Supporting information to "Interpreting toxicity data in a DEB framework; a case study for nonylphenol in the marine polychaete *Capitella teleta*"

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October 25, 2010

1 The standard scaled DEB model

Several formulations of DEB theory are available that are useful for different purposes. We use the DEB3 version with scaled reserves and maturity of Kooijman and co-workers [4], which is phrased only in terms of the dimensions length and time. Reserves and maturity are scaled with the maximum assimilation rate per unit of surface area, which removes the unit 'mole' from the system (and one parameter). All stage transitions are initiated by maturity levels; $U_H = U_H^b$ for birth (start of feeding) and $U_H = U_H^p$ for puberty (start of investment in reproduction, and stop investment in maturity).

The change in scaled reserve is given by:

$$\frac{d}{dt}U_E = \left\{ \begin{array}{ll} -S_C & \text{if } U_H < U_H^b \\ fL^2 - S_C & \text{otherwise} \end{array} \right. \quad \text{with } U_E(0) = U_E^0 \tag{1}$$

The entire feeding process is lumped into a single parameter f, the scaled functional response. Under unlimiting food conditions $f = 1$ and under limiting food densities $f < 1$.

It turns out to be handy to work with the scaled reserve density:

$$e = \dot{v}\frac{U_E}{L^3} \tag{2}$$

Under constant conditions, and the absence of toxic stress on feeding or assimilation, $e = f$.

The scaled mobilisation flux of the reserves is given by:

$$S_C = L^2 \frac{ge}{g+e}\left(1 + \frac{\dot{k}_M L}{\dot{v}}\right) \tag{3}$$

The change in structural length is given by:

$$\frac{d}{dt}L = \frac{1}{3L^2}\left(\frac{\dot{v}}{g}S_C - \dot{k}_M L^3\right) \quad \text{with } L(0) \approx 0 \tag{4}$$

This equation is different from the one given in [4], although it is mathematically equivalent. This form more clearly reveals the close links with the maturation and reproduction process; growth is the net result of the mobilised reserved that are allocated to growth and somatic maintenance (κ is included in g), minus the maintenance needs.

The change in scaled maturity is given by:

$$\frac{d}{dt}U_H = \left\{ \begin{array}{ll} (1-\kappa)S_C - \dot{k}_J U_H & \text{if } U_H < U_H^p \\ 0 & \text{otherwise} \end{array} \right. \quad \text{with } U_H(0) = 0 \tag{5}$$

Note that at birth $U_H = U_H^b$ and at puberty $U_H = U_H^p$. The energy flux into the reproductive buffer is given by:

$$\frac{d}{dt}U_R = \left\{ \begin{array}{ll} 0 & \text{if } U_H < U_H^p \\ (1-\kappa)S_C - \dot{k}_J U_H^p & \text{otherwise} \end{array} \right. \quad \text{with } U_R(0) = 0 \tag{6}$$

At certain points in time, the reproduction buffer will be converted to eggs. Ignoring the buffer, the mean reproduction rate is given by:

$$\dot{R} = \frac{\kappa_R}{U_E^0} \frac{d}{dt} U_R \tag{7}$$

These equations define the full DEB model, but one problem is left open: the determination of the scaled initial reserves in the egg, U_E^0. However, following the standard assumptions of the DEB model, this quantity does not require additional parameters. The key assumption is that the initial reserves must be such that the embryo will hatch at the same reserve density (e) as its mother had at egg formation. The easiest way to solve this problem would be to simply simulate the embryonic development with different values of U_E^0 until we observe the correct reserve density at hatching. However, more efficient procedures are available in [3].

In this formulation, two compound parameters have been introduced to remove the dimension 'energy' from the complete parameter set: $\dot{k}_M$ and g, defined as:

$$\dot{k}_M = \frac{[\dot{p}_M]}{[E_G]} \quad \text{and} \quad g = \frac{[E_G]}{\kappa[E_m]} \tag{8}$$

When $\dot{k}_J$ equals $\dot{k}_M$ we have the situation where stage transitions take place at the same structural length for different food levels. This situation is of special interest as a constant size at puberty appears to be common in many of the invertebrates that are used as standard test organisms in ecotoxicology. For this reason, we introduce the ratio of the two rate constants as a new parameter (with a default value of 1). Similarly, we introduce a parameter for the ratio of the maturity at birth and at puberty:

$$k = \frac{\dot{k}_J}{\dot{k}_M} \quad \text{and} \quad u_H^{bp} = \frac{U_H^b}{U_H^p} \tag{9}$$

The reason for introducing this new parameter u_H^{bp} is that the absolute value of U_H is difficult to interpret because of the non-intuitive dimensions. All U are scaled using the maximum surface-specific assimilation rate. This rate depends on details of food quality and can therefore differ between experiments. The ratio of the two maturity threshold is likely to remain constant in the same species under different conditions.

This leaves the following complete set of parameters: g, $\dot{v}$, $\dot{k}_M$, k, κ, κ_R, U_H^p, u_H^{bp} and f. For κ_R, a standard value of 0.95 is usually taken [4].

2 One-compartment model for toxicokinetics

For toxicokinetics, we used the scaled one-compartment model as presented in [2]. The real (but unknown) internal concentration is divided by the real (but also unknown) bioconcentration factor. The resulting variable is proportional to the real internal concentration, but has the dimension of an external concentration (see [1] for more explanation). This formulation accounts for dilution by growth and the changing surface:volume ratio during growth. The model equation is:

$$\frac{d}{dt} c_V = \dot{k}_e \frac{L_{m0}}{L} \left(c_d - c_V \right) - c_V \dot{r} \tag{10}$$

In this way, $\dot{k}_e$ has the interpretation of the elimination rate of an organism at the maximum size reached under control conditions, L_{m0} (smaller individuals will have a larger elimination rate).

The specific volumetric growth rate $\dot{r}$ is given by:

$$\dot{r} = \frac{1}{V} \frac{d}{dt} V = \frac{3}{L} \frac{d}{dt} L \tag{11}$$

The maximum structural length in the control is given by:

$$L_{m0} = \frac{\dot{v}}{\dot{k}_M g} \tag{12}$$

with all three required parameters under unexposed conditions.

3 Effects of toxicants on DEB parameters

For the effects of toxicants, we introduce a stress function as function of the scaled internal concentration:

$$s = \frac{1}{c_T} \max\left(0, c_V - c_0\right) \tag{13}$$

In this definition, s is a dimensionless indicator of the degree of stress on a DEB parameter. Below the no-effect concentration c_0, there is no effect. When the scaled internal concentration exceeds the NEC, the stress function increases in a linear fashion. Subsequently, s can be applied to one or more primary DEB parameters (see [2]). In the case of nonylphenol in *Capitella*, we applied the stress factor on the costs for growth, and the costs for reproduction and maturation. This latter is not a parameter in the standard model, but we can define an overhead for maturation κ_H in analogy to the overheads for reproduction κ_R (in the control, κ_H is set to 1). The equation for maturation than becomes:

$$\frac{d}{dt} U_H = \begin{cases} \kappa_H \left((1-\kappa)S_C - \dot{k}_J U_H\right) & \text{if } U_H < U_H^p \\ 0 & \text{otherwise} \end{cases} \quad \text{with } U_H(0) = 0 \tag{14}$$

The stress factor s is then applied as follows:

$$
\begin{aligned}
g & \rightarrow & g(1+s) & \tag{15} \\
k_M & \rightarrow & k_M(1+s)^{-1} & \tag{16} \\
\kappa_R & \rightarrow & \kappa_R(1+s)^{-1} & \tag{17} \\
\kappa_H & \rightarrow & \kappa_H(1+s)^{-1} & \tag{18}
\end{aligned}
$$

The addition of the stress factor to k_M is needed because the growth costs are part of this coefficient too (see Eq. 8)

References

[1] T. Jager and S. A. L. M. Kooijman. A biology-based approach for quantitative structure-activity relationships (qsars) in ecotoxicity. *Ecotoxicology*, 18:187–196, 2009.

[2] T. Jager, T. Vandenbrouck, J. Baas, W. M. De Coen, and S. A. L. M. Kooijman. A biology-based approach for mixture toxicity of multiple endpoints over the life cycle. *Ecotoxicology*, 19:351–361, 2010.

[3] S. A. L. M. Kooijman. What the egg can tell about its hen: embryonic development on the basis of dynamic energy budgets. *Journal of Mathematical Biology*, 58(3):377–394, 2009.

[4] S. A. L. M. Kooijman, T. Sousa, L. Pecquerie, J. Van der Meer, and T. Jager. From food-dependent statistics to metabolic parameters, a practical guide to the use of dynamic energy budget theory. *Biological Reviews*, 83:533–552, 2008.

Symbol	Description	Dimensions
c_0	scaled no-effect concentration (NEC)	$\#l^{-3}$
c_d	concentration of a toxicant in the environment	$\#l^{-3}$
c_T	scaled tolerance concentration	$\#l^{-3}$
c_V	scaled internal toxicant concentration	$\#l^{-3}$
e	scaled reserve density	$-$
$[E_G]$	energy costs per unit of structural volume	eL^{-3}
$[E_m]$	maximum reserve density	eL^{-3}
f	scaled functional response	$-$
g	energy investment ratio	$-$
k	maintenance ratio $\dot{k}_J/\dot{k}_M$	$-$
$\dot{k}_e$	elimination rate constant	t^{-1}
$\dot{k}_J$	somatic maintenance rate coefficient	t^{-1}
$\dot{k}_M$	specific maturity maintenance	t^{-1}
L	structural length of organism	L
L_{m0}	maximum structural length of organism in control	L
$[\dot{p}_M]$	somatic maintenance per unit of structural volume	$eL^{-3}t^{-1}$
$\dot{r}$	specific volumetric growth rate	t^{-1}
$\dot{R}$	reproduction rate	$\#t^{-1}$
s	stress factor for toxic stress	$-$
S_C	scaled catabolic flux	L^2
u_H^{bp}	ratio of maturity at birth and at puberty $u_H^{bp} = U_H^b/U_H^p$	$-$
U_E	scaled reserve level, $U_E^0 = U_E(0)$ ($t = 0$ is at egg production)	tL^2
U_H	scaled maturity level, at birth $U_H = U_H^b$, at puberty $U_H = U_H^p$	tL^2
U_R	scaled reproduction buffer	tL^2
$\dot{v}$	energy conductance	Lt^{-1}
V	structural volume of organism L^3	L^3
κ	allocation fraction to growth and maintenance	$-$
κ_H	fraction of allocated energy fixed in maturity	$-$
κ_R	fraction of allocated energy fixed in eggs	$-$

Table 1: Symbols used in this section, with explanation, and dimensions in terms of numbers ($\#$), body length (l), environmental length (L), energy (e) and time (t). Square brackets indicate a parameter per volume (a density), curly braces per surface area. A dot on a parameter specifies it as a rate (per time).