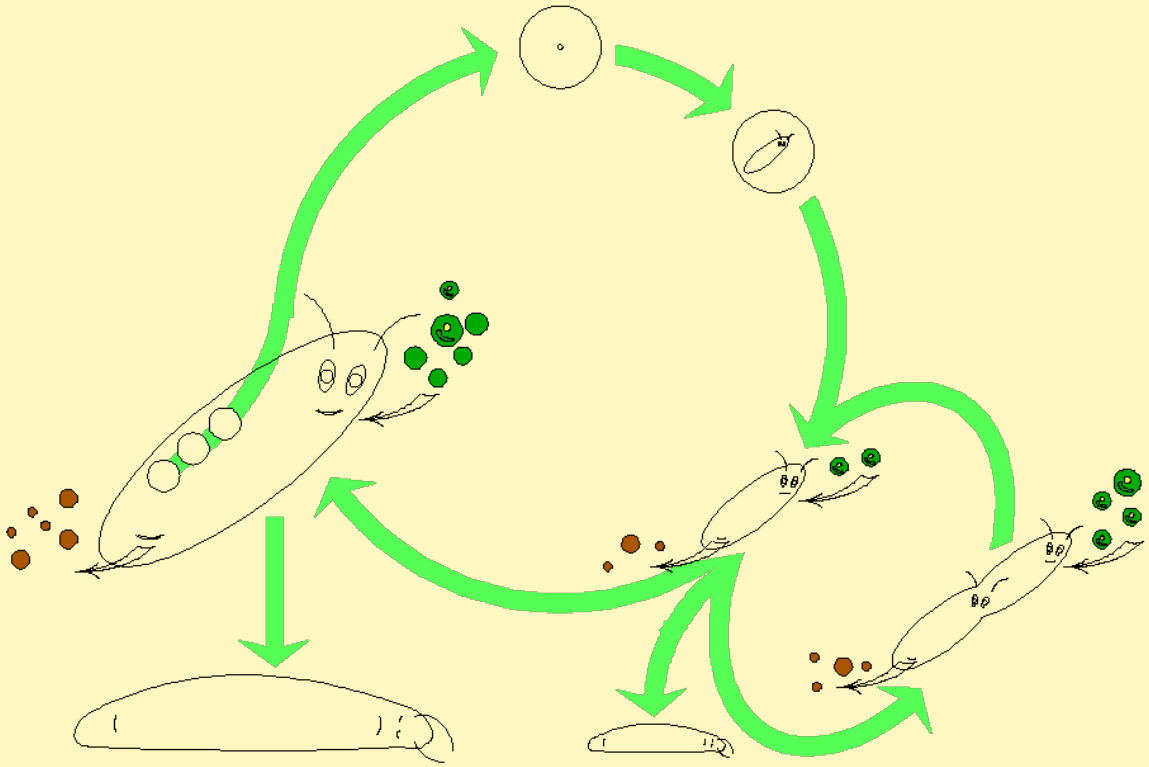
Exercises + answers for

Dynamic Energy Budget tele-course



DEB theory for metabolic organisation

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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.

Answer:

Formally: no problems if $\dim(b) = \sqrt{\text{time}}$ and $\dim(a) = \dim(y)/\sqrt{\text{time}}$. It is unlikely, however, that the model has a (simple) physical interpretation with such dimensions.

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?

Answer:

This model can have a simple physical interpretation if $\dim(c) = \text{time}$ and b is dimensionless, while $\dim(a) = \dim(y)\text{time}^{-1}$. More generally: $\dim(c) = \text{time}\ \dim(d)^2$, which implies $\dim(b) = \text{time}\ \dim(d)^{-1}$, where d has simple but otherwise arbitrary physical dimensions. The fitting of this model to data $\{t_i, y_i\}_{i=1}^n$ yields two parameters only, not three.

If you multiply a and b with a number and divide c by that number, y does not change.

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.

Answer:

$\dim K = \dim(S)$ because $f = \frac{S}{S+K}$
f is dimensionless because $f = \frac{S}{S+K}$
$\dim(j_S) = \dim(S)/(\text{time}\ \dim(X))$
$\dim(y_{XS}) = \dim(X)/\dim(S)$
$\dim(\dot{r}) = \text{time}^{-1}$

A possible choice for the dimension of S and X is: C-mol . length^{-3}. This does not imply, however, that y_{XS} is necessarily dimensionless; we have $\dim(y_{XS}) = \frac{\text{C-mol X}}{\text{C-mol S}}$ and $\dim(j_S) = \frac{\text{C-mol S}}{\text{time . C-mol X}}$.

0.2.2 Question:

What are the parameters of the model?

Hint:

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

Answer:

Five parameters: initial substrate concentration $S(0)$, initial population density $X(0)$, saturation coefficient K, max specific uptake rate j_S, yield coefficient y_{XS}.

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?

Answer:

The scaled system will have $5 - 3 = 2$ parameters, because we can (usually) remove one parameter per variable.

One choice for rescaling is: $s = S/K$, $x = X/(K\, y_{XS})$, $\tau = t\, j_S\, y_{XS}$. The system then becomes

$$\begin{aligned} \frac{d}{d\tau}s &= -fx \\ \frac{d}{d\tau}x &= fx \end{aligned}$$

with $f = \frac{s}{1+s}$ and two parameters: $s(0) = S(0)/K$, $x(0) = X(0)/(K\, y_{XS})$.

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.

Answer:

Since we have no information about $X(t)$, we choose $x = X/(K\, y_{XS})$.

$$\begin{aligned} \frac{d}{dt}S &= -\dot{r}_m K f x \\ \frac{d}{dt}x &= x f \dot{r}_m \end{aligned}$$

with four parameters: $S(0)$, $x(0)$, K, $\dot{r}_m = j_S\, y_{XS}$. The latter parameter has the interpretation of the maximum specific growth rate.

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 $x(0)$.

Answer:

Theoretically: yes, because we can estimate $x(0)$ and K, so $y_{XS} = X(0)/(K\,x(0))$. This is remarkable, because we have no direct measurements about the conversion from substrate to biomass. Practically, however, we will see that in presence of a little scatter, the uncertainty in the values for $x(0)$ and K is large, which makes the uncertainty in the value of y_{XS} huge. More elaborate models for biomass growth not necessarily allow to extract the conversion efficiency from these data.

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.

Answer:

$\dim(K) = \dim(X)$, because $f = \frac{X}{X+K}$.
f must be dimensionless, because $f = \frac{X}{X+K}$.
$\dim(L_b) = \dim(L) =$ length, because $L(0) = L_b$.
$\dim(L_m) = \dim(L) =$ length, because $L(\infty) = fL_m$, and f is dimensionless.
$\dim(\dot{r}_B) =$ time^{-1}, because $t\dot{r}_B$ must be dimensionless; it occurs as an argument of a transcendental function.
$\dim(\dot{k}_M) = \dim(\dot{r}_B) =$ time^{-1}, because $\dot{r}_B = (3/\dot{k}_M + 3fL_m/\dot{v})^{-1}$.
$\dim(\dot{v}) =$ length/time, because $\dim((fL_m/\dot{v})^{-1}) = \dim(\dot{r}_B) =$ time^{-1}.
g must be dimensionless because $\dim(\frac{\dot{v}}{g\dot{k}_M}) = \dim(L_m) =$ length; $\dim(\dot{v})$ and $\dim(\dot{k}_M)$ are known.

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?

Answer:

Three (compound) parameters only: L_b, fL_m and $\dot{r}_B$.

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?

Answer:

Five parameters are identifiable: L_b, K, $\dot{k}_M$, g and $\dot{v}$. Functions of these parameters, such as f, $\dot{r}_B$ and L_m are identifiable as well, obviously. The relationship between L and t gives information about L_b, $L(\infty)$ and $\dot{r}_B$ (see previous question); the relationship of $L(\infty)$ with X gives information about K and L_m; the relationship between $\dot{r}_B$ with $L(\infty)$ gives information about $\dot{k}_M$ and $\dot{v}$; the relationship between V_m and $\{\dot{v}, \dot{k}_M, g\}$ gives information about g. There might well be *practical* problems with obtaining these parameter values from the two data sets.

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?

Answer:

$\dim(d_V) = \dim(d_E) = \text{weight}\,.\,\text{length}^{-3}$. Six parameters: $\frac{d_V+f_1d_E}{d_V+f_2d_E}$, K, $(d_V + f_1d_E)V_b$, $V_b/(f_1^3V_m)$, $\dot{k}_M^{-1}+f_1V_m^{1/3}/\dot{v}$, $\dot{k}_M^{-1}+f_2V_m^{1/3}/\dot{v}$. In conclusion we can state that these compound parameters are not very informative.

The parameter $\dot{v}$ is not identifiable, because it has dimension length/ time, but no lengths are measured.

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?

Answer:

Six parameters are identifiable: d_VV_b, d_E/d_V, K, $\dot{k}_M$, g and $d_V^{1/3}\dot{v}$, or functions of these (compound) parameters. Knowledge about the values of X can be used in this case to obtain K and f; this is because the relationship between $W_b = (d_V + fd_E)V_b$ and X has three parameters, K, d_VV_b and d_EV_b, and we have three observations.

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.

Answer:

After setting the path to debtool/lib, the required code of a script file with the name `exer.m` should read something like this:

```
aL = [0 1; 1 4; 2 5; 3 5.5]; % age-length data

function L = bert(p,aL) % define the von Bert curve
L = p(2) - (p(2) - p(1)) * exp(-p(3) * aL(:,1));
end

p = nrregr('bert', [1 6 1]', aL); % estimate parameters
[cov, cor, sd] = pregr('bert', p, aL); % get standard deviation
[p, sd] % show result
shregr_options('default') % initiate plot settings
shregr('bert', p, aL) % make a plot
```

This should work when you save this script file and run `exer` in the directory where you parked `exer.m`. You can check the correct location by typing `ls`, which should list `exer.m`.

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.

Answer:

Inner product: x'*y. Outer product: x*y'.

0.5.2 Question:

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

Answer:

sum(x.*y). Notice that this equals x'*y.

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.

Answer:

Your function can look like this:

```
function [m, cov, cor] = mcc (x)
[n, k] = size(x);
m = sum(x,1)'/ n;
cov = x' * x/ n - m * m';
sd = diag(cov).^0.5
cor = cov./ (sd * sd');
endfunction
```

Fill variable x like: x = [1 1.5; 2 1.5; 3 2]
Run your function mcc like: [m, cov, cor] = mcc x
We get

$$m = \begin{pmatrix} 2.00 \\ 1.66 \end{pmatrix} \quad cov = \begin{pmatrix} 0.666 & 0.166 \\ 0.166 & 0.055 \end{pmatrix} \quad cor = \begin{pmatrix} 1.000 & 0.866 \\ 0.866 & 1.000 \end{pmatrix}$$

Notice that this function also works for more than 2 variables.

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.

Answer:

The ln likelihood function for data $\{x_i\}_{i=1}^n$ is $\ell(\lambda) = \ln\lambda \sum_{i=1}^n x_i - n\lambda - \sum_{i=1}^n \ln x_i!$. The ML-estimate is $\hat{\lambda} = \sum_i x_i/n$. The profile ln likelihood function is

$$\ell_p(\lambda) \quad = \quad 2(\ell(\hat{\lambda}) - \ell(\lambda)) = 2n(\lambda - \hat{\lambda}) - 2\ln(\lambda/\hat{\lambda}) \sum_{i=1}^n x_i = 2n\lambda - 2n\hat{\lambda}(1 + \ln(\lambda/\hat{\lambda}))$$

We have to subtract the first term in the second-order Tayler expansion and multiply by 2 to arrive at a function that is comparable with the profile ln likelihood function and obtain

$$\ell_t(\lambda) \quad = \quad (\lambda - \hat{\lambda})^2 \frac{d^2}{d\lambda^2}\ell_(\hat{\lambda}) = (\lambda - \hat{\lambda})^2 \hat{\lambda}^{-2} \sum_i x_i = n(\lambda - \hat{\lambda})^2/\hat{\lambda}$$

The 95% confidence interval is given by

$$\{\lambda | \ell_p(\lambda) < 3.8415\} \quad \text{or} \quad \{\lambda | \ell_t(\lambda) < 3.8415\}$$

Large sample theory has been applied here, so the results only holds for large n. Practice learns, however, that the first confidence interval is close to correct for much smaller values of n than the second interval. The practical problem is that the calculation of the profile likelihood function is generally computationally intensive.

The code can look like this: we create an empty script-file with the name prof.m and write in that file for Octave:

```
x = [3, 2, 4, 3]; % data
n = length(x); % number of data-points
lm = mean(x); % ML estimate for Poisson-parameter
l = linspace(0,3 * lm, 100); % vector of parameter values
f1 = 2 * n * l - 2 * n * lm * (1 + log(l/ lm)); % prof-lik function
f2 = n * (l - lm) .^ 2/ lm; % tangent parabola
plot(l, f1, 'g', l, f2, 'r', ... % plot functions in green and red
[0; 3 * lm], [3.84; 3.84], '6'); % draw line for conf. intervals in black
```

We now run the script-file by typing prof in the Octave comment-line.

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.

Answer:

We first specify the function for which we want to find the root. Your function looks like

```
function f = finda (a)
global x y;
[nx k] = size(x); [ny k] = size(y);
varx = sum((x(:,2) - a * x(:,1)).^2)/ nx;
vary = sum((y(:,2) - a * y(:,1)).^2)/ ny;
v = x(:,1)' * x(:,2)/varx + y(:,1)' * y(:,2)/ vary;
w = x(:,1)' * x(:,1)/varx + y(:,1)' * y(:,1)/ vary;
f = a - v/w;
end
```

Now we find the root and use your function like:

```
x = [1 2; 2 2.2; 3 2.3]; y = [2 5; 3 6; 4 6.1]; global x y;
[a, error] = fsolve('finda', 0.1)
[a, error] = fsolve('finda', 2)
```

Check the value of error to make sure that the numerical procedure converged. It can easily result in nonsense. Notice that the two calls have different results; the one with the highest value for the likelihood function is the proper estimate. Consult Matlabs' manual for 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?

Answer:

Physical length depends on shape and requires a definition of how the length is taken; volumetric length is independent of shape and represents the cubic root of the physical volume. Both reserve and structure contribute to physical volume; structural length is

the cubic root of structural volume. Isomorphy implies that physical length is proportional to volumetric length. Auxiliary theory assumes that a well-chosen physical length is proportional to structural 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).

Answer:

We should expect a rate of $0.2\exp(8000/(273+20) - 8000/(263+37))\,\mathrm{cm\,d^{-1}}$.

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?

Answer:

No, mussels and sparrows don't have the same shape, so a direct comparison of these rates makes no sense. We can remove the effect of shape by turning to volumetric lengths, but we still have the problem that mussels would rapidly die at 40°C, and a sparrow at 20°C. We can infer a theoretical Arrhenius temperature for the sparrow if we know some characteristic rate (such as the energy conductance) for the mussel at 20° and the sparrow

at 41°C, and assume that they are the same for both species. This Arrhenius temperature can then be used to make the comparison, given that our assumption holds.

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.

Answer:

Let $h = k = 0$, and $b = a$, so $x^2 - y^2 = a^2$. Introduce $v = x + y$ and $w = x - y$, so $x = (v + w)/2$ and $y = (v - w)/2$. Substitution gives $vw = a^2$. Translate $v = X + K$,

$v = 1 - Y$ and set $a^2 = K$, which results in $(1 - Y)(X + K) = K$, or $X = Y(X + K)$, or $Y = (1 + K/X)^{-1}$.

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 $y = \exp\{-ct\}$.

Answer:

$\frac{\partial z}{\partial x} = ay(t)$ and $\frac{\partial z}{\partial y} = ax(t)$; $\frac{dx}{dt} = b$ and $\frac{dy}{dt} = -c\exp\{-ct\}$, so $\frac{dz}{dt} = ab\exp\{-ct\}(1 - ct)$.

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

$$\begin{array}{lrcl} 1: & f(x,y) & = & x^3 - 3xy^2 + y^3 \\ 2: & f(x,y) & = & \dfrac{xy}{\sqrt{x^2+y^2}} \\ 3: & f(x,y) & = & \exp\{x/y\} \end{array}$$

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

Answer:

1 degree 3

2 degree 1

3 degree 0

4 degree 3

5 degree 3:

6 degree 1:

7 non-homogeneous

8 degree 0:

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 $t = 1$.

Answer:

Let $g(t) = f(tx,ty) = t^n f(x,y)$ and introduce $x = tX$ and $y = tY$. Use the chain rule for differentiation to prove that

$$\frac{d}{dt}g(t) = nt^{n-1}f(X,Y) = X\frac{\partial}{\partial x}f(tX,tY) + Y\frac{\partial}{\partial y}f(tX,tY)$$

then let $t = 1$.

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.

Answer:

Structural mass M_V relates to structural volume V as $M_V = [M_V]V$, where $[M_V]$ is constant due to the assumption of strong homeostasis. So $\dot{r} = M_V^{-1}\frac{d}{dt}M_V = V^{-1}\frac{d}{dt}V$. Structural (volumetric) length L relates to structural volume V as $V = L^3$ by definition. Since $\frac{d}{dt}V = \frac{d}{dt}L^3 = 3L^2\frac{d}{dt}L$, we have $\dot{r} = 3L^{-1}\frac{d}{dt}L$. The change in reserve density is

$$\begin{aligned}\frac{d}{dt}m_E &= M_V^{-1}\frac{d}{dt}M_E - \dot{r}m_E \\ &= j_{EA} - M_V^{-1}M_E(\frac{\dot{v}}{L} - \dot{r}) - \dot{r}m_E \quad \text{for } j_{EA} = \dot{J}_{EA}/M_V \\ &= j_{EA} - m_E\frac{\dot{v}}{L}\end{aligned}$$

No change in reserve density occurs if $m_E = j_{EA}L/\dot{v}$. It remains constant during growth (of juveniles and adults) if $j_{EA} \propto L$ and the proportionality factor is constant. This holds if $\dot{J}_{EA} \propto L^2$ and food density remains constant. DEB theory assumes that $\dot{J}_{EA} = f\{\dot{J}_{EAm}\}L^2$, where the scaled functional response is a function of food density, with a maximum of 1 and the proportionality factor $\{\dot{J}_{EAm}\}$ is constant. Reserve density in juveniles and adults is at maximum at steady state if assimilation is at maximum; For $M_V = [M_V]L^3$ it then has value $m_{Em} = \frac{j_{EAm}L}{\dot{v}} = \frac{\dot{J}_{EAm}L}{M_V\dot{v}} = \frac{\{\dot{J}_{EAm}\}L^3}{[M_V]L^3\dot{v}} = \frac{\{\dot{J}_{EAm}\}}{[M_V]\dot{v}}$. Weak homeostasis means that the chemical composition of the whole body (reserve and structure) remain constant during growth at constant food density. This reserve dynamics as function of the states of the individual (amounts of reserve and structure) is the only one that satisfies this condition. The assumptions behind this reserve dynamics are

1 food is first converted to reserve that is mobilised

2 the mobilisation rate only depends on the state of the individual: amounts of reserve and structure

3 reserve and structure obey strong homeostasis

4 the individual is isomorphic

5 weak homeostasis applies

The difference with first order dynamics is in the dilution by growth. First order dynamics would result in $\dot{J}_{EC} = M_E\frac{\dot{v}}{L}$ rather than $\dot{J}_{EC} = M_E(\frac{\dot{v}}{L} - \dot{r})$. Since the DEB reserve dynamics uniquely follows from assumption 1-5, first order dynamics is not weakly homeostatic, even if assumptions 1-4 apply. The mean residence time of a molecule in reserve is $\frac{M_E}{\dot{J}_{EC}} = \frac{M_E}{M_E(\frac{\dot{v}}{L} - \dot{r})} = (\frac{\dot{v}}{L} - \dot{r})^{-1}$. Notice that is time decreases with increasing length.

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.

Answer:

At constant food, length changes as $\frac{d}{dt}L = \dot{r}_B(L_\infty - L)$, so $\frac{d^2}{dt^2}L = -\dot{r}_B^2(L_\infty - L)$. Since the latter continuously decreases, growth in length is maximal at birth, so $L = L_b$.

Weight is proportional to cubed length, and cubed length changes as $\frac{d}{dt}L^3 = 3L^2\frac{d}{dt}L = 3L^2\dot{r}_B(L_\infty - L)$ and $\frac{d^2}{dt^2}L^3 = 3\dot{r}_B^2(L_\infty - L)(2L_\infty - 3L)$. The latter equals zero if $L = \frac{2}{3}L_\infty$, so growth in weight is maximal at $L = \max(L_b, \frac{2}{3}L_\infty)$.

Relative growth of length is maximal if $\frac{d}{dt}\left(L^{-1}\frac{d}{dt}L\right) = 0$, i.e. if $L\frac{d^2}{dt^2}L = \left(\frac{d}{dt}L\right)^2$. Substitution shows that the equation has no meaningful solution, while the relative growth in length only decreases. This implies that it is maximal at birth.

Relative growth of weight is maximal if $\frac{d}{dt}\left(L^{-3}\frac{d}{dt}L^3\right) = 0$, which leads to the same result as for relative growth of length.

Notice that growth of length and weight behave quite differently, but relative growth of length and weight are behave quite similar.

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.

Answer:

Observe that lengths and reproduction satiate monotoneously to an asymptotic value for isomorphs at constant food, while weight-curves are sigmoidal, because they relate to cubed length. Also observe that organisms do not complete the juvenile stage at low food levels.

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.

Answer:

Allocation to reproduction is in continuous time, so allocation per time increment is incrementally small only, not sufficient to produce an embryo. Buffer handling rule can span a wide spectrum:

- some rotifers produce on egg after the other.
- waterfleas produce eggs clutch-wise, coupled to the moulting cycle.
- mussels spawn once a year, coupled to the season.
- albatrosses nest every other year.
- bamboo trees set seed once every seven or so years.

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?

Answer:

If we exclude contributions from the reproduction buffer to weight for simplicity's sake, the relationship between mass in gram and C-mole is for $* = E, V$

$$\begin{aligned} W_d &= w_E M_E + w_V M_V; \quad w_* = 12 n_{C*} + 1 n_{H*} + 16 n_{O*} + 14 n_{N*} \\ W_w &= w_E^w M_E + w_V^w M_V; \quad w_*^w = 12 n_{C*} + 1 n_{H*}^w + 16 n_{O*}^w + 14 n_{N*} \end{aligned}$$

where $n_{CE} = n_{CV} = 1$ per definition (of C-mole) and $n^w_{HE} = n_{HE} + 2x_E$, $n^w_{OE} = n_{OE} + x_E$, $n^w_{HV} = n_{HV} + 2x_V$, $n^w_{OV} = n_{OV} + x_V$. So $w_E + 18x_E = w^w_E$ and $w_V + 18x_V = w^w_V$. Notice that water does not affect the quantification of mass in C-moles (M_E and M_V), only the molecular weights (w_E and w_V). The question is to specify the moles of water per carbon in reserve and structure, x_E and x_V. The values of x_E and x_V must be found from

$$\begin{aligned} 0 &= 10W_d - W_w \quad \text{which was given} \\ 0 &= 10(w_E M_E + w_V M_V) - w^w_E M_E - w^w_V M_V \\ 0 &= (10w_E - w^w_E)m_E + 10w_V - w^w_V \\ 0 &= (9w_E - 18x_E)m_E + 9w_V - 18x_V \end{aligned}$$

As implied from what was given, the ratio of dry weight W_d and wet weight W_w (both in gram) does not seem to depend on the ratio $m_E = M_E/M_V$ of mass of reserve M_E and mass of structure M_V (both in C-mole). Our result shows that this is only possible if the molecular weights of dry reserve and structure are equal, $w_E = w_V$ and the fraction of water in reserve and structure must be equal, $x_E = x_V = x$. The implication is $x = w_V/2 = w_E/2$. So for $n_{HE} = n_{HV} = 1.8$, $n_{OE} = n_{OV} = 0.5$ and $n_{NE} = n_{NV} = 0.2$, we have for dry mass $w_E = w_V = 24.6\,\mathrm{g/mol}$, $x = 12.3\,\mathrm{g/mol}$ and the chemical indices for wet mass are $n^w_{HE} = n^w_{HV} = 1.8 + 2 \times 12.3 = 26.4$ and $n^w_{OE} = n^w_{OV} = 0.5 + 12.3 = 12.8$. The resulting molecular weight for wet mass is $w^w_E = w^w_V = 12{+}1{\times}26.4{+}16{\times}12.8{+}14{\times}0.2 = 246\,\mathrm{g\,mol^{-1}}$, which checks the result. Our result also shows that a constant (so nutrition independent) ratio between wet and dry weight can only be an approximation at best.

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?

Answer:

The definition of the fraction of energy in ingested food that is fixed in reserve is $\kappa_X = \dot{p}_A/\dot{p}_X$. The definition of the yield coefficient of reserve on food is $y_{EX} = \dot{J}_{EA}/\dot{J}_{XA}$. The relationship between energy and mass fluxes for food and reserve is $\dot{p}_X = \dot{J}_{XA}\mu_X$ and $\dot{p}_A = \dot{J}_{EA}\mu_E$, respectively. So $\kappa_X = \frac{\dot{J}_{EA}\mu_E}{\dot{J}_{XA}\mu_X} = y_{EX}\mu_E/\mu_X$. Notice that κ_X is really dimensionless, but the units of y_{EX} are a mole of E per mole of X; y_{EX} is not really dimensionless because E and X are different types.

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?

Answer:

In the context of the standard DEB model, carbon in food can end up in reserve, faeces and carbon dioxide. The conservation of carbon implies $1 = y_{CX} + y_{PX} + y_{EX}$. The yield of carbon dioxide on food is given by $y_{CX} = 1 - y_{PX} - y_{EX}$. If $y_{EX} = 1$, we must have $y_{CX} = y_{PX} = 0$.

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?

Answer:

Section 4.3.1 on metabolic transformation applies Section 3.5 on macrochemical transformation. The three transformations are for $Y^A_{XX} = Y^G_{EE} = Y^D_{EE} = 1$:

assimilation A**:** $Y^A_{XX}\,\mathrm{X} + Y^A_{OX}\,\mathrm{O} \to Y^A_{EX}\,\mathrm{E} + Y^A_{PX}\,\mathrm{P} + Y^A_{CX}\,\mathrm{C} + Y^A_{HX}\,\mathrm{H} + Y^A_{NX}\,\mathrm{N}$

growth G**:** $Y^G_{EE}\,\mathrm{E} + Y^G_{OE}\,\mathrm{O} \to Y^G_{VE}\,\mathrm{V} + Y^G_{CE}\,\mathrm{C} + Y^G_{HE}\,\mathrm{H} + Y^G_{NE}\,\mathrm{N}$

dissipation D**:** $Y^D_{EE}\,\mathrm{E} + Y^D_{OE}\,\mathrm{O} \to Y^D_{CE}\,\mathrm{C} + Y^D_{HE}\,\mathrm{H} + Y^D_{NE}\,\mathrm{N}$

Since assimilation is the only process that involves Y^A_{EX} or Y^A_{PX}, the superscript A is suppressed; a similar reason applies to superscript G for Y^G_{VE}. Moreover Y is replaced by $-y$ in these cases to express that the yield coefficients are constant and to make y positive. Eq (3.12) can be applied to find the yield coefficients. For assimilation we have for the chemical element C, H O and N in the rows with $y_{XX} = 1$:

$$\begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \end{pmatrix} = \begin{pmatrix} 1 & 0 \\ 1.8 & 0 \\ 0.5 & 2 \\ 0.2 & 0 \end{pmatrix} \begin{pmatrix} -y_{XX} \\ Y^A_{OX} \end{pmatrix} + \begin{pmatrix} 1 & 1 & 1 & 0 & 0 \\ 2 & 1.8 & 0 & 2 & 3 \\ 0.5 & 0.5 & 2 & 1 & 0 \\ 0.15 & 0.15 & 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} y_{EX} \\ y_{PX} \\ Y^A_{CX} \\ Y^A_{HX} \\ Y^A_{NX} \end{pmatrix}$$

This can be rearranged to separate known from unknown

$$\begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 2 & 0 & 3 \\ 2 & 1 & 2 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} Y^A_{CX} \\ Y^A_{HX} \\ Y^A_{OX} \\ Y^A_{NX} \end{pmatrix} = - \begin{pmatrix} 1 & 1 & 1 \\ 1.8 & 2 & 1.8 \\ 0.5 & 0.5 & 0.5 \\ 0.2 & 0.15 & 0.15 \end{pmatrix} \begin{pmatrix} -y_{XX} \\ y_{EX} \\ y_{PX} \end{pmatrix}$$

and solved

$$\begin{pmatrix} Y^A_{CX} \\ Y^A_{HX} \\ Y^A_{OX} \\ Y^A_{NX} \end{pmatrix} = - \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 2 & 0 & 3 \\ 2 & 1 & 2 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix}^{-1} \begin{pmatrix} 1 & 1 & 1 \\ 1.8 & 2 & 1.8 \\ 0.5 & 0.5 & 0.5 \\ 0.2 & 0.15 & 0.15 \end{pmatrix} \begin{pmatrix} -1 \\ y_{EX} \\ y_{PX} \end{pmatrix} = - \begin{pmatrix} 1 & 1 & 1 \\ 0.6 & 0.775 & .675 \\ -1.05 & -1.138 & -1.088 \\ 0.2 & 0.15 & 0.15 \end{pmatrix} \begin{pmatrix} -1 \\ y_{EX} \\ y_{PX} \end{pmatrix}$$

The same can be done for growth for $y_{EE} = 1$ with the results

$$\begin{pmatrix} Y^G_{CE} \\ Y^G_{HE} \\ Y^G_{OE} \\ Y^G_{NE} \end{pmatrix} = -\begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 2 & 0 & 3 \\ 2 & 1 & 2 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix}^{-1} \begin{pmatrix} 1 & 1 \\ 2 & 1.8 \\ 0.5 & 0.5 \\ 0.15 & 0.15 \end{pmatrix} \begin{pmatrix} -y_{EE} \\ y_{VE} \end{pmatrix} = -\begin{pmatrix} 1 & 1 \\ 0.775 & 0.675 \\ -1.24 & -1.09 \\ 0.15 & 0.15 \end{pmatrix} \begin{pmatrix} -1 \\ y_{VE} \end{pmatrix}$$

And for dissipation

$$\begin{pmatrix} Y^D_{CE} \\ Y^D_{HE} \\ Y^D_{OE} \\ Y^D_{NE} \end{pmatrix} = -\begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 2 & 0 & 3 \\ 2 & 1 & 2 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix}^{-1} \begin{pmatrix} 1 \\ 2 \\ 0.5 \\ 0.15 \end{pmatrix} \begin{pmatrix} -y_{EE} \end{pmatrix} = \begin{pmatrix} 1 \\ 0.775 \\ -1.137 \\ 0.15 \end{pmatrix}$$

The assumptions that we used are

- the basic structure of the standard DEB model (food is first converted to reserve that is mobilised for other transformations)
- strong homeostasis (the chemical indices are fixed)
- dioxygen is a substrate that is non-limiting (Chapter 5 deals with multiple substrates)

Notice that reproduction is only represented in the form of overhead costs as part of the dissipation flux. From a chemical point of view reserve of the mother is 'transformed' into reserve of the offspring, which has the same composition.

The yields relate to the fluxes as $Y^A_{EX} = \dot{J}_{EA}/\dot{J}_{XA} = -y_{EX}$ and $Y^A_{VE} = \dot{J}_{VG}/\dot{J}_{EG} = -y_{VE}$. The dissipation flux collects all fluxes that represent the mineralisation of reserve; this includes somatic and maturity maintenance, maturation and overhead of reproduction.

The yield coefficients have units $\dim(y_{EX}) = \frac{\text{mol } E}{\text{mol } X}$ and $\dim(y_{VE}) = \frac{\text{mol } V}{\text{mol } E}$. Although the difference is subtle, the yield coefficients are not dimensionless, since X, E and V represent different types.

The relationships between mass and energy fluxes are $\dot{p}_X = \mu_X \dot{J}_{XA}$, $\dot{p}_A = \mu_E \dot{J}_{EA}$, $\dot{p}_G = \mu_E \dot{J}_{EG}$ and $\dot{p}_D = \mu_E \dot{J}_{ED}$, were μ_X and μ_E are the chemical potentials of food and reserve, respectively. The flux $\dot{p}_G$ represents the flux allocated to growth, while $\kappa_G \dot{p}_G = \mu_V \dot{J}_{VG}$ is the flux fixed in new structure. So $y_{VE} = \frac{\dot{J}_{VG}}{\dot{J}_{EG}} = \frac{\kappa_G \dot{p}_G/\mu_V}{\dot{p}_G/\mu_E} = \frac{\kappa_G \mu_E}{\mu_V}$.

The total flux of dioxygen is $\dot{J}_O = Y^A_{OX}\dot{p}_X/\mu_X + Y^D_{OD}\dot{p}_D/\mu_E + Y^G_{OG}\dot{p}_G/\mu_E$.

3.2.2 Question:

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

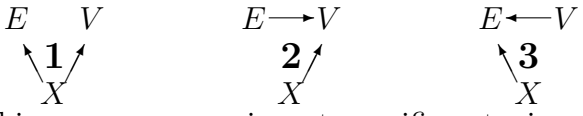
Hint:

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 $\dot{J}_{XA}$.

Answer:

The situation in standard DEB model with its two pools is much simpler: food is transformed to reserve and reserve to structure. While food density might fluctuate wildly, growth changes smoothly are a result of the buffering capacity of the reserve pool. Now this buffering does not exist. What are the implications?

The four possible transformations are $X \to y_{EX}E$, $X \to y_{VX}V$, $E \to y_{VE}V$ and $V \to y_{EV}E$, suppressing all mineral substrates and products. We have here $y_{VE} \neq y_{EV}^{-1}$ and the values must be such that possibly limiting mineral compounds (such as ammonia) are always products, never substrates. (Dioxygen is a typically substrate under aerobic conditions, but is supposed to be non-limiting; facultative fermentation is discussed Chapter 4.) This also applies to the standard DEB model, but we now have 4 transformations, not 2. The interconversion of E and V causes a non-uniqueness that must but eliminated, somehow, for instance by assuming that for each time increment we have one of three possible cases:



Suppose that biomass was growing at specific rate $\dot{r}_0 = \dot{r}(t)$ at t, so $\frac{d}{dt}M_W(t,\dot{r}_0) = \dot{r}_0 M_W(t,\dot{r}_0)$, with $M_W(t,\dot{r}_0) = M_V(t)\,(1+m_E(\dot{r}_0))$ and $m_E(\dot{r})$ is some known smooth function of $\dot{r}$. To make it more concrete for $m_E = \frac{e\{\dot{J}_{EAm}\}}{\dot{v}[M_V]}$ (see Table 3.3), the standard DEB model assumes $e = g\frac{\dot{k}_M(1+L_T/L)+\dot{r}}{\dot{v}/L-\dot{r}}$ (Eq (2.21)), so $m_E(\dot{r})$ is monotonically increasing (for $\dot{r} < \dot{v}/L$, which is always the case). This can only be linked to the intake rate if the scaled functional response is constant for sufficiently long period; the difference with the present situation is that this link is direct, and $m_E(\dot{r})$ might be a different function.

The amount of food that is transformed in the infinitesimally small time interval $(t, t+dt)$ is $M_X(t) = \dot{J}_{XA}(t)\,dt$, where $\dot{J}_{XA}(t)$ might fluctuate wildly, including a white-noise process. This food is converted to biomass at some unknown specific rate $\dot{r}_1 = \dot{r}(t+dt)$, so $M_W(t+dt,\dot{r}_1) = M_V(t+dt)\,(1+m_E(\dot{r}_1))$, where we need to find $\dot{r}_1 = (M_W(t+dt,\dot{r}_1)/M_W(t,\dot{r}_0) - 1)\,/dt$. Given m_E and $\dot{r}_o$ and M_E and M_V at t such that $M_E/M_V = m_E(\dot{r}_0)$, we need to solve $\dot{r}_1$ and so θ in one of three cases

Case 1: $$\frac{M_E + \theta y_{EX} M_X}{M_V + (1-\theta) y_{VX} M_X} = m_E(\dot{r}_1) \quad \text{with } \dot{r}_1 = \dot{J}_{XA}\frac{\theta y_{EX} + (1-\theta) y_{VX}}{M_E + M_V}$$

Case 2: $$\frac{M_E - \theta M_E}{M_V + y_{VX} M_X + \theta y_{VE} M_E} = m_E(\dot{r}_1) \quad \text{with } \dot{r}_1 = \frac{y_{VX}\dot{J}_{XA} + (y_{VE} - 1)\theta M_E/dt}{M_E + M_V}$$

Case 3: $$\frac{M_E + y_{EX} M_X + \theta y_{EV} M_V}{M_V - \theta M_V} = m_E(\dot{r}_1) \quad \text{with } \dot{r}_1 = \frac{y_{EX}\dot{J}_{XA} + (y_{EV} - 1)\theta M_V/dt}{M_E + M_V}$$

Case 1 applies if a solution for θ exists between 0 and 1. If not, case 2 applies if $\dot{r}_1 < \dot{r}_0$ and $\frac{d}{d\dot{r}} m_E(\dot{r}_1) > 0$ or $\dot{r}_1 > \dot{r}_0$ and $\frac{d}{d\dot{r}} m_E(\dot{r}_1) < 0$. Otherwise case 3 applies.

The problem we have to study is that a sudden change in food density $X(t)$ translates into a sudden change in ingestion rate $\dot{J}_{XA}$ and so in growth rate $\dot{r}_1$ and biomass composition $m_E(\dot{r}_1)$. In the cases 2 and 3, θ is not necessarily small (so θ/dt can be large), so that a possibly large fraction of one generalized compound needs to be transformed into the other and in the next incrementally small time interval it might be reversed. These backward and forward transformations represent not only an energy (and mineral) loss, but it might be physically impossible to do this within a time increment. Stochasticity in the feeding rate directly translates into stochasticity in the composition. Animals are organisms that feed on other organisms. If food organisms would also follow this rule, food would have a stochastic composition, which translates into a stochastic conversion efficiency. So apart from being physically impossible, the construct also becomes hopelessly complex in situations where food availability is erratic. The discrete nature of food particles also causes problems of a related nature, since nothing is smoothing the transitions. The conclusion is that working with a variable composition in absence of a smoothing buffer is asking for problems and the only way to avoid these problems is to partition biomass into pools of constant composition.

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?

Answer:

The RU then resembles enzyme kinetics better for increasing $\dot{k}_A$ and $\dot{k}_B$, the SU for decreasing values. This relates directly to the way RU and SU are obtained as limiting cases of enzyme kinetics.

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.

Answer:

The maximum relative difference is about 0.25, which is reached for $n_A = n_B \to \infty$ and $\dot{J}_A = \dot{J}_B \to 0$; under these conditions the impact is maximal of the waiting time of the other compound. The relative difference is not much in many practical cases (i.e. low values for n_A and n_B), which is important because we frequently do not know the absolute stoichiometry.

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?

Answer:

Yes; we can decrease the amount of time that transformations have to be delayed because the SU has to wait for the last-arriving substrate by increasing the number of copies of substrate and that of product.

3.3.4 Question:

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

Hint:

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

Answer:

The relative differences in binding fractions can be considerable; the substrate-SU complex is relative more abundant than the substrate-RU or substrate-enzyme complexes, because the dissociation rates for SUs is zero.

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 $n_A A + n_B B \rightarrow C$.

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?

Answer:

The end-result is a mix of enzyme, product in concentration $X_C = \min(X_A/n_A, X_B/n_B)$ and substrate A in the concentration $X_A - n_A X_C$ or substrate B in concentration $X_B - n_B X_C$; one of the substrates completely disappeared.

If substrate i, for $i \in \{A, B\}$, is left over, and the other substrate hardly limited the transformation, the initial appearence rate of product C is $\dot{J}_C = J_{Cm}/(1 + X_i^{-1}\dot{k}_C/\dot{b}_i)$.

The rate is almost constant, most of the time, but later drops gradually, depending on the parameter values. If this applies, we can solve the waiting time t till the practical end of the transformation from $t\dot{J}_C = n_i X_i$, which gives $t = n_i(X_i + \dot{k}_C/\dot{b}_i)/\dot{J}_{Cm}$. This is an underestimation, because the transformation slows down, and the other substrate could have been co-limiting. The latter can be taken into account in a rough way, by $t = n_i(X_i + \dot{k}_C/\min(\dot{b}_i, \dot{b}_j))/\dot{J}_{Cm}$. This still represents an underestimation.

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.

Answer:

For the sequential-substitutable case we have for $\boldsymbol{\theta} = \begin{pmatrix} \theta_{..} & \theta_{A.} & \theta_{.B} & \theta_{AB} \end{pmatrix}^T$

$$\begin{aligned}
\frac{d}{dt}\theta_{..} &= \dot{k}_A\theta_{A.} + \dot{k}_B\theta_{.B} - (\rho_A\dot{J}_A + \rho_B\dot{J}_B)\theta_{..} \\
\frac{d}{dt}\theta_{A.} &= \rho_A\dot{J}_A\theta_{..} - \dot{k}_A\theta_{A.} \\
\frac{d}{dt}\theta_{.B} &= \rho_B\dot{J}_B\theta_{..} - \dot{k}_B\theta_{.B} \\
\frac{d}{dt}\theta_{AB} &= 0 \quad \text{so} \\
\frac{d}{dt}\boldsymbol{\theta} &= \dot{\boldsymbol{k}}_{ss}\boldsymbol{\theta} \quad \text{with} \quad \dot{\boldsymbol{k}}_{ss} = \begin{pmatrix} -\rho_A\dot{J}_A - \rho_B\dot{J}_B & \dot{k}_A & \dot{k}_B & 0 \\ \rho_A\dot{J}_A & -\dot{k}_A & 0 & 0 \\ \rho_B\dot{J}_B & 0 & -\dot{k}_B & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}
\end{aligned}$$

For the sequential-complementary case

$$\frac{d}{dt}\theta_{..} = \dot{k}_C\theta_{AB} - \rho_A\dot{J}_A\theta_{..}$$

$$\begin{aligned}
\frac{d}{dt}\theta_{A\cdot} &= \rho_A \dot{J}_A \theta_{\cdot\cdot} - \rho_B \dot{J}_B \theta_{A\cdot} \\
\frac{d}{dt}\theta_{\cdot B} &= 0 \\
\frac{d}{dt}\theta_{AB} &= \rho_B \dot{J}_B \theta_{A\cdot} - \dot{k}_C \theta_{AB} \quad \text{so} \\
\frac{d}{dt}\boldsymbol{\theta} &= \dot{\boldsymbol{k}}_{sc}\boldsymbol{\theta} \quad \text{with} \quad \dot{\boldsymbol{k}}_{sc} = \begin{pmatrix} -\rho_A \dot{J}_A & 0 & 0 & \dot{k}_C \\ \rho_A \dot{J}_A & -\rho_B \dot{J}_B & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & \rho_B \dot{J}_B & 0 & -\dot{k}_C \end{pmatrix}
\end{aligned}$$

For the parallel-substitutable case

$$\begin{aligned}
\frac{d}{dt}\theta_{\cdot\cdot} &= \dot{k}_A \theta_{A\cdot} + \dot{k}_B \theta_{\cdot B} - (\rho_A \dot{J}_A + \rho_B \dot{J}_B)\theta_{\cdot\cdot} \\
\frac{d}{dt}\theta_{A\cdot} &= \rho_A \dot{J}_A \theta_{\cdot\cdot} + \dot{k}_B \theta_{AB} - \rho_B \dot{J}_B \theta_{A\cdot} - \dot{k}_A \theta_{A\cdot} \\
\frac{d}{dt}\theta_{\cdot B} &= \rho_B \dot{J}_B \theta_{\cdot\cdot} + \dot{k}_A \theta_{AB} - \rho_A \dot{J}_A \theta_{\cdot B} - \dot{k}_B \theta_{\cdot B} \\
\frac{d}{dt}\theta_{AB} &= \rho_B \dot{J}_B \theta_{A\cdot} + \rho_A \dot{J}_A \theta_{\cdot B} - \dot{k}_A \theta_{AB} - \dot{k}_B \theta_{AB} \quad \text{so} \\
\frac{d}{dt}\boldsymbol{\theta} &= \dot{\boldsymbol{k}}_{ps}\boldsymbol{\theta} \quad \text{with} \quad \dot{\boldsymbol{k}}_{ps} = \begin{pmatrix} -\rho_A \dot{J}_A - \rho_B \dot{J}_B & \dot{k}_A & \dot{k}_B & 0 \\ \rho_A \dot{J}_A & -\rho_B \dot{J}_B - \dot{k}_A & 0 & \dot{k}_B \\ \rho_B \dot{J}_B & 0 & -\rho_A \dot{J}_A - \dot{k}_B & \dot{k}_A \\ 0 & \rho_B \dot{J}_B & \rho_A \dot{J}_A & -\dot{k}_A - \dot{k}_B \end{pmatrix}
\end{aligned}$$

For the parallel-complementary case

$$\begin{aligned}
\frac{d}{dt}\theta_{\cdot\cdot} &= \dot{k}_C \theta_{AB} - (\rho_A \dot{J}_A + \rho_B \dot{J}_B)\theta_{\cdot\cdot} \\
\frac{d}{dt}\theta_{A\cdot} &= \rho_A \dot{J}_A \theta_{\cdot\cdot} - \rho_B \dot{J}_B \theta_{A\cdot} \\
\frac{d}{dt}\theta_{\cdot B} &= \rho_B \dot{J}_B \theta_{\cdot\cdot} - \rho_A \dot{J}_A \theta_{\cdot B} \\
\frac{d}{dt}\theta_{AB} &= \rho_A \dot{J}_A \theta_{\cdot B} + \rho_B \dot{J}_B \theta_{A\cdot} - \dot{k}_C \theta_{AB} \quad \text{so} \\
\frac{d}{dt}\boldsymbol{\theta} &= \dot{\boldsymbol{k}}_{pc}\boldsymbol{\theta} \quad \text{with} \quad \dot{\boldsymbol{k}}_{pc} = \begin{pmatrix} -\rho_A \dot{J}_A - \rho_B \dot{J}_B & 0 & 0 & \dot{k}_C \\ \rho_A \dot{J}_A & -\rho_B \dot{J}_B & 0 & 0 \\ \rho_B \dot{J}_B & 0 & -\rho_A \dot{J}_A & 0 \\ 0 & \rho_B \dot{J}_B & \rho_A \dot{J}_A & -\dot{k}_C \end{pmatrix}
\end{aligned}$$

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 $\frac{d}{dt}L_D$.

Answer:

Volume V grows as $\frac{d}{dt}V = 0.1\frac{d}{dt}L\,\mathrm{m}^3/\mathrm{a}$, and diameter L_D grows in a ways that can easily be expressed in terms of L.

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?

Answer:

Since wood production ceases, if we believe Preston et al, wood production cannot be associated with assimilation and dissipation, because these processes do not cease. It must therefore be associated with growth only. Other data, however, suggest that wood production continues if the tree is already fully grown.

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}
$\mathrm{CH}_{n_{HE}}\mathrm{O}_{n_{OE}}\mathrm{N}_{n_{NE}} + Y_{OE}\,\mathrm{O_2} \rightarrow$

$$y_{VE}\,\mathrm{CH}_{n_{HV}}\mathrm{O}_{n_{OV}}\mathrm{N}_{n_{NV}} - Y_{CE}\,\mathrm{CO}_2 - Y_{HE}\,\mathrm{H_2O} - Y_{NE}\,\mathrm{NH_3}$$

with $\begin{cases} Y_{CE} &= y_{VE} - 1 \\ Y_{HE} &= -n_{HE}/2 + n_{HV}\,y_{VE}/2 - Y_{NE}3/2 \\ Y_{OE} &= -n_{OE}/2 + n_{OV}\,y_{VE}/2 - Y_{CE} - Y_{HE}/2 \\ Y_{NE} &= -n_{NE} + n_{NV}\,y_{VE} \end{cases}$

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.

Answer:

The carbon dioxide flux cannot be zero if $y_{EX} < 1$, because the anabolic component of assimilation is than *producing* carbon dioxide, and no other process is fixing it. The condition is, however, more stringent. The specific substrate flux is $j_{XA} = f j_{XAm}$, the specific maintenance flux of reserve is $j_{EM} = y_{EV}\,\dot{k}_M$ and that for growth is $j_{EG} = y_{EV}\,\dot{r} = y_{EV}\frac{f-l_d}{f+g}\dot{k}_E$, with $y_{EV} = y_{VE}^{-1}$ and $l_d = g\dot{k}_M/\dot{k}_E$. So the carbon dioxide flux is zero if

$$y_{VE}(y_{EX} - 1)f j_{XAm} = \dot{k}_M + (1 - y_{VE})\dot{k}_E\frac{f - l_d}{f + g}$$

or

$$0 = (y_{EX} - 1)j_{XAm}f^2 + \left(g(y_{EX} - 1)j_{XAm} - \dot{k}_M y_{EV} - (y_{VE} - 1)\dot{k}_E\right)f + (y_{EV} - 1)\dot{k}_M$$

This can be summarized by $0 = af^2 + bf + c$. The scaled functional response f can be solved from this quadratic equation in f. A positive real solution for f exists if $y_{EX} > 1$, and $0 < f < 1$ if $\sqrt{b^2 - 4ac} - b > 2a$, or $-c < b + a$. A zero carbon dioxide flux is possible for some substrate density if

$$(1 + g)(y_{EX} - 1)j_{XAm} + (1 - y_{VE})\dot{k}_E > \dot{k}_M$$

Some text books mention that for each produced carbon dioxide molecule, two methane molecules have been consumed by a methanotroph. This exercise shows, however, that such a fixed relationship does not exist; it is very sensitive for environmental conditions.

Methane burning in assimilations' catabolic component should generate enough energy to drive assimilations' anabolic component. So $\mu_X \, j^C_{XA} > (\mu_E - \mu_X) j^A_{XA}$ or $\mu_X(1 - y_{EX}) > (\mu_E - \mu_X) y_{EX}$ or $y_{EX} > \mu_E/\mu_X$.

Notice that, like carbon dioxide, ammonia is taken up as well as excreted. We know apriori that ammonium uptake always exceeds excretion at steady state.

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?

Answer:

Initially embryos have a negligibly small structure, which implies that the structure-specific fluxes are very large. Weights include reserve and structure. The initial amount of reserve is substantial, so weight-specific fluxes are not blown up. Embryos get more reserve from the mother than juveniles can possibly obtain by eating. This is why embryos can grow faster than juveniles on a relative basis.

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.

Answer:

You will see that if the elemental compositions of reserve and structure do not differ a lot, the respiration ratio stays more or less constant. This explains why respiration ratios are usually taken to be constant in experimental animal physiology. You can also see that if the composition differ substantially, the respiration ratio varies a lot with size. This explains why respiration ratios are usually not taken to be constant in microbiology.

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.

Answer:

The comment for section 4.3.3 explains the evaluation.

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.

Answer:

The constraint on the maintenance rate coefficients implies that stage transitions occur at fixed amounts of structure. We need (compound) DEB parameters first, which are independent of food availability, and then use these to obtain the quantities of interest. Start Octave, set the path to DEBtool/animal and type `p = [1; 1; 5; 7; 0.01]; [q, U] = get_pars_g(p)` . The result $U_E = 7.195$, 1.6606 d.cm^2 represents the scaled reserve at age 0 and a_b, so the fraction of reserve that is left over at birth is $1.66/7.195 = 0.23$. We now type `[r, U] = iget_pars_g(.7,q)` . The result $U_E = 6.7707$, 1.1624 d.cm^2 shows that the fraction of reserve that is left over at birth now equals $1.16/6.77 = 0.17$, and that the ultimate length is r(3) = 3.5 cm, the age at birth r(4) = 7.4 d, and the von Bertalanffy growth rate r(5) = 0.0108 d^{-1}. Notice that the von Bertalannfy growth rate is now higher, and the ultimate length lower than at abundant food, but the growth curves at different food levels do not intersect. The effect of the reduced food availability on the fraction of reserve that is left over at birth is relatively large because the reserve density at birth drops from 1 till 0.7, and because a lower initial reserve increases the age at birth, and so the cumulative maintenance costs.

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 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` .

Answer:

Type `get_pars_r([1; 1; 3; 5; 7; 0.01; 0.7])` and find the answer $\kappa = 0.729$. This estimate depends on the length at puberty because of the maturity maintenance costs are competing with allocation to reproduction.

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`.

Answer:

Type `[q, U] = get_pars_s([1 0.7; 4.4 4.4; 10.2 10.1; 25 17.5; 0.03 0.042; 2.6 1]')` . The answer is: $\kappa = 0.81$, $g = 0.21$, $\dot{k}_J = 0.36\,\mathrm{d}^{-1}$, $\dot{k}_M = 0.54\,\mathrm{d}^{-1}$, $\dot{v} = 2.8\,\mathrm{cm/d}$, $M_H^b/\{\dot{J}_{EAm}\} = 1.46\,\mathrm{d\,cm^2}$ and $M_H^p/\{\dot{J}_{EAm}\} = 20.7\,\mathrm{d\,cm^2}$.

The fractions of reserve that are left over at birth is $30.46/41.65 = 0.73$ for $f = 1$ and $21.14/32.57 = 0.65$ for $f = 0.7$. The ages at birth are $a_b = 5.1\,\mathrm{d}$ for $f = 1$ and $5.2\,\mathrm{d}$, respectively.

All values that have cm in their units depend on length. these are $\dot{v}$, $M_H^b/\{\dot{J}_{EAm}\}$ and $M_H^p/\{\dot{J}_{EAm}\}$.

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	**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?

Answer:

If the temperature is constant, rate parameters are constant. Living in the thermal neutral zone means no energy is required to maintain a constant body temperature (at $37^/circ$C), so $\{\dot{p}_T\} = 0$. The von Bertalannfy growth rate is $\dot{r}_B = \frac{\dot{k}_M/3}{1+f/g}$, see Eq. (2.24), and the energy investment ratio is $g = \frac{\dot{v}[M_V]}{\kappa\{\dot{J}_{EAm}y_{VE}} = \frac{\dot{v}d_V y_{EV}}{\kappa w_V\{\dot{p}_{Am}\mu_E}$, see Table 3.3.

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.

Answer:

You will see large effects for small throughput rates. When you think of a community as a more complex chemostat, this observation should motivate you to include nutrient recycling in all basic community models.

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.

Answer:

We can expect this for non-limiting reserves that are hardly excreted.

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.

Answer:

You will see that for proper combinations of parameter values plants' allocation to roots versus shoots partly compensates adverse effects on growth rates, despite the fact that such a response is not incorporated explictly in the DEB model.

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.

Answer:

You will see that for proper combinations of parameter values a peak in shoots' reserve density occurs during a short period, just after germination. Notice that the occurrence of this behaviour has not been incorporated explicitly in the DEB model; it is a consequence of how roots and shoots exchange metabolites. This, however, does not exclude the existence of regulation mechanisms for the growth and absorption of cotyledons.

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.

Answer:

The flux of nitrogen waste can be written as $\dot{J}_N = \eta_{NA}\dot{p}_A + \eta_{ND}\dot{p}_D + \eta_{NG}\dot{p}_G$ (cf page 147 of the DEB book). All powers $\dot{p}_*$ are cubic polynomials in (scaled) length (cf page 123). This means that nitrogen waste production can be written as a cubic polynomial in (scaled) length

$$\dot{J}_N = \dot{J}_{N3}l^3 + \dot{J}_{N2}l^2 + \dot{J}_{N1}l + \dot{J}_{N0}$$

The coefficients $\dot{J}_{N*}$ can be obtained by straightforward substitution in the expressions given at page 123 where we take $e = 1$.

A reasonable approximation for the cortex volume is $V_c = \delta\,(L^3 - (L - L_c)^3)$, where δ is a dimensionless coefficient that takes care of the kidney shape, L is a typical length measure of the kidney, and L_c is the thickness of the cortex.

If cortex thickness L_c would be proportional to kidney length L, cortex volume would be proportional to L^3, and so proportional to body volume. Since nitrogen waste production is a weighted sum of squared and cubed length, this would imply that the work load of the cortex tissue decreases with body size.

Let us now allow more complex relationships between cortex thickness and kidney length, and linearize this function: $L_c(L) = L_{c0} + \delta_c L$. Obviously we must have $L > L_{c0}$, and we assume that the kidney is not functional for smaller body sizes. The cortex volume now amounts for $\delta_m = 1 - \delta_c$ to

$$V_c = \delta\left((1 - \delta_m^3)L^3 + 3\delta_m^2 L_{c0} L^2 - 3\delta_m L_{c0}^2 L + L_{c0}^3\right)$$

The workload of cortex tissue remains constant during development if

$$\begin{aligned}
\dot{J}_{N3} &= \dot{J}_{Nr}(1 - \delta_m^3) \\
\dot{J}_{N2} &= 3\dot{J}_{Nr}\delta_m^2 L_{c0}/L_0 \\
\dot{J}_{N1} &= -3\dot{J}_{Nr}\delta_m L_{c0}^2/L_0^2 \\
\dot{J}_{N0} &= \dot{J}_{Nr} L_{c0}^3/L_0^3
\end{aligned}$$

Where $\dot{J}_{Nr}$ is a reference flux, and L_0 a reference length. These 4 equations determine $\dot{J}_{Nr}$, L_0, $\delta_c = 1 - \delta_m$ and L_{c0} as function of parameters of the DEB.

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'.

Answer:

The DEB module has 2 ageing parameters: the ageing acceleration $\ddot{h}_a$ and the Gompertz stress coefficient s_G. If the growth period is short, these two parameters can be reformulated in the Weibull and Gompertz ageing rates, $\dot{h}_W$ and $\dot{h}_G$. Both the Weibull and the Gompertz ageing models also have 2 parameters. The general Gompertz model and the Weibull model with shape parameter 3 are special cases of the DEB module, but because of the larger

shape plasticity of the DEB module, the general Weibull model can be approximated very well, see Section 6.1.1 of the comments on 'Empirical Weibull curves'. Part of this larger plasticity is due to the energetics module of the DEB model; the Weibull and the Gompertz models don't have such a coupling. Only if tissue differentiation is irreversible and if other causes of death play a minor role, species are affected by ageing (as an effect if free radicals).

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.

Answer:

See DEBtool/tox/mydata_acc. The result is an elimination rate of $0.9\,\mathrm{d}^{-1}$, and a BCF of 4.88 l/g. The standard deviations are very large.

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?

Answer:

See DEBtool/tox/mydata_acceli. The result is an elimination rate of $0.58\,\mathrm{d}^{-1}$, and a BCF of 5.47 l/g. The standard deviations are still large, but much smaller than for accumulation data only. Notice that the fit for the accumulation phase is less good, because the elimination phase suggest different parameter values.

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.

Answer:

Because the size of the animals differed, it is likely that the BCF is constant, but the elimination rates differ, so we choose for the parametrization $C(t) = K(1 - \exp\{-\dot{k}_e t\}$.

We now write a script file where we fill the data, define the regression functions, estimate the parameters and obtain the standard deviations.

```
tc1 = [0 1 2 3 4 5; 0, 3.1 5.9 8.1 9.  9.5]';
tc2 = [0 1 2 3 4 5; 0, 2.9, 5.7, 7.9 8.9 9.4]';
function f = myacc0(p,tc)
K = p(1); ke = p(2);
f = K*(1-exp(-tc(:,1)*ke));
end
p0 = nrregr("myacc0",[10 .3]',[tc1;tc2]);
ssq0 = ssq("myacc0",p0,[tc1;tc2]);
function [f1,f2] = myacc1(p,tc1,tc2)
K = p(1); ke1 = p(2); ke2 = p(3);
```

```
f1 = K*(1-exp(-tc1(:,1)*ke1));
f2 = K*(1-exp(-tc2(:,1)*ke2));
end
p1 = nrregr("myacc1",[15 .3 .3]', tc1, tc2);
ssq1 = ssq("myacc1",p1, tc1, tc2);
6 * log(ssq0/ssq1)
```

The result is 0.414, which is not significant at the 5 % level, because under the null hypothese this represents a random trial from a Chi-square distribution with 1 degree of freedom.

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.

Answer:

Type `t = [0 1]'; c = [0 1 2 4 8 16]';`

```
S = [10 10 10 10 10 10; 10 9 10 8 4 1];
p = nmsurv2(''fomort'', [.02 1.5 .6 1]',t,c,S);
p = nmsurv2(''fomort'', p, t, c, S);
lc50(p([2 3 4]),1);
```

The elimination rate walks to large values in this example, which explains the convergence problems. The standard deviation of the NEC can only be obtained here by fixing the elimination rate. The standard deviations appear after:

```
[cov, cor, sd] = psurv2(''formort'', [p, [1 1 1 0]'], t, c, S); [p, sd]
```

The result is NEC = 2.9 (sd 1.1) mg/l, the LC50.1d = 6.9 mg/l.

6.3.2 Question:

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

Answer:

Without any recalculation we know that the blank mortality rate , the killing rate and the elimination rate is two times as small. This follows directly from a change in time-units.

6.3.3 Question:

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

Answer:

The NEC will be multiplied by the factor x, and the killing rate will be divided by that factor.

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?

Answer:

Type `t = [0 1 2 3 4 5]'; c = 5; S = [100 69 17 3 0 0]'; p = scsurv2('fomort', [1e-8 1.5 .6 1; 0 1 1 1]', t, c, S); lc50(p([2 3 4],1),t)`

The result is NEC = 0.73 mM, the LC50 for day 1 2 3 4 5 is 7.2, 2.9, 1.9, 1.5, 1.3 mM.

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.

Answer:

Set 1 has the lowest ultimate LC50, because the LC50 for set 1 decreases more between day 2 and 3.

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?

Answer:

Type:

```
tc1 = [1 2 3; 23.5 8 4.5]';
tc2 = [1 2 3; 23.5 7.9 4.5]';
p1 = lc503(tc1, [.5 1 .1]);
lc50(p1,4); p2 = lc503(tc2,p1); lc50(p2,4);
```

The LC50.4d appears because the output of lc50 is not assigned to a variable. The ultimate LC50's equal the NEC, which are in `p1(1)` and `p2(1)`, respectively. They appear by typing: `[p1, p2]` . This can be checked by typing:

```
lc50(p1,1e8); lc50(p2,1e8)
```

The values are 0.362 and 0.748 mg/l.

Notice that the small difference between the LC50.2d for the two sets, results in a factor 2 difference in the NEC. This illustrates the unstability of extrapolation while the LC50 is still decreasing.

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?

Answer:

Type: `shregr(''lc50'',p1,tc1)` . The mean squared deviation is zero, because three LC50 values exactly determine three parameter values.

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.

Answer:

Type: `tc=[tc1;4 3]; p=nrregr(''lc50'',p1,tc); lc50(p,[5 6]);`
The answer is LC50.5d = 2.25 mg/l and LC50.6d = 1.78 mg/l.

The graphical check is done by typing:
`shregr_options(''default''); shregr(''lc50'',p,tc);`
The fit should by quite good, but the mean squared deviation is not longer zero.

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.

Answer:

The ratio of the P_{ow} values for compound 2 and 1 is $10^8/10^7 = 10$. The toxicity parameters for compound 2 are: NEC = 1/10 mM, killing rate = 10 $\mathrm{mM}^{-1}\,\mathrm{d}^{-1}$ and the elimination rate = $0.01/\sqrt{10}\,\mathrm{d}^{-1}$. The LC50.2d is found from DEBtool/tox/lc50, by typing: `lc50([0.1, 10, 0.01/sqrt(10)],2)`
The result is 35.63 mM. The LC50.2d for compound 1 is 113.27 mM.

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.

Answer:

Type: `t = [0 1 2 3 4]';`

```
cph = [0 2 4 8 16; 7.8 7.7 7.4 7.0 6.5]';
S = [10 10 10 10 10; 10 10 10 10 8; 10 10 10 8 4; 10 10 9 6 1; 10 9 6 3 0];
p = [1e-8 0.1 4 .2 0.5 1 8.0; 0 1 1 1 1 1 0]';
q = nmsurv2("fomortph",p,t,cph,S);
p = scsurv2("fomortph",q,t,cph,S);
```

The routine nmsurv2 does not come to full conversion, but that is not necessary to get scsurv2 converged. The calculations lead to NECS of 0.00665 and 0.00678 mM for the molecular and ionic forms. Notice that the number of estimated parameters is rather large relative to the available information from data. This implies substantial uncertainty in the values. Check this with the standard deviations.

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.

Answer:

The result is

mode of action	NEC	EC50.21 d	EC50.∞ d
assimiliation	1.61	2.72	2.58
maintenance costs	1.38	2.75	2.20
growth costs	$*$	2.95	2.82
reproduction costs	0.50	2.50	0.81
neonate survival	1.38	2.51	1.82

$*$: Effects via growth resulted in slow kinetics, with a NEC-time of 11.72 mM d.
The NEC differ by a factor 3 for the various modes of action.

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?

Answer:

If the change in body length is always of the log-logistic type, it amounts to:

$$\frac{d}{dt}\ln L(c,t) \;=\; \frac{d}{dt}\ln L_{0,t} - \beta_t \frac{\left(\frac{d}{dt}\ln\beta_t\right)\ln\frac{c}{c_{e,t}} - \frac{d}{dt}\ln c_{e,t}}{1 + (c_{e,t}/c)^{\beta_t}}$$

The first observation is that relative growth at any given concentrations is that in the blank minus something that depends on concentration and exposure time.

Since it is very probable that $\frac{d}{dt}c_{e,t} < 0$ and $\frac{d}{dt}\beta_t > 0$, growth at any given concentration ceases before that in the blank. Suppose that shrinking can be excluded. While $\frac{d}{dt}L(c,t) = 0$, we must have that

$$\frac{d}{dt}\ln L_{0,t} = \beta_t \frac{\left(\frac{d}{dt}\ln\beta_t\right)\ln\frac{c}{c_{e,t}} - \frac{d}{dt}\ln c_{e,t}}{1+(c_{e,t}/c)^{\beta_t}}$$

We here see an unpleasant implication: the change in the EC50 and the slope depends on the behaviour in the blank. This line of thought should be worked out in further detail. The aim of this exercise has been to show that fitting a sigmoid curve to length data comes with implicit assumptions of 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.

Answer:

We find that for $\dot{R}(c,t) = \frac{d}{dt}N(c,t)$ and $\dot{R}_{0,t} = \frac{d}{dt}N_{0,t}$, and $N_{0,t} = N_{0,t_0} + (t-t_0)\dot{R}_0$ for some appropriate value for t_0 (after which the reproduction in the blank is constant):

$$\begin{aligned}
\frac{d}{dt}\ln N(c,t) &= \frac{d}{dt}\ln N_{0,t} - \beta_t \frac{\left(\frac{d}{dt}\ln\beta_t\right)\ln\frac{c}{c_{e,t}} - \frac{d}{dt}\ln c_{e,t}}{1+(c_{e,t}/c)^{\beta_t}} \\
\frac{\dot{R}(c,t)}{N(c,t)} &= \frac{\dot{R}_0}{N_{0,t_0}+(t-t_0)\dot{R}_0} - \beta_t \frac{\left(\frac{d}{dt}\ln\beta_t\right)\ln\frac{c}{c_{e,t}} - \frac{d}{dt}\ln c_{e,t}}{1+(c_{e,t}/c)^{\beta_t}}
\end{aligned}$$

Suppose that some exposure time exists after which the reproduction rate at concentration c remains constant, so $N(c,t) = N_{c,t_0} + (t-t_0)R_c$. The slope and the EC50 can then also no longer change ($\frac{d}{dt}\beta_t = 0$ and $\frac{d}{dt}c_{e,t} = 0$), because the slope and the EC50 would become functions of N_{0,t_0}, while they should be independent of what happens in the blanc. So

the second term disappears, and the equation applies for all t, which results in $N_{c,t_0}/\dot{R}_c = N_{0,t_0}/\dot{R}_0$. This result cannot hold, because it depends on an arbitrary choice for t_0.

Generally, the concentration-response curve at 22 d cannot be of the log-logistic type if that at 21 d is of the log-logistic type. This devalidates the routine application of this response curve in cases like this, and all the statistics that comes after the assumption that this model would be correct. The present derivation rests on the existence of moments in time after which the reproduction rate does not change. This is consistent with empirical data; this line of thought might be generalized to relax this condition. For the time being, again the conclusion must be that fitting a sigmoid curve to the cumulative number of offspring per female comes with far reaching implicit assumptions about the reproduction process. In this case it might well be that the result can only imply non-sense.

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.

Answer:

The result is

mode of action	NEC	EC50.2d	EC50.∞d	unit
init mort	2.85	4.34	4.34	mM
mort.	2.98	4.31	2.99	mM
growth rate	3.39	4.21	3.41	mM

Notice that the EC50 does not depend on time if the compound affects initial mortality only. The NECs differ just a little, the EC50.2d even less; the EC50.∞d is more sensitive to the mode of action. The goodness of fit is excellent in all cases.

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?

Answer:

Population growth is assumed to be exponential in the blank, although this cannot be checked in the present numerical example. The living populations are always growing exponentially at all modes of action, but the measurements include dead cells. This means that the measured populations deviate from exponential growth if the effects are on mortality and initial mortality. The population growth rate (of the living population) equals that in the blank for effects on initial mortality.

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.

Answer:

The reponses can be ranked as follows

-1 Migration to avoid (predictable) starvation.

0 No response; the reserve will decrease according to the same rules as during feeding. Growth will cease at a certain reserve density threshold; reproduction continues.

1 Allocation to maturity maintenance and reproduction is ceased at a certain reserve density threshold; this threshold is decreased to the no-growth threshold.

2 Structure is degraded to pay somatic maintenance costs.

3 Somatic maintenance is reduced by ceasing activety (dormancy) and allocation to heating (in endotherms).

4 Suicide reproduction or spore formation. The individual sacrifices itself for the benefit of its progeny.

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.

Answer:

The waiting time is $t = -[M_{sm}]V^{1/3} \ln \alpha / \{\dot{J}_{Xm}\}$.

7.2.2 Question:

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

Hint:

Use eqn (3.6) on {81}.

Answer:

Gut residence time is also proportional to length.

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?

Answer:

The ratio of the waiting times for stomach emptying of mother and baby is $(4/64)^{1/3} = 2.5$, which implies that the baby has to eat $2.5 \times 3 = 7.5$ times a day to experience the same fluctuations. It is because the baby takes milk, and the mother less nutritial food, that the baby can do with a lower frequency.

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?

Answer:

$K = \{\dot{J}_{XAm}\}/\{\dot{F}_m\}$ is a compound parameter, but $\{\dot{J}_{XAm}\} = \{\dot{J}_{EAm}\}/y_{EX}$ is that as well, like $E_m = \{\dot{J}_{EAm}\}/\dot{v}$. Since y_{EX} is basic to the biochemical machinery, which all eukaryotes

share, it must a primary parameter and is intensive. $\{\dot{J}_{EAm}\}$ is preferred above $\{\dot{J}_{XAm}\}$ as primary parameter, because it is evolutionarily easier to change the feeding capacity than the assimilation capacity. Moreover, it is more close to the maximum length, which depends on maintenance. The searching rate $\{\dot{F}_m\}$ is close to the underlying processes, compared with the half-saturation coefficient K and is an intensive parameter. The energy conductance has a direct relationship with the mechanism of reserve mobilisation, so it is chosen to be a primary parameter, and is intensive. Moreover the maximum reserve capacity shares the property with the maximum length as being a ratio of incomming and outgoing fluxes; both ratios are compound parameters. With the choice of $\{\dot{F}_m\}$, y_{EX}, $\{\dot{J}_{EAm}\}$, $\dot{v}$ as primary parameter and K, $\{\dot{J}_{XAm}\}$, E_m as compound parameters, only one primary parameter is a design parameter, the rest is intensive.

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?

Answer:

1) All parameters can be classified as intensive or design parameters.
2) Simply functions of design parameters are intensive.
3) Maximum length is a function of only one design parameter.

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?

Answer:

1) Effects per molecule inside the individual don't depend of the partition coefficient.
2) Toxico-kinetics is quantified by the one-compartment model (or extensions of it)
3) This model is based on fugacity, which implies a skew symmetry for the roles of both media.

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.

Answer:

If you decrease κ, investment to reproduction increases, but this does not necessarily translate into more offspring. This is because food uptake is coupled to size, and so to growth, and offspring has to be produced from food (via reserves). An increase maintenance has many consequences for scaling relationships and size control.

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".

Answer:

You will see that biomass density is at maximum in absence of maintenance, while it is zero in presence of maintenance. The rate at which biomass density increases as a function of very small troughput rates depend on the specific maintenance costs.

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.

Answer:

Product density can be a rather complex function of throughput rate if the coupling coefficients to assimilation and growth become negative.

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.

Answer:

The substrate balance in the chemostat is

$$\frac{d}{dt}X = (X_r - X)\dot{h} - \frac{X j_{XAm}}{X+K} X_V$$

which gives $X_V^* = \frac{(X_r - X)(X+K)\dot{h}}{X j_{XAm}}$ at steady state. The specific growth rate equals the throughput rate at steady state, so $\dot{r}^* = \frac{f^* \dot{k}_E - g\dot{k}_M}{f^* + g} = \dot{h}$. So $f^* \equiv \frac{X^*}{X^*+K} = g\frac{\dot{k}_M + h}{\dot{k}_E - h}$ and $X = K\frac{f}{1-f}$. Product formation (see page 148 of the DEB book) equals: $j_P = \zeta_{PM}\dot{k}_M g + \zeta_{PA}\dot{k}_E f^* + \zeta_{PG} g\dot{h}$. The product balance in the chemostat is

$$\frac{d}{dt}X_P = X_V j_P - X_P \dot{h}$$

so that the steady state product concentration is $X_P^* = X_V^* j_P / \dot{h}$. This completes the biological part. Reactor's design parameters are the reactor volume V, the substrate concentration in the feed X_r and the throughput rate $\dot{h}$.

The balance equation for the financial costs is simple: The total money flux is

$$\dot{S} = \$_P \dot{J}_P - \$_X \dot{J}_X - \$_V \dot{J}_V$$

where $\$_*$ represents the mole-specific financial costs, and the molar product flux $\dot{J}_P = \dot{h}VX_P^*$, the molar substrate flux in the feed $\dot{J}_X = \dot{h}VX_r$, and the biomass flux $\dot{J}_V = \dot{h}VX_V^*$.

We now maximize S as function of the design parameters of the reactor. Since the money flux is linear in the reactor volume, the latter cannot be optimised yet. A realistic inclusion of the financial costs for stirring and cooling into the money flux can define the optimal size of the reactor.

This scheme can be made more realistic by including costs for labour and maintenance of the reactor, climate control, marketing, processing of substrate and medium in the effluent, or regeneration costs for the medium, for instance. Some costs, such as costs for transportation and for the medium, can be included in the coefficients $\$_*$ as long as they are linear in the amounts.

The next step is to code the money flux and maximise is numerically given estimates of the parameter values. This is not difficult in Octave or Matlab.

This application illustrates the typical situation that the DEB theory has to be supplemented with application-specific components to arrive at practical results.

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.

Answer:

Since the chemostat is dwelled by V1-morphs, their total biomass can be conceived of as a single individual. The unusual elements are that this 'super' V1-morph grows without becoming bigger, because the chemostat has a drain, and that the growth rate is human-controlled rather that the result of physiological processes that can be manipulated in an indirect way only.

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.

Answer:

It is possible to find combinations of parameter values for which the grazer hardly benefits (i.e. becomes more abundant) from grazing: it is killing the "chicken with the golden eggs". It is also possible to find parameter combinations for which the prey/predator ratio is rather insensitive to changes in substrate, which corresponds with a weak homeostasis situation. This marks the transition to a symbiontic system that can be captured with a single structural component.

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?

Answer:

The primary function of reserve is to incorporate metabolic memory. Bacteria live off many substrate, which they take up from the environment independently, while animals live off other organisms that already have all substrates that they need.

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?

Answer:

Partitionning, and especially merging, occurred frequently as part of the process of coupling and uncoupling of reserves, so increasing and decreasing the number of reserves, such that the overall dynamics is not affected. Organisational simplicity of integrated units is a functional constraint for robustness and regulatory systems.

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?

Answer:

The earliest mammals were carnivores, which explains why feeding on plants was rather problematic and the conversion efficiency from grass to cow is that low. The chemical composition of plants and animals differ more than within animals. Increasing the number of reserves was not an option (for several reasons). Quite a few plant taxa are not green and can't, therefore use photons as energy substrate. The earliest eukaryotes where heterotrophic; plants acquired phototrophy by symbiogenesis, but without refraining from heterotrophy. To mention another example: All plants and animals have mitochondria, which they acquired by symbiogenesis.

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.

Answer:

The explanations are given in Tables 11.2 and 11.3 of the comments.

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?

Answer:

SfG models typically ignore the embryo stage and subtract respiration from assimilation before considering production. Maintenance is typically identified with respiration (but not in DEB theory). Explicitly or not, growth overheads are typically included in respiration, which points to a fundamental problem in SfG-models. They also have problems to combine weak homeostasis with reserve, see Section 11.3 of the comments on topological alternatives.