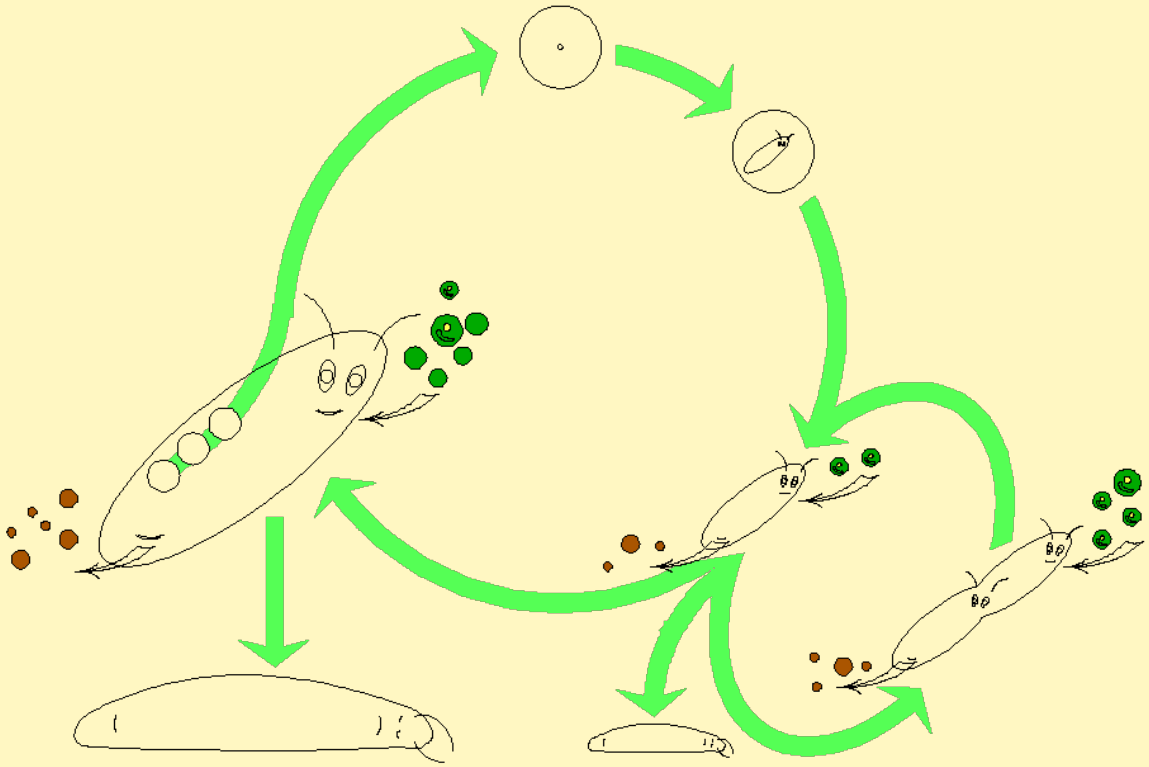
Exercises for

Dynamic Energy Budget tele-course



DEB theory for metabolic organisation

Cambridge University Press, third edition 2010

Authors:

Tânia Sousa & Gonçalo Marques: questions 2.3, 3.2, 4.5, 11.1
Bas Kooijman (the rest)

Advisory Board:

Chapter 0

Basic methods

These exercises concern the background document Basic methods for Theoretical Biology, which is assumed to be known to participants of the DEB tele-course.

0.1 Dimensions

Motivation:

If a model suffers from dimensional problems, it will be rarely useful. It, therefore, makes sense to start with a dimensional analysis of any new model, before anything else. If a model survives this check, it may still fail other consistency checks, however.

Given:

Suppose that we have a model

$$y(t) = a(t/b + b)$$

for a variable y as a function of time t with parameters a and b.

0.1.1 Question:

Does the model suffer from dimension problems?

Hint:

Try to identify the dimensions of the parameters, starting with that of b.

0.1.2 Question:

a What about the model $y(t) = a(t/b + bc)$, where t represents time again?

b How many identifiable parameters has this model?

Hint:

Is it possible to choose $\dim(c)$ such that $\dim(b)$ becomes simple? Is it possible to multiply a with a number and multiply or divide b and c with that number without any consequence for y?

0.2 Scaling of dynamic systems

Motivation:

One reason to scale a dynamic system is to remove parameters that cannot be estimated from data. Scaling can usually be done in different ways.

Given:

The Monod model for the growth of a microbial population with density X on a substrate in concentration S in a batch reactor is given by

$$\begin{aligned} \frac{d}{dt}S &= -j_S f X \\ \frac{d}{dt}X &= \dot{r} X \end{aligned}$$

where t stands for time, f for the scaled functional response $f = \frac{S}{S+K}$, j_S is the biomass-specific uptake rate, and $\dot{r}$ is the specific growth rate: $\dot{r} = y_{XS}\, j_S\, f$.

0.2.1 Question:

What are the dimensions of all symbols, using only the given information?

Hint:

Start with f and use the rule that you can only add quantities with the same dimension, and consider $\dim(S)$ and $\dim(X)$ as given.

0.2.2 Question:

What are the parameters of the model?

Hint:

Does a differential equation fully specify the time-trajectories of the variables?

0.2.3 Question:

a Can you scale the dynamic system $\{S, X\}$ to dimensionless quantities?

b How many parameters will a system with three variables and five parameters have after rescaling to dimensionless variables?

Hint:

Compare the dimensions of the parameters and the variables, and try to multiply of divide variables with parameters such that the dimensions disappear. How many variables has the system? What about time itself?

0.2.4 Question:

Suppose that we have a scatter-free data set $\{t_i, S(t_i)\}_{i=1}^{n}$. Can you rescale the dynamic system $\{S, X\}$ such that it only has (theoretically) identifiable parameters?

Hint:

Remove all biomass-related dimensions from variables and parameters.

0.2.5 Question:

Suppose that we know the initial biomass density $X(0)$, but not how it changes in time due to growth on the substrate. Can find we an estimate for the yield coefficient y_{XS}, so the efficiency with which substrate is converted into biomass?

Hint:

Have a close look at $x(0)$.

0.3 Theoretical identification of parameter values

Motivation:

Mechanistic models usually have parameters and variables that cannot be observed directly. Whether or not parameter-values can be identified, depends on the combination of the model and the available (type of) data. Theoretical and practical identification of parameter-values are different concepts; the next chapter will deal with practical parameter identification problems.

Given:

In the DEB book Chap 2, Eq (2.23), {49}, we will see that the (volumetric) structural length of an isomorph at constant food density X develops during the juvenile and adult stage as

$$L(t) = fL_m - (fL_m - L_b)\exp\{-t\dot{r}_B\}$$

where the von Bertalanffy growth rate $\dot{r}_B$ is given by $\dot{r}_B = (3/\dot{k}_M + 3fL_m/\dot{v})^{-1}$, and the maximum length L_m by $L_m = \frac{\dot{v}}{g\dot{k}_M}$, and scaled functional response f is given by $f = \frac{X}{X+K}$, where X is the food density and K the saturation coefficient. Time t and food density X are variables (although X is kept constant), and saturation coefficient K, energy conductance $\dot{v}$, maintenance rate coefficient $\dot{k}_M$, investment ratio g, (volumetric) length at birth L_b are parameters.

0.3.1 Question:

What are the dimensions of all symbols, using only what has been given here?

Hint:

Use the rule that you can only add quantities that have the same dimension, and consider $\dim(X)$ as given.

0.3.2 Question:

Suppose that we have a set of scatter-free length-at-time observations $\{t_i, L(t_i)\}_{i=1}^n$, for a single food level (so a single but unkown value for f). Which parameters are theoretically identifiable?

Hint:

How many quantities fully determine the relationship between V and t?

0.3.3 Question:

Suppose that we have two sets of observations $\{t_i, V(t_i)\}_{i=1}^n$, for two (sufficiently different) known food levels X_1 and X_2. Which parameters are now theoretically identifiable?

Hint:

What do we know more now? How many parameters does the ultimate length have as function of food density?

0.3.4 Question:

Suppose that we have two sets of scatter-free observations on *weights*, rather than on structural volumes, $\{t_i, W(t_i)\}_{i=1}^{n}$, for two (sufficiently different) known food levels X_1 and X_2. Given is that weights relate to the structural volumes as (cf (2.6) at {31} for $E_R = 0$ and $E = fE_m$ and $d_E = [E_m]w_E/\mu_E$)

$$W = (d_V + fd_E)V$$

where d_V and d_E are (unknown) parameters.

a What are the dimensions of d_V and d_E and which parameters are now theoretically identifiable?

b Can you give a direct and simple argument why the parameters $\dot{v}$ is not identifiable?

Note: both structure and reserve contribute to weight, and we have no a-priori rule to quantify their contributions; only weights can be measured in a straightforward way. So data on weights have less information than data on structural volume.

Hint:

How many parameters has ultimate weight as a function of food denity? Does that exceed the number of observations?

0.3.5 Question:

Suppose that we have now data sets of weights-at-time for three, rather than two (sufficiently different) known food levels. Which parameters are then identifiable?

Hint:

How many parameters has ultimate weight as a function of food denity?

0.4 Fitting data

Motivation:

DEBtool is meant to facilitate the application of DEB theory. Parameter estimation and checking goodness of fit is among the tasks. This excersize show how to do this in a relatively simple way. This simple task can be done by many packages, but we will meet more complex tasks, where most packages are useless. We use Octave in the exercises; read the manual of DEBtool to see the differences with Matlab.

Given:

We measured the lengths 1, 4, 5 and 5.5 cm at days 0, 1, 2 and 3.

0.4.1 Question:

a What is the von Bertalanffy growth rate and its standard deviation?

b Do the data fit this curve well?

Hint:

Check the code for figure 2.11, i.e. `Bert_examples.m` in `DEBtool/fig_3/ch2`, and replace a data set by this one.

0.5 Inner and outer products

Motivation:

Octave and Matlab are matrix-oriented languages. Their strength only reveals when you make use of this.

Given:

Two column-vectors of numbers of equal length: x = [1 2]'; y = [3 4]';.

0.5.1 Question:

What is the inner and outer product of these two vectors? Use Octave or Matlab.

0.5.2 Question:

Calculate the sum of the products of the elements of the two vectors.

0.6 Mean and variance

Motivation:

Mean and variances, covariances and correlations are basic concepts. Coding them in Matlab/Octave helps to familiarize yourself with this language. This exercise is also about maxtrix manipulation.

Given:

The list of paired data $\{x, y\}_{i=1}^{3}$: (1, 1.5), (2, 1.5), (3, 2).

0.6.1 Question:

What is the mean and estimated variance of x and y, their covariance, and their correlation coefficient? Write a function that calculates the vector of means, the variance-covariance matrix, and the correlation matrix for any (n,2)-matrix with n pairs of data.

Hint:

Look into some DEBtool/lib/regr/ functions to see examples of code and consult the manual. Notice that, when the list $\{x_i\}_{i=1}^n$ represents n random trials from some probability distribution of a random variable $\underline{x}$, the expected value for $\underline{x}$ is estimated by the mean $\sum_{i=1}^n x_i/n$. A similar result applies for products of two variables. When the list $\{x_i, y_i\}_{i=1}^n$ represents n random trials from some probability distribution of a pair of random variables $(\underline{x}, \underline{y})$, the expected value for the product $\underline{xy}$ is estimated by the mean $\sum_{i=1}^n x_i y_i/n$. Manipulate matrices the solve the problem.

0.7 Profile likelihood

Motivation:

Profile likelihood function provide valuable information about the accuracy of an parameter estimation.

Given:

The list $\{3, 2, 4, 3\}$ represents random trials from a Poisson distribution.

0.7.1 Question:

What is the 95% confidence interval of the parameter of the Poisson distribution? Compare the likelihood-based estimate with that based on a parabolic approximation of the likelihood function near the maximum. Make plots of the profile likelihood function, and the one based on the parabolic approximation.

Hint:

The second-order Taylor approximation to the ln likelihood function in the point $\hat{\lambda}$ is $\ell(\lambda) \simeq \ell(\hat{\lambda}) + (\lambda - \hat{\lambda}) \frac{d}{d\lambda} \ell(\hat{\lambda}) - 0.5(\lambda - \hat{\lambda})^2 \frac{d^2}{d\lambda^2} \ell(\hat{\lambda})$. The middle term of the taylor expansion of the ln likelihood function is zero by definition; this function represents a parabola in λ. DEBtool's routine survi_chi calculates the inverse survivor function of the chi-square distribution. So survi_chi(1, 0.05) gives the value for which a chi-squared distributed variable with parameter 1 (known as the degree of freedom) exceeds that value with probablility 0.05.

0.8 Root finding

Motivation:

Many practical problems involve the finding of roots using numerical methods. Likelihood function can have more than one local extremes. We need the global maximum only. Roots finding methods for the derivatives of the likelihood function can be used to identify the values for which the likelihood function has extremes. We still have to make sure that the root corresponds to the global maximum, rather than to a local extreme (minimum or maximum).

Given:

Two sets of paired data x = [1 2; 2 2.2; 3 2.3] and y = [2 5; 3 6; 4 6.1]; The first columns represent independent variables, the second column dependent variables, which are normally distributed with a mean that is proportional to the dependent variable and a constant variance. The variances of the two data sets don't need to be equal, the proportionality factor in their means are equal.

0.8.1 Question:

What is the ML estimate for the proportionality factor?

Hint:

This estimate is given in implicit form in the statistical document in the section "More sample case"; write a function to get a numerical estimate, using fsolve.

Chapter 1

Basic concepts

1.1 Physical versus volumetric length

Motivation:

Lengths are important in DEB theory because of the role of surface areas in assimilation and mobilisation (of reserve), in combination with that of volume in maintenances. Moreover, auxiliary theory uses physical length to access the amount of structural length.

Given:

The standard DEB model applies.

1.1.1 Question:

a What is the difference between physical and volumetric length?

b What is the difference between volumetric and structural length?

c What is the implication of isomorphy for the relationship between physical and volumetric length?

d Which assumption does auxiliary theory make about their relationships?

Hint:

What is the role of shape in length?

1.2 Temperature correction

Motivation:

All physiological rates depend on temperature, which should be taken into account when rates are compared at different temperatures.

Given:

A typical Arrhenius temperature for ectotherms is 8 kK, see Table 8.1.

1.2.1 Question:

Suppose that we measure a shell growth rate of 0.2 $\mathrm{cm\,d^{-1}}$ at 20°C in a mussel and the Arrhenius relationship applies, what would this rate be at 41°C?

Hint:

Have a look at Eq (1.2).

1.2.2 Question:

How does this rate relate to a body growth rate of, say, 2 $\mathrm{mm\,d^{-1}}$ of a sparrow with a body temperature of 41°C? Discuss the comparison.

Hint:

Do they have the same shape? Are sparrows ectothermic?

Chapter 2

Standard DEB Model

2.1 Hyperbola

Motivation:

The DEB's functional response is frequently called a hyperbola, but its standard representation seems to be quite different at first sight. This exercise aims to clarify the link.

Given:

A hyperbola is the set of all points (x, y) the difference of whose distances from distinct fixed points (*foci*) is constant. In formula

$$\frac{(x-h)^2}{a^2} - \frac{(y-k)^2}{b^2} = 1$$

The intersections of the line through the foci with the hyperbola are called *vertices*; the line segment connecting the vertices is called the *transverse axis*; the midpoint of the transverse axis is called the *center*. The center is at (h, k), the vertices are a units from the center, the foci c units, with $b^2 = c^2 - a^2$.

2.1.1 Question:

Show that the function $f(X) = (1 + K/X)^{-1}$ for $X > 0$ is (part of) a hyperbola.

Hint:

Set center at origin; make hyperbola rectangular; rotate 45 degrees; translate.

2.2 Homogeneous functions

Motivation:

Reserve dynamics belongs to the core of the DEB theory, but its derivation is not the most easy part of the DEB book; the comments on the DEB book gives a more simple derivation. This exercise aims to clarify the background of homogeneous functions, which occur in the derivation of reserve dynamics; we start with total and partial derivatives, which we need to understand Euler's theorem, see Basic Methods for Theoretical Biology.

Given:

If $z = f(x, y)$ and $x = g(t)$ and $y = h(t)$, and the functions f, g and h are all differentiable, then

$$\frac{dz}{dt} = \frac{\partial z}{\partial x}\frac{dx}{dt} + \frac{\partial z}{\partial y}\frac{dy}{dt}$$

The quantity $dz = \frac{\partial z}{\partial x}\Delta x + \frac{\partial z}{\partial y}\Delta y$ is known as the total differential of z.

2.2.1 Question:

Evaluate the total derivative of z for $z(t) = ax(t)y(t)$, $x(t) = bt$ and $y = \exp\{-ct\}$.

Given:

A function is homogeneous of degree n if

$$f(tx, ty) = t^n f(x, y)$$

for all $t > 0$ and all $(x, y) \neq (0, 0)$.

2.2.2 Question:

Find the degree of the given function

$$\begin{aligned}
1: \quad f(x,y) &= x^3 - 3xy^2 + y^3 \\
2: \quad f(x,y) &= \frac{xy}{\sqrt{x^2+y^2}} \\
3: \quad f(x,y) &= \exp\{x/y\} \\
4: \quad f(x,y) &= 2x^3 - 3xy^2 \\
5: \quad f(x,y) &= x^2y - 4x^3 + 3xy^2 \\
6: \quad f(x,y) &= x\exp\{x/y\} + y\sin\{y/x\} \\
7: \quad f(x,y) &= 1 + x + y \\
8: \quad f(x,y) &= \frac{x-y}{x+y}
\end{aligned}$$

2.2.3 Question:

Show that if $f(x, y)$ is homogeneous of degree n, then

$$x\frac{\partial}{\partial x}f(x,y) + y\frac{\partial}{\partial y}f(x,y) = nf(x,y)$$

a result known as Euler's theorem for homogeneous functions. The converse also holds true.

Hint:

Let $g(t) = f(tx, ty) = t^n f(x, y)$ and introduce $x = tX$ and $y = tY$; evaluate $\frac{d}{dt}g$ and set $t = 1$.

2.3 Reserve dynamics

Motivation:

DEB theory assumes that food-derived metabolites are first converted to reserve(s), and reserve is mobilised for other metabolic purposes. The mobilisation of reserve, therefore, drives metabolism and its dynamics is key to DEB theory.

Given:

The change in mass of reserve is the difference between the assimilation and mobilisation fluxes of reserve: $\frac{d}{dt}M_E = \dot{J}_{EA} - \dot{J}_{EC}$. For an individual with structural mass M_V and structural length L, the mobilisation flux is $\dot{J}_{EC} = M_E(\frac{\dot{v}}{L} - \dot{r})$, where $\dot{r} = M_V^{-1}\frac{d}{dt}M_V$ represents the (varying) specific growth rate and $\dot{v}$ the (constant) energy conductance.

2.3.1 Question:

a Express the specific growth rate in terms of change in structural volume and of change in structural length.

b Give the expression for the change in reserve density, i.e. the ratio of the amounts of reserve and structure $m_E = M_E/M_V$.

c Under what condition is the reserve density constant?

d Assuming that the assimilation flux has a maximum $\dot{J}_{EAm}$, what is the maximum reserve density?

e What are the assumptions behind this reserve dynamics?

f What is the difference with first order kinetics?

g What is the mean residence time of a molecule in reserve?

Hint:

You are only asked to express the specific growth rate in terms of change in structural volume and length, not in terms of amounts of reserve and structure. What relationships exist between mass, volume and length? What assumptions are used for these relationships? Remember the chain-rule for differentiation: $\frac{d}{dx}g(x)f(x) = f(x)\frac{d}{dx}g(x)+g(x)\frac{d}{dx}f(x)$. What does the concept of weak homeostasis mean? A transformation follows first kinetics if each substrate molecule partakes to the transformation with a constant probability rate.

2.4 Maximum growth

2.4.1 Question:

When is juvenile and/or adult growth maximal at constant food? Consider relative and absolute measures for lengths and weights.

Hint:

Growth is maximal if the second derivetive of the size measure equals zero, while weight is proportional to cubed length. Use DEBtool-function "shtime" in domain "animal" to see that growth in length and weight differ considerably in morphology.

2.5 Numerical behaviour of growth and reproduction

Motivation:

The numerical behaviour of the standard DEB model for isomorphs is important to know when we want to go from data to model parameters. This knowledge can help to detect data sets that cannot be described by the model, which call for extra attention to the cause.

2.5.1 Question:

How do lengths, weights and reproduction develop as functions of food density?

Hint:

Use DEBtool-animal routines "shmics" and "shtime" to make plots, after editing the parameters values in "pars.m". Try to predict the effect of changes that you will see, before use actually see them. Notice the (sometimes rather complex) contraints on "reasonable" parameter values.

2.6 Reserve buffer for reproduction

2.6.1 Question:

Why is the existence of a reserve buffer for reproduction basic in DEB models? Mention some examples of rules for using this buffer which involve an increasing number of offspring.

Hint:

These rules are discussed in 2.7.2.

Chapter 3

Energy, compounds and metabolism

3.1 Body mass and composition

Motivation:

It is not easy to measure the dry mass of a whale, or the wet mass of a bacterium (for very different reasons). We, therefore, have to interconvert measurements in wet and dry mass to link DEB predictions to measurements. It can also be hard to measure energy fluxes (especially if they are small. We, therefore, need to be able to convert from mass fluxes to energy fluxes and *vice versa*.

Given:

Suppose that wet weight equals ten times the dry weight, and the chemical indices of dry reserve and structure are known.

3.1.1 Question:

What are the chemical indices of wet reserve and structure?

Hint:

The ratio of dry and wet weight does not seem to depend on the ratio of mass of reserve and structure. What does this imply?

3.1.2 Question:

What is the relationship between the fraction of energy in ingested food that is fixed in reserve, κ_X, and the yield of reserve on food, y_{EX}?

Hint:

What is the relationship between energy fluxes and mass fluxes in C-moles?

3.1.3 Question:

Why do we need to specify the yield of faeces on food, y_{PE}, to quantify the carbon dioxide production that is associated with assimilation?

Hint:

What are the possible destinies of carbon in food? What is the consequence of the yield of reserve on food $y_{EX} = 1$ for faecal production?

3.2 Metabolic transformation

Motivation:

The standard DEB model has three degrees of freedom for metabolic transformations: assimilation, growth and dissipation. This is key to the method of indirect calorimetry as well as to the conceptual structure of the model. Although Chapter 4 deals with the application of the material presented in Chapter 3, we here apply the concept of macrochemical reaction equations to make it more concrete.

Given:

Biomass, in the standard DEB model, consists of reserve E and structure V. Assume that they have composition $CH_2O_{0.5}N_{0.15}$ and $CH_{1.8}O_{0.5}N_{0.15}$, respectively. Food X has composition $CH_{1.8}O_{0.5}N_{0.2}$ and faeces P has composition $CH_{1.8}O_{0.5}N_{0.15}$. Only 4 mineral compounds are involved: carbon dioxide C (CO_2), water H (H_2O), dioxygen O (O_2) and ammonia N (NH_3).

3.2.1 Question:

a Compute the stoichiometry for the assimilation process (for a C-mole of food) as a function of the DEB parameters y_{EX} and y_{PX}.

b Compute the stoichiometry for the dissipation process (for a C-mole of reserve).

c Compute the stoichiometry for the growth process (for a C-mole of reserve) as a function of the DEB parameters y_{VE}.

d What are the dimensions and the meaning of DEB parameters y_{EX}, y_{PX} and y_{VE}?

e What is the relationship between the fluxes feeding $\dot{J}_{XA}$, assimilation $\dot{J}_{EA}$, growth $\dot{J}_{EG}$ and dissipation $\dot{J}_D = \dot{J}_{ES} + \dot{J}_{EJ} + (1 - \kappa_R)\dot{J}_{ER}$ and the equations above? And between these mass fluxes and energy fluxes $\dot{p}_A$, $\dot{p}_G$ and $\dot{p}_D$?

f What is the total consumption of dioxygen as a function of $\dot{p}_A$, $\dot{p}_D$ and $\dot{p}_G$?

g Which assumptions are used in these expressions?

Hint:

What are the substrates and the products in each transformation? Use the conservation of chemical elements to obtain the stoichiometric coefficients. Is dioxygen substrate or product? What assumption about its availability is involved?

3.2.2 Question:

Is it really necessary to introduce a reserve pool to capture growth rate related changes in biomass composition?

Hint:

Suppose that food X of constant composition is transformed to biomass W in one step and that biomass at growth rate $\dot{r}$ and time t can be written as $M_W(t, \dot{r}) = M_V(t)\,(1 + m_E(\dot{r}))$ for some specified smooth function $m_E(\dot{r})$, where the composition of V and E is constant. This strong restriction of possibilities is based on the idea that if we cannot obtain the quantitative specification with the simplest change in composition, we cannot get it for more complex changes. Write out the macro-chemical reaction equation of the conversion of food to biomass and solve the specific growth rate, given an ingestion rate $\dot{J}_{XA}$.

3.3 Enzyme kinetics

Motivation:

The behaviour of Synthesizing Units will be a module in multivariate extensions of DEB theory. In its most basic form, it has a straightforward relationship with classic enzyme kinetics, but it is much easier to apply in complex situations, especially for systems that do not fully specify the fate of all intermediates and the overall transformation is not reversible. We discuss SUs at the beginning to show that univariate formulations are consistent with the more elaborate ones that will follow.

3.3.1 Question:

a When we increase the values for the turnover rates of the enzyme-substrate complexes in the transformation $1A + 1B \rightarrow 1C$, will the Rejection Unit resemble enzyme kinetics better than the Synthesizing Unit, or not?

b Why?

c What if we *de*crease the values?

Hint:

Use DEBtool, toolbox `enzyme`; edit `k_A` and `k_B` in `pars_enzyme.m` and increase the values. Run: `clear; pars_enzyme; shcontsu`. Does this affect the SU behaviour? Why?

3.3.2 Question:

a What is the largest relative difference between the SU's product formation rates of the transformation $n_A A + n_B B \to C$, given the substrate arrival fluxes $\dot{J}_A$ and $\dot{J}_B$, and of $1A + 1B \to C$, given the fluxes $\dot{J}_A/n_A$ and $\dot{J}_B/n_B$?

b For what ratio of arrival fluxes do you expect the largest relative difference?

c What is the significance of this result?

Hint:

Use DEBtool/enzyme routine `su` and try different values for n_A and n_B, starting with (1, 2), (2, 1), (2, 2), (1, 3), (2, 3), (3, 3). Calculate `(su(X_A/n_A, X_B/n_B, 1, 1) - su(X_A, X_B, n_A, n_B))/su(X_A, X_B, n_A, n_B)`. Observe that the problem is symmetric in the two substrates, and that the relative difference is most extreme for a particular ratio of substrate arrival rates, and a certain limiting case of these rates.

3.3.3 Question:

Can Liebig's law of a single limiting substrate be written as a limiting case of SU kinetics?

Hint:

How does the SU behave in the transformation $n_C n_A A + n_C n_B B \to n_C C$, for increasing values of n_C?

3.3.4 Question:

Compare the fractions of free-enzyme, and enzyme-substrate complexes for the SU, RU and classic enzyme, in the transformation $1A + 1B \to 1C$.

Hint:

Use DEBtool/enzyme routines `su11`, `ru11` and `enz11`, and select conditions where SUs and enzymes are close, and RUs and enzymes are close.

Given:

Suppose that we have a batch reactor with substrate A in concentration X_A, substrate B in concentration X_B, and enzyme that catalises the transformation $n_A A + n_B B \to C$.

3.3.5 Question:

What will be the end-result, and how long do we have to wait to approximate this result, if the enzyme behaves as a SU. Check your answer with DEBtool/enzyme routine `shbatch`.

Hint:

One of the substrates will not disappear completely; which one? Suppose that the other substrate limited the transformation completely. It then disappeared as a zero-th-order process, with what parameter? How long do we have to wait at least for almost complete disappearance if the disappearance rate did not decrease?

Given:

SU-dynamics are orderly, i.e. not more that one event can occur during a time increment. SUs bind irreversibly, i.e. substrates don't dissociate from the SU-substrate complex, only products can dissociate from the SU-product complex.

3.3.6 Question:

Figure 3.4 presents 4 basic classes of transformations $A + B \rightarrow C$. The changes in the fractions of bounded SUs can be written as $\frac{d}{dt}\boldsymbol{\theta} = \dot{\boldsymbol{k}}\boldsymbol{\theta}$. What are the 4 matrices $\dot{\boldsymbol{k}}$ for these classes?

Hint:

What are the possible states of the SUs in terms of fractions? Write out the changes of these states in terms of sources and sinks. Check that all fraction sum to 1, so the sum does not change.

Chapter 4

Univariate DEB models

4.1 Wood production

Motivation:

Some parts of organisms are neither reserve nor structure. Failure to recognize this easily leads to the conclusion that trees have exceptionally small specific maintenance costs, which they have not.

Given:

Peterson et al 1997, *Ecology and management of Sitka spruce*, UBC Press, Vancouver, present data for Queen Charlotte Islands in British Columbia showing that the height in m of *Picea sitchensis* grows von Bertalanffy, $L(t) = 56 - (56 - 12.5)\exp\{-0.02t\}$ for $t > 10\,\mathrm{a}$. The fit is so close that the data were probably generated by this relationship. Merchantable wood volume relates to height as $V = 35(L - 12.5)\,\mathrm{m}^3/\mathrm{ha}$ for $L > 12.5\,\mathrm{m}$, with about 350 trees per hectare.

4.1.1 Question:

How does the trunk diameter L_D grow? Make a plot.

Hint:

Assume that the trees' shape is somewhere between a cone and a pillar, so volume $V = \alpha L_D^2 L$, with $\pi < 12\alpha < 3\pi$. Write the von Bertalanffy growth in the differential equation $\frac{d}{dt}L = 0.02(56 - L)$, and consider $\frac{d}{dt}L_D$.

4.1.2 Question:

Can you link wood production to assimilation, maintenance and/or growth?

Hint:

Assume that trees in a forest behave as V0-morphs, so change in structural mass equals $\frac{d}{dt}M_V \propto M_{V\infty} - M_V$, see Eq. (4.10). Assume also that structural mass $M_V \propto L$. What is the asymptotic behaviour of wood production?

4.2 Carbon dioxide production

Motivation:

Some essential compounds that are taken up are also excreted, which might seem inefficient by human judgement. Photosynthesis is not the only process that fixes carbon dioxide. The stoichiometric macro-reaction equation can be decomposed into several constituting processes; the relative importance of these sub-processes depends on environmental conditions.

Given:

Methanotrophs use methane (CH_4) as energy source; methane is the only carbon source in Type I methanotrophs, such as *Methylomonas*, *Methylomicrobium*, *Methylobacter* and *Methyloccus*, which use the monophosphate pathway to process formaldehyde (CH_2O), a metabolite of methane. Methane and carbon dioxide (CO_2) are carbon sources for Type II methanotrophs, such as *Methylosinus* and *Methylocystis*, which use the serine pathway to process formaldehyde. These organisms can also fix di-nitrogen.

4.2.1 Question:

What are the contraints for the absence of carbon dioxide consumption *and* production for Type II methanotrophs under methane-limiting conditions, with ammonia as nitrogen source?

Hint:

The catabolic and anabolic aspects of assimilation can written as generalized transformations. We here use classic notation for chemical transformations with yield coefficient's Y_{**}, which are negative if one of the compounds disappears and the other appears; this is why yield coefficients on the right-hand side of the arrow have a minus-sign. This points to a notational problem that is hard to deal with in a consequent way, due to the various possible levels of organisation that can be considered. Yield coefficients Y are ratio's of fluxes, but notice that yield coefficients y_{**} have almost the same interpretation, but they are treated as positive constant mass-mass couplers. Specific fluxes j_* are here taken to be positive, although it might be better to take them negative if the compound disassears (but this has counter-intuitive consequences at other places.)

Assimilation energy generation at specific rate j^C_{XA}

$\mathrm{CH_4} + 2\,\mathrm{O_2} \rightarrow \mathrm{CO_2} + 2\,\mathrm{H_2O}$ (plain methane oxidation, as in your kitchen)

Assimilation Type I anabolism at specific rate j^A_{XA}

$$\mathrm{CH_4} + Y_{OX}\,\mathrm{O_2} \;+n_{NE}\,\mathrm{NH_3} \rightarrow \mathrm{CH}_{n_{HE}}\mathrm{O}_{n_{OE}}\mathrm{N}_{n_{NE}} \;-\; Y_{HX}\,\mathrm{H_2O}$$

$$\text{with} \left\{ \begin{array}{rcl} Y_{HX} &=& -2 + n_{HE}/2 - n_{NE}3/2 \\ Y_{OX} &=& -y_{HX}/2 + n_{OE}/2 \end{array} \right.$$

Assimilation Type II anabolism at specific rate j^A_{XA}

$$\mathrm{CH_4} + Y_{CX}\,\mathrm{CO_2} + Y_{OX}\,\mathrm{O_2} + n_{HE}\,\mathrm{NH_3} \;\rightarrow\; y'_{EX}\,\mathrm{CH}_{n_{HE}}\mathrm{O}_{n_{OE}}\mathrm{N}_{n_{NE}} \;-\; Y_{HX}\,\mathrm{H_2O}$$

$$\text{with} \left\{ \begin{array}{rcl} Y_{CX} &=& y'_{EX} - 1 \\ Y_{HX} &=& -2 - n_{HE}3/2 - n_{HE}\,y'_{EX}/2 \\ Y_{OX} &=& -Y_{CX} + n_{OE}\,y'_{EX}/2 - Y_{HX}/2 \end{array} \right.$$

Assimilation , total (for Type I and II methanotrophs) at specific rate $j_{XA} = j^C_{XA} + j^A_{XA}$

$$\mathrm{CH_4} + Y_{CX}\,\mathrm{CO_2} + Y_{OX}\,\mathrm{O_2} + n_{HE}\,\mathrm{NH_3} \;\rightarrow\; y_{EX}\,\mathrm{CH}_{n_{HE}}\mathrm{O}_{n_{OE}}\mathrm{N}_{n_{NE}} - Y_{HX}\,\mathrm{H_2O}$$

$$\text{with} \left\{ \begin{array}{rcl} Y_{CX} &=& y_{EX} - 1 \\ Y_{HX} &=& -2 - n_{HE}3/2 - n_{HE}\,y_{EX}/2 \\ Y_{OX} &=& -Y_{CX} + n_{OE}\,y_{EX}/2 - Y_{HX}/2 \end{array} \right.$$

The yield of reserve on substrate can be written as $Y_{EX} = -y_{EX} = -j^A_{XA}/j_{XA}$.

Apart from assimilation, which converts substrate, here methane $\mathrm{CH_4}$, into reserve $\mathrm{CH}_{n_{HE}}\mathrm{O}_{n_{OE}}\mathrm{N}_{n_{NE}}$, we have

Maintenance transformation at specific rate j_{EM}

$$\mathrm{CH}_{n_{HE}}\mathrm{O}_{n_{OE}}\mathrm{N}_{n_{NE}} + Y_{OE}\,\mathrm{O_2} \;\rightarrow\; \mathrm{CO_2} - Y_{HE}\,\mathrm{H_2O} + n_{NE}\,\mathrm{NH_3}$$

$$\text{with} \left\{ \begin{array}{rcl} Y_{HE} &=& n_{NE}3/2 - n_{HE}/2 \\ Y_{OE} &=& 1 - n_{OE}/2 - Y_{HE}/2 \end{array} \right.$$

Maintenance burns reserve, only minerals result,

Growth transformation at specific rate j_{EG}

$$\mathrm{CH}_{n_{HE}}\mathrm{O}_{n_{OE}}\mathrm{N}_{n_{NE}} + Y_{OE}\,\mathrm{O_2} \rightarrow$$
$$y_{VE}\,\mathrm{CH}_{n_{HV}}\mathrm{O}_{n_{OV}}\mathrm{N}_{n_{NV}} - Y_{CE}\,\mathrm{CO_2} - Y_{HE}\,\mathrm{H_2O} - Y_{NE}\,\mathrm{NH_3}$$

$$\text{with} \left\{ \begin{array}{rcl} Y_{CE} &=& y_{VE} - 1 \\ Y_{HE} &=& -n_{HE}/2 + n_{HV}\,y_{VE}/2 - Y_{NE}3/2 \\ Y_{OE} &=& -n_{OE}/2 + n_{OV}\,y_{VE}/2 - Y_{CE} - Y_{HE}/2 \\ Y_{NE} &=& -n_{NE} + n_{NV}\,y_{VE} \end{array} \right.$$

Growth transforms reserve into structure plus minerals. The latter not only result from stoichiometric constraints, but also represent overhead costs for growth. The growth process can be partitioned into catabolic and anabolic components $j^A_{EG} = y_{VE}j_{EG}$ and $j^C_{EG} = (1 - y_{VE})j_{EG}$, just like assimilation. The transformation of the catabolic component of growth is the same as that of maintenance, while the anabolic component does not generate carbon dioxide.

The Type II anabolic component of assimilation is the only process that fixes carbon dioxide. The yield of carbon dioxide on substrate, Y_{CX}, can be positive as well as negative. The total carbon dioxide flux is zero if:

$$0 = -Y_{CX}\, j_{XA} + j_{EM} - Y_{CE}\, j_{EG}$$

Write now the fluxes j_{XA}, j_{EM} and j_{EG} in terms of substrate availability. Consider steady states to symplify the result and use the decomposition of assimilation into a catabolic and anabolic component to judge whether or not the carbon dioxide flux *can* be zero.

4.3 Numerical behaviour of fluxes and states

Motivation:

The numerical behaviour of the standard DEB model for isomorphs is important to know when we want to go from data to model parameters. This knowledge can help to detect data sets that cannot be described by the model, which call for extra attention to the cause.

4.3.1 Question:

How do fluxes of compounds in and out the organism depend on food density? How do absolute fluxes compare with relative fluxes with respect to the amount of structure and to weight?

Hint:

Use DEBtool-animal routines "shflux", "shflux_struc", "shflux_weight" and "shpower", after editing the parameters values in "pars.m". Try to predict the effect of changes that you will see, before use actually see them. Can you explain the differences between structure-specific and weight-specific fluxes in early embryo's? Why can the relative growth of embryos be larger than that of juveniles?

4.3.2 Question:

a How do respiration ratios depend on body size and food density?

b How does this depend on the elemental composition of reserve and structure?

Hint:

Use DEBtool-animal routine "shratio", and edit the composition values in "pars_animal.m". Starting from an equal composition of reserve and structure, make the reserve richer in lipids than the structure, and predict the effect on the ratios before you see the result. The table 4.2 of the DEB book gives typical compositions of lipids and proteins.

4.3.3 Question:

Eggs have initially a certain amount of reserve, hardly any structure and zero maturity. How is this reserve spend at birth? In what respect differs foetal development from this pattern?

Hint:

What are the possible destinies of reserve? Is all reserve used? Does a foetus develop faster or slower than an egg? Why? Use DEBtool routine birth_pie and birth_pie_foetus in toolbox animal, but try to understand the result.

4.4 Practical identification of parameter values

Motivation:

Since quantities that are easy to measure (weight, respiration) have contributions from different processes, they cannot serve as variables in mechanistic models, while such variables (structure, reserve) can typically not be measured directly. This calls for auxiliary theory that links the easy-to-measure quantities to explanatory variables. See KooySous2008 for more details.

Given:

Suppose that a certain length measure has hardly contributions from reserve and that the standard DEB model applies with the somatic and maturity maintenance rate coefficients being equal, $\dot{k}_M = \dot{k}_J$, the surface-linked maintenance costs are absent $\{\dot{J}_{ET}\} = 0$, and the overhead costs of reproduction are 0.05, so $\kappa_R = 0.95$. At abundant food we measured length at birth $L_b = 1$ cm, ultimate length $L_\infty = 5$ cm, age at birth $a_b = 7$ d, von Bertalanffy growth rate $\dot{r}_B = 0.01$ d.

4.4.1 Question:

a What fraction of the initial reserve is left over at birth?

b What is this fraction for a scaled functional response $f = 0.7$, and what values for the measured quantities can we expect at this functional response?

Hint:

What is the implication of $\dot{k}_M = \dot{k}_J$? Which of the measured values depend on food availability? What do we need to obtain these values for other food availabilities? Look at `get_pars_g` and `iget_pars_g` in DEBtool/animal.

4.4.2 Question:

a If in addition to what is given in the previous question we measured a length at puberty of $L_p = 3$ cm and an ultimate reproduction rate of $0.7\,\mathrm{d}^{-1}$, what is the fraction of mobilised reserve that is allocated to somatic maintenance plus growth, and what is the energy conductance?

b Why is this fraction depending on the length at puberty?

Hint:

Look at `get_pars_r` .

Given:

Suppose that we have measured at abundant food ($f = 1$) length at birth $L_b = 4.4\,\mathrm{cm}$, length at puberty $L_p = 10.2\,\mathrm{cm}$, ultimate length $L_\infty = 55\,\mathrm{cm}$, von Bertalanffy growth rate $\dot{r}_B = 0.03\,\mathrm{d}^{-1}$, and ultimate reproduction rate $\dot{R} = 2.6\,\mathrm{d}^{-1}$. In addition we have measured at scaled functional response $f = 0.7$: $L_b = 4.4$ cm, $L_p = 10.1$, $L_\infty = 17.5\,\mathrm{cm}$, $\dot{r}_B = 0.042\,\mathrm{d}^{-1}$ and ultimate reproduction rate $\dot{R} = 1\,\mathrm{d}^{-1}$. We don't want to use information about age at birth, because we are not certain that our organism don't delay the start of the development. Again we assume that the standard DEB model applies, the surface-linked maintenance costs are absent $\{\dot{J}_{ET}\} = 0$, and the overhead costs of reproduction are 0.05, so $\kappa_R = 0.95$. This time, we don't want to make assumptions about the maturity maintenance costs relative to the somatic maintenance costs.

4.4.3 Question:

a What values have the following DEB parameters: fraction of mobilised reserve allocated to soma κ, energy investment ratio g, maturity and somatic maintenance rate coefficient $\dot{k}_J$ and $\dot{k}_M$, energy conductance $\dot{v}$, scaled maturity at birth and puberty $M_H^b/\{\dot{J}_{EAm}\}$ and $M_H^p/\{\dot{J}_{EAm}\}$?

b Which of these parameters depend on the shape of the organism, so on the definition of the length measure that we have used?

c What fractions of initial reserve are left over at birth?

Hint:

Look at `get_pars_s` in DEBtool/animal. The numerical procedure has a very small domain of attraction, so it might be difficult to find the answer; the initial conditions might need some editing in `get_pars_s`.

4.5 Parameter estimation

Motivation:

Understand some problem on parameter estimation; most applications of DEB theory require knowledge of parameter values.

Given:

Consider, for the sake of giving an example, the following data for *Homo sapiens* at abundant food living at constant temperature in the thermal neutral zone. The bold-typed values are just rough guesses based on scaling relations.

Length at birth	$50\,\mathrm{cm}$
Length at puberty	$150\,\mathrm{cm}$
Ultimate length	$180\,\mathrm{cm}$
Wet weight at birth	$3500\,\mathrm{g}$
Wet weight at puberty	$45000\,\mathrm{g}$
Ultimate wet weight	$85000\,\mathrm{g}$
Age at birth	$266\,\mathrm{d}$
Age at puberty	$12 \times 365\,\mathrm{d}$
Daily energy intake at ultimate length	$2500 \times 4.18\,\mathrm{kJ\,d^{-1}}$
Density of dry biomass	$0.125\,\mathrm{g\,cm^{-3}}$
Composition of dry structure	$CH_2O_{0.5}N_{0.15}$
Composition of dry reserve	$CH_{1.8}O_{0.5}N_{0.15}$
Yield of food on reserve y_{XE}	$\mathbf{1.3}\,\mathrm{mol\,mol^{-1}}$
Yield of reserve on structure y_{EV}	$\mathbf{1.2}\,\mathrm{mol\,mol^{-1}}$
Fraction of mobilised reserve allocated to soma	$\mathbf{0.8}$

The wet weight - dry weight ratio is 8.

4.5.1 Question:

a Using only the given observations, estimate shape coefficient $\delta_{\mathcal{M}}$, specific somatic maintenance rate $[\dot{p}_M]$ specific costs for structure $[E_G]$ energy conductance $\dot{v}$, maximum specific assimilation rate $\dot{p}_{Am}$, chemical potential for reserve μ_E, maturity maintenance rate coefficient $\dot{k}_J$, maturity threshold at birth E_H^b, maturity threshold at puberty E_H^p,

b Estimate the wet weights at birth, puberty and ultimate length.

c Are they reasonable? If not, redo the calculations with new values for any of the parameters highlighted (in bold) in the table.

d What fraction of weight represents reserve?

Hint:

Write a subroutine for `nmregr` that gives the expected observations as function of the parameters that must be estimated and obtain all estimates simultaneously. To find initial estimates, first use the observations one by one to get an approximation (and an understanding of the relationships). What are the implications of temperature being constant and of living in the thermal neutral zone? How does age relate to size at birth for foetal developmetn? What is the von Bertalanffy growth rate in terms of the parameters that must be estimated? How can this help to get length and age at at puberty? How does physical length relate to structural (volumetric length)? How does the energy investment ratio g relate the chemical potential of reserve μ_E? How does the maximum specific assimilation relate to the maximum food intake rate?

Chapter 5

Multivariate DEB models

5.1 Simultaneous nutrient limitation

Motivation:

Most literature deals with population rather than system dynamics, and is sloppy with the treatment of nutrients. This is partly due to the absence of proper nutrient balances for most models.

5.1.1 Question:

What is the effect of the metabolic availability of excreted nutrients on chemostat dynamics?

Hint:

Use DEBtool-alga routine "shchem" and "shchem1" for the comparison.

5.1.2 Question:

When can we expect situations where reserve densities *in*crease for *de*creasing growth rates?

Hint:

Use DEBtool-alga routine "shchem" and "shchem1" for the comparison. Look for effects of the excretion parameters.

5.2 Plant physiology

Motivation:

Plants are difficult to model, due to their plasticity of responses to environmental factors (light, water, nutrients). Many of such responses follow from simple allocation rules, and do not need explicit regulatory mechanisms to mimic such responses in a DEB-based model.

5.2.1 Question:

How do plants react to reductions of light and water in terms of growth of roots and shoots, and changes in the ratio of shoot over root biomass?

Hint:

Use DEBtool-plant routine "shtime" to see such affects. Try to predict them before you play with parameter values.

5.2.2 Question:

Most flowering plants first produce one or two special leaves after germination, which are very rich in reserves. These leaves, named cotyledons, usually differ in shape from normal leaves. Can you find this back in the simulation? Does the occurrence of a peak in reserve density depend on combinations of parameter values?

Hint:

Use DEBtool-plant routine "shtime" to see such affects.

5.3 Kidney size and function

Motivation:

Rules for substrate uptake and use of individuals imply constraints for lower levels of organisation. Surface area/volume relationships are basic for understanding the quatitative aspects of metabolism at all levels of organisation.

Given:

The primary function of kidneys is to remove wastes that are dissolved in the body fluid of animals, especially nitrogen waste. Kidneys also have a function in the regulation the ion and water balance of the body. Adult human kidneys typically produce 160-180 litre of filtrate each day. Most of this is fed back to the body fluid, a fraction of 0.005 typically ends up as urine.

The two kidneys of vertebrates have a particular anatomy. The central tissue consists of the medulla, where most of the reabsorption occurs, and the renal pelvis, that collects fluids for the ureter, i.e. the outgoing tube that feeds the bladder. Kidneys' peripheral tissue consists of the cortex, where the filtering occurs.

5.3.1 Question:

a How relates kidney function to kidney size in a strict isomorph?

b What are the constraints for a constant work load for the cortex?

Hint:

Focus on the maximum nitrogen removal rate, which occurs during maximum feeding rate, so $f = 1$. Write it as a weighted sum of squared and cubed body length. Assume that kidney volume is isomorphic and write the volume of the cortex as a weighted sum of squared and cubed kidney length. The latter is proportional to body length. Equate the weight coefficients for squared length for removal to that for size. Do this also for the weight coefficients for cubed length. This give a constraint for the relative size of the cortex in terms of parameter values.

Chapter 6

Effects of compounds on budgets

6.1 Ageing

Motivation:

Ageing, as a module in DEB theory, is an effect of free radicals that applies most organisms.

Given:

The growth period is short relative to the life span.

6.1.1 Question:

a How many parameters has the ageing module of the standard DEB model?

b How many parameters have the Weibull and the Gompertz models for ageing?

c How can both these different models be special cases of the DEB module?

d Which species are affected by ageing?

Hint:

What does plasticity mean for a model? See section 1.9 of the document Basic methods in Theoretical Biology on 'Realism'.

6.2 Toxicokinetics

Motivation:

Effects are linked to internal concentrations. First order accumulation/elimination is the most simple and basic kinetics, on which countless variations can be based.

Given:

Suppose that we have measured the intenal concentrations 0, 3, 4, 4.5, 4.75, and 4.9 mmol/g during 0, 1, 2, 3, 4, and 5 days of exposure to a compound with external concentration of 1 mM.

6.2.1 Question:

a Give an estimate for the elimination rate and the Bio-Concentration Factor.

b How accurate are these estimates?

Hint:

Use DEBtool/tox/acc for the regression model.

Given:

Suppose that we also have measured the internal concentrations 5, 3, 2, 1, 0.5, 0.25 mmol/g during 0, 1, 2, 3, 4, and 5 days of elimination, where the compound has been absent in the environment.

6.2.2 Question:

a What are the estimates for the elimination rate and the Bio Concentration Factor, using this extra information?

b How accurate are these estimates?

Given:

Two data sets of internal concentrations at a constant concentration of some compound in the water in small and larger test animals at 0, 1, 2, 3, 4, 5 days: 0, 3.1 , 5.9, 8.1, 9., 9.5 μM/g for the small ones and 0, 2.9, 5.7, 7.9 8.9 9.4 μM/g for the larger ones.

6.2.3 Question:

Do the accumulation and elimination rates differ significantly?

Hint:

If they differ, is it likely that the BCF is equal? Fit the two curves under the nill and the alternative hypothesis, and compare the differences in goodness of fit.

6.3 Concentration-Survival relationships

Motivation:

Current practice is to standardize the exposure period to a test compound and use the data at the end of the bioassay only. This means that hardly anything is known about the dynamic aspects of toxic effects.

Given:

The exposure time of 1 day, to a test compound at concentrations 0, 1, 2, 4, 8, 16 mM, and surviving individuals 10, 9, 10, 8, 4, 1, starting with 10 individuals in all concentrations.

6.3.1 Question:

Determine the NEC and the LC50.

Hint:

Use DEBtox or DEBtool/tox/fomort and DEBtool/tox/lc50.

6.3.2 Question:

What would be the toxicity parameters if the exposure period was not 1 day, but 2 days?

6.3.3 Question:

What would be the toxicity parameters if the concentrations are multiplied by a factor x?

Given:

Suppose that survival at 5 mM is monitored only. The observed number of survivors at exposure times 0, 1, 2, 3, 4, 5 days is 100, 69, 17, 3, 0, 0.

6.3.4 Question:

What are the NEC and the LC50 if blank mortality can be excluded?

6.4 Extrapolation from acute to chronic LC50 values

Motivation:

Many bioassays concern short-term exposures to compounds, while the actual interest is frequently in long-term effects.

Given:

Two sets of LC50 values for 1, 2 and 3 days of exposure to a compound in mg/l: 23.5, 8, 4.5 for set 1 and 23.5, 7.9, 4.5 for set 2.

6.4.1 Question:

Which of these sets has the lowest LC50? (Don't calculate them; just look at the data.)

Hint:

The LC50.1d and LC50.3d are the same for these sets, only the LC50.2d differs a little.

6.4.2 Question:

What is the LC50.4d and the ultimate LC50 for the two sets?

Hint:

First obtain the parameter values using DEBtool/tox/lc503, then use lc50 to obtain the values for 4d. Do we need to calculate the ultimate LC50?

6.4.3 Question:

a Can you make a plot for the two sets where the data points and the predicted lc50-time curves are shown?

b What is the mean squared deviation of the data from the curve?

Hint:

Use DEBtool/lib/regr/shregr for this purpose; Don't forget to make a path to this sub-directory.

6.4.4 Question:

What is the best estimate for LC50.5d and LC50.6d if LC50.4d = 3 mg/l, given data set 1?

Hint:

Use DEBtool/lib/regr/nrregr to estimate the parameters, then lc50 to obtain the LC50.5d. Check the result graphically.

6.5 Extrapolation of effects from one compound to that of another

Motivation:

For an optimal experimental design, not-yet-known effect levels of a compound must be guessed from known effects of another compound, with a similar mode of action; such expectations can also be useful for environmental risk assessment, in absence of adequate data. We here deal with effects on survival on the same test species and otherwise identical conditions.

Given:

The $P_{ow} = 10^7$, NEC = 1 mg/l, killing rate = $1\,\mathrm{mg}^{-1}\,\mathrm{l}\,\mathrm{d}^{-1}$ and elimination rate = 0.01 d^{-1} for compound 1, and the $P_{ow} = 10^8$ for compound 2.

6.5.1 Question:

What is the expected LC50.2d for compound 2?

Hint:

First obtain the three toxicity parameters for compound 2, then use these values to obtain the LC50.2d using DEBtool's function lc50.

6.6 Effects of pH on toxicity

Motivation:

Quite a few chemical compounds tend to ionize in water, and affect the pH. The toxicity of the molecular and the ionic form are not necessarily ideltical. The response surface of such compounds differs from that of non-ionizing compounds.

Given:

The ionization product constant is 8.0, observation times [0 1 2 3 4] days, the concentrations [0 2 4 8 16] mM, the pH values [7.8 7.7 7.4 7.0 6.5] and the number of surviving individuals

10	10	10	10	10
10	10	10	9	1
10	10	10	1	0
10	10	5	0	0
10	10	1	0	0

6.6.1 Question:

What are the NECs of the molecular and the inonic forms?

Hint:

Use DEBtool/tox/formortph; inspect mydata_fomortph for an example of application.

6.7 Effects on reproduction

Motivation:

Reproduction is frequently most sensitive to toxic agents. Several modes of action can be delineated.

Given:

The cumulative number of offspring per female daphnid at 21 d, for concentrations concentration 0, 1, 2, 4, 16 mM are 600, 650, 550, 40, and 2, for the different concentrations. The following physiological parameters are known: the von Bertalanffy growth rate is $0.1\,\mathrm{d}^{-1}$, the scaled length at birth is 0.13, and at puberty 0.42, and the energy investment ratio is 1.

6.7.1 Question:

Calculate the NEC and the EC50 for the different modes of action (assimilation rate, maintenance costs, growth costs, reproduction costs, neonate survival). How does the EC50 behave as a function of exposure time?

Hint:

Use DEBtox; fill data, select mode of action, press flag to start calculations; look under "statistics" to obtain EC50, change number of days to see ultimate EC50. Change mode of action and repeat. Notice that the data information is extremely small in this case (no information how effects built up in time, so the shape of the dose-response curve is the only source of information for the elimination rate), which makes the numerical procedures somewhat tricky and the standard deviations unreliable.

6.8 Interpolation methods for sublethal effects

Motivation:

Fitting a sigmoid curve (usually the log-logistic one) to response data and obtaining an ECx from that is still popular practice. The result becomes sensitive to the model choice

if x deviates from 50 %. The goodness of fit is just one criterion to test the "validity" of the model, and this criterion is not the strongest one. Consistency arguments come first in importance.

Given:

A 36 d body growth test on fish; we fit a log-logistic curve to the body length as a function of the concentration test compound. So $L(c,t) = L_{0,t}\left(1 + (c/c_{e,t})^{\beta_t}\right)^{-1}$, where the blank body length $L_{0,t}$, the EC50 $c_{e,t}$ and the slope parameter β_t are parameters, which can (in principle) all depend on exposure time t.

6.8.1 Question:

If the concentration-response curve happens to be log-logistic at 36 d as well as e.g. at 37 d, what are the implicit assumptions about the growth process?

Given:

A 21 d *Daphnia* reproduction test; we fit a log-logistic curve to the cumulative number of offspring per female as a function of the concentration test compound. So $N(c,t) = N_{0,t}\left(1 + (c/c_{e,t})^{\beta_t}\right)^{-1}$, where the blank number $N_{0,t}$, the EC50 $c_{e,t}$ and the slope parameter β_t are parameters, which can (in principle) all depend on exposure time t. Also is given that the reproduction rate around 21 d is constant for each female in the blank.

6.8.2 Question:

If the concentration-response curve happens to be log-logistic at 21 d, will it be still log-logistic at 22 d (with possibly different parameters)?

Hint:

Make use of the fact that the reproduction rates become constant and that toxicity parameters should not depend on blank parameters.

6.9 Effects on populations

Motivation:

Although most ecotoxicity tests focus on effects on individuals, the societal interest is in that on populations (and ecosystems). Population consequences can be derived theoretically from effects on individuals, but for a few species (algae, bacteria, duck weed) standardized bioassays directly deal with populations.

Given:

The inoculated population density is 10^3 cells/ml. After 2 days, the population densities in concentrations 0, 1, 2, 4, 8, 16 mM were 100, 109, 98, 60, 10 and 2 times 10^3 cells/ml.

6.9.1 Question:

Give the NEC, the EC50.2d and the EC50.∞d if the compound would affect initial mortality, mortality or the growth rate.

Hint:

Use DEBtox and select the various modes of action. The "adaptation" model assumes initial mortality only; the "hazard" model assumes that mortality continues during exposure.

6.9.2 Question:

Does the population always grow exponentially for all modes of action?

Hint:

What do we mean by exponentially growing populations? The growth of living cells, of the change of the measured densities? Do the measurements represent the number of living cells?

Chapter 7

Extensions of DEB models

7.1 Responses to starvation

Motivation:

The response to starvation is basic to life and to DEB models. The two classes of DEB models, production and assimilation models, differ most in the implementation of responses to starvation, as is discussed in chapter 11.

7.1.1 Question:

Rank the different responses to starvation with respect to the length of the starvation period or the increased saving of reserves.

Hint:

These responses to starvation area discussed in section 4.1.

7.2 Stomach dynamics

Motivation:

Some implications of the DEB theory are really straightforeward, and worth noticing for creative use of the concepts.

Given:

Suppose that stomach dynamics follows a first order dynamics as given by (7.66).

7.2.1 Question:

How long does it take to empty a fully filled stomach to $100\alpha\%$ while starving?

Hint:

What is the value for the scaled functional response f during starvation? Can you solve the ordinary differential equation for stomach contents as a function of time? Solve the equation where stomach contents equals α times its original value.

7.2.2 Question:

How does the gut residence time behave as a function of structural volume?

Hint:

Use eqn (3.6) on {81}.

7.2.3 Question:

Suppose that an adult human mother weighs 64 kg, and her baby 4 kg. The mother eats three times a day. How frequently should a baby eat to experience similar fluctuations in stomach and gut contents?

Hint:

Suppose that food density is constant or high; does the ratio of weights equal the ratio of structural volumes? Are any parameters left in the ratio of the waiting times till a certain fraction of the initial stomach filling?

Chapter 8

Co-variation of parameters

8.1 Identification of primary parameters

Motivation:

Which parameters are primary and which are compound is, from a mathematical perspective, arbitrary, but not from a biological one.

Given:

The standard DEB model applies.

8.1.1 Question:

Which parameters are primary and which are compound and why in the following cases?

a What is the relationship between the half saturation coefficient K, the maximum specific feeding rate $\{\dot{J}_{XAm}\}$, and the maximum specific searching rate $\{\dot{F}_m\}$?

b What is the relationship between the maximum specific feeding rate $\{\dot{J}_{XAm}\}$, the maximum specific assimilation rate $\{\dot{J}_{EAm}\}$ and the yield of reserve on food y_{EX}?

c What is the relationship between the energy conductance $\dot{v}$, the maximum specific assimilation rate $\{\dot{J}_{EAm}\}$ and the maximum reserve capacity $[E_m]$?

Hint:

Are the parameters intensive or design parameters? How does this relate to the choice for primary versus compound parameters?

8.2 Scaling relationships

Motivation:

The implied scaling relationships are very powerful properties in applications of DEB theory.

8.2.1 Question:

What are the three properties of the standard DEB model that imply the scaling relationships with no degree of freedom?

Hint:

The standard DEB model is mechanistic, meaning that all its parameters have a clear relationship with the underlying physics and chemistry. This allows a classification of parameters in two categories. Which categories?

8.2.2 Question:

What are the assumptions in the standard toxicity module of DEB theory that specify how (lethal and sublethal) effects of chemicals vary with the partition coefficient?

Hint:

How are such effects specified for a single chemical compound? What is fugacity?

8.3 Effect of changes in parameter values

Motivation:

Scaling relationships for the standard DEB model depend on parameter values of the reference, so a 'typical' isomorph; a correct prediction of trends in parameter values among (isomorphic) species is essential for all useful models for eco-energetics.

8.3.1 Question:

Can you predict affects of changes in parameter values on body size scaling relationships of isomorphs? Have special attention for κ and the maintenance costs.

Hint:

Use DEBtool-animal routine "shscale". Have a look at the manual for odd effects of the size of the window that you are using on the appearance of log-log plots. The book gives more relationships and the book is not exhaustive too.

Chapter 9

Living together

9.1 Chemostat dynamics

Motivation:

Chemostats are attractive for their symplicity as a system, and as a device to obtain biological material with a prescibed physiological state. Yet their dynamics is sometimes counter-intuitive. DEB theory can be used for very practical purposes, such a optimisation of industrial bioproduction.

9.1.1 Question:

a How does the biomass at equilibrium depend on small throughput rates?

b How does this behaviour depend on the maintenance costs?

Hint:

Use DEBtool-microbe routine "shchemostat", after changing the maintenance costs in the parameter file "pars.m".

9.1.2 Question:

a How does the equilibrium concentration of product depend on the throughput rate?

b Can the relationship have more than one optimum?

Hint:

Modify the coefficients that relate product formation to assimilation, maintenance and growth. Try (small) negative values for coupling to assimilation and growth.

9.1.3 Question:

Can you work out a scheme for optimal product (e.g. penicillin) formation in terms of financial costs and profits?

Hint:

Assign financial costs for substrate and medium in the input, and product and biomass in the output. Make a few simplifying assumptions, such as the costs of processing product and biomass are independent of the concentration (or density), the costs associated with substrate in the effluent and with stirring and cooling is zero. The financial costs for biomass can be positive or negative, depending on its fate. Optimize the result as function of the concentration of substrate in the feed, the throughput rate and the size of the reactor.

9.1.4 Question:

Can you relate the fluxes to and from the chemostat at steady state to the concentrations of substrate, biomass and product; How does this compare to the fluxes to and from a isomorph?

Hint:

Use DEBtool-microbe routine "shflux" to study the numerical behaviour of fluxes to and from the chemostat, and compare with DEBtool-animal routine "shflux" for isomorphs. Notice that the fluxes are plotted against the throughput rate for chemostats, and against scaled length for isomorphs.

9.2 Alga-grazer systems

Motivation:

Nutrient limited prey-predator systems can make a smooth transition to a symbiosis, due to the excretion of carbohydrates and nutrients. The dynamics of these compounds affect the prey-predator dynamics profoundly, which makes studies of prey-predator without nutrient dynamics rather academic.

9.2.1 Question:

What is the affect of a decrease in grazing activity at constant affinity for dissolved nutrients, hydrocarbons and substrate in a alga-grazer community that lives in a chemostat with a constant input of substrate and nutrient?

Hint:

Use DEBtool-symbi routines “shsubstr2graz” and “shthrou2graz” to study effects of varying grazing intensity, substrate input and throughput rates. These routines take a considerable amount of computing time.

Chapter 10

Evolution

10.1 Homeostasis

Motivation:

DEB theory is basically about the evolution of homeostasis. To capture the gradual process of its evolutionary ontogeny, the theory delineates 5 types in Section 1.2: strong, weak, structural, thermal and acquisition. The list could be extended with the reduction of the number of reserves.

10.1.1 Question:

Why do bacteria need many reverse and animals, which evolved from them, only one?

Hint:

What is the primary function of reserve and how does this relate to types of substrate?

10.2 Reorganisation

Motivation:

As a consequence of an increasing homeostasis during evolution, life did become increasing depending on itself and symbiosis became increasingly important.

10.2.1 Question:

Why are the processes of partitionning and merging of reserves key to evolution?

Hint:

What do theses processes mean?

10.3 Evolutionary memory

Motivation:

The reason why a metabolic system functions in a particular way is because it evolved from earlier metabolic systems.

10.3.1 Question:

Give an animal and a plant example that illustrates its evolutionary history.

Hint:

Many examples could be given. What was the diet of the first mammals? Are all plants green?

Chapter 11

Evaluation

11.1 Empirical evidence

Motivation:

Explore the links between empirical evidence and DEB theory

Given:

The list of empirical facts, as presented in Table 11.1 of the comments on the DEB book.

11.1.1 Question:

Explain why the empirical evidence F2, G1 and O4 is compatible with the standard DEB model.

Hint:

The most important aspects of the metabolic organization are here: the individual is composed of structure and reserve and the κ-rule.

11.2 Production versus assimilation models

Motivation:

Most models for energetics in the literature are time-dependent Static Energy Budget models, also known as net-production models or Scope for Growth (SfG) models.

11.2.1 Question:

a What is the characterizing property of production models?

b How do production models typically deal with overhead costs for growth?