated that the slope $\beta$ has the largest impact on the output range calculated by the model, followed by an equal contribution of the other parameters (Fig. 1). In case of specific analysis, values applicable to specific species or substances were used.

Validation

**Intrinsic rate of increase affected by toxic stressors.** The model specified by Equation 4 and calibrated according to Table 2 yielded a near-linear relationship between the standardized intrinsic rate of increase $r(C)/r(0)$ and the standardized concentration $C/\text{LC50}$ (Fig. 1). As such, it provides a mechanistic basis for linear regressions assumed but not underpinned in early studies [2,8].

The model calculations corresponded well to the largely independent data on rates of increase as collected in the review (Fig. 1). The fifth, 50th, and 95th percentiles of the slopes obtained in 109 experiments matched the model estimations with parameters set at the unfavorable, mean, and favorable values of their 95% CI (see Methods for details). All single-toxicant studies were included in this data set, with exception of those on algae where LC50 values are not available. Both model and data show that in more than 95% of the cases, toxicants cause no substantial reduction of the population growth below 1/100 of the LC50. Exposure at one-fifth of the LC50 causes a 50% reduction of the intrinsic rate of increase. Steep slopes, that is, with reproduction affected far below lethal concentrations, were observed for some arthropods exposed to bromide, 3,4-dichloroaniline, and, to a lesser extent, cadmium [35–37]. Flat slopes were noted for various toxicants and species. Some of these studies were characterized by high food densities that may have reduced bioavailability of the toxicant [38,39].

The variability between toxicants and conditions was explored by selecting and comparing data on D. magna, a well-studied species. All experiments with this daphnid were included, with the exception of those on suboptimal food density and deviating temperatures, as discussed in the section on multiple stressors below. Despite variability in laboratory conditions, most curves were within the interval expected from the model (Fig. 2a and b). Bromide (curve 2, as shown on Fig. 2a) affected population increase at concentrations far below the acute lethal level [35]. Of the metals that were represented by more than one data set, curves for chromium (9–10 on Fig. 2a) and copper (12–15 on Fig. 2a) tended to be at the lower and higher end of the interval expected from the

Fig. 1. Ratio of exposed and control population intrinsic rate of increase $r(C)/r(0)$ versus ratio of exposed and median lethal concentration $C/\text{LC50}$ on a linear and logarithmic axis. Model estimations with parameters at average and 95% confidence interval of Table 2 (dashed curves). Largely independent validation data of actual measurements and the fifth, 50th, and 95th percentiles of the 109 linear regressions obtained from laboratory studies with single toxicants and animals listed in Table 1 (dots and solid curves).
Fig. 2. Ratio of exposed and control population intrinsic rate of increase $r(C)/r(0)$ versus ratio of exposed and median lethal concentration $C/\text{LC50}$ or $2(C/\text{LC50})$. Model estimations with parameters at average and 95% confidence interval for the substance and species groups concerned as given in Table 2 (dashed curves). Laboratory measurements on species and various toxic substances, usually at optimal food density and temperature ($T = 20^\circ\text{C}$) with references listed in Table 1 (solid curves).

(a) 1 = As, 2 = Br, 3–8 = Cd, 9–11 = Cr, 12–15 = Cu, 16 = Pb, 17 = Hg, 18 = Ni, 19 = Se, 20 = Zn, 21 = γ irradiation with Daphnia pulex. (b) 1 = pentachlorobenzene, 2–3 = dichloroanilines, 4–5 = 4-nitrophenol, 6–7 = bromoxynil, 8 = endosulfan, 9 = γ-hexachlorocyclohexane, 10 = fenitrothion, 11 = fonofos, 12 = methylenebisthiocyanate, 13 = tetraethylthiuram disulfide, 14 = tetramethylthiourea, 15 = tetramethylthiuram disulfide, 16 = zinc ethylenebisthiocarbamate, 17–19 = Dispersogen A. (c) 1 = Thalassiosira weissflogii, 2 = Amphidinium carteri, 3 = Brachionus calyciferus, 4 = Chydorus piger, 5–10 = Daphnia magna, 11–12 = Daphnia pulex, 13 = Echinosea triseriata, 14–15 = Moina macrocopa, 16 = Folsomia candida, 17–18 = Orchesella cincta, 19 = Platynothrus pelletier, 20 = Lumbricus rubellus. (d) 1 = Scenedesmus, 2 = Brachionus calyciferus, 3–4 = Ceriodaphnia quadrangularis, 5 = Chydorus, 6 = Keratella, 7–8 = Daphnia magna, 9 = Poecilia reticulata. (e) 1–3 = Ceriodaphnia cornuta, 4 = Daphnia pulex, 5–7 = Moina micrura, 8–10 = Moinodaphnia macleayi with different algae strains. (f) 1 = Chlorella pyrenoidosa and effluent, 2–3 = Daphnia magna and As, Cd, Cr, Cu, Ni, Hg, Pb, Zn, 4–5 = Daphnia magna and Cd, Cr, Zn, 6 = Onychiurus armatus and Cu, Pb.

model, respectively. Effects of γ irradiation to Daphnia pulex were also close to the average estimated by the model (21 on Fig. 2a). Response was also quite similar and close to the model average for organic substances with different modes of action. These include narcotics (1–5 on Fig. 2b), phytotoxicity (6–7 on Fig. 2b), and chloro- (8–9 on Fig. 2b), phosphorus- (10–11 on Fig. 2b), and sulfur (12–16 on Fig. 2b) neurotoxicity. Some narcotics (1–3 on Fig. 2b) tended to be at or below the lower end expected from the model.

The standardized intrinsic rate of increase in static systems was equal to or lower than that of flow-through exposure to the same concentration ($4 = 5, 6 < 7$ on Fig. 2b) [40,41].
Juveniles that experienced pre-exposure to the same or previous generation were less resilient than naive offspring (1i 1, 18 < 19 on Fig. 2b) [16,42]. Standardized rates of increase \( r(C)/r(0) \) in whole-population experiments were lower than in cohort studies for Dispersogen A (17 < 19 on Fig. 2b) [42] but not for cadmium (7 = 8 on Fig. 2a) [43]. Exposure of parents thus appears to affect juveniles in some but not all cases.

The variability between species and conditions was explored by comparing data on cadmium, 3,4-dichloroaniline, and microcystein-LR, three well-studied toxic stressors (Fig. 2c to e). To extend the number of species, algae growth rates were included into the set after standardization to the maximum test concentration instead of the LC50. The data suggested some reduction of algae growth within this range (1–2 on Fig. 2c, 1 on Fig. 2d). Patterns for animals were generally close to the model calculations. For cadmium, deviations applied to some terrestrial species that stop laying eggs already after minor contamination (18 on Fig. 2c) [36]. For 3,4-dichloroaniline, Ceriodaphnia quadrangula reproduction appears to be affected far below the LC50 (3–4 on Fig. 2d). For microcystein-LR, data apply to experiments in which animals were exposed to increasing ratios of toxic blue algae and edible green algae [44]. Despite the different experimental design, toxins appeared to follow the model well. Measured growth rates for individuals instead of populations were also close to the average estimated by the model [45, data not shown].

For mixtures, standardized rates of increase were calculated as a function of standardized concentrations with \( C/LC50 \) replaced by toxic units, that is, the sum of the tested versus acute lethal concentrations of each contaminant \( \Sigma(C/LC50) \). The patterns in the few studies found on mixtures were similar to those of individual toxicants (Fig. 2f). The curves for metals added in equitoxic mixtures and combinations with ratios equivalent to quality standards are similar. It suggests that the ratio in which contaminants are added makes no difference (2–3 on Fig. 2f) [46]. Differences between naive and pre-exposed in mixtures were somewhat less than observed for single substances (4–5 on Fig. 2f) [16].

The model estimations thus matched the regressions on experimental data well for toxicants, toxins, irradiation, and mixtures. However, exceptional conditions, substances, and species were identified.

**Intrinsic rate of increase affected by multiple stressors.** A small number of research workers have measured the intrinsic rate of increase during exposure to a toxicant and another stressor, usually food (starvation) or temperature. In general, standardized rates of increase \( r(C)/r(0) \) decreased with standardized concentrations \( C/LC50 \) at different levels of temperature or food, similar to that of single toxicants and the model (Fig. 3). For cadmium, standardized rates of increased \( r(C)/r(0) \) for Echinisca triserialis declined with decreasing food levels, whereas variation of algae density induced only minimal differences in \( D. magna \) populations (1 > 2 = 3 and 4 = 5 = 6 = 7 on Fig. 3a) [38,47]. For 3,4-dichloroaniline, C. quadrangula numbers collapsed already below 0.001-LC50 for all food levels, partly because of an unusually high LC50 (1 = 2 = 3 = 4 on Fig. 3b) [37]. All \( D. magna \) populations dropped at the lower end predicted by the model, with exception of the cohorts that received the lowest algae density (5 ≥ 6 = 7 ⇒ 8 on Fig. 3b). For parathion-methyl, Brachionus patusus experienced a slight decrease due to food levels (1 > 2 > 3 > 4 on Fig. 3c) [48]. With the exception of the lowest temperature during deltamethrin exposure, population development was reduced more seriously by insecticides with increasing temperatures (2 > 1 > 3, 6 > 5 > 4 on Fig. 3d) [49]. With one exception (6 on Fig. 3e), \( D. magna \) intrinsic rates of increase generally declined with decreasing food levels at the same temperature and with increasing temperatures at the same food density (1 > 2 > 3, 4 > 6 > 5, 7 > 8 = 9, 7 > 4 > 1, 8 = 2 > 5, 9 ≥ 6 > 3 on Fig. 3e) [50]. Variability was not reduced by relating population development to internal concentrations measured at the end of the exposure period (on Fig. 3f).

Decreasing food levels and increasing temperatures thus enhances impact of toxicants usually only slightly. Variability in population development due to differences in toxicants and species (Fig. 2) was higher than variability induced by differences in food and temperature levels (Fig. 3). With the exception of extreme cases, the impact of multiple stressors can thus be described by response multiplication.

**Carrying capacity affected by toxicants and by multiple stressors.** Reduction of carrying capacity due to contamination has rarely been studied (Fig. 4). Despite substantial variation, standardized carrying capacities \( K(C)/K(0) \) decreased proportionally to standardized rates \( r(C)/r(0) \) at the same concentration \( C \) (Fig. 4). Pollution thus affects populations twice. A concentration of one-fifth of the LC50 reduces the population growth and carrying capacity to 50 and 40% of the control, respectively (Figs. 1 and 4). It suggests that the competition coefficient \( q_K = r/K \) is indeed fairly constant for various levels of contamination. The largest deviations were noted for algae, where the chlorophyll content in the stationary phase was reduced more than proportionally compared to the growth rate [51].

**DISCUSSION**

We have specified, calibrated, and validated a model to estimate impact of toxicants and other environmental stressors at the population level in simple laboratory systems. The equations were selected from traditional formulas used in toxicology and ecology. The parameters were set at universal values, considered applicable to all substances and species of the group selected. Survival and reproduction were considered to affect each age class proportionally, whereas the generation time and the crowding coefficient were set constant. Despite these rigorous assumptions, characteristics of the overall data set as well as individual experiments are generally well anticipated by the model. Nevertheless, some restrictions must be made. Both calibration and validation data sets were biased toward metals and crustaceans. Acute LC50 values for algae, some mixtures, as well as benthic, terrestrial, and rarely tested aquatic animals are not available and were derived from chronic data.

Keeping in mind these limitations, the model can thus be used to predict the average and range of the standardized intrinsic rate of increase \( r(C)/r(0) \) and carrying capacity \( K(C)/K(0) \) as a function of the actual \( C \) and acute lethal LC50 concentration. The standardized values can be converted to absolute levels by allometric regressions on intrinsic rates of increase \( r(0) \) and carrying capacity \( K(0) \) (for a review, see [26]). Obviously, our simple model cannot be used to simulate complex dynamics of interacting species in (semi-)field conditions.

With this average and range at hand, exceptional deviations can be easily identified. Bromide and dichloro-aniline reduced
the intrinsic rate of increase $r$ at concentrations substantially below the acute lethal level. It suggests that reproduction is affected via another mode of action than survival. Indeed, these substances are known to kill embryos at concentrations far below those that affect juveniles and adults [52]. For the other substances, population decline is largely within the range covered by the model. In these cases, reproduction may be inhibited via a reduction of the production or consumption by the parents. Even more, patterns for substances with different modes of action are quite similar. Apparently, potential differences in impact at the individual level such as (de-)activation of metabolism do not induce large differences at the population level [53]. *Orchesella cincta* population growth also stopped below the acute lethal level of cadmium [36]. Additional experiments with *Platynothrus peltifer* did not confirm the extreme sensitivity of this species (Van Straalen, personal communication). More than average tolerance was inconsistently noted for some toxicants and species. Some of these studies were characterized by high food densities that may have reduced bioavailability.
The impact of simultaneous exposure to several toxicants or stressors can generally be well anticipated by the model. The few available data available indicate that mixtures of toxicants of similar and different modes of action can often be accounted for by concentration addition. Likewise, combinations of stressors can be incorporated by response multiplication. The reduction of the intrinsic rate of increase \( r \) can be described by \( r(C,X_1)/r(0,X_1) = r(C,X_2)/r(0,X_2) \) with toxicant concentration \( C \) and nontoxicant stressor \( X \) at levels 1 and 2 (Fig. 3). This equation can be rewritten to \( r(C,X_1)/r(0,X_1) = r(C,X_2)/r(0,X_2) \). A reduction of \( r \) by 10% due to a toxicant and by 20% due to another stressor \((X_1 \rightarrow X_2)\) should thus lead to 90%–80% = 72% of the control in a combined exposure. In general, multiple stress for daphnid reproduction and population growth was best described by (antagonistic) multiplication [50, 54].

The model estimations are thus generally confirmed by experiments with spiked contaminants. In addition, we may qualitatively explore its usefulness for application to environmental monitoring. In the Rhine–Meuse delta, laboratory experiments with river water generally show no increase of *D. magna* population growth with dilution [55]. Instead, some decrease is noted, probably due to reduced food availability. As expected from the model, population growth and acute survival decreased after 5 to 10 and 25 times of XAD concentration, respectively [56]. Development of daphnids in biological early warning systems or field cages can be corrected for temperature and food availability [55, 57].

Some model implications are in line with general observations on trends expected in stressed ecosystems, such as increased proportion of r-strategists, reduced efficiencies, and an increase of ungrazed primary production [58]. Other implications, such as the correlation between the standardized intrinsic rate of increase and the carrying capacity \((K[C]/K[0]) = r(C)/r(0)\), are not necessarily in line with these trends.

**CONCLUSION**

The present study shows that a first estimate of the population intrinsic rate of increase \( r \) and the carrying capacity \( K \) as affected by a toxicant concentration \( C \) can be obtained from some classical toxicological and ecological equations with a few fixed constants. These parameters are the concentration–response relationships \( \beta \), the lethal–sublethal concentration ratio \( q_L \), acute–chronic concentration ratio \( q_{ac} \) and the lifetime offspring of an adult \( R_0 \). More specifically, the average and range of the population intrinsic rate of increase \( r \) predicted by the model coincided with the 5 to 95% interval and mean of largely independent data from single substance experiments. In approximately 5% of the cases, population growth seized below 1% of acute lethal concentration LC50. The reduction safety factors (large \( q_L \), \( q_{ac} \)) and few offspring (small \( R_0 \)). Although the relative importance of each of these parameters remains to be determined in a more in-depth sensitivity and statistical analysis, it is evident that identification of chemical properties that induce exceptional acute–chronic \( q_L \) and lethal–sublethal \( q_{ac} \) ratios, such as different modes of action, should be given priority. Because of the nonlinear nature of Equation 4, species with many small young are expected to withstand toxic stress better than those with a few large offspring, but in case of food (starvation) stress the reverse may be true. Quantitative tests of these implications are lacking so far, and experimental investigations in this area are therefore more valuable than additional routine tests. In general, further development of population toxicology is likely to benefit most from empirical studies on nonstandard conditions, nontraditional chemicals, and nonclassical test species with the previously mentioned risk characteristics.

![Graph](image)  
**Fig. 4.** Ratios of exposed and control population carrying capacity \( K[C]/K[0] \) versus ratios of exposed and control population intrinsic rate of increase \( r(C)/r(0) \). Both carrying capacity and intrinsic rate of increase measured in laboratory studies.
of the carrying capacity $K$ was correlated to the inhibition of the population growth.

Population-level effects of mixtures as estimated by concentration addition were confirmed by the observations in the experiments. The impact of a toxicant and another stressor on the intrinsic rate of increase $r$ could generally be described by response multiplicity. Substantial deviations were noted in case of extreme stress. With this restriction, multistress appears predictable from single-stress conditions.

Data sets on population laboratory experiments are biased to metals and crustaceans. Consistent differences between conditions and substance or species groups are difficult to detect. However, deviations from this general pattern were identified. These include substances that affect reproduction at concentrations far below lethal levels (large $k_R$), possibly due to different modes of action. Also, species that have a small number of offspring (small $R_n$) or that are sensitive to any disturbances are vulnerable. Population toxicology will therefore benefit most from empirical investigations on nonstandard conditions, nontraditional chemicals, and nonclassical test species with such risky characteristics.

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