Supplementary information for: "Simplified Dynamic Energy Budget model for analysing ecotoxicity data"

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November 15, 2011

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1 The standard DEB model

1.1 A word on notation

In this file, we strictly follow the notation rules for DEB theory as laid down by Kooijman [4]. Symbols with a dot (like $\dot{k}_e$) indicate a parameter that is a rate (i.e., with a dimension that includes t^{-1}). Parameters between square brackets relate to the parameter without these brackets in a division by structural volume (e.g., $[E] = E/L^3$). Similarly, a parameter between curly braces relates to the normal parameter through division by a structural surface area (e.g., $\{\dot{p}_{Am}\} = \dot{p}_{Am}/L^2$). Symbols with the same leading symbol have the same dimensions. All parameter symbols are explained in Table 1.

1.2 Basic DEB model in powers

We start with a global description of DEB in terms of 'powers' (energy fluxes, in et^{-1}) as indicated in Figure 1; in Section 1.3 and 1.4, these powers will be further specified. In the standard DEB

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Symbol	interpretation	dimensions
$\dot{b}_\dagger$	scaled killing rate	$L^3\#^{-1}t^{-1}$
c_0	scaled internal threshold concentration	$\#L^{-3}$
$c_{0\dagger}$	scaled internal threshold for survival	$\#L^{-3}$
c_d	dissolved external concentration of toxicant	$\#L^{-3}$
c_T	scaled internal tolerance concentration	$\#L^{-3}$
c_V	scaled internal concentration of toxicant	$\#L^{-3}$
e	scaled reserve density (generally 0-1)	$[-]$
E	absolute reserve	e
$[E]$	absolute reserve density (E/L^3)	el^{-3}
E_0	energy content of a single egg	e
$[E_G]$	volume-specific costs for structure, in control $[E_{G0}]$	el^{-3}
E_H	investment into maturity, at birth E_H^b, at puberty E_H^p	e
$[E_m]$	maximum reserve density	el^{-3}
E_R	reserves in the reproduction buffer	e
f	scaled functional response (0-1), in control f_0	$[-]$
g	energy investment ratio, in control g_0	$[-]$
$\dot{h}$	total hazard rate for survival	t^{-1}
$\dot{h}_0$	background hazard rate for survival	t^{-1}
$\dot{h}_Q$	hazard rate due to the toxicant	t^{-1}
$\dot{k}_e$	elimination or 'dominant' rate constant ($L = L_m$)	t^{-1}
$\dot{k}_J$	maturity maintenance rate coefficient	t^{-1}
$\dot{k}_M$	somatic maintenance rate coefficient, in control $\dot{k}_{M0}$	t^{-1}
L	structural body length	l
L_0	structural body length at start of experiment	l
L_p	structural body length at puberty	l
L_m	maximum structural body length, in control at $f = 1$	l
M_Q	mass of toxicant in an organism	$\#$
$[M_Q]$	density of toxicant in an organism	$\#l^{-3}$
$\dot{p}_A$	assimilation power	et^{-1}
$[\dot{p}_A]$	volume-specific assimilation power	$et^{-1}l^{-3}$
$\{\dot{p}_{Am}\}$	surface-specific maximum assimilation power	$et^{-1}l^{-2}$
$\dot{p}_C$	mobilisation power	et^{-1}
$[\dot{p}_C]$	volume-specific mobilisation power	$et^{-1}l^{-3}$
$\dot{p}_J$	maturity maintenance power, at puberty $\dot{p}_J^p$	et^{-1}
$\dot{p}_M$	somatic maintenance power	et^{-1}
$[\dot{p}_M]$	volume-specific somatic maintenance power, in control $[\dot{p}_{M0}]$	$et^{-1}l^{-3}$
P_{Vd}	volumetric bioconcentration factor between water and organism	L^3l^{-3}
$\dot{r}$	relative growth rate of individual	t^{-1}
$\dot{r}_B$	Von Bertalanffy growth rate constant, in control at $f = 1$	t^{-1}
$\dot{R}$	reproduction rate	$\#t^{-1}$
$\dot{R}_m$	maximum reproduction rate ($f = 1$, $L = L_m$), in control $\dot{R}_{m0}$	$\#t^{-1}$
s	stress factor (0 in control)	$[-]$
S	survival probability	$[-]$
$\dot{v}$	energy conductance	lt^{-1}
$\dot{v}_Q$	conductance for toxicant uptake	lt^{-1}
κ	fraction of mobilised reserves allocated to the soma	$[-]$
κ_H	fraction of reserve flux to maturation fixed in maturity, 1 in control	$[-]$
κ_R	fraction of allocated reserves fixed in eggs, in control κ_{R0}	$[-]$

Table 1: DEB model parameters used in this paper with their symbols, interpretation and dimensions (# for numbers, e for energy, L for length of environment, l for length of organism, t for time).

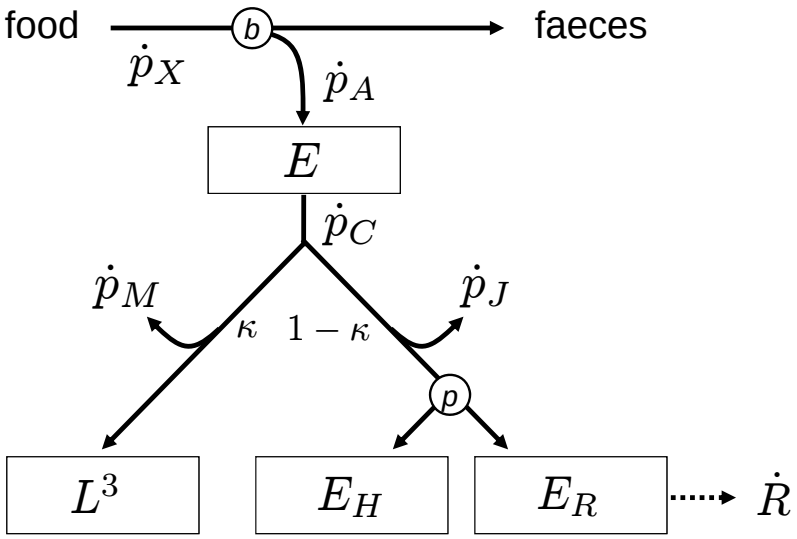

Figure 1: Schematic diagram of the energy flows in a standard DEB animal, with the associated parameter symbols. The nodes b and p denote switches at birth (start of feeding) and puberty (start of reproductive investment). The mobilisation flux is split according to a constant fraction κ.

animal model, there are two types of biomass: structure (which requires maintenance) and reserve (which fuels metabolic processes). Structure and reserve have a constant composition (strong homeostasis) and at constant food density (and when reserves are in steady state with the food level) the ratio between reserves and structure is constant from birth to death (weak homeostasis). Both structure and reserve are state variables. DEB identifies three life-cycle stages: embryo, juvenile and adult. The switch from embryo to juvenile is marked by the initiation of feeding, the switch from juvenile to adult marks the end of maturation and the start of investment in reproduction. The switching is determined by the 'complexity' of the organism, which is captured by the DEB state variable 'maturity' (the cumulated investment of reserves in development). There are thus maturity thresholds for birth E_H^b and puberty E_H^p. Note that $t = 0$ indicates the start of embryonic development, unless specified otherwise.

The change in absolute amount of reserves (E) is given by the difference between the powers for assimilation ($\dot{p}_A$) and mobilisation ($\dot{p}_C$):

$$\frac{d}{dt}E = \begin{cases} -\dot{p}_C & \text{if } E_H < E_H^b \\ \dot{p}_A - \dot{p}_C & \text{otherwise} \end{cases} \quad \text{with } E(0) = E_0 \tag{1}$$

For embryos, $\dot{p}_A = 0$ by definition. Structural body volume L^3 is calculated from the allocated mobilisation flux to the soma, after withdrawing the maintenance power $\dot{p}_M$. The energy flux is converted into structural volume using the energetic costs for structure $[E_G]$:

$$\frac{d}{dt}L^3 = \frac{1}{[E_G]}\left(\kappa\dot{p}_C - \dot{p}_M\right) \quad \text{with } L(0) \approx 0 \tag{2}$$

Maturation (as cumulated reserve investment into maturity, for embryos and juveniles) is given in the same manner, as the difference between the allocated mobilisation power, after withdrawing maturity maintenance $\dot{p}_J$:

$$\frac{d}{dt}E_H = \begin{cases} \kappa_H\left((1-\kappa)\dot{p}_C - \dot{p}_J\right) & \text{if } E_H < E_H^p \\ 0 & \text{otherwise} \end{cases} \quad \text{with } E_H(0) = 0 \tag{3}$$

In addition to DEB theory, we include here κ_H as the fraction of the energy flux available for maturity that is fixed in maturation. Normally, we do not have to bother with this parameter, and set it to 1, as we define maturity in terms of the reserves used to build it up. However, we need this parameter when we add toxicants, to include an effect on the costs for maturation.

The investment in maturation stops when the invested reserves hit the threshold for puberty E_H^p. At that point (thus for adults only), the energy flux is channelled into the reproduction buffer E_R:

$$\frac{d}{dt}E_R = \begin{cases} 0 & \text{if } E_H < E_H^p \\ (1-\kappa)\dot{p}_C - \dot{p}_J^p & \text{otherwise} \end{cases} \quad \text{with } E_R(0) = 0 \tag{4}$$

For adults, the maturity maintenance costs are fixed to the level at puberty. The mean reproduction rate can be calculated using the costs for a single egg (E_0), and assumes that a fraction κ_R of the allocated flux is fixed into eggs (the remainder is lost as overheads):

$$\dot{R} = \frac{\kappa_R}{E_0}\frac{d}{dt}E_R \tag{5}$$

In the standard DEB model, the egg costs need to be found in such a way that they lead to hatching of an animal with the same reserve density $[E]$ as its mother had at the moment of egg formation (a maternal effect). The egg starts with a very small amount of structure, no maturity, no reproduction buffer, and an amount E_0 of reserves. It hatches when the maturity hits the birth threshold E_H^b. Note that in the simplified DEB model, we will assume constant egg costs, and do not deal with the embryo stage.

1.3 Specification of the powers for assimilation and maintenance

The assimilation flux (for juveniles and adults) scales with the structural surface area and depends on the available food. The surface-area specific maximum assimilation power $\{\dot{p}_{Am}\}$ is a species-specific constant. The actual assimilation power $\dot{p}_A$ is than given by:

$$\dot{p}_A = fL^2\{\dot{p}_{Am}\} \tag{6}$$

where f is the scaled functional response, which is 1 at maximum food and 0 when there is no food available. Further details of the feeding process (i.e., how f relates to the available food in the environment) are not dealt with here.

The somatic maintenance power is proportional to the structural volume. The volume-specific somatic maintenance power is thus a species-specific constant $[\dot{p}_M]$:

$$\dot{p}_M = [\dot{p}_M]L^3 \tag{7}$$

The maturity maintenance power is proportional to the cumulated investment into maturation:

$$\dot{p}_J = \dot{k}_J E_H \tag{8}$$

1.4 Specification of the mobilisation power

For the mobilisation power, we have to do a bit more work. We start with the differential equation for the reserve, Eq. 1, which we rewrite to an equation for the reserve density $[E] = E/L^3$:

$$\frac{d}{dt}[E] = [\dot{p}_A] - [\dot{p}_C] - [E]\dot{r} \tag{9}$$

The last term stands for the dilution of the reserves by growth, where:

$$\dot{r} = \frac{1}{L^3}\frac{d}{dt}L^3 \tag{10}$$

The weak homeostasis assumption of DEB theory [4] demands that $[E]$ does not change at constant food density, and thus does not depend on body size. However, we know that $[\dot{p}_A]$ scales with L^{-1}, because $\dot{p}_A$ scales with L^2 (see Eq. 6). For $\frac{d}{dt}[E]$ to stay zero when $[\dot{p}_A]$ scales with L^{-1}, the last two terms in Eq. 9 ($-[\dot{p}_C] - [E]\dot{r}$) should together be some function that scales with L^{-1}. We can write this in Eq. 9 by introducing some function H of $[E]$, where the other parameters of this function (θ) cannot depend on L:

$$\frac{d}{dt}[E] = [\dot{p}_A] - \frac{1}{L}H([E];\theta) \tag{11}$$

Following an argument about partitionability of the reserves, Kooijman [4] argues that the only possible function for H is a simple one: $H = \dot{v}[E]$. This implies that the volume-specific mobilisation power ($[\dot{p}_C]$) should be found by combining the last terms in Eq. 9 and 11:

$$-[\dot{p}_C] - [E]\dot{r} = -\frac{\dot{v}}{L}[E] \tag{12}$$

and thus:

$$[\dot{p}_C] = [E]\left(\frac{\dot{v}}{L} - \dot{r}\right) \tag{13}$$

$$\dot{p}_C = E\left(\frac{\dot{v}}{L} - \dot{r}\right) \tag{14}$$

Next, we can fill in $\dot{r}$, using Eq. 10 and the equation for growth Eq. 2, using the maintenance power of Eq. 7:

$$\dot{p}_C = E\left(\frac{\dot{v}}{L} - \frac{1}{L^3[E_G]}\left(\kappa\dot{p}_C - [\dot{p}_M]L^3\right)\right) \tag{15}$$

$$= E\frac{\dot{v}}{L} - E\frac{\kappa\dot{p}_C}{L^3[E_G]} + E\frac{[\dot{p}_M]}{[E_G]} \tag{16}$$

Next, we can move all terms including $\dot{p}_C$ to the left side of the equation:

$$\dot{p}_C + E\frac{\kappa\dot{p}_C}{L^3[E_G]} = E\frac{\dot{v}}{L} + E\frac{[\dot{p}_M]}{[E_G]} \tag{17}$$

$$\dot{p}_C\left(1 + \frac{[E]\kappa}{[E_G]}\right) = E\left(\frac{\dot{v}}{L} + \frac{[\dot{p}_M]}{[E_G]}\right) \tag{18}$$

Which leads to:

$$\dot{p}_C = E\frac{\dot{v}/L + \frac{[\dot{p}_M]}{[E_G]}}{1 + \frac{[E]\kappa}{[E_G]}} \tag{19}$$

$$= E\frac{[E_G]\dot{v}/L + [\dot{p}_M]}{[E_G] + [E]\kappa} \tag{20}$$

This is the equation that is also derived in the DEB book, Page 39, Eq. 2.12 (when multiplied with structural volume, L^3). We can further use Equation 19, introducing the somatic maintenance rate coefficient $\dot{k}_M = [\dot{p}_M]/[E_G]$, the scaled reserve densiy $e = [E]/[E_m]$ (where $[E_m]$ is the maximum reserve density, which is taken as a constant), and the energy investment ratio $g = [E_G]/(\kappa[E_m])$:

$$\dot{p}_C = E\frac{\dot{v}/L + \dot{k}_M}{1 + \kappa\frac{[E]}{[E_G]}} \tag{21}$$

$$= e[E_m]L^3\frac{\dot{v}/L + \dot{k}_M}{1 + e\kappa\frac{[E_m]}{[E_G]}} \tag{22}$$

$$= [E_m]L^3\left(\frac{\dot{v}}{L} + \dot{k}_M\right)\frac{eg}{e+g} \tag{23}$$

2 DEBtox simplification

The simplified system that we derive here follows from two additional assumptions:

1. There is always a constant ratio between structure and maturity for juveniles and embryos, also under (toxicant) stress. The start of investment into reproduction (puberty) therefore occurs at a fixed structural length, and we do not need to follow maturity as a state variable.

2. Egg costs are constant, unless there is a direct toxicant effect on them. This assumption overrides the 'maternal effect' of DEB theory (see [4]).

In contrast to the original DEBtox equations [6], we include the scaled reserves (e) as a dynamic state variable. Thus, we do not have to assume that the reserve density is always in steady state.

Assumption 1 limits the parameters that are allowed to change under stress. For example, if we increase the costs for structure, this implies a change in the length at puberty, unless the costs for maturation are affected by the same factor. Similarly, a change in κ will affect the length of puberty. To allow a change in such DEB parameters, one would have to use a full DEB model (see [3]). The use of scaled reserves implies that we cannot incorporate an effect on the energy conductance $\dot{v}$ (as a change in $\dot{v}$ would affect $[E_m]$ that is used to scale the reserves, see next section).

2.1 Reserve dynamics

From the derivation in Section 1.4 (Eq. 11 and 6), it follows that (see also the DEB book [4] Page 39, Eq. 2.10-2.11):

$$\frac{d}{dt}[E] = [\dot{p}_A] - [E]\frac{\dot{v}}{L} = \frac{\{\dot{p}_{Am}\}f - [E]\dot{v}}{L} \tag{24}$$

The maximum reserve density is achieved ($[E] = [E_m]$) when $f = 1$, and thus $\frac{d}{dt}[E] = 0$ when $[E_m] = \{\dot{p}_{Am}\}/\dot{v}$. The scaled reserve density was defined as $e = [E]/[E_m]$, and because $[E_m]$ is taken as constant, we can rewrite the reserve equation to:

$$\frac{d}{dt}e = (f - e)\frac{\dot{v}}{L} \tag{25}$$

When the dynamics of the reserves are fast, or when f is constant, we can take $f = e$, and effectively ignore the reserve altogether.

2.2 Maturity is a constant fraction of structure

In this section, we will remove maturity as a state variable, using assumption 1 above. The change in structural volume L^3 and in the investment in maturity E_H are given by the following two equations:

$$\frac{d}{dt}L^3 = \frac{1}{[E_G]}\left(\kappa\dot{p}_C - [\dot{p}_M]L^3\right) \tag{26}$$

$$\frac{d}{dt}E_H = \kappa_H\left((1-\kappa)\dot{p}_C - \dot{k}_J E_H\right) \tag{27}$$

When maturity is always a constant fraction of structural volume, we can work with length instead of maturity; investment in reproduction will always start at a constant structural size. Both structure and maturity start at embryonic development approximately at zero. Thus we demand that:

$$\frac{E_H}{L^3} = \frac{\frac{d}{dt}E_H}{\frac{d}{dt}L^3} = \frac{E_H^p}{L_p^3} = [E_H] = \text{constant} \tag{28}$$

and thus (note that $\dot{k}_M = [\dot{p}_M]/[E_G]$):

$$\frac{d}{dt}E_H = [E_H]\frac{d}{dt}L^3 \tag{29}$$

$$\kappa_H\left((1-\kappa)\dot{p}_C - \dot{k}_J E_H\right) = \frac{[E_H]}{[E_G]}\left(\kappa\dot{p}_C - [\dot{p}_M]L^3\right) \tag{30}$$

$$\kappa_H(1-\kappa)\dot{p}_C - \kappa_H\dot{k}_J E_H = \frac{\kappa[E_H]}{[E_G]}\dot{p}_C - [E_H]\frac{[\dot{p}_M]}{[E_G]}L^3 \quad (31)$$

$$\kappa_H(1-\kappa)\dot{p}_C - \kappa_H\dot{k}_J[E_H]L^3 = \frac{\kappa[E_H]}{[E_G]}\dot{p}_C - [E_H]\dot{k}_M L^3 \quad (32)$$

$$\kappa_H\frac{1-\kappa}{[E_H]}\dot{p}_C - \kappa_H\dot{k}_J L^3 = \frac{\kappa}{[E_G]}\dot{p}_C - \dot{k}_M L^3 \quad (33)$$

For $\dot{p}_C$, we can include Eq. 23:

$$\kappa_H\frac{(1-\kappa)[E_m]}{[E_H]}L^3\left(\frac{\dot{v}}{L}+\dot{k}_M\right)\frac{eg}{e+g} - \kappa_H\dot{k}_J L^3 = \frac{\kappa[E_m]}{[E_G]}L^3\left(\frac{\dot{v}}{L}+\dot{k}_M\right)\frac{eg}{e+g} - \dot{k}_M L^3 \quad (34)$$

$$\kappa_H\frac{(1-\kappa)[E_m]}{[E_H]}\left(\frac{\dot{v}}{L}+\dot{k}_M\right)\frac{eg}{e+g} - \kappa_H\dot{k}_J = \frac{\kappa[E_m]}{[E_G]}\left(\frac{\dot{v}}{L}+\dot{k}_M\right)\frac{eg}{e+g} - \dot{k}_M \quad (35)$$

$$\kappa_H\frac{1-\kappa}{[E_H]}H(L) - \kappa_H\dot{k}_J = \frac{\kappa}{[E_G]}H(L) - \dot{k}_M \quad (36)$$

We thus have only a single function H of L, times two constants, and minus two constants. This equality can only hold when $\kappa_H\dot{k}_J = \dot{k}_M$, and when the factors before $H(L)$ are the same. This latter requirement translates into:

$$\kappa_H\frac{1-\kappa}{[E_H]} = \frac{\kappa}{[E_G]} \quad (37)$$

$$\kappa_H\frac{1-\kappa}{\kappa}[E_G] = [E_H] \quad (38)$$

We can use this result to obtain an expression that links E_H^p to L_p, because we would like to use the latter as a model parameter (and remove the first):

$$\kappa_H\frac{1-\kappa}{\kappa}[E_G] = \frac{E_H^p}{L_p^3} \quad (39)$$

$$E_H^p = \kappa_H\frac{1-\kappa}{\kappa}[E_G]L_p^3 \quad (40)$$

Thus, we now have a constraint for using a constant length at puberty ($\kappa_H\dot{k}_J = \dot{k}_M$) and an expression for how the length at puberty (L_p^3) relates to the invested reserves into maturation (E_H^p). Because we assume that E_H^p is constant, this implies that an increase in $[E_G]$ needs to be accompanied by a decrease of κ_H by the same factor (note that $\dot{k}_M$ includes $[E_G]$, so the equality $\kappa_H\dot{k}_J = \dot{k}_M$ still holds). Furthermore, a change in somatic maintenance costs $\dot{k}_M$ should be accompanied by the same change in maturity maintenance costs $\dot{k}_J$.

2.3 Rewriting the reproduction rate

In this section, we will rewrite the reproduction equation in such a way that many of the model parameters are combined into a new compound parameter, the maximum reproduction rate $\dot{R}_m$. Starting from the energy-based equation for reproduction, we can use the results derived in the previous section ($\kappa_H\dot{k}_J = \dot{k}_M$ and the expression for E_H^p in Eq. 40) to rewrite the equation:

$$\dot{R} = \frac{\kappa_R}{E_0}\left((1-\kappa)\dot{p}_C - \dot{k}_J E_H^p\right) \quad (41)$$

$$= \frac{\kappa_R}{E_0}\left((1-\kappa)\dot{p}_C - \frac{\dot{k}_M}{\kappa_H}\kappa_H\frac{1-\kappa}{\kappa}[E_G]L_p^3\right) \quad (42)$$

$$= \frac{\kappa_R}{E_0}\frac{1-\kappa}{\kappa}[E_G]\left(\frac{\kappa}{[E_G]}\dot{p}_C - \dot{k}_M L_p^3\right) \quad (43)$$

Next, we need expressions for the mobilisation flux, which was already derived in Section 1.4 (Eq. 23), as well as the maximum mobilisation flux (without stress, with $L = L_m$ and $e = 1$). We need this maximum flux because we will write the reproduction equation in terms of the maximum reproduction rate later on, to remove a number of parameters. For that purpose, we introduce the maximum length L_m, and parameters in the control $\dot{k}_{M0}$ and g_0 (remember that we do not consider stress on $\dot{v}$ or κ as they violate the simplifying assumptions). This is necessary to correctly introduce stress factors due to the toxicant at a later stage. The maximum mobilisation power is:

$$\dot{p}_{Cm} = [E_m] L_m^3 \left(\frac{\dot{v}}{L_m} + \dot{k}_{M0} \right) \frac{g_0}{1+g_0} \tag{44}$$

Note that $L_m = \dot{v}/(\dot{k}_{M0} g_0)$ is the maximum length in the control, and thus:

$$\begin{aligned}
\dot{p}_{Cm} &= [E_m] L_m^3 \left(\dot{k}_{M0} g_0 + \dot{k}_{M0} \right) \frac{g_0}{1+g_0} && (45)\\
&= [E_m] L_m^3 \dot{k}_{M0} \left(1+g_0\right) \frac{g_0}{1+g_0} && (46)\\
&= [E_m] L_m^3 \dot{k}_{M0} g_0 && (47)\\
&= [E_m] \dot{v} L_m^2 && (48)
\end{aligned}$$

The maximum reproduction rate (in the control, at maximum size, and $e = 1$) is now given by introducing the expression for $\dot{p}_{Cm}$ into Eq. 43, and using control parameters only (κ_{R0}, $[E_{G0}]$, $\dot{k}_{M0}$) (note that $g = [E_G]/(\kappa[E_m])$):

$$\begin{aligned}
\dot{R}_m &= \frac{\kappa_{R0}}{E_0} \frac{1-\kappa}{\kappa} [E_{G0}] \left(\frac{\kappa}{[E_{G0}]} [E_m] \dot{v} L_m^2 - \dot{k}_{M0} L_p^3 \right) && (49)\\
&= \frac{\kappa_{R0}}{E_0} \frac{1-\kappa}{\kappa} [E_{G0}] \left(\frac{\dot{v}}{g_0} L_m^2 - \dot{k}_{M0} L_p^3 \right) && (50)\\
&= \frac{\kappa_{R0}}{E_0} \frac{1-\kappa}{\kappa} [E_{G0}] \dot{k}_{M0} \left(L_m^3 - L_p^3 \right) && (51)
\end{aligned}$$

The reproduction rate of Eq. 43 can be filled in with the regular mobilisation flux too:

$$\begin{aligned}
\dot{R} &= \frac{\kappa_R}{E_0} \frac{1-\kappa}{\kappa} [E_G] \left(\frac{\kappa}{[E_G]} [E_m] L^3 \left(\frac{\dot{v}}{L} + \dot{k}_M \right) \frac{eg}{e+g} - \dot{k}_M L_p^3 \right) && (52)\\
&= \frac{\kappa_R}{E_0} \frac{1-\kappa}{\kappa} [E_G] \left(L^3 \left(\frac{\dot{v}}{L} + \dot{k}_M \right) \frac{e}{e+g} - \dot{k}_M L_p^3 \right) && (53)\\
&= \frac{\kappa_R}{E_0} \frac{1-\kappa}{\kappa} [E_G] \dot{k}_M \left(\left(\frac{\dot{v}}{\dot{k}_M} L^2 + L^3 \right) \frac{e}{e+g} - L_p^3 \right) && (54)
\end{aligned}$$

We can remove a number of parameters from this equation by calculating the ratio $\dot{R}/\dot{R}_m$, and use that to form an expression for $\dot{R}$ that includes $\dot{R}_m$ as parameter:

$$\begin{aligned}
\frac{\dot{R}}{\dot{R}_m} &= \frac{\kappa_R}{\kappa_{R0}} \frac{[E_G]}{[E_{G0}]} \frac{\dot{k}_M}{\dot{k}_{M0}} \frac{\left(\frac{\dot{v}}{\dot{k}_M} L^2 + L^3 \right) \frac{e}{e+g} - L_p^3}{L_m^3 - L_p^3} && (55)\\
\dot{R} &= \frac{\dot{R}_m}{L_m^3 - L_p^3} \frac{\kappa_R}{\kappa_{R0}} \frac{[E_G]}{[E_{G0}]} \frac{\dot{k}_M}{\dot{k}_{M0}} \left(\left(\frac{\dot{v}}{\dot{k}_M} L^2 + L^3 \right) \frac{e}{e+g} - L_p^3 \right) && (56)\\
&= \frac{\dot{R}_m}{L_m^3 - L_p^3} \frac{\kappa_R}{\kappa_{R0}} \frac{[\dot{p}_M]}{[\dot{p}_{M0}]} \left(\left(\frac{\dot{v}}{\dot{k}_M} L^2 + L^3 \right) \frac{e}{e+g} - L_p^3 \right) && (57)
\end{aligned}$$

The last step makes use of the fact that $\dot{k}_M = [\dot{p}_M]/[E_G]$. The stress-to-control ratios κ_R/κ_{Ro} and $[\dot{p}_M]/[\dot{p}_{M0}]$ are of course only relevant when there is exposure to a toxicant, otherwise they are one and can be removed. These two model parameters only appear as a ratio. The advantage is that a stress on κ_R or $[\dot{p}_M]$ does not require the absolute value of these parameters. The stress factor s can simply be applied on the parameter $\dot{R}_m$.

2.4 Rewriting the growth equation

Starting with the growth equation in terms of energetics (making use of $\dot{k}_M = [\dot{p}_M]/[E_G]$):

$$\frac{d}{dt}L^3 = \frac{1}{[E_G]}\left(\kappa\dot{p}_C - [\dot{p}_M]L^3\right) \tag{58}$$

$$3L^2\frac{d}{dt}L = \frac{1}{[E_G]}\left(\kappa\dot{p}_C - [\dot{p}_M]L^3\right) \tag{59}$$

$$\frac{d}{dt}L = \frac{1}{3}\left(\frac{\kappa\dot{p}_C}{[E_G]L^2} - \dot{k}_M L\right) \tag{60}$$

Next, we can include Eq. 23 for the mobilisation rate (making use of $g = [E_G]/(\kappa[E_m])$):

$$\frac{d}{dt}L = \frac{1}{3}\left(\frac{\kappa[E_m]}{[E_G]}L\left(\frac{\dot{v}}{L} + \dot{k}_M\right)\frac{eg}{e+g} - \dot{k}_M L\right) \tag{61}$$

$$= \frac{1}{3}\left(\left(\dot{v} + \dot{k}_M L\right)\frac{e}{e+g} - \dot{k}_M L\right) \tag{62}$$

$$= \frac{1}{3}\left(\dot{v}\frac{e}{e+g} + \dot{k}_M L\frac{e}{e+g} - \dot{k}_M L\right) \tag{63}$$

$$= \frac{1}{3}\left(\dot{v}\frac{e}{e+g} + \dot{k}_M L\left(\frac{e}{e+g} - 1\right)\right) \tag{64}$$

$$= \frac{1}{3}\left(\dot{v}\frac{e}{e+g} + \dot{k}_M L\frac{e-(e+g)}{e+g}\right) \tag{65}$$

$$= \frac{1}{3(e+g)}\left(\dot{v}e - \dot{k}_M Lg\right) \tag{66}$$

$$= \frac{\dot{k}_M g}{3(e+g)}\left(e\frac{\dot{v}}{\dot{k}_M g} - L\right) \tag{67}$$

This is the Von Bertalanffy result of DEB theory, as long as the parameters are constant.

2.5 Deriving the scaled toxicokinetics equation

In this section, we derive the equation for the scaled internal concentration from 'first principles'. We require the scaled concentration to deal with cases where we want to use the DEBtox equations without (relevant) measured body residues (see [2]).

Here, we consider toxicokinetics to be well represented by a diffusion process for a single, well-mixed, compartment. First consider an organism made up of water, exposed to a chemical dissolved in water. According to Fick's first law, diffusion of a chemical in a single solvent is proportional to the surface area for exchange and the concentration difference between two regions ΔC. The surface area for diffusive exchange is proportional to the volumetric length of the organism squared. The mass flux between environment and organism is thus given by (M_Q is the moles of chemical in the organism):

$$\frac{d}{dt}M_Q = \dot{v}_Q L^2 \Delta C \tag{68}$$

The proportionality constant $\dot{v}_Q$ is the ratio of the diffusion coefficient (dimensions l^2t^{-1}) and the distance over which transport takes place (dimension l). This constant is a conductance (dimensions of a length per time) and is known in environmental chemistry as a mass-transfer coefficient or 'piston velocity'. The chemical conductance depends on the chemical (mainly on molecular weight, when considering transport in a single solvent), on the nature of the interface over which the toxicant transfer takes place, and on the temperature, but $\dot{v}_Q$ does not depend on the size of the organism.

We can change this mass flux into a concentration change by dividing both sides of Eq. 68 by the volume of the organism, L^3 (note that $[M_Q] = M_Q/L^3$). However, the volume is not

necessarily constant; the organism may grow or shrink in a particular manner. Using the product rule for the derivative:

$$\frac{d}{dt}[M_Q] = \frac{d}{dt}\frac{M_Q}{L^3} = \frac{1}{L^3}\frac{d}{dt}M_Q + M_Q\frac{d}{dt}\frac{1}{L^3} \tag{69}$$

and using the chain rule for the last term:

$$\begin{aligned}\frac{d}{dt}[M_Q] &= \frac{1}{L^3}\frac{d}{dt}M_Q - M_Q\frac{3}{L^4}\frac{d}{dt}L &(70)\\ &= \frac{1}{L^3}\frac{d}{dt}M_Q - [M_Q]\frac{3}{L}\frac{d}{dt}L &(71)\end{aligned}$$

We can use Eq. 68 to rewrite this equation to:

$$\begin{aligned}\frac{d}{dt}[M_Q] &= \dot{v}_Q\frac{L^2}{L^3}\Delta C - [M_Q]\frac{3}{L}\frac{d}{dt}L &(72)\\ &= \frac{\dot{v}_Q}{L}\Delta C - [M_Q]\frac{3}{L}\frac{d}{dt}L &(73)\end{aligned}$$

The last term accounts for the effects of a change in volume on the concentration. The parameter combination $\dot{v}_Q/L$ forms the 'elimination rate constant', which is the concentration-specific elimination rate from the organism. Even though this elimination rate is here a function of the size of the organism, we can still work with an elimination rate constant as a parameter, but we would have to define a reference situation. A logical reference is the situation where $L = L_m$:

$$\frac{d}{dt}[M_Q] = \dot{k}_e\frac{L_m}{L}\Delta C - [M_Q]\frac{3}{L}\frac{d}{dt}L \tag{74}$$

We still need to think about ΔC. In ecotoxicology, we are not dealing with a chemical in a single solvent but with the transfer from the environment to an organism. This can be considered as a situation with two solvents (still, a rather heroic simplification). We cannot directly compare the concentration in the environment to the concentration in the organism, but we can use the difference between the actual and the final concentration as the driving force:

$$\Delta C = [M_Q]_\infty - [M_Q] = P_{Vd}c_d - [M_Q] \tag{75}$$

Where the bioconcentration factor P_{Vd} is defined as the ultimate concentration in the organism $[M_Q]_\infty$, divided by the dissolved external concentration, c_d. With that, the full equation for the body density of toxicant becomes:

$$\frac{d}{dt}[M_Q] = \dot{k}_e\frac{L_m}{L}\left(P_{Vd}c_d - [M_Q]\right) - [M_Q]\frac{3}{L}\frac{d}{dt}L \tag{76}$$

The scaled internal concentration is derived by dividing both sides of this equation by the bioconcentration factor P_{Vd} and take $c_V = [M_Q]/P_{Vd}$:

$$\frac{d}{dt}c_V = \dot{k}_e\frac{L_m}{L}\left(c_d - c_V\right) - c_V\frac{3}{L}\frac{d}{dt}L \tag{77}$$

2.6 Including toxicant effects

The principle of the DEBtox approach is that some internal concentration affects the value of one or more parameters in a DEB model. For the relationship between the scaled internal concentration and the stress on a model parameter, we assume a linear relationship with a threshold:

$$s = \frac{1}{c_T}\max\left(0, c_V - c_0\right) \tag{78}$$

In this definition, s is a dimensionless parameter; $s = 0$ indicates no stress. This stress factor can subsequently be applied to model parameters. The assumption that maturity is a constant proportion of structure severely limits the number of parameters we are allowed to change, see

Mode of action	DEB parameters under stress
Decrease in assimilation from food	$f = f_0 \max(0, 1-s)$
Increase in somatic and maturity maintenance	$\dot{k}_M = \dot{k}_{M0}(1+s)$, $\dot{R}_m = \dot{R}_{m0}(1+s)$
Increase in costs for structure and maturation	$g = g_0(1+s), \dot{k}_M = \dot{k}_{M0}(1+s)^{-1}$
Increase in overhead costs for making an egg	$\dot{R}_m = \dot{R}_{m0}(1+s)^{-1}$
Hazard during oogenesis	$\dot{R}_m = \dot{R}_{m0}\ \exp(-s)$

Table 2: Possible physiological modes of action for the simplified DEBtox model (combinations of these 5 are also possible). Parameters that are not mentioned in the table for a specific mode of action are set to their value in the control (e.g., $f = f_0$, for all but the first mode).

Table 2. The stress-to-control ratios κ_R/κ_{Ro} and $[\dot{p}_M]/[\dot{p}_{M0}]$ of Eq. 57 are absorbed into an effect on $\dot{R}_m$. Therefore, an effect on maintenance costs will effect $\dot{R}_m$ too. An effect on the costs for structure also affects $\dot{k}_M$ too, as $\dot{k}_M = [\dot{p}_M]/[E_G]$. The model for hazard during oogenesis links to the approach for survival in Eq. 82. The stress factors is the integrated hazard rate over the sensitive period of development.

2.7 The model for survival

In a DEB context, mortality is treated as a chance process [1, 2]. Chance processes in time are modelled using the hazard rate. The hazard rate is the instantaneous probability to die, or more precisely:

$$\dot{h}(t) = \lim_{\Delta t \to 0} \frac{S(t) - S(t+\Delta t)}{\Delta t S(t)} = -\frac{1}{S}\frac{d}{dt}S \tag{79}$$

Thus, the hazard rate times a very small time increment gives the probability to die in that interval, given that you are alive at the start of that interval. Effects on mortality are modelled somewhat independently from effects on the energy budget. In principle, the same scaled internal concentration c_V should be used as for growth and reproduction, but survival has its own threshold for effects and its own proportionality:

$$\dot{h}_Q = \dot{b}_\dagger \max(0, c_V - c_{0\dagger}) \tag{80}$$

The hazard rate due to toxicant exposure ($\dot{h}_Q$) can simply be added to other hazard rates, assuming that they are independent effects. Some deaths are accidental, and can be included by a (low) constant background hazard rate ($\dot{h}_0$). For short laboratory experiments, this is usually sufficient. For full life-cycle situations, we probably want to use a dedicated ageing module. The total hazard is thus:

$$\dot{h} = \dot{h}_Q + \dot{h}_0 \tag{81}$$

If we know the hazard rate as function of time, we can calculate the survival probability over time as:

$$S(t) = \exp\left(-\int_0^t \dot{h}(\tau)\, d\tau\right) \tag{82}$$

2.8 Summary of the simplified model

The final equation for the reserve dynamics is (see Eq. 25; note that $t = 0$ now indicates the start of the experiment):

$$\frac{d}{dt}e = (f-e)\frac{\dot{v}}{L} \quad \text{with } e(0) = 1 \tag{83}$$

Here, we assume that the animals that are used to start the experiment are from an ad-libitum fed culture. Reserve dynamics does not require any additional parameters, but it does require an additional state variable to calculate. To take out the reserve dynamics, this ODE can be replaced by $e = f$.

For growth, the final equation is (Eq. 67, $t = 0$ again indicates the start of the experiment):

$$\frac{d}{dt}L = \frac{\dot{k}_M g}{3(e+g)}\left(e\frac{\dot{v}}{\dot{k}_M g} - L\right) \quad \text{with } L(0) = L_0 \tag{84}$$

In DEB theory, L stands for structural length, which is not the same as physical length or body size (see main text).

For the reproduction rate we can use the following (Eq. 57):

$$\dot{R} = \begin{cases} 0 & \text{if } L < L_p \\ \frac{\dot{R}_m}{L_m^3 - L_p^3}\left(\left(\frac{\dot{v}}{\dot{k}_M}L^2 + L^3\right)\frac{e}{e+g} - L_p^3\right) & \text{otherwise} \end{cases} \tag{85}$$

Instead of $\dot{k_M}$ and $\dot{v}$, we can use the more intuitive maximum length (in the control at maximum food) and Von Bertalanffy growth rate constant (in the control at maximum food) as our parameters:

$$\dot{r}_B = \frac{\dot{k}_{M0} g_0}{3(1+g_0)} \quad \text{and} \quad L_m = \frac{\dot{v}}{\dot{k}_{M0} g_0} \tag{86}$$

Therefore, if g_0 is given:

$$\dot{k}_{M0} = \dot{r}_B \frac{3(1+g_0)}{g_0} \quad \text{and} \quad \dot{v} = L_m \dot{k}_{M0} g_0 \tag{87}$$

For the scaled toxicokinetics we use:

$$\frac{d}{dt}c_V = \dot{k}_e \frac{L_m}{L}(c_d - c_V) - c_V \frac{3}{L}\frac{d}{dt}L \tag{88}$$

The scaled internal concentration is subsequently used to calculate a stress factor:

$$s = \frac{1}{c_T}\max(0, c_V - c_0) \tag{89}$$

The parameters under stress can be calculated using this stress factor, following the rules in Table 2.

The scaled internal concentration can also be used to calculate the hazard rate:

$$\dot{h}_Q = \dot{b}_\dagger \max(0, c_V - c_{0\dagger}) \tag{90}$$

The hazard rate relates to survival probability as:

$$S(t) = \exp\left(-\int_0^t \dot{h}_Q(\tau) + \dot{h}_0 \, d\tau\right) \tag{91}$$

This brings the list of input parameters for the DEB model in the blank to: L_0, L_p, L_m, $\dot{r}_B$, $\dot{R}_{m0}$, g_0, f_0 and h_0. The internal parameters k_{M0} and $\dot{v}$ are calculated from this set. For the toxicant, we require the external dissolved concentration c_d, and as additional parameters: $\dot{k}_e$, c_0, c_T, $c_{0\dagger}$, $b_\dagger$. This makes 13 parameters in total. When food is provided ad libitum, we can fix $f = 1$, thus reducing the parameter count to 12. This parameter set can be used to calculate the effects on survival, growth and reproduction, simultaneously over a large part of the life cycle. For effects on growth only (as in [5]), the number of parameters reduces even further to 7 (with $f = 1$) or 8.

3 Likelihood functions

3.1 Continuous endpoints (body size and reproduction)

Here, we will go into a bit more detail about normal likelihood functions, and especially on treating the standard deviation of the error distribution as a nuisance parameter, and working with the means of replicate observations.

Our reference situation is the log-likelihood function for a data set Y (with time points i, concentrations j, and replicate observations r) where the deviations from the model predictions $\hat{Y}$ are normal, independent and homoscedastic, and depend on the parameter set θ:

$$\ell(\theta, \sigma^2|Y) = -\frac{N}{2}\ln(2\pi\sigma^2) - \frac{1}{2\sigma^2}\sum_{j=1}^{m}\sum_{i=1}^{k_j}\sum_{r=1}^{n_{ij}}(Y_{ijr} - \hat{Y}_{ij}(\theta))^2 \tag{92}$$

where N is the total number of data points:

$$N = \sum_{j=1}^{m}\sum_{i=1}^{k_j} n_{ij} \tag{93}$$

3.2 Standard deviation known

If the standard deviation of the scatter is known, the first term in Eq. 92 becomes trivial (it does not depend on the parameters, so it is a constant). The log-likelihood function thus reduces to:

$$\ell(\theta|Y, \sigma^2) = -\frac{1}{2\sigma^2}\sum_{j=1}^{m}\sum_{i=1}^{k_j}\sum_{r=1}^{n_{ij}}(Y_{ijr} - \hat{Y}_{ij}(\theta))^2 + C \tag{94}$$

To include heteroscedasticity in the analysis, we can also take different error variances for each time and concentration:

$$\ell(\theta|Y, \sigma^2) = -\sum_{j=1}^{m}\sum_{i=1}^{k_j}\frac{1}{2\sigma_{ij}^2}\sum_{r=1}^{n_{ij}}(Y_{ijr} - \hat{Y}_{ij}(\theta))^2 + C \tag{95}$$

We can easily work with means ($\bar{Y}_{ij}$)instead of individual data points (Y_{ijr}), as long as the correct error variance is used. Note that:

$$\sigma^2_{\bar{Y}_{ij}} = \frac{\sigma^2}{n_{ij}} \tag{96}$$

And thus if σ^2 is known:

$$\ell(\theta|Y, \sigma^2) = -\frac{1}{2\sigma^2}\mathrm{wSSQ}_n(\theta; Y) + C \tag{97}$$

$$\mathrm{wSSQ}_n(\theta; Y) = \sum_{j=1}^{m}\sum_{i=1}^{k_j} n_{ij}(\bar{Y}_{ij} - \hat{Y}_{ij}(\theta))^2 \tag{98}$$

The SSQ is thus replaced by the weighted sum-of-squares; each residual is weighted with the number of replicates for each mean. If the variance of the error is known, no information is lost when we work with the means instead of the individual replicates.

3.3 Standard deviation as a nuisance parameter

Usually, we are not interested in the value of the residual variation σ^2, and we can replace it with its maximum-likelihood estimate. The variation is given by:

$$\hat{\sigma}^2(\theta, Y) = \frac{1}{N}\sum_{j=1}^{m}\sum_{i=1}^{k_j}\sum_{r=1}^{n_{ij}}(Y_{ijr} - \hat{Y}_{ij}(\theta))^2 \tag{99}$$

In fact, replacing σ^2 with its maximum likelihood estimate leads to a profile likelihood where σ^2 is 'profiled out' as a nuisance parameter. This profile likelihood can be treated like a normal likelihood in all respects [7]. The log-likelihood simplifies to:

$$\ell(\theta|Y) = -\frac{N}{2}\ln\left(\sum_{j=1}^{m}\sum_{i=1}^{k_j}\sum_{r=1}^{n_{ij}}(Y_{ijr} - \hat{Y}_{ij}(\theta))^2\right) + C \tag{100}$$

All constant terms (that do not depend on the parameters) are absorbed in C, including the factor $\ln 2\pi/N$, and can subsequently be ignored.

In practice, we might have to work with the mean observed values at each timepoint and concentration $\bar{Y}_{ij}$. This requires some consideration because the simplification rests on the estimation of σ^2 from the data (see Eq. 99), and the number of replicates on which mean is based might differ between the observation times or the tested concentrations. We can make use of the relationship between the standard error of the mean (the expected deviation between the average of a number of replicates and the true mean) and the standard deviation of a number of replicates (the expected deviation between individual replicate and the true mean). Consider a set of replicate observations for one timepoint i and one treatment j:

$$\sigma^2_{\bar{Y}_{ij}} = \frac{\sigma^2}{n_{ij}} \tag{101}$$

$$\mathcal{E}\left((\bar{Y}_{ij} - \hat{Y}_{ij}(\theta))^2\right) = \frac{1}{n_{ij}}\mathcal{E}\left((Y_{ijr} - \hat{Y}_{ij}(\theta))^2\right) \tag{102}$$

We can estimate the expected squared deviations $(Y_{ijr} - \hat{Y}_{ij})^2$ with the standard deviation:

$$\mathcal{E}\left((Y_{ijr} - \hat{Y}_{ij}(\theta))^2\right) \approx \frac{1}{n_{ij}}\left(\sum_{r=1}^{n_{ij}}(Y_{ijr} - \hat{Y}_{ij}(\theta))^2\right) \tag{103}$$

Combining Eq. 102 and 103, we can therefore estimate the sum-of-squares over the replicate observations by the following:

$$\sum_{r=1}^{n_{ij}}(Y_{ijr} - \hat{Y}_{ij}(\theta))^2 \approx n_{ij}^2(\bar{Y}_{ij} - \hat{Y}_{ij}(\theta))^2 \tag{104}$$

Even though these expressions are not necessarily equal, their expectations are the same. We can thus estimate the error variance from the data using the n^2-weighted sum-of-squares (see Eq. 99):

$$\hat{\sigma}^2(\theta, Y) = \frac{1}{N}\mathrm{wSSQ}_{n^2}(\theta; Y) \tag{105}$$

$$\mathrm{wSSQ}_{n^2}(\theta; Y) = \sum_{j=1}^{m}\sum_{i=1}^{k_j} n_{ij}^2(\bar{Y}_{ij} - \hat{Y}_{ij}(\theta))^2 \tag{106}$$

Now, we have to go back to the full log-likelihood of Eq. 92, and fill in Eq. 105 and 98:

$$\ell(\theta, |Y) = -\frac{N_Y}{2}\ln\left(\frac{2\pi}{N}\mathrm{wSSQ}_{n^2}(\theta; Y)\right) - \frac{N}{2\mathrm{wSSQ}_{n^2}(\theta; Y)}\mathrm{wSSQ}_n(\theta; Y) \tag{107}$$

Where N_Y is the total number of means (whereas N is the total number of observations on individuals):

$$N_Y = \sum_{j=1}^{m}\sum_{i=1}^{k_j} 1 \tag{108}$$

We can further simplify the log-likelihood function by including all constant terms (that do not depend on the parameters) into a constant C:

$$\ell(\theta|Y) = -\frac{N_Y}{2}\ln(\mathrm{wSSQ}_{n^2}(\theta; Y)) - \frac{N\mathrm{wSSQ}_n(\theta; Y)}{2\,\mathrm{wSSQ}_{n^2}(\theta; Y)} + C \tag{109}$$

In contrast to the likelihood with fixed error variance, in this case, information is lost when using the means instead of the replicate observations. The reason is that the individual data points allow for a better estimation of the variance.

3.4 Multinomial distribution for mortality

For survival, the likelihood function follows from the multinomial distribution. The log-likelihood of the parameter set θ, given the data set Y, is given by (see e.g., [1, 2]).

$$\ell(\theta|Y) = \sum_{j=1}^{m}\sum_{i=1}^{k}(Y_{ij} - Y_{i+1j})\ln(S_{ij}(\theta) - S_{i+1j}(\theta)) + C \tag{110}$$

In this equation, Y_{ij} is the number of surviving organisms at observation time i at concentration j. Similarly, S_{ij} is the survival probability at that point (Eq. 82). Note that the subscript $i+1$ in this equation means that we have to deal with the situation where $i = k+1$. This is an additional interval which catches the organisms that survive until the end of the experiment (they will die in the interval from the end of the experiment to infinity). Therefore we can specify:

$$Y_{k+1j} = 0 \quad \text{and} S_{k+1j} = 0 \tag{111}$$

For this likelihood function, the fact the follow the same group of animals over time is not a problem because we only use one observation for each individual (in which interval it dies). Precondition is that the death of one individual in a container does not affect the death probability of the others.

In some cases, we can have the situation that organisms are removed from the survival test for destructive analysis (e.g., measurement of body residues), or that have escaped from the test container. We can still use the observations from these organisms for our likelihood, as they still contain information (they were alive up to the point where they were removed for analysis or lost). We can still use Equation 110 for the individuals that have actually died, but add to it another log-likelihood function for the ones that were removed or lost (Z):

$$\ell(\theta|Z) = \sum_{j=1}^{m}\sum_{i=1}^{k} Z_{ij}\ln S_{ij}(\theta) + C \tag{112}$$

3.5 SSQs for reproduction

In the main text, we suggest to compare the number of offspring produced by an individual mother in an interval between $t-1$ and t, Y_{ijr}, to the integrated reproduction rate over that interval:

$$\mathrm{SSQ}(\theta; Y) = \sum_{j=1}^{m}\sum_{i=2}^{k_j}\sum_{r=1}^{n_{ij}}\left(\int_{t_{i-1}}^{t_i} R_j(\tau,\theta)d\tau - Y_{ijr}\right)^2 \tag{113}$$

Often, we have observations for the number of offspring produced by a group of mothers in an interval, Y_{ij}. We can derive a weighted SSQ by calculating an average reproduction per female, using the average number of mothers alive in that interval, and again compare it to the integrated reproduction rate over that interval. We also have to weigh the residuals with the average number of mother over the interval:

$$\mathrm{wSSQ}_n(\theta; Y) = \sum_{j=1}^{m}\sum_{i=2}^{k_j}\left(\frac{n_{ij}+n_{i-1j}}{2}\right)\left(\int_{t_{i-1}}^{t_i} R_j(\tau,\theta)d\tau - \frac{2\,Y_{ij}}{n_{ij}+n_{i-1j}}\right)^2 \tag{114}$$

The n^2-weighted SSQ can be derived by scaling with the average number of mothers squared.

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