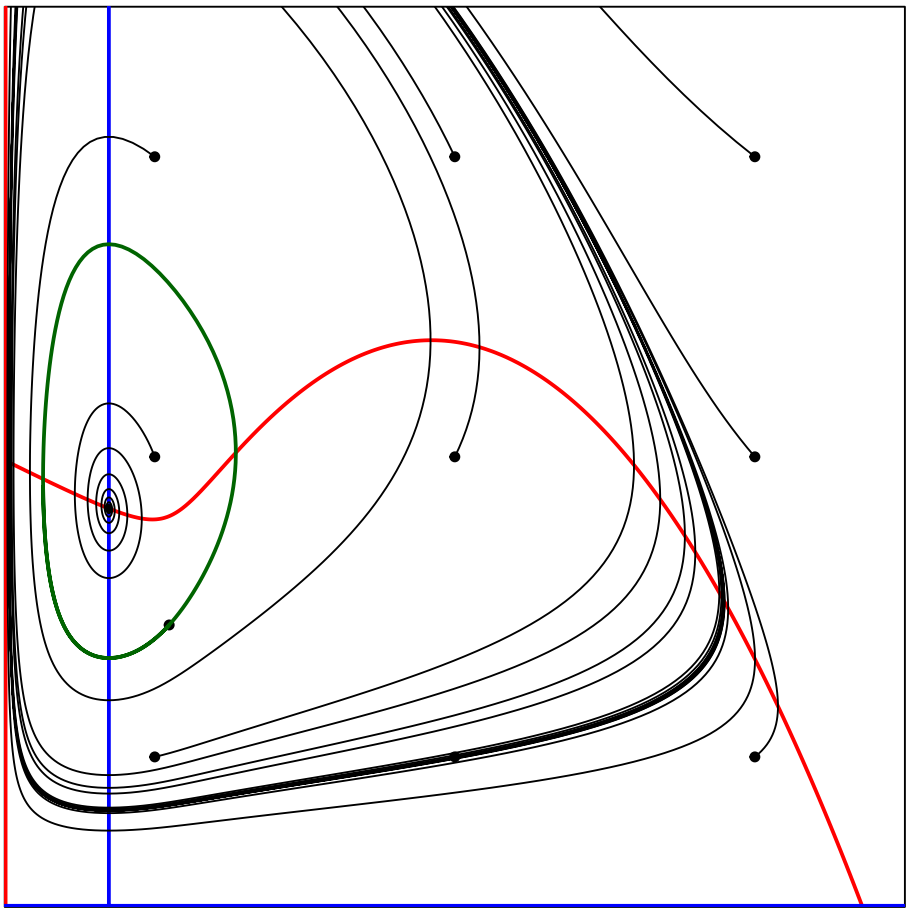
Biological Modeling of Populations

2025

Answers to Questions



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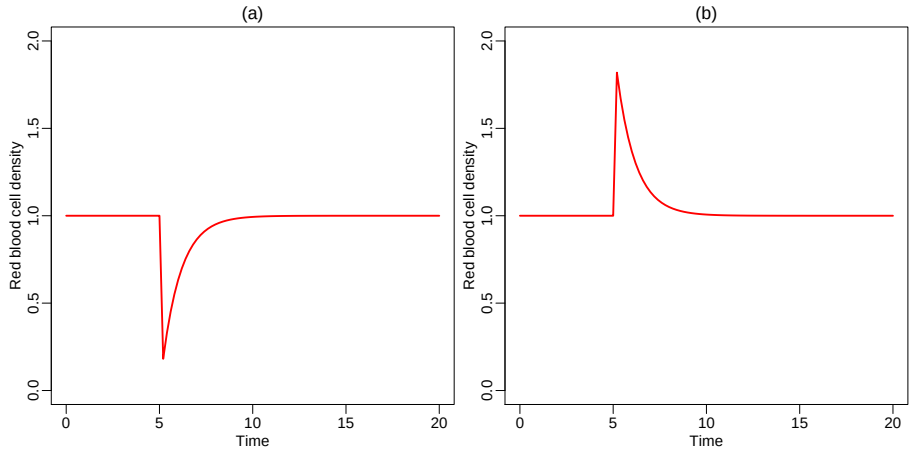
This addendum provides short answers to the questions in the ebook "Biological Modeling of Populations". Since many of the questions can be approached by using several different models, these answers are typically just one of the many possible answers. When you get stuck on a particular question, you may peek into its answer to obtain a hint enabling you to proceed. When you are done with a question, use this addendum to check if your own answer is correct and complete. Do not give up if your own answer is different, as it could very well be correct (and hopefully even better). Please report errors and suggestions for improvement, for instance by emailing me Rob de Boer at `r.j.deboer@uu.nl`.

Ebooks publicly available at:
tbb.bio.uu.nl/rdb/books/bm.pdf and books/bmAnswers.pdf

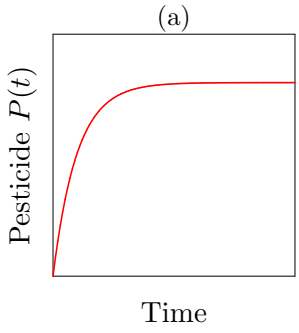
Answers to Chapter 2

Question 2.1. Red blood cells
Figure made with `blood.R`:



a. Since the production of red blood cells relies on a source we use Eq. (2.3), and rewrite that as $\mathrm{d}N/\mathrm{d}t = m - dN$.
b. Donating blood corresponds to Panel (a), where blood is taken at $t = 5$, and the steady state, $\bar{N} = m/d$, has been scaled to one (by setting $m = d = 1$).
c. Receiving blood corresponds to Panel (b), where blood is given at $t = 5$.

Question 2.2. Pesticides on apples
Figure made with a previous version of Grind:



a. An expected time course is depicted in Panel (a).
b. The pesticide concentration would approach its steady state $\bar{P} = \sigma/\delta$.
c. The model becomes $\mathrm{d}P/\mathrm{d}t = -\delta P$ with the initial condition $P(0) = \sigma/\delta$. Solving $P(0)/2 = P(0)\mathrm{e}^{-\delta t}$ yields $t_{1/2} = \ln[2]/\delta$.
d. From $\mathrm{d}P/\mathrm{d}t = 2\sigma - \delta P$ with $\bar{P} = 2\sigma/\delta$, one obtains the same $\ln 2/\delta$ days for the half life.
e. From $50 = \ln 2/\delta$ one obtains $\delta = 0.014$ per day.

Question 2.3. ATP
a. Since $\mathrm{d}A/\mathrm{d}t$ is measured in grams per day, p would be grams of ATP produced per day. Note that ADP and ATP cycle, according to the reaction $\mathrm{ADP} + \mathrm{P} \underset{\delta}{\overset{k}{\rightleftharpoons}} \mathrm{ATP}$, meaning that ATP is resynthesized when its end-product ADP spends energy to bind phosphate. Thus, the parameter p combines the mass-action parameter k and the concentrations of ADP and phosphate.
b. The steady state $\bar{A} = p/\delta$ g, and because we know there is 60 g of ATP we know that $p/\delta = 60$ g.
c. When $\delta\bar{A} = \delta 60 = 60\times10^3$ g of ATP per day, we estimate that $\delta = 10^3$ per day, or $\delta = 0.69$ per minute. The expected 'life span' on an ATP molecule would therefore be about $1/0.69 = 1.44$

minutes.

Question 2.4. Bacterial growth

a. The doubling time is defined as $t = \ln[2]/r$.

b. Since the neutrophil have to prevent bacterial growth we require that $\mathrm{d}B/\mathrm{d}t < 0$. Solving $\mathrm{d}B/\mathrm{d}t = rB - kNB = 0$, and neglecting the trivial $B = 0$ solution, we obtain $N = r/k$ for the critical number of neutrophils in a ml of blood.

c. The dimension of r is per hour. Since the total term kNB has dimension "number of bacterial per hour" (as measured in a ml of blood), the dimension of k should be "per neutrophil per hour". This can also be checked from the expression $N = r/k$ that should be "neutrophils" on the both the left- and right-hand side.

d. "bacteria per neutrophil per hour". This is the maximum number of bacteria that one neutrophil can encounter and kill per hour.

e. The critical number now depends of the concentration of bacteria, i.e., solving $\mathrm{d}B/\mathrm{d}t = rB - \frac{kNB}{h+B} = 0$ for N now gives $N = \frac{r}{k}(h + B)$. This is a straight line with slope r/k, intersecting the vertical axis at $N = rh/k$. Thus, the larger the infection, the more neutrophils are required. Note that this line is a nullcline: below this line $\mathrm{d}B/\mathrm{d}t > 0$, and above it $\mathrm{d}B/\mathrm{d}t < 0$.

f. h has the dimension number of bacteria per ml. When $B = h$ the model is $\mathrm{d}B/\mathrm{d}t = rB - kN/2$ saying the neutrophils are killing at a rate $k/2$, i.e., half their half-maximal killing rate.

Question 2.5. Physics: a cup of tea

a. Setting $\mathrm{d}T/\mathrm{d}t = c(T_E - T) = 0$ readily gives $\bar{T} = T_E$, i.e., ultimately the tea approaches room temperature.

b. c is a rate, with dimension $1/t$.

c. Three parameters: c, T_E and the initial value T_0.

Question 2.6. Physics: acceleration

a. The dimension of the velocity, v, is m/s and that of the acceleration, a, is m/s^2, which makes perfect sense.

b. For the plastic we write $\mathrm{d}p/\mathrm{d}t = k(t) = at + k(0)$, and the corresponding solution is $p(t) = \frac{1}{2}at^2 + k(0)t + p(0)$.

c. No, the amount of plastic will continue to increase at an accelerating rate.

Answers to Chapter 3

Question 3.1. Carrying capacity

a. The *per capita* birth rate is minimal when a population approaches its carrying capacity.

b. the *per capita* death rate is maximal when a population approaches its carrying capacity.

c. The individual well-being is expected to be best in an expanding population: the *per capita* birth rate is maximal and the *per capita* death rate is minimal.

d. With $\mathrm{d}N/\mathrm{d}t = rN[1 - N/(k\sqrt{N})] = 0$ one obtains the carrying capacity from $N/(k\sqrt{N}) = 1$ or $\sqrt{N} = k$ giving $\bar{N} = k^2$. This still is a finite carrying capacity, at which circumstances are poor. For the best circumstances the population has to remain below its carrying capacity.

Question 3.2. Homeostasis

a. No, the steady state of $\mathrm{d}B/\mathrm{d}t = m - dB = \alpha P - dB$ is $\bar{B} = \frac{\alpha P}{d}$. In such a model the number of peripheral B cells remains proportional to the number of bone marrow precursors, P.

b. For instance with density dependent death, $\mathrm{d}B/\mathrm{d}t = m - dB(1 + eB)$, or with density dependent production, $\mathrm{d}B/\mathrm{d}t = m/(1 + eB) - dB$, because with such a negative density dependence the steady state, $\bar{B}$, will depend less than proportional on $m = \alpha P$. Actually, the steady state of both density dependent models is solved from $m - dB - deB^2 = 0$, i.e.,

$$\bar{B} = \frac{d \pm \sqrt{d^2 + 4edm}}{-2ed} \quad \text{with one positive root} \quad \bar{B} = \frac{\sqrt{d^2 + 4edm}}{2ed} - \frac{1}{2ed} \ ,$$

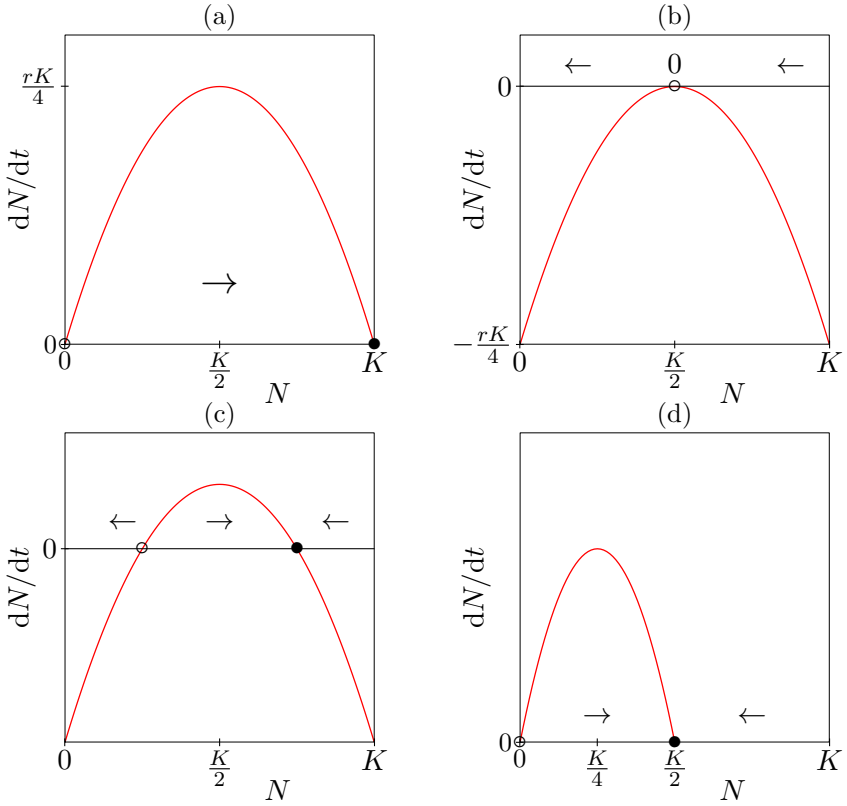
in which we see that steady state depends on the square root of the source $m = \alpha P$. Thus both models allow for some of the saturation observed by Agenes *et al.* [1], but do not predict a plateau at large numbers of progenitors. You may want to try alternative models starting with the Grind model provided as `agenes.R`.

c. Yes clearly, in the absence of homeostasis the steady number of peripheral B cells is proportional to the number of bone marrow precursors, and in the data it is not.

d. No, it is accounting for a steady state, but not for density dependent population regulation.

Question 3.3. Overfishing herring

Figure made with `herring.R`. Bullets and circles denote stable and unstable steady states, respectively:



a. Plotting $\mathrm{d}N/\mathrm{d}t = f(N) = rN(1 - N/K)$ as a function of N (or $y = rx(1 - x/K)$ as function of x), yields a parabola crossing the horizontal axis at $N = 0$ and $N = K$. The maximum of the function $f(N) = rN - rN^2/K$ is found by setting its derivative, $\partial_N f = r - 2rN/K$, to zero. This gives $\hat{N} = K/2$. Substituting this maximum into the population growth function, one obtains the maximum population growth of $f(\hat{N}) = rK/4$; see Panel (a).

b. The optimal population size is the one yielding maximum growth, i.e., $N = K/2$. At this optimal density, the total population growth, $rK/4$, could in principle be harvested.

c. We just add the harvest as a negative term to the model: $\mathrm{d}N/\mathrm{d}t = rN(1 - N/K) - Q$, with a total catch of $Q = rK/4$ herring per unit of time. The new model only has one steady state at $N = K/2$, which is unstable in the direction of lower densities; see Panel (b). Starting above this state, e.g., at $N = K$, while allowing for this maximum harvest, one would mathematically still expect an approach to this equilibrium. However, any disturbance of the population size bringing it below the level $N = K/2$, leads to extinction because the population entered the basin of attraction of $\bar{N} = 0$. Harvesting less than the maximum yield, $Q < rK/4$, allows for two steady states; see Panel (c). The upper one is stable and the lower one is unstable (a saddle point). The population remains vulnerable to extinction after large perturbations bringing the population size below the saddle point.

d. The first thing one needs to think about is the parameter values of the model. One could con-

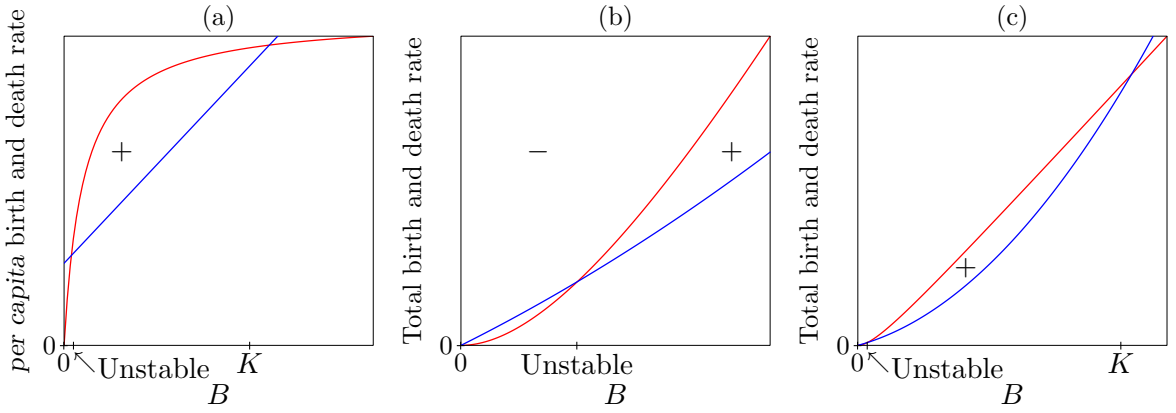
sider the Herring population in the North sea, and realize that a natural non-harvested population will have a carrying capacity amounting to huge number of individuals (or biomass). Fortunately, one can always scale the population density by the carrying capacity of the population. Thus, we can define a scaled carrying capacity, $K = 1$, defining that $H = 1$ corresponds to a natural Herring population at carrying capacity in the North sea. The next parameter to consider is the natural rate of increase, r. We first need to define a time scale, and for a Herring population with a yearly reproduction cycle, a time scale of years seems a proper choice. Then we are thinking of a growth rate per year, and using our biological intuition about fish of the size of Herring, it seems obvious that a growth rate of 1% per year seems slow and that they will not easily grow faster than 100% per year. Thus, setting $r = 0.1$ per year, or $r = 0.2$ per year, seem reasonable choices. One can actually check this by studying the recovery rate of a crashed Herring population in the absence of fishing: setting $H = 0.1$ and $Q = 0$, and run the model for a few decades to test how long it takes for the population to recover and approach its carrying capacity. Running the `herring.R` script for $Q = rK/4$ with a noisy carrying capacity reveals that the population ultimately goes extinct, confirming that a fixed quota of $Q = rK/4$ is not sustainable.

e. The steady state is computed from $\mathrm{d}H/\mathrm{d}t = rH(1-H/K) - fH = 0$, which gives the trivial $\bar{H} = 0$ and the non-trivial $\bar{H} = K(1-f/r)$ as long as $f < r$. The total harvest at steady state is $f\bar{H} = fK(1-f/r)$. The derivative of the harvest, $\partial_f(f\bar{H})$, is $K - (2K/r)f$, and setting that to zero to find a maximum gives $f = r/2$. Substituting that into $\bar{H}$ gives $\bar{H} = K/2$, i.e., half of the carrying capacity. For the total harvest we compute $f\bar{H} = rK/4$, which is the same as the fixed quota, Q, defined above. Thus, economically this should be the same.

f. The model $\mathrm{d}H/\mathrm{d}t = rH(1-H/K) - fH$ with $f = r/2$, is mathematically the same as a model with a linear density dependent birth rate and a density independent death rate (as discussed in Eq. (3.6)), and since this has a stable steady state at $\bar{H} = K(1-f/r) = K/2$, one no longer expects the population to go extinct; see Panel (d). This is confirmed by subjecting the model to the same fluctuations of the K parameter (using the `herring.R` script). We conclude that defining a fixed or a fractional quota does not make a difference for the total yearly harvest, but makes a huge difference in sustainability. A very simple model therefore suggest that it is much better to define fractional quota, and that this need not have any economic consequences.[1]

Question 3.4. Biofilm

Figures made with the model `biofilm.R`:



a. The function $y = \frac{bx}{h+x}$ is an increasing saturation function intersecting the vertical axis in the origin, and the function $y = d + ex$ is a straight line intersecting the vertical axis in $y = d$; see Panel (a). When $d < b$ these lines tend to intersect in two points, where the *per capita*

[1] A simpler argument leading to the same result is to see that the optimal harvest is obtained when the harvest function, fH, crosses the growth function, $rH(1-H/K)$, in its maximum, i.e., in $rK/4$ obtained at $H = K/2$.

birth rate equals the *per capita* death rate. The steady state at low population densities is unstable, and the one at high densities corresponds to the stable carrying capacity.

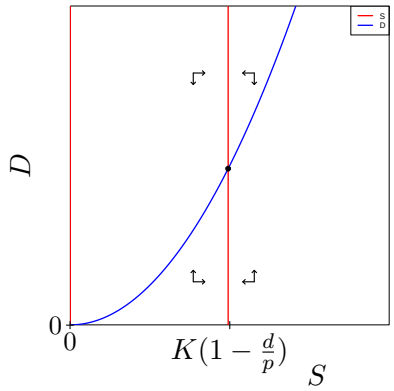
b. Because the birth function goes from quadratic to linear, and the death function from linear to quadratic, these tend to intersect three times: in the origin, at a low density and at a high density. See Panels (b) and (c) where (b) is a zoom-in at low population densities depicting the unstable intersect. (The red line depicts the birth rate and the blue line the death rate.)

c. We therefore find three steady states, with a stable origin and a stable carrying capacity, and a saddle point in the middle defining the population threshold corresponding to an Allee effect.

d. When the biofilm enhances survival, one should decrease the death rate, e.g., $\mathrm{d}B/\mathrm{d}t = \frac{bB}{1+B/k} - \frac{dB}{1+B/h}$, where we have put the negative density dependence in the birth rate to allow for a carrying capacity (and the Allee effect in the death rate). The *per capita* death rate is d when the population is small, decreases to $d/2$ when $B = h$, and approaches zero when $B \to \infty$.

Question 3.5. Stem cells

The Figure was made with the model `stem.R`:



a. Defining p as the division rate, and d as a death rate, a natural model would be $\mathrm{d}S/\mathrm{d}t = pS(1-S/K) - dS$, where we could define a time scale of days, i.e., the dimension of p and d are d^{-1}, and that of K is cells. Because the size of the substrate naturally limits the number of stem cells, the division (birth) rate is density dependent. Note that this equation corresponds to the logistic growth model of Eq. (3.6).

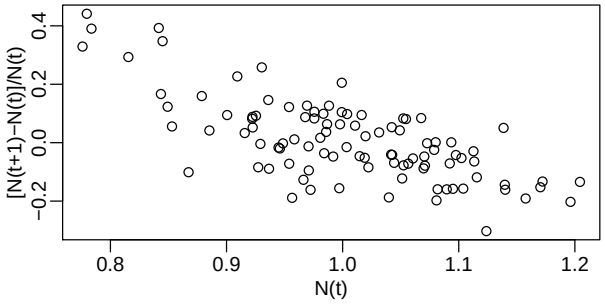
b. Solving $\mathrm{d}S/\mathrm{d}t = 0$ gives the non-trivial solution $\bar{S} = K(1-\frac{d}{p})$, which is smaller than K because sites are continuously freed up by cell death.

c. Because the fraction S/K of the dividing stem cells differentiates, one obtains $\mathrm{d}D/\mathrm{d}t = \frac{p}{K}S^2 - \delta D$.

d. The production rate is $\frac{p}{K}S^2$, which has the parabolic form of $y = ax^2$. Note that this despite the quadratic form this production has a correct dimension cells d^{-1} because p has a dimension d^{-1}, and K has dimension cells. The production rate remains bounded, however, because there can be no more than $\bar{S} = K(1-\frac{d}{p})$ stem cells, i.e., the maximum production is $pK(1-\frac{d}{p})^2$ cells d^{-1}.

e. The $\mathrm{d}S/\mathrm{d}t = 0$ nullcline is given by $\bar{S} = K(1-\frac{d}{p})$ and the $\mathrm{d}D/\mathrm{d}t = 0$ nullcline by $D = \frac{p}{K\delta}S^2$, which is a parabola going through the origin (see the figure). Since $\mathrm{d}D/\mathrm{d}t > 0$ when S is large and D is small the differentiated cells increase on the right-hand side of their nullcline. Stem cells increase below their steady state. The vector field reveals that this steady state is stable.

Question 3.6. Regression to the mean



a. Since everything is random, the first expectation is that one should find not correlation between the *per capita* change,$(N_{t+\Delta} - N_t)/N_t$, and the previous density, N_t.

b. We nevertheless find a significant correlation. Although all N_t values are random, relatively small N_t values tend to create a large deviate $N_{t+\Delta} - N_t$, which is subsequently "boosted" by dividing by a small N_t value. In statistics this is known as the "regression to the mean" phenomenon. Thus, testing for density dependence in a random time series is expected to lead to statistically significant evidence.

c. This "tought-experiment" illustrating the main message of the Shenk *et al.* [14] and Freckleton *et al.* [4] papers tells us that one needs to be careful when searching for evidence for density dependence in time-series data.

Question 3.7. Fitting the Logistic growth Gause data from 1934

a. Yes, the fits look quite reasonable and we obtain very similar estimates for the two growth rates and carrying capacities of both species. Apparently, the logistic equation can adequately capture the *in vitro* growth curves of these two *Paramecium* species.

b. Fitting both the initial condition, $N(0)$, and the natural rate of increase, r, does not work well because they are correlated, i.e., a high r can be compensated for by a low $N(0)$. Both parameters are therefore not identifiable from this data (see the low P-value for $N(0)$). To obtain a more reliable estimate for r, we therefore fix $N(0)$ by the first data point in the data. Finally, we check the confidence range of r and K by bootstrapping (sampling) the data a 100 times. Now both parameters seem identifiable.

c. The confidence ranges of the parameter estimates of *P. aurelia*, $1 \lesssim r \lesssim 1.2$ and $99 \lesssim K \lesssim 108$, and these of *P. caudatum*, $0.75 \lesssim r \lesssim 1.4$ and $53 \lesssim K \lesssim 70$, overlap in the growth rates, but not in the carrying capacities. Thus, the two species clearly have a markedly different carrying capacity, but need not have different growth rates.

d. Fitting the data with four free parameters, or with a shared growth rate (i.e., with three free parameters), provides quite similar fits that nevertheless differ considerably in the summed squared residuals, i.e., SSR=1111 and SSR=1282, respectively. An F-test, i.e., $F[1, 24] = 3.69$ indicates that this difference is not significant ($P = 0.067$). Hence the 4-parameter model is not significantly better than the 3-parameter model.

e. The two species differ markedly in their carrying capacity and hardly in their growth rate. Since *P. aurelia* has the highest carrying capacity its usage of the resource should be more efficient. Since we can only estimate a net growth rate, r, and do not know their birth and death rates, we cannot estimate their R_0s, and we therefore no nothing about the difference in fitness between the two species.

Question 3.8. Habitat destruction

a. Solving the non-trivial solution of $cP(1-P)-eP = 0$, i.e., of $c-cP-e = 0$, gives $\bar{P} = 1-e/c$. The model is actually a scaled version of Eq. (3.6).

b. According to the $\bar{P} = 1 - e/c$ result, the species is absent from a fraction e/c of the patches in a pristine environment. Since the fraction of empty patches increases with the extinction rate, and decreases with the colonization rate, this is a quite natural property of the model.

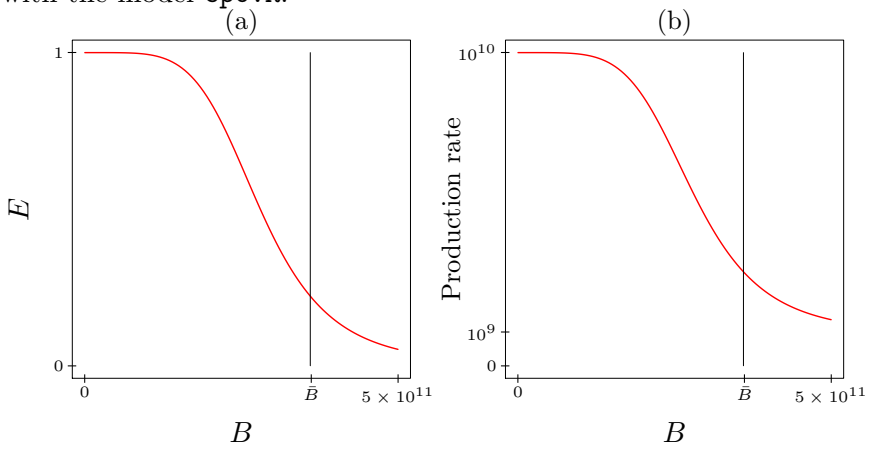
c. Solving the non-trivial solution of $cP(\alpha - P) - eP = 0$, i.e., of $c\alpha - cP - e = 0$, gives $\bar{P} = \alpha - e/c$, which has a similar form as the answer from the pristine environment.

d. Solving $\bar{P} = \alpha - e/c = 0$ gives $\alpha = e/c$.

e. A species that was present at a frequency $\bar{P} = 1 - e/c = 0.01$ in the pristine environment has an extinction to colonization ratio $e/c = 0.99$. For the perturbed environment one therefore finds that the species is expected to go extinct when $\alpha = 0.99$, i.e., when just 1% of the patches is destroyed ($\Delta = 1 - \alpha = 0.01$). This counterintuitive result could well be realistic because this species is so rare because it is a poor colonizer that easily goes extinct. Such a species needs many patches to survive globally.

Question 3.9. Red blood cells

Figure made with the model `epo.R`:



a. Scaling the maximum concentration of EPO to one, we write the declining Hill function $E = \frac{1}{1+(B/h)^n}$. Because this should be a steep sigmoid function we set $n = 5$; see Panel (a), where we have set $h = 2.8 \times 10^{11}$ (see below).

b. We defined a minimum production rate, $s_0 \simeq 10^9$ cells kg^{-1} d^{-1}, in the absence of EPO. Hence we could write $s_0 + s_1 E$ for the total production rate. Because the maximum production when $E = 1$ is 10^{10} cells kg^{-1} d^{-1}, i.e., $s_0 + s_1 = 10^{10}$, we obtain that $s_1 \simeq 9 \times 10^9$. The total production is plotted in Panel (b).

c. Together this leads to

$$\frac{\mathrm{d}B}{\mathrm{d}t} = s_0 + s_1 E - dB \quad \text{where} \quad E = \frac{1}{1 + (B/h)^n} \ ,$$

$s_0 \simeq 10^9$, $s_1 \simeq 9 \times 10^9$, and $d = 1/120$. Knowing that the normal steady state is $\bar{B} = 3.6 \times 10^{11}$ RBC, one can solve the unknown h parameter from $\mathrm{d}B/\mathrm{d}t = 0$. For $n = 1$ one can do this by hand,

$$s_0 + \frac{s_1}{1 + \bar{B}/h} = d\bar{B} \quad \leftrightarrow \quad \frac{s_1}{1 + \bar{B}/h} = d\bar{B} - s_0 \quad \leftrightarrow \quad \frac{s_1}{d\bar{B} - s_0} = 1 + \frac{\bar{B}}{h} \quad \leftrightarrow$$

$$\frac{s_1}{d\bar{B} - s_0} - 1 = \frac{\bar{B}}{h} \quad \leftrightarrow \quad \frac{s_1 - d\bar{B} + s_0}{d\bar{B} - s_0} = \frac{\bar{B}}{h} \quad \leftrightarrow \quad h = \bar{B}\frac{d\bar{B} - s_0}{s_0 + s_1 - d\bar{B}} \simeq 1.03 \times 10^{11} \ .$$

The general case, i.e., $n > 1$ can be solved by Mathematica (see the `epo.nb` script), or by the function `uniroot.all()` in R (see the `epo.R` script), and for $n = 5$ this leads to $h = 2.8 \times 10^{11}$.

d. Running the model for these parameters indeed leads to the normal steady state of $\bar{B} = 3.6 \times 10^{11}$ cells kg^{-1}. Patients not producing EPO have the steady state of $\bar{B} = s_0/d = 1.2 \times 10^{11}$ cells kg^{-1}, which is 3-fold lower than the normal number of RBC.

e. Running the model after halving s_0 and s_1 leads to a 23% loss of the RBC in the blood, i.e., for $s_0 = 5 \times 10^8$ and $s_1 = 4.5 \times 10^9$ one finds $\bar{B} = 2.7 \times 10^{11}$ cells kg^{-1}, which is quite a decrease from the normal $\bar{B} = 3.6 \times 10^{11}$ cells kg^{-1}. For the current parameters, the model therefore fails to perfectly explain the similar RBC numbers in elderly individuals (if a 50% reduction in productive bone marrow tissue is realistic).

Question 3.10. Generalized logistic growth

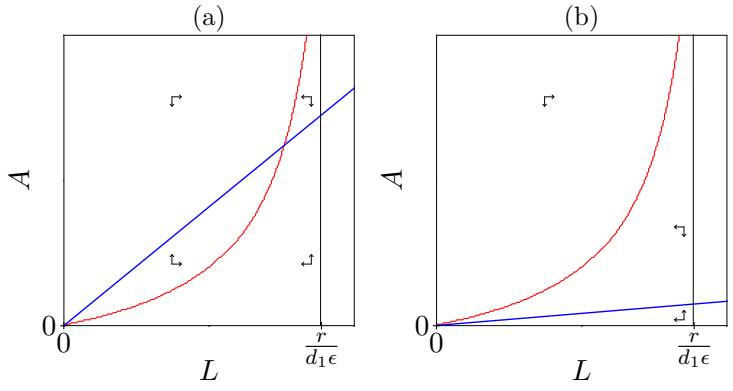
a. The *per capita* growth term in the standard logistic equation is of the form $r(1 - N/K) = r - kN$, where $k = r/K$. Summing *per capita* birth and death rates of the form $b(1 - N/k_b)$ and $d(1 + N/k_d)$, respectively, also yields a *per capita* growth rate of the form $r - kN$, where $r = b - d$ and k is a combination of all four parameters.

b. This would be a *per capita* birth rate of the form $b(1-(N/k)^m)$, which is concave when $m > 1$ (like blue red line in Fig. 3.3c, and convex when $m < 1$ (like the green line in Fig. 3.3c). The concave shape would mean that the negative density dependence on the birth process kicks in at relatively high population densities, which would be realistic when resources become limiting only after the population has expanded. The convex shape would imply that effect of competition on the birth rate is steepest at low densities, which would be realistic for a population expanding spatially, and growing at its border. Thus, any positive value of m seems legitimate.

c. The death rate would be of the form $d(1 + (N/k)^m)$, which for $m > 1$ would mean that the increase of *per capita* death rate keeps accelerating when the population expands. For $m < 1$ the increase of the *per capita* death rate decelerates with the population size. Both could be realistic and hence any positive value of m seems legitimate.

Question 3.11. Life stages

Figure made with a previous version of Grind:



a. To define how the mortality of larvae depends on the density of the adults, A, we need to define a function, $f(A)$, that increases with A. Choosing for simplicity, e.g., $f(A) = d_1(1+\epsilon A)$, we would have a linearly increasing function, where d_1 defines the natural death rate of larvae in the absence of adults, and $1/\epsilon$ is the adult density at which the death rate doubles (to $2d_1$). For the larvae, L, and the adults one would then write

$$\frac{\mathrm{d}L}{\mathrm{d}t} = rA - mL - f(A)L = rA - mL - d_1(1 + \epsilon A)L \quad \text{and} \quad \frac{\mathrm{d}A}{\mathrm{d}t} = mL - d_2 A \ ,$$

where m is the maturation rate of the larvae, and r the rate of reproduction by the adults.

b. To simplify the algebra we rewrite the ODE for the larvae into $\mathrm{d}L/\mathrm{d}t = rA - m'L - d_1'LA$, where $m' = m + d_1$ and $d_1' = d_1\epsilon$, and solve the larvae nullcline from $rA - m'L - d_1'LA = 0$. Solving for A we define A as the vertical axis, and L as the horizontal axis, and obtain $A = \frac{m'L}{r - d_1'L}$. This is zero when $L = 0$ (i.e., goes through the origin), and has a vertical asymptote at $L = r/d_1'$. The slope in the origin is computed from the derivative $\partial_L A$,

$$\frac{m'}{r - d_1'L} + \frac{m'd_1'L}{(r - d_1'L)^2} \quad \text{which for } L = 0 \text{ gives} \quad \frac{m'}{r} \ .$$

See Panel (a). For the adults $\mathrm{d}A/\mathrm{d}t = mL - d_2A = 0$ gives $A = \frac{mL}{d_2}$, which is a straight line through the origin with slope m/d_2. If $m/d_2 > m'/r = (m + d_1)/r$ the

two nullclines intersect in a non trivial stable steady state. Otherwise the origin is the only steady state (see Panel (b)). (Also see the online tutorial for sketching nullclines on tbb.bio.uu.nl/rdb/bm/clips/nullclines for the a rotated version of the same phase space).

c. Assuming a quasi steady state for the larvae, one has to solve L from $\mathrm{d}L/\mathrm{d}t = 0$, giving $\hat{L} = \frac{rA}{m'+d_1'A}$.

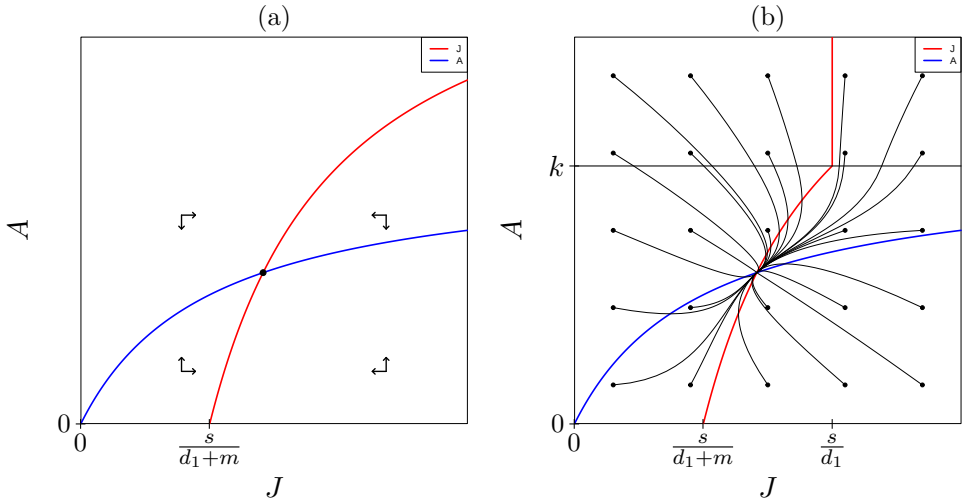
d. Substituting $\hat{L}$ into the adult equation gives $\mathrm{d}A/\mathrm{d}t = \frac{mrA}{m'+d_1'A} - d_2A$ for the quasi steady state model. This is one of the models with a density dependent birth rate (see Table 3.1).

e. From $A = (m/d_2)L$ we get $\mathrm{d}L/\mathrm{d}t = (r'-m')L - dL^2$ where $r' = rm/d_2$ and $d = d_1'm/d_2$, which has the form of a logistic growth equation.

f. In many insect species the adults live much shorter than the larvae. Then $\mathrm{d}A/\mathrm{d}t = 0$ would be most realistic.

Question 3.12. Seedlings over-shadowed by adult plants

Figure made with the model `seedling.R`:



a. Because shadowing is expected to be linear (i.e., proportional to A), a natural model would look like:

$$\frac{\mathrm{d}J}{\mathrm{d}t} = s - d_1J - mJ(1-A/k) \quad \text{and} \quad \frac{\mathrm{d}A}{\mathrm{d}t} = mJ(1-A/k) - d_2A \ ,$$

where $f(A) = 1 - A/k$ defines a "shadowing" function. For the nullcline of the seedlings we set $\mathrm{d}J/\mathrm{d}t = 0$, i.e.,

$$s - d_1J - mJ + \frac{m}{k}JA = 0 \leftrightarrow s - d_1J - mJ = -\frac{mJ}{k}A \leftrightarrow A = \frac{k(d_1+m)}{m} - \frac{sk}{mJ} \leftrightarrow A = \alpha - \frac{\beta}{J} \ ,$$

where $\alpha = \frac{k(d_1+m)}{m} = k + kd_1/m$ and $\beta = sk/m$. To sketch this we define A as the vertical axis and J as the horizontal axis. Next we

1. find the intersection with x-axis by solving $A = 0$, i.e.,

$$\alpha = \beta/J \quad \text{or} \quad J = \beta/\alpha = \frac{sk}{m}\,\frac{m}{k(d_1+m)} = \frac{s}{d_1+m} \ ,$$

2. find a horizontal asymptote by sending $J \to \infty$, which gives $A \to \alpha$, or $A \to k + kd_1/m$,
3. find a vertical asymptote by sending $J \to 0$, which gives $A \to -\infty$,
4. and compute the derivative, $A' = \frac{\beta}{J^2}$, to find out that the slope is always positive, i.e., there are no minima and maxima,

(see the online tutorial on sketching functions). So this is a hyperbola approaching the negative y-axis, intersecting the x-axis, and approaching the horizontal asymptote $A = k + \frac{kd_1}{m}$; see Panel (a). For the nullcline of the adult plants one sets $\mathrm{d}A/\mathrm{d}t = 0$:

$$mJ - \frac{m}{k}JA - d_2A = 0 \leftrightarrow mJ = A(d_2 + mJ/k) \leftrightarrow A = \frac{mJ}{d_2 + mJ/k} = \frac{kJ}{kd_2/m + J} = \frac{kJ}{h + J}$$

where $h = kd_2/m$. This is a Hill function when A is plotted as a function of J. Indeed,

1. setting $J = 0$ gives $A = 0$, which is the origin of the phase space,
2. letting $J \to \infty$ gives $A \to k$, which is a horizontal asymptote,
3. we ignore the vertical asymptote at $J = -h$, because one can safely ignore negative population densities,
4. we fill in the special point $J = h = kd_2/m$ because that gives $A = k/2$.

(see the online tutorial on sketching functions). So this is an increasing Hill function starting in the origin and approaching the horizontal asymptote $A = k$; see Panel (a). The point where the nullclines intersect is a stable steady state because the vector field is pointing towards it in all four regions around it.

Actually, our shadowing function, $f(A) = 1 - A/k$, is not completely correct because $f(A)$ will become negative whenever $A > k$, i.e., above the horizontal line in Panel (a). To prevent this one can write $f(A) = \max[0, 1 - A/k]$, which returns $f(A) = 0$ when $A > k$. This is depicted in Panel (b), and has little effect because the steady state is necessarily located below the line $A = k$.

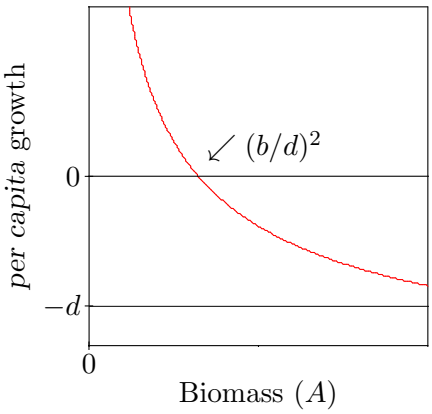
b. Yes, these nullclines cross whenever $k + \frac{kd_1}{m} > k$, which is always true. Intuitively, this can be understood because the seed bank always allows some seedlings to be present, and some of these should always mature to become adult plants. The population cannot become infinitely large because the seedlings are limited by the seed bank, and on top of that the adult plants are limiting their own production.

c. Yes, the vector field points towards the steady state in every section of the phase space. Note that arrows point rightwards on the left-hand side of the $\mathrm{d}J/\mathrm{d}t = 0$ nullcline because $\mathrm{d}J/\mathrm{d}t > 0$ for small values of J, and that arrows point upwards below the $\mathrm{d}A/\mathrm{d}t = 0$ nullcline because $\mathrm{d}A/\mathrm{d}t > 0$ for small values of A. Hence, this is a feasible model because it allows the vegetation to approach some carrying capacity.

d. Yes, this model allows for homeostasis because there is a negative density dependence from adults onto juveniles: the higher the adult density the more juveniles die (the minimum fraction being $\frac{d_1}{d_1+m}$).

Question 3.13. Tumor growth

Figure made with a previous version of Grind:



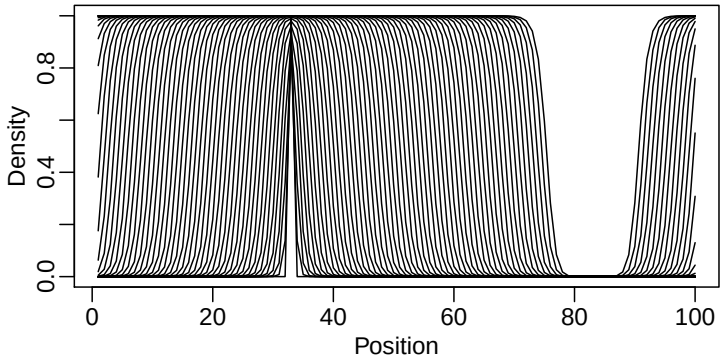
a. Since the total biomass is given by $A = c\pi r^2$, one obtains that the radius $r = \sqrt{\frac{A}{c\pi}} =$

$c'\sqrt{A}$, where c' is a new scaling constant. The total growth rate, G, is proportional to the circumference, i.e., $G \propto 2\pi r$, which after substituting the radius becomes $G \propto 2\pi c'\sqrt{A}$ or $G = b\sqrt{A}$, where b is a "birth rate" that is proportional to the square root of the biomass. On the other hand, the total death rate should be proportional to the total biomass, A. A natural model would therefore be $\mathrm{d}A/\mathrm{d}t = G - dA = b\sqrt{A} - dA$.

b. The carrying capacity is solved from $b\sqrt{A} - dA = 0$, or $b - d\sqrt{A} = 0$ giving $\bar{A} = (b/d)^2$. There is a trivial steady state, $A = 0$, corresponding to having no tumor.

c. The *per capita* growth $\frac{\mathrm{d}A/\mathrm{d}t}{A} = \frac{b}{\sqrt{A}} - d$. Which for $A \to \infty$ approaches the horizontal asymptote $-d$, which is perfectly reasonable (see the Figure). However, for small population sizes, i.e., $A \to 0$, the *per capita* growth rate blows up, which is not a good property of the model.

Question 3.14. The Fisher equation



a. The model defines a vector of left and right neighbors by initializing two vectors filled with with zeros. The left neighbor of compartment i is then defined as compartment $i-1$, and the left neighbor of the first compartment is set as the last compartment. For the right neighbors this is just the other way around. The `dtN` line then computes the derivatives for the whole vector of compartments.

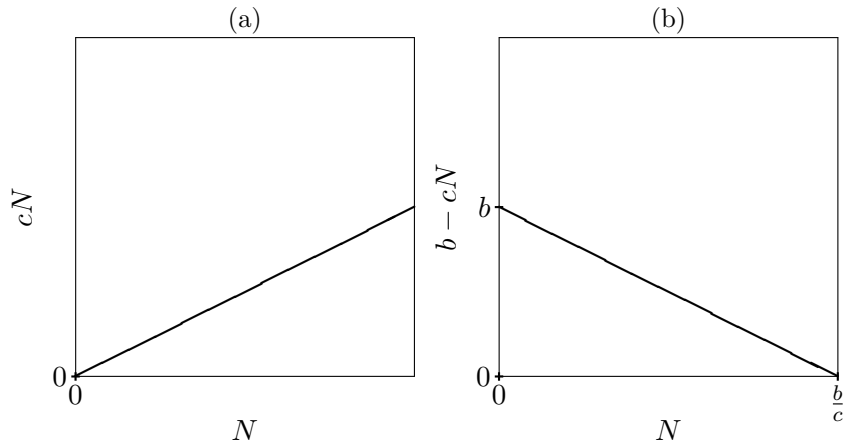
b. Starting at position 30, this code creates a wave traveling left- and right-wards. The wave traveling left-wards re-enters the space on the right (see the Figure).

c. If the Allee effect is sufficiently strong and the diffusion sufficiently slow it should be possible to stop the wave. Try this!

Answers to Chapter 4

Question 4.1. Density dependent death

Figure made with a previous version of Grind:



a. In the model $\mathrm{d}N/\mathrm{d}t = (b - cN)N$, the *per capita* death rate is cN: see Panel (a)
b. The net *per capita* growth rate is $b - cN$: see Panel (b).
c. The trivial steady state is $N = 0$, and solving $b - cN = 0$ gives the non-trivial steady state $\bar{N} = b/c$.
d. The R_0 is not defined because the individuals have no expected life span, i.e., at low densities the generation time goes to infinity .
e. The derivative with respect to N is $b - 2cN$. Substituting $N = b/c$ yields $\lambda = -b < 0$. Thus the return time $T_R = 1/b$ is fully determined by the birth rate and is independent of the density dependent death rate c.

Question 4.2. Return time

a. For $\mathrm{d}N/\mathrm{d}t = f(N) = bN(1 - N/k) - dN$ there are two steady states, the origin $\bar{N} = 0$, and the carrying capacity $\bar{N} = k(1 - d/b)$. For the return time to the carrying capacity one computes the derivative $\partial_N f(N) = b - d - 2bN/k$ and substitutes the steady state value to obtain

$$\lambda = b - d - \frac{2b}{k}\, k(1 - d/b) = d - b \quad \text{and} \quad T_R = \frac{-1}{\lambda} = \frac{1}{b - d}\ .$$

For $\mathrm{d}N/\mathrm{d}t = g(N) = bN - dN(1 + N/K)$ there are also two steady states, the origin $\bar{N} = 0$, and the carrying capacity $\bar{N} = k(b/d - 1)$. For the return time to the carrying capacity one computes the derivative $\partial_N g(N) = b - d - 2dN/k$ and substitutes the steady state value to obtain

$$\lambda = b - d - \frac{2d}{k}\, k(b/d - 1) = d - b \quad \text{and} \quad T_R = \frac{-1}{\lambda} = \frac{1}{b - d}\ .$$

Thus, in both models the return time decreases when the net rate of increase, $r = b - d$, increases (which underlies the r versus K-selected paradigm).

b. For $\mathrm{d}N/\mathrm{d}t = f(N) = s - dN$ with steady state $\bar{N} = s/d$, the derivative $\partial_N f(N) = -d$, which immediately gives $\lambda = -d$ and $T_R = 1/d$.
c. The s and k parameters are not rates, but have dimension $[N\ \text{time}^{-1}]$ and $[N]$, respectively. Because both depend on the units of the population size, one can always scale the population size such that $s = 1$ and $k = 1$. For instance, scaling the non-replicating population by its steady state, $\bar{N} = s/d$, by defining a scaled population as $n = \frac{d}{s}N$, and then substitute $N = \frac{s}{d}n$ into $\mathrm{d}N/\mathrm{d}t = s - dN$, one obtains the scaled ODE

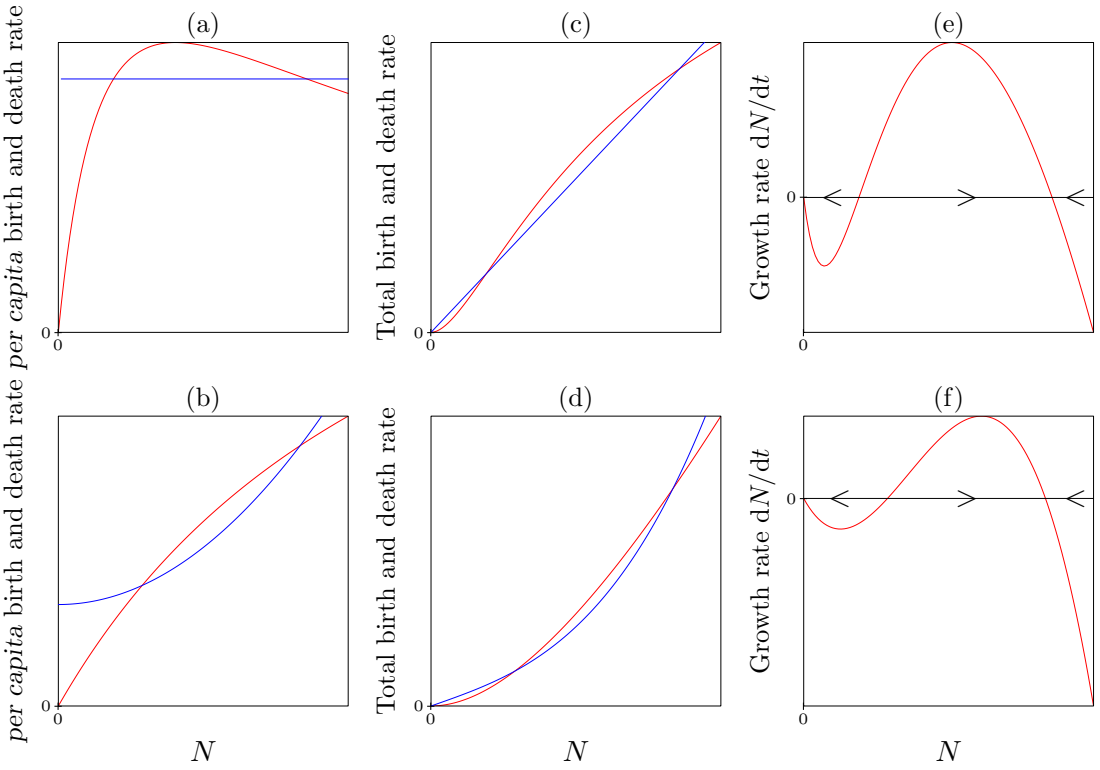
$$\frac{s}{d}\,\frac{\mathrm{d}n}{\mathrm{d}t} = s - \frac{s}{d}dn \quad \text{or} \quad \frac{\mathrm{d}n}{\mathrm{d}t} = d - dn\ ,$$

which has the death rate as its only parameter, see Section 15.4.

d. The ODE $\mathrm{d}N/\mathrm{d}t = s(1 - N/k) - dN$ can be written as $\mathrm{d}N/\mathrm{d}t = s - (s/k + d)N = s - \delta N$, where $\delta = s/k + d$. This is of the same form as $\mathrm{d}N/\mathrm{d}t = s - dN$, and hence the return time is given by $R_T = \frac{1}{\delta} = \frac{1}{s/k+d}$, which is shorter than $1/d$. Note that the parameter s is now part of the return time because s/k is a rate.

Question 4.3. Whales

Figures made with the model `whales.R`:



After defining the probability that an individual female finds a male as a saturation function, $p(N) = N/(h + N)$, one needs to allow for a carrying capacity by including negative density dependence in the birth and/or the death terms:

a. Assuming density dependent birth one would write something like

$$\frac{\mathrm{d}N}{\mathrm{d}t} = \frac{bN}{1 + N/K}\,\frac{N}{h + N} - dN\ , \tag{A.4.1}$$

and assuming density dependent death one could write

$$\frac{\mathrm{d}N}{\mathrm{d}t} = bN\frac{N}{h + N} - dN(1 + (N/k)^2)\ , \tag{A.4.2}$$

and in reality one could have a combination of the two. Curves corresponding to Eq. (A.4.1) are depicted in the upper row; those corresponding to Eq. (A.4.2) in the lower row.

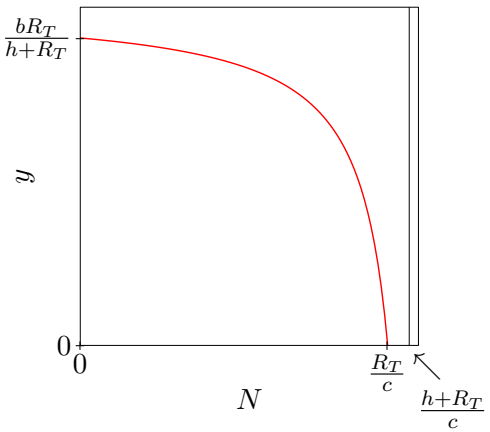
b. The *per capita* birth rate (in red) and the death rate (in blue) are depicted in Panels (a) and (b). The total birth rate (in red) and the death rate (in blue) are depicted in Panels (c) and (d).

c. The population growth rates are shown in Panels (e) and (f). The basins of attraction are defined by the intersections by the black line located at $\mathrm{d}N/\mathrm{d}t = 0$ (see the arrows).

Answers to Chapter 5

Question 5.1. Sketch the *per capita* birth rate

Figure made with the file `birth.R`:

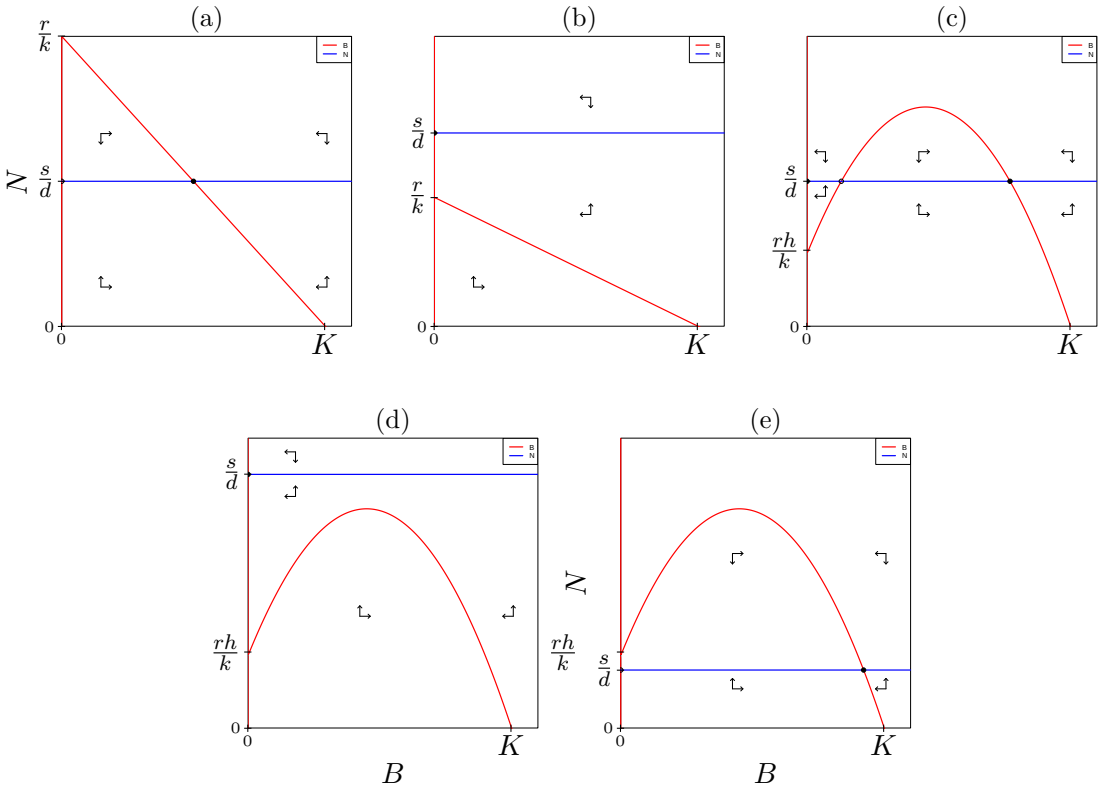


a. Plotting $y = \frac{b(R_T - cN)}{h+R_T-cN}$ as a function of N needs to be done in several steps. First, $y = 0$ when $N = R_T/c$, i.e., when all of the nutrient is contained in the cells. At low population densities the population approaches the birth rate $y = \frac{bR_T}{h+R_T}$, and when the saturation constant, h, is much smaller than the total resource density, R_T, this will approach the maximum birth rate b. When N increases the *per capita* birth rate will decrease. The full function has a vertical asymptote at $N = \frac{h+R_T}{c}$, which is located beyond the point, $N = R_T/c$, where $y = 0$. We find the horizontal asymptote by first writing $y = \frac{bR_T/N - bc}{h/N+R_T/N-c}$, and then taking the limit $N \to \infty$ to find that $y \to b$. We therefore obtain the concave hyperbolic function depicted above.

b. This concave shape is what we considered most realistic in Chapter 3. For instance see Fig. 3.3c and Fig. 3.5b.

Question 5.2. Neutrophils

Figure made with `neutrophils.R`:



a. The nullcline is derived by setting $\mathrm{d}B/\mathrm{d}t = rB(1 - B/K) - kNB = 0$ giving $B = 0$ and

$N = \frac{r}{k}(1 - B/K)$. Plotting N on the vertical axis and B on the horizontal axis, the latter is a straight declining line starting at $N = r/k$ and ending at $B = K$ (just like the prey nullcline of the Lotka-Volterra model). The nullcline of the neutrophils is defined by the line $N = s/d$. These lines will only intersect when $\frac{r}{k} > \frac{s}{d}$. In Panel (a) the uninfected state, $(\bar{B}, \bar{N}) = (0, s/d)$, is unstable because bacteria can invade, and there is a stable state corresponding to a chronic infection. In Panel (b) the uninfected state is stable, as small infections cannot grow.

b. Comparing Panel (a) with (b) we observe that bacterial invasions are immediately controlled when $s/d > r/k$ (which is similar to the $kN > r$ obtained in Chapter 2).

c. The nullcline of the ODE for the bacteria is derived by setting $\mathrm{d}B/\mathrm{d}t = rB(1-B/K) - \frac{kNB}{h+B} = 0$ giving $B = 0$ and the parabola $N = \frac{r}{k}(1 - B/K)(h + B)$.[2] This parabola intersects the horizontal axis at $B = -h$ and $B = K$, intersects the vertical axis at $N = rh/k$, and has a maximum at $R = (K - h)/2$. All qualitatively different situations are sketched in Panels (c)–(e). The situation in Panel (d) is like that of Panel (b), where small infections cannot grow. In Panel (e) the situation is like that in Panel (a), with one stable state corresponding to a chronic infection. In Panel (c) the uninfected state, $(\bar{B}, \bar{N}) = (0, s/d)$, is a stable node, the steady state marked by the open circle is a saddle point, and the steady state marked by the bullet is a stable node, corresponding to a chronic infection.

d. In Panel (d) the normal neutrophil level $\bar{N} = s/d$ is sufficient for controlling an infection of any size, which happens whenever s/d is larger the top of the parabola. Technically, this can be computed by substituting $B = (K - h)/2$ into the equation for the nullcline $N = \frac{r}{k}(h + B)(1 - B/K)$, giving $\frac{s}{d} > \frac{r(h+K)^2}{4kK}$. In Panel (e) the normal neutrophil level $\bar{N} = s/d$ is too low to control any bacterial infection, which happens when s/d is smaller than the intercept of the parabola with the vertical axis at $\frac{rh}{k}$, giving $\frac{s}{d} > \frac{hr}{k}$ as the condition for immediate control. In Panel (c) this condition is fulfilled and small infections are immediately controlled by normal neutrophil levels, whereas large bacterial infections grow. The situation of Panel (c) occurs when s/d is higher than the intercept and lower than the top of the parabola. Technically, this means that

$$\frac{rh}{k} < \frac{s}{d} < \frac{r(h+K)^2}{4kK} \ .$$

The maximum size of a controllable infection can be computed by substituting $N = s/d$ into the equation for the nullcline of the bacteria, i.e., $\frac{s}{d} = \frac{r}{k}(1 - B/K)(h + B)$ and solving this quadratic equation for B (not shown).

e. A large transient output from the bone marrow tends to overcome the thresholds defined above.

Question 5.3. Lotka-Volterra models

a. This would indeed be compatible with $\mathrm{d}T/\mathrm{d}t = rT(1-T/K) - kTN$ and $\mathrm{d}N/\mathrm{d}t = aTN - dN$ for the tumor, T, and natural killer cells, N, respectively. Here k is a mass-action killing rate and a the mass-action activation rate allowing the natural killing cells to divide.

b. In Chapter 6 we will encounter the SI model, $\mathrm{d}S/\mathrm{d}t = rS(1 - S/K) - \beta SI$ and $\mathrm{d}I/\mathrm{d}t = \beta SI - dI$, for the susceptible individuals, S, and infected individuals, I, respectively. Here β is an infection rate and d the death rate of infected individuals.

c. The natural killer cells probably have a maximum killing rate, and a maximum rate of activation, which would change the model to $\mathrm{d}T/\mathrm{d}t = rT(1 - T/K) - \frac{kTN}{h_k+T}$ and $\mathrm{d}N/\mathrm{d}t = \frac{aTN}{h_a+T} - dN$ (see Chapter 7). The SI model is frequently written as $\mathrm{d}S/\mathrm{d}t = rS(1-S/K) - \frac{\beta SI}{S+I}$ and $\mathrm{d}I/\mathrm{d}t = \frac{\beta SI}{S+I} - dI$, because $\frac{I}{S+I}$ is the fraction of infected individuals in the population

[2] This is identical to the prey equation of the Monod-saturated predator-prey model in Chapter 7.

(see Chapter 6). This is a more natural term when the susceptible individuals tend to meet an average number of other people, irrespective of their health status.

Question 5.4. Scaling
The Lotka-Volterra equations are

$$\frac{\mathrm{d}R}{\mathrm{d}t} = [r(1 - R/K) - aN]R \quad \text{and} \quad \frac{\mathrm{d}N}{\mathrm{d}t} = [caR - d]N \ .$$

a. Defining $x = R/K$ and scaling time by dividing all rates by r one obtains

$$\frac{\mathrm{d}Kx}{\mathrm{d}t} = [(1 - Kx/K) - aN/r]Kx \quad \text{and} \quad \frac{\mathrm{d}N}{\mathrm{d}t} = [\frac{ca}{r}Kx - d/r]N \ ,$$

where the "new" t runs r-fold faster that the non-scaled t. Defining $\alpha = a/r$ this simplifies into

$$\frac{\mathrm{d}x}{\mathrm{d}t} = [(1 - x) - \alpha N]x \quad \text{and} \quad \frac{\mathrm{d}N}{\mathrm{d}t} = [c\alpha Kx - d/r]N \ ,$$

with only one parameter in the resource equation. Defining $y = \alpha N$, i.e., $N = y/\alpha$, we remove that parameter from $\mathrm{d}x/\mathrm{d}t$

$$\frac{\mathrm{d}x}{\mathrm{d}t} = [(1 - x) - y]x \quad \text{and} \quad \frac{1}{\alpha}\frac{\mathrm{d}y}{\mathrm{d}t} = [c\alpha Kx - \frac{d}{r}]\frac{y}{\alpha} \ ,$$

where $\mathrm{d}y/\mathrm{d}t$ can be simplified by lumping the parameters

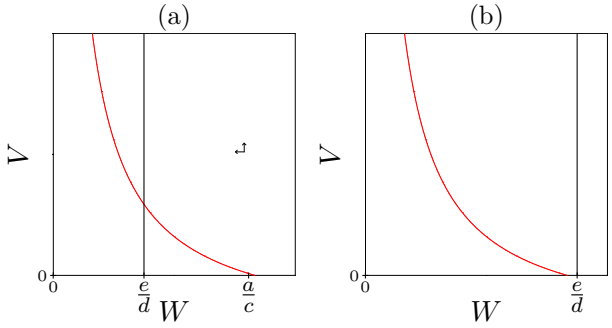
$$\frac{\mathrm{d}y}{\mathrm{d}t} = [\gamma x - \delta]y \ ,$$

where $\gamma = c\alpha K = cKa/r$ and $\delta = d/r$.

b. We went from five to two parameters for which we even know the scaled fitness $R_0 = \gamma/\delta$, and that $\gamma/\delta > 1$ is required for co-existence.

c. The δ parameter is the time-scaled death rate of the predator, and has a dimension t^{-1} on the new time scale. The γ parameter is a dimensionless conversion rate.

Question 5.5. Desert
Figures made with a previous version of Grind:



a. If there is no vegetation one sets $V = 0$ to obtain $\mathrm{d}W/\mathrm{d}t = a - cW$ with the steady state $\bar{W} = a/c$

b. If there is twice the amount of rain the parameter a becomes $2a$, which means $\bar{W} = 2a/c$.

c. The steady state is now solved from the system $\mathrm{d}W/\mathrm{d}t = \mathrm{d}V/\mathrm{d}t = 0$. Since $V = 0$ cancels from $\mathrm{d}V/\mathrm{d}t = 0$ one obtains the steady state $\bar{W} = e/d$ from the vegetation equation. This is independent of rain and evaporation!

d. Knowing that $\bar{W} = \frac{e}{d}$, we solve V from $\mathrm{d}W/\mathrm{d}t = 0 = a - b\ \frac{e}{d}\ V - c\ \frac{e}{d}$, or $\bar{V} = \frac{ad}{eb} - \frac{c}{b}$.

e. The steady state remains $\bar{W} = e/d$ and because $\bar{V}$ depends on a we see that the extra water ends up in the vegetation.

f. The vegetation nullcline is solved from $\mathrm{d}V/\mathrm{d}t = dWV - eV = 0$ which means that $V = 0$ and $W = e/d$. The water nullcline is solved from $\mathrm{d}W/\mathrm{d}t = a - bWV - cW = 0$ or $a - cW = bWV$, i.e., $V = \frac{a}{bW} - \frac{c}{b}$, which is a decreasing hyperbolic function with horizontal asymptote $V = -(c/b)$ and vertical asymptote $W = 0$. There are two possibilities: See Panel (a) and (b). The vector field shows steady state $\bar{W} = a/c$ without a vegetation is a unstable saddle in Panel (a) and is stable in Panel (b). For the non-trivial steady state in Panel (a) we can derive the full Jacobian

$$J = \begin{pmatrix} -b\bar{V} - c & -b\bar{W} \\ d\bar{V} & d\bar{W} - e \end{pmatrix} = \begin{pmatrix} -b\bar{V} - c & -b\bar{W} \\ d\bar{V} & 0 \end{pmatrix} ,$$

because $\bar{W} = \frac{e}{d}$, and giving $\mathrm{tr}J = -b\bar{V} - c < 0$ and $\det J = 0 + bd\bar{W}\bar{V} > 0$. One can also retrieve the graphical Jacobian from the local vector field, i.e.,

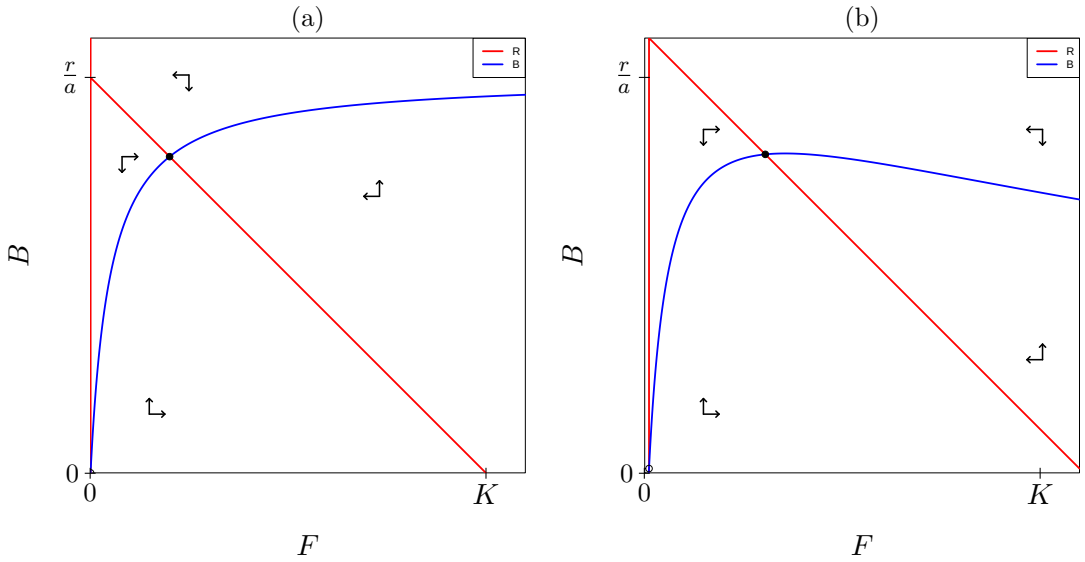
$$J = \begin{pmatrix} - & - \\ + & 0 \end{pmatrix} \quad \text{also giving} \quad \mathrm{tr}J < 0 \quad \text{and} \quad \det J > 0 \ .$$

Both methods agree that the non-trivial steady state in Panel (a) is stable.

g. Increased rainfall increases a, which will move the water nullcline up and its intersection with the horizontal axis to the right. Since the vertical vegetation nullcline is unaffected, the amount of water in the soil remains the same, and the vegetation increases.

Question 5.6. Kingfishers

Figures made with the model `kingfisher.R`:



The answer in Chapter 14 suggests the following model

$$\frac{\mathrm{d}F}{\mathrm{d}t} = rF(1 - F/K) - aFB \quad \text{and} \quad \frac{\mathrm{d}B}{\mathrm{d}t} = i(B_T - B)F - aFB - eB \ ,$$

for the fish, F, and the birds, B. The nullcline of the fish is a conventional straight Lotka-Volterra nullcline going from $B = r/a$ when $F = 0$ to $F = K$ when $B = 0$. The nullcline of the birds is solved from $0 = i(B_T - B)F - aFB - eB$, which has only one solution

$$B = \frac{iB_TF}{iF + aF + e} \ ,$$

which is a saturation function of F, i.e., $B = 0$ when $F = 0$, and $B \to \frac{iB_T}{i+a}$ when $F \to \infty$. Plotting the fish on the horizontal axis and the birds on the vertical axis we obtain Panel (a) depicted above, which has two steady states, the origin and a non-trivial steady state. Note that the fish at carrying capacity is not a steady state because the birds increase by immigration when $B = 0$. The graphical Jacobian of the non-trivial steady state is $J = \begin{pmatrix} -a & -b \\ +c & -d \end{pmatrix}$, showing that it is stable because the trace, $-a - d$, is negative and the determinant, $ad + bc$, is positive. The origin is unstable because both the birds and the fish increase in its neighborhood.

a. This phase portrait looks very reasonable, suggesting that the model is fine.

b. In the absence of the eB term, $\mathrm{d}B/\mathrm{d}t = 0$ whenever $F = 0$. Hence the initial number of birds present at an empty lake would never change.

c. If we had chosen the model where the immigration is a saturation function of the fish, we would have to solve

$$\frac{\mathrm{d}B}{\mathrm{d}t} = i(B_T - B)\frac{F}{h+F} - aFB - eB = 0 \quad \leftrightarrow \quad iB_TF - iBF - aFB(h+F) - eB(h+F) = 0$$

to obtain

$$B = \frac{iB_TF}{eh + F(i + ah + e) + aF^2} \ ,$$

which is an optimum function which resembles an increasing Hill function when F^2 is small, and approaches zero when F is large; see Panel (b) depicted above. For the steady state this brings little novelty, both are therefore reasonable.

Question 5.7. Biotic and abiotic resources

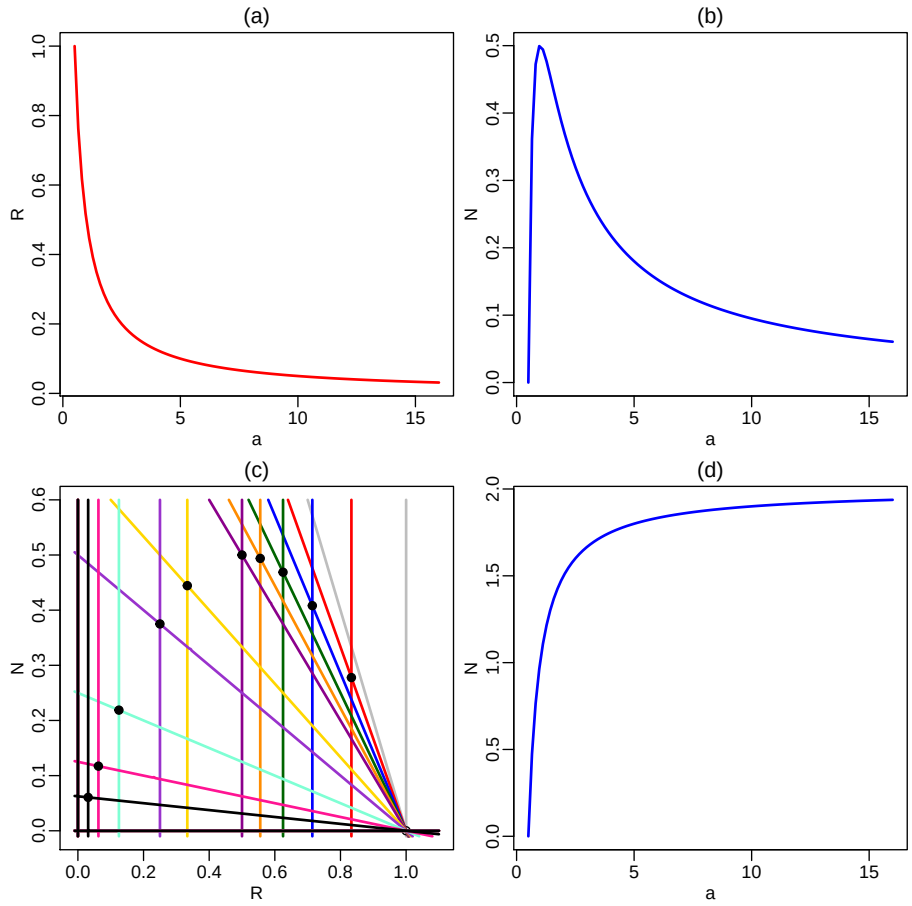
a. For the abiotic resource, R, we first write a source term, s, and a loss term, d, i.e., $\mathrm{d}R/\mathrm{d}t = s - dR$. For the consumer we define a *per capita* birth rate $\frac{bR}{h+R}$ that obeys a Monod saturation of the resource concentration. Adding the same loss rate we arrive at $\mathrm{d}N/\mathrm{d}t = \frac{bRN}{h+R} - dN$, where d is the rate of outflow from the chemostat (which we assume to be much larger than the death rate of the consumers), and h is the resource concentration at which the birth rate is half of its maximum. Since the resource is only used when the consumer grows, we add this birth rate as a consumption term to the ODE of the resource, i.e., $\mathrm{d}R/\mathrm{d}t = s - dR - \frac{cbRN}{h+R}$, where c is the amount of resource contained in a single consumer individual.

b. The biotic resource maintains itself by growth and because it has a carrying capacity, we write a logistic growth model $\mathrm{d}R/\mathrm{d}t = rR(1 - R/K)$. Adding mass-action consumption we arrive at $\mathrm{d}R/\mathrm{d}t = rR(1 - R/K) - aRN$, where a is an attack rate, and aR is the daily consumption per consumer. Since the birth rate is a saturation function of the consumption, we write $\mathrm{d}N/\mathrm{d}t = \frac{baRN}{h+aR} - dN$, where h is the level of consumption, aR, at which the birth rate is half of its maximum, and d is the death rate of the consumers.

c. The consumer equations are mathematically identical, because both are based upon a saturated birth rate and density independent death rate. The resource equations differ in the form of the consumption term, and in the process whereby the resource is produced. Hence, for abiotic resource the consumption is proportional to the birth rate (e.g., algae consuming nitrogen), and otherwise the birth rate should be a saturation function of the *per capita* consumption.

Question 5.8. Evolution to self-extinction

Figure made with `extinction.R`:



a. Since the consumer can only invade when $caR > \delta$ we find that $aK > \delta/c$.

b. In the script `extinction.R` we plot $\bar{R}$ and $\bar{N}$ using the curve function; see Panels (a) and (b). The non-monotonic nature of the $\bar{N}$ function is a consequence of the parabolic nature of the Logistic growth equation: the total growth rate of the resource is highest at intermediate resource densities, i.e., when $R = K/2$, which is approached when

$$\bar{R} = \frac{\delta}{ca} = \frac{K}{2} \quad \text{or} \quad a = \frac{2\delta}{cK} \ ,$$

which corresponds to the maximum of $\bar{N}$ in Panel (b). The same script also draws nullclines for various values of the attack rate to show that $\bar{N}$ depends non-monotonically on a due to concomitant shifting of the $\mathrm{d}R/\mathrm{d}t = 0$ nullcline and rotation of the $\mathrm{d}R/\mathrm{d}t = 0$ nullcline. See Panel (c).

c. Yes. Define the ODE for the invader (or mutant) as $\mathrm{d}M/\mathrm{d}t = c\alpha aRM - \delta M$, where α defines the fold change in the attack rate. Fill in the non-trivial steady state of the resource, $\bar{R} = \frac{\delta}{ca}$, to see that

$$\frac{\mathrm{d}M}{\mathrm{d}t} = c\alpha a \frac{\delta}{ca} M - \delta M > 0 \quad \leftrightarrow \quad \alpha - 1 > 0 \quad \leftrightarrow \quad \alpha > 1 \ ,$$

which proves that the invader expands whenever its attack rate exceeds that of the resident consumer.

d. No, a mutant consumer with a higher attack rate will always outcompete the resident consumer. Hence, in the absence of trade-offs, one would expect resource-consumer systems to evolve extremely high attack rates, and host-parasite systems to evolve extremely high infection rates. As a consequence they become vulnerable to extinction by stochastic events.

e. In consumer-resource systems the attack rate is also affected by evasion mechanisms of the resource, i.e., there is a selection pressure on the resource to decrease a. Additionally, in a spatial environment patches in which resources or consumers go extinct will be invaded by

immigrants from nearby patches. However, a chronic virus like HIV that is evolving for many generations within a host, is similarly expected to increase its infection rate, a, while the host's target cells are incapable to co-evolve.

f. According to Eq. (5.3) the steady state of the resource remains $\bar{R} = \frac{\delta}{ca}$, which suggests that $\bar{R} \to 0$ when $a \to \infty$. The steady state of the consumer, $\bar{N} = \frac{sc}{\delta} - \frac{d}{a}$, which was solved by substituting $\bar{R}$ into Eq. (5.2), reveals that $\bar{N}$ is an increasing function of a. When $a \to \infty$ this function approaches $\bar{N} \to \frac{sc}{\delta}$; see Panel (d). Since consumers with a higher attack rate are expected to invade, one expects the resource to go extinct, while the consumers approach $\bar{N} = \frac{sc}{\delta}$, i.e., approach the scaled production of the resource divided by the loss rate of the consumers.

Question 5.9. Cryptic oscillations

a. Since bacteria rapidly evolve resistance to bacteriophages, it is quite likely that at this time point the bacterial population is largely taken over by phage-resistant *E. coli*, which then approach the carrying capacity of the medium.

b. One could postulate that a small subpopulation of sensitive *E. coli* remains present, and maintains the predator-prey oscillations with the T4 phage. This would be visible in the phage densities, but not in the bacteria when these are dominated by the phage-resistant *E. coli*.

c. If the sensitive subpopulation remains small due to the dominance of the phage-resistant *E. coli*, it seems quite natural that the phage densities decline. This major decline of both densities could even explain the longer period of the oscillation. Given what we learned about the Paradox of enrichment in Fig. 5.6, it would be best to test this with a dedicated mathematical model.

d. A mathematical model would require four variables: sensitive uninfected bacteria, S, resistant bacteria, R, infected bacteria, I, and phages P. In its most simple form it would be something like

$$\frac{\mathrm{d}S}{\mathrm{d}t} = b_B S(1-B/k) - d_B S - \beta SP \ , \quad \frac{\mathrm{d}R}{\mathrm{d}t} = b_B(1-s)R(1-B/k) - d_B R \ ,$$
$$\frac{\mathrm{d}I}{\mathrm{d}t} = \beta SP - d_I I \quad \text{and} \quad \frac{\mathrm{d}P}{\mathrm{d}t} = b d_I I - d_P P \ ,$$

where $B = S + R + I$ is the total number of bacteria, b_B is the maximum birth rate of bacteria, k is the bacterial density at which the birth rate vanishes, s is the fitness cost of the resistance, d_x are death rates, and b a burst size. A first model like this, which also allows for resistance mutations of the bacteria is available on the website as `phages.R`. Note that you may have to change the mass-action infection rate into a saturated term to obtain oscillations (see Chapter 7).

Question 5.10. Phages and bacteria

a. The time delay λ defines that bacteria that become infected at time t, i.e., the term $\delta B_0(t)P(t)$, will burst and disappear at time $t+\lambda$, see the term $-\delta B_0(t-\lambda)P(t-\lambda)$. Bursting bacteria then produce b phages. In the R-script the function `lagvalue(tlag)` returns a vector with the values of all 5 variables at time $t-\lambda$. The second and fifth element of that vector correspond to $B_0(t-\lambda)$ and $P(t-\lambda)$, respectively.

b. The `fig2B0` data correspond to bacterial growth in the absence of phages, and the `fig2B` data comes from an experiment with phages.

c. Fitting the first data provides a very similar estimate for the consumption rate, v.

d. Yes, this looks like a good fit, and the parameter estimates are similar. Since the resistant bacteria are growing slower than predicted, it would have been better to also estimate a fitness cost.

e. No the data are equally well described with an ODE model without a fixed time delay. The value of the eclipse time, $1/\lambda$, is much longer now because it is exponentially distributed. The estimated fitness cost hardly changes.

f. The model has no death rate of the bacteria and no clearance of the phages. Given the short time scale of the experiment this is probably not important.

Question 5.11. Gillespie algoritm

a. If we were to set $d = 0$ and hence interpret b as a natural rate of increase, one obtains that the replication rate becomes zero, and looses its natural stochasticity, when $R = k$ (we would definitely lose all the stochasticity when $N = 0$ and $R = k$).

b. One would need to define an additional event for the division of killer cells, happening at a rate βRN, independently of the kill events happening at a rate aRN.

c. One would have to define predators having consumed a particular number of prey, e.g.

$$\frac{\mathrm{d}R}{\mathrm{d}t} = bR(1 - R/k) - dR - aR\sum_{i=0}^{n} N_i \ , \quad \frac{\mathrm{d}N_0}{\mathrm{d}t} = 2\beta N_n - aRN_0 - \delta N_0 + rN_1 \ ,$$

$$\frac{\mathrm{d}N_1}{\mathrm{d}t} = aRN_0 - aRN_1 - \delta N_1 - rN_1 + rN_2 \ , \ldots \ , \frac{\mathrm{d}N_n}{\mathrm{d}t} = aRN_{n-1} - \delta N_n - rN_n - \beta N_n \ ,$$

where the new parameter r defines a reversal to a previous satiation level, and N_n are the satiated predators giving birth at a rate β. Note that both the mother and the offspring revert to N_0 after birth, and that one would need to define many more different events.

d. Run say a 100 simulations starting at $R = 100$ and $N = 0$ with $b = 0$, and find in each simulation the time point where $R = 50$. Report the average of these 100 time points and compare that to $t = \ln[2]/d$.

Question 5.12. Return time

We calculate the return time of the non-trivial steady state of the Lotka-Volterra model considering both density dependent birth and density dependent death. For simplicity we do this for the case where this equilibrium is a stable spiral point. To save time we first write the model in a general form and compute the return time for this general model. The two cases of density dependent birth and death can then be "substituted" into the general form. A general form of the Lotka-Volterra model is

$$\frac{\mathrm{d}R}{\mathrm{d}t} = rR - \gamma R^2 - aRN \quad \text{and} \quad \frac{\mathrm{d}N}{\mathrm{d}t} = caRN - \delta N \ .$$

a. For the return time of the general form we first solve the non-trivial steady state by setting $\mathrm{d}N/\mathrm{d}t = 0$ and $\mathrm{d}R/\mathrm{d}t = 0$, which gives

$$\bar{R} = \frac{\delta}{ca} \quad \text{and} \quad \bar{N} = \frac{r}{a} - \frac{\gamma}{a}\bar{R} = \frac{r}{a} - \frac{\gamma\delta}{ca^2} \ ,$$

respectively. The Jacobian of the general model is

$$J = \begin{pmatrix} r - 2\gamma\bar{R} - a\bar{N} & -a\bar{R} \\ ca\bar{N} & ca\bar{R} - \delta \end{pmatrix} = \begin{pmatrix} -\frac{\gamma\delta}{ca} & -\frac{\delta}{c} \\ cr - \frac{\gamma\delta}{a} & 0 \end{pmatrix} \ ,$$

where $cr - \gamma\delta/a > 0$ because $ca\bar{N} > 0$. The trace of this matrix is negative, i.e., $\mathrm{tr} = -\frac{\gamma\delta}{ca}$, and the eigenvalues of this Jacobian are given by

$$\lambda_{\pm} = \frac{\mathrm{tr} \pm \sqrt{\mathrm{tr}^2 - 4\det}}{2} = -\frac{\gamma\delta}{2ca} \pm \frac{\sqrt{D}}{2} \ ,$$

where $D = \mathrm{tr}^2 - 4\det$ is the discriminant of the matrix (and "det" the determinant). Since we are considering a spiral point, the eigenvalues have to be complex, implying that the discriminant $D < 0$. The imaginary part of the eigenvalues defines the period of the dampened oscillation, and the real part how fast its amplitude grows or contracts, i.e., the return

time depends on the real part only. Thus, for the return time we consider the real part, $\mathrm{Re}(\lambda) = -\frac{\gamma\delta}{2ca}$, to obtain a return time

$$T_R = \frac{-1}{\mathrm{Re}(\lambda)} = \frac{2ca}{\gamma\delta} = \frac{2}{\gamma}\,\frac{1}{\bar{R}} \ .$$

Thus, the return time is independent of the net rate of increase, r, depends on the density dependence parameter, γ, and is inversely related to the steady state of the resource.

b. We write the model with density dependent birth as

$$\frac{\mathrm{d}R}{\mathrm{d}t} = bR(1 - R/k) - dR - aRN = bR - bR^2/k - dR - aRN \ ,$$

which in the general form means that $r = (b - d)$ and $\gamma = b/k$. To obtain the return time of the non-trivial steady state of this model, we only need to substitute $\gamma = b/k$ into the general expression for the return time, because the return time is independent of r, and because $\bar{R}$ came from $\mathrm{d}N/\mathrm{d}t = 0$, which has not changed. We obtain that

$$T_R = \frac{2}{b}\frac{k}{\bar{R}} = \frac{2cak}{b\delta} \ ,$$

where $k/\bar{R}$ is a ratio of resource densities (i.e., k is the density at which the birth rate become zero). Note that the dimension is correct: $k/\bar{R}$ is dimensionless and $2/b$ has the dimension time. Thus, the return time of this density dependent birth depends on the birth rate parameters, b and k, and not on the density independent death rate, d.

c. We write the model with density dependent death as

$$\frac{\mathrm{d}R}{\mathrm{d}t} = bR - dR(1 + R/k) - aRN = bR - dR - dR^2/k - aRN \ ,$$

which in the general form means that $r = (b - d)$ and $\gamma = d/k$. Now we substitute $\gamma = d/k$ into T_R and obtain that

$$T_R = \frac{2}{d}\frac{k}{\bar{R}} = \frac{2cak}{d\delta} \ ,$$

where $k/\bar{R}$ is another ratio of resource densities (i.e., k is the density at which the death rate doubles). Now the return time depends on the density dependent death rate parameters, d and k.

d. In both cases the return time is determined by a self-dampening effect of the resource onto itself, i.e., $\mathrm{Re}(\lambda) = -(\gamma/2)\bar{R}$. Increasing the birth rate, or the death rate, decreases the return time because it speeds up the dynamics around the steady state. Increasing k increases the return time because it weakens the density dependent regulation. Weakening the consumer, i.e., increasing $\bar{R}$, decreases the return time because that also increases the self-dampening effect of the resource.

Answers to Chapter 6

Question 6.1. SARS

a. First count the total number of infected patients $I(t)$. $R_0 = 3$ in two weeks means that $\beta = 1.5$ per week. For a time scale of weeks the model therefore is $\mathrm{d}I/\mathrm{d}t = 1.5I - 0.5I = I$. The equation to solve is $3 \times 10^9 = I(0)\mathrm{e}^{rt}$, where $r = (\beta - \delta) = 1$, and where one starts with one infected individual, i.e., $I(0) = 1$. Solving $3 \times 10^9 = \mathrm{e}^t$ yields $t = 22$ weeks for the time required to have $I(t) = 3 \times 10^9$.

For completeness, one could argue that it is more interesting to calculate the time required to have killed half of the population, but this is more difficult. For that one also should

keep track of the total number of dead individuals $\mathrm{d}D/\mathrm{d}t = \delta I$. With $I(t) = \mathrm{e}^{(\beta-\delta)t}$ and $D(0) = 0$ the solution of $\mathrm{d}D/\mathrm{d}t = \delta \mathrm{e}^{(\beta-\delta)t}$ is $D(t) = \frac{\delta[\mathrm{e}^{(\beta-\delta)t}-1]}{\beta-\delta}$. Solving $I(t)+D(t) = 3\times 10^9$ for $\beta = 1.5$ and $\delta = 0.5$ per week gives a total time of $t = 21$ weeks. The difference is small because the number of dead patients approaches a fixed fraction $\frac{\delta}{\beta-\delta} = 0.5$ of the total number of patients that are alive.

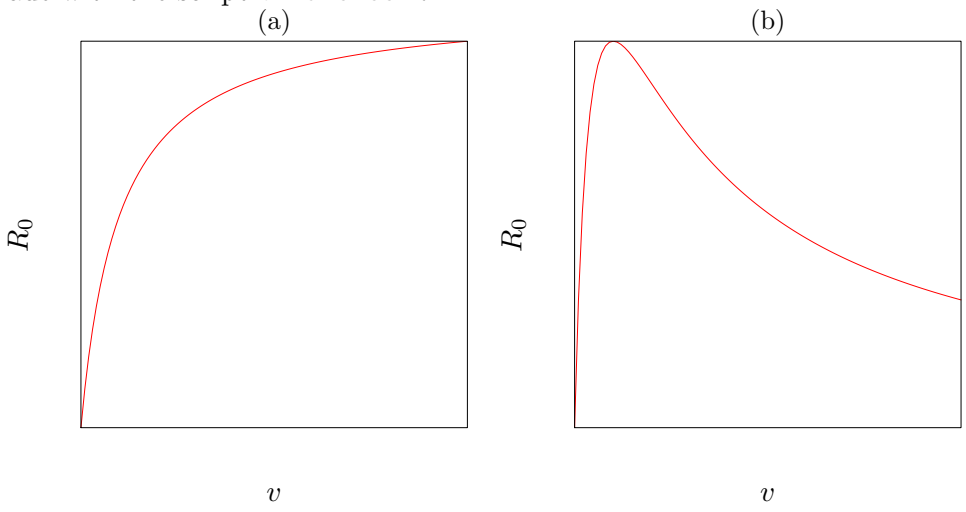
b. No, it should go slower because the pandemic will limit itself by depleting the number of susceptibles. Thus it seems much better to study this with an SI model with a frequency dependent transmission rate, with the same R_0. Because the SARS pandemic went so much faster than the human birth and death rates, Eq. (6.2) would simplify to

$$\frac{\mathrm{d}S}{\mathrm{d}t} = -\beta SI/N \quad \text{and} \quad \frac{\mathrm{d}I}{\mathrm{d}t} = \beta SI/N - \delta I \quad \text{where} \quad N = S + I \ ,$$

which initially, i.e., when $S = N$, is indeed identical to the above $\mathrm{d}I/\mathrm{d}t = \beta I - \delta I$. Simulating this model for $S(0) = 6 \times 10^9$ and $I(0) = 1$, with $\beta = 1.5$ and $\delta = 0.5$ per week with the R-script `sars.R` shows that this still takes about 21 weeks (because such a pandemic grows exponentially and susceptibles only become depleted when the pandemic has spread all over the world). Another improvement of the model that would slow down the pandemic is to allow for an incubation period, and use a a frequency dependent SEIR model (for a deadly disease, i.e., $r = 0$). Allowing for an incubation time for half a week would marked slow down the pandemic (see the R-script `sars.R`).

Question 6.2. Evolution of virulence

Figure made with the script `virulence.R`:



a. Since infected individuals appear at a maximum rate $\beta\bar{S}$, and have an expected life span of $1/(d+v)$ time units, the $R_0 = \frac{\beta\bar{S}}{d+v} = \frac{\beta}{d+v}\ \frac{s}{d}$.

b. Substituting $\beta = cv$ we obtain $R_0 = \frac{cv\bar{S}}{d+v} = \frac{cv}{d+v}\ \frac{s}{d}$.

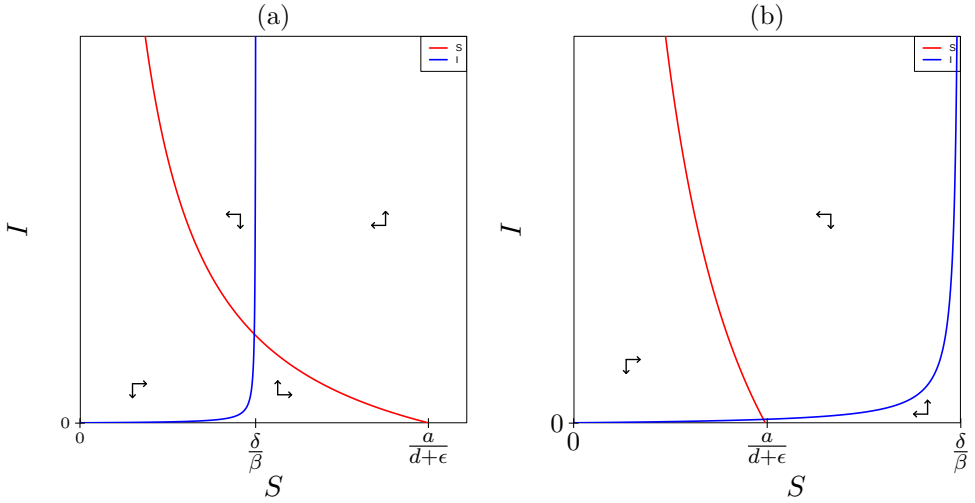
c. The R_0 of the infection is a saturation function of the virulence (see Panel (a)). Since one expects the variant with the highest reproductive number, R_0, to win the competition, one expects the most virulent variant to win. Virulence is therefore expect to increase over time.

d. When $\beta = \frac{cv}{h+v}$ one obtains $R_0 = \frac{cv}{h+v}\ \frac{1}{d+v}\ \frac{s}{d}$.

e. To sketch the latter as a function of the virulence, v, we observe that for $v \to 0$ the fitness approaches $R_0 \simeq \frac{cv}{h}\ \frac{1}{d}\ \frac{s}{d}$, which is an increasing function of v. When $v \gg h$, the fitness approaches $R_0 = \frac{c}{d+v}\ \frac{s}{d}$, which is a decreasing function of v. In combination one therefore expects a curve with an optimal virulence (see Panel (b)), where the trade-off between the increased transmission and the decreased life span is balanced (see the tutorial on sketching functions). Thus, one expects the virulence to evolve towards this optimum.

Question 6.3. Sexually transmitted disease (STD)

Figure made with the model `aids.R`:



a. In the absence of foreign infections infected individuals appear at a maximum rate $\beta\bar{S}$, and have an expected life span of $1/\delta$ days, meaning that the $R_0 = \frac{\beta\bar{S}}{\delta} = \frac{\beta}{\delta}\,\frac{a}{d}$.

b. No the infection will never disappear from this subpopulation because there is always a small source of infected individuals. The steady state number of infected individuals will always be larger than $\bar{I} = \epsilon\bar{S}/\delta$, which is the minimum approached when $\beta \to 0$.

c. The $\mathrm{d}S/\mathrm{d}t = 0$ nullcline is defined as $I = \frac{a}{\beta S} - \frac{d+\epsilon}{\beta}$. The nullcline has a vertical asymptote at $S = 0$ because when $S \to 0$ the first term goes to infinity. The nullcline has a horizontal asymptote because when $S \to \infty$ the number of infected individuals approaches $I = -\frac{d+\epsilon}{\beta}$. The nullcline intersects the horizontal axis in the carrying capacity $S = \frac{a}{d+\epsilon}$; see Panel (a) and (b). The $\mathrm{d}I/\mathrm{d}t = 0$ nullcline is defined by $I = \frac{\epsilon S}{\delta - \beta S}$, which has the vertical asymptote at $S = \frac{\delta}{\beta}$. When $S \to 0$ the slope of the nullcline approaches $\frac{\epsilon}{\delta}$, which increases with S (see Panel (a) and (b)). Note that this vertical asymptote corresponds to the classical vertical nullcline of the SI model without a source, i.e., the epidemic grows at the right-hand side of this asymptote. Panel (a) therefore corresponds to the case where $R_0 > 1$ because the epidemic can maintain itself without a source, and Panel (b) reveals the opposite case where $R_0 < 1$ and the source maintains a small infection. In both Panels the Jacobi matrix of the non-trivial steady state is given by

$$J = \begin{pmatrix} - & - \\ + & - \end{pmatrix} \quad \text{giving} \quad \mathrm{tr}J < 0 \quad \text{and} \quad \det J > 0\ ,$$

i.e., the endemic state is stable (even if $R_0 < 1$).

d. Because the probability of becoming infected by an HIV-infected partner is relatively low for heterosexual couples, implying that β and R_0 are small, the situation depicted in Panel (b) is quite realistic for non-promiscuous Dutch subpopulations.

e. A model defining both the people at home and those on holidays would look like

$$\frac{\mathrm{d}S}{\mathrm{d}t} = a - dS - \beta SI - hS + r\hat{S}\ , \quad \frac{\mathrm{d}I}{\mathrm{d}t} = \beta SI - \delta I + r\hat{I}$$

$$\frac{\mathrm{d}\hat{S}}{\mathrm{d}t} = hS - r\hat{S} - \hat{\beta}\hat{S} \quad \text{and} \quad \frac{\mathrm{d}\hat{I}}{\mathrm{d}t} = \hat{\beta}\hat{S} - r\hat{I}\ ,$$

where $\hat{S}$ and $\hat{I}$ define the individuals on holidays (people go on vacation at rate h and return at rate r), and $\hat{\beta}$ is the infection rate due to having sex with foreigners. Since the typical time scale of a vacation (weeks) is much shorter than that of an HIV infection (years), it is fair to make the Quasi Steady State Assumption (QSSA), $\mathrm{d}\hat{S}/\mathrm{d}t = \mathrm{d}\hat{I}/\mathrm{d}t = 0$, and to write

that

$$\bar{S} \simeq \frac{h}{r+\hat{\beta}}\ S \quad \text{and} \quad \hat{I} \simeq \frac{\hat{\beta}}{r}\hat{S} = \frac{\hat{\beta}}{r}\ \frac{h}{r+\hat{\beta}}\ S\ .$$

Hence the $hS - r\hat{S}$ in $\mathrm{d}S/\mathrm{d}t$ can be simplified into

$$\left(h - \frac{rh}{r+\hat{\beta}}\right) S = \left(\frac{h(r+\hat{\beta})}{r+\hat{\beta}} - \frac{rh}{r+\hat{\beta}}\right) S = \frac{-h\hat{\beta}}{r+\hat{\beta}} S = -\epsilon S\ .$$

Similarly, the $r\hat{I}$ in $\mathrm{d}I/\mathrm{d}t$ can be simplified to

$$r\hat{I} = r\ \frac{\hat{\beta}}{r}\frac{h}{r+\hat{\beta}} S = \epsilon S\ .$$

Thus, the ϵ parameter in the first model of the question can be derived mechanistically by a QSSA, and is defined as $\epsilon = \frac{h\hat{\beta}}{r+\hat{\beta}}$.

Question 6.4. COVID-19 herd immunity in the Brazilian Amazon

a. A recovery time of 10 days would correspond to $r = 0.1\ \mathrm{d}^{-1}$. Solving the death rate, d, from $f = \frac{d}{d+r}$ yields $d = \frac{fr}{1-f} \simeq fr = 0.0002\ \mathrm{d}^{-1}$. From $\beta \simeq rR_0$ one would estimate that $\beta \simeq 0.25$. Although the 106 day half life of the antibodies is not the same as the half life of protective immunity, we could use it to define an initial guess of the waning rate, w. Solving $\ln[2]/w = 106$ yields $w \simeq 0.006$ (which corresponds to assuming that recovered individuals become susceptible again when their antibody levels have halved).

b. The daily number of deaths is defined as dI in the model. In the R-script this is added as an extra column to the output of the model (using Grind's `tweak` option).

c. It al seems correct. The model starts with $S = 2.2 \times 10^6$ susceptible inhabitants of Manaus.

d. The summary statistics provided by `summary(fit1)` suggest that all 5 free parameters are identifiable. The parameter values are estimated to be $\beta \simeq 0.36\ \mathrm{d}^{-1}$, $r \simeq 0.14\ \mathrm{d}^{-1}$, $f \simeq 0.0016\ \mathrm{d}^{-1}$, $w \simeq 0.005\ \mathrm{d}^{-1}$ and $I(0) = 15750$, from which one can compute that $d \simeq 0.0002\ \mathrm{d}^{-1}$ and $R_0 = 2.48$. The waning rate, w, appears to be an identifiable parameter, and hence the estimated half life of the immunity is $\ln[2]/0.005 \simeq 134$ days; a little more than 3 months. This small waning rate explains the late increase in the epidemic, which seems realistic (and may be a prelude to the second peak).

e. Assuming exponential growth one would solve $I(t) = \mathrm{e}^{\rho_0 t}$, i.e., $\ln[I(t)] = \rho_0 t$, or $\ln[15750]/0.215 \simeq 45$ days before 1 April 2020 (i.e., around 15 February). This can be checked by running the model with one infected individual, and shifting time 45 days in the data. For instance,

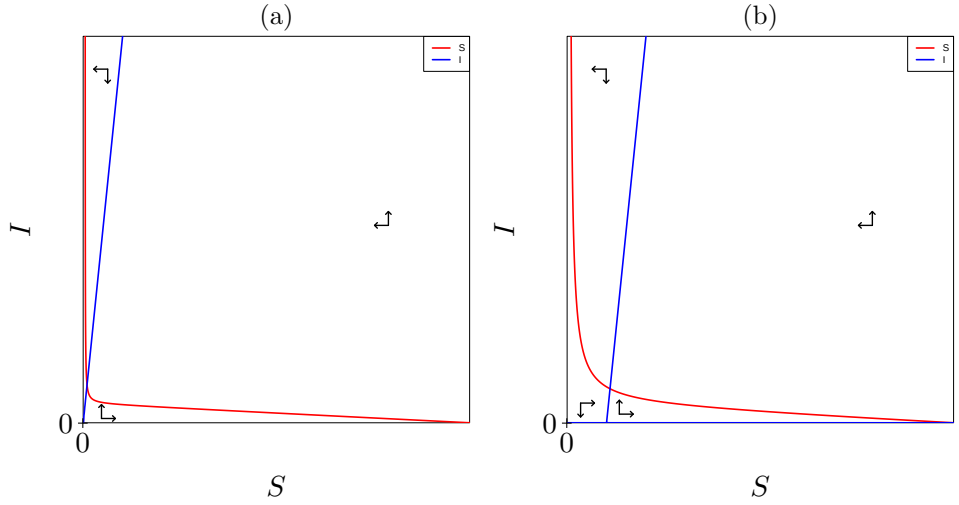
```
s["I"] <- 1
run(250,1,ymax=150,tweak=tweak,show="D")
points(data$time+45,data$D)
```

reveals an excellent correspondence with the shifted data.

f. No it is impossible to have a larger second peak when part of the population still has some immunity. The second wave is caused by a novel variant of SARS CoV-2. One would at least need to define an ODE for people infected with the second variant (I_2), a novel infection rate for (waned) susceptibles ($\beta_2 S I_2/N$), and a third one for reinfection of recovered people ($\beta_3 R I_2/N$).

Question 6.5. SIR model

Figure made with the model `sir.R`:



a. The $R_0 = \frac{\beta}{\delta+r}$ and the initial growth rate $\rho_0 = \beta - \delta - r$.

b. Because $\bar{S} = N$ in the uninfected steady state the Jacobian is

$$J = \begin{pmatrix} -d & -\beta \\ 0 & \beta - \delta - r \end{pmatrix} , \tag{A.6.3}$$

and hence the largest eigenvalue $\lambda_1 = \beta - \delta - r$. This eigenvalue indeed defines the initial growth rate r_0, and since requiring instability means $\lambda_1 > 0$, or $\beta > \delta + r$, this also corresponds to requiring $R_0 > 1$.

c. Setting

$$\frac{\mathrm{d}I}{\mathrm{d}t} = \frac{\beta SI}{S+I} - (\delta + r)I = 0 \quad \text{gives} \quad \frac{\beta S}{\delta + r} = I + S ,$$

or $I = S(R_0 - 1)$, which is a line through the origin with slope $R_0 - 1$. For the other nullcline we set

$$\frac{\mathrm{d}S}{\mathrm{d}t} = s - dS - \frac{\beta SI}{S+I} = 0 \quad \text{giving} \quad (s - dS)(S + I) = \beta SI \quad \text{or} \quad I = \frac{sS - dS^2}{(\beta + d)S - s} ,$$

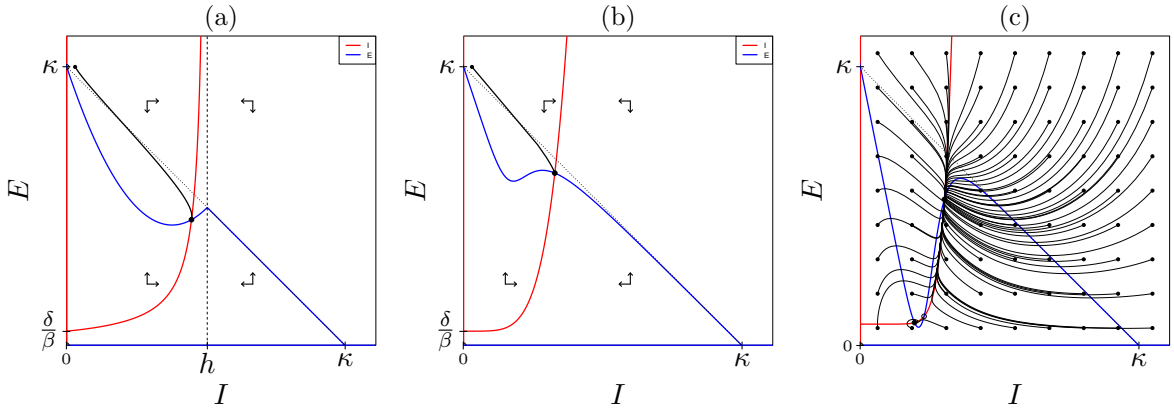
which defines a line that is too unpleasant to sketch by hand. Better use the `sir.R` model (see the Panel (a)).

d. The fact that the $\mathrm{d}I/\mathrm{d}t = 0$ nullcline goes through the origin means that the epidemic can grow when the susceptible population is extremely small (see the upward arrow near the origin). This is a unpleasant consequence of using the fraction of infected individuals in the number of daily encounters: at low population densities the number of individuals encountered should actually go to zero. Thus, this problem should be solved by realizing that the infection term should depend on both the expected number, n, of individuals encountered per day, and the fraction, $f = \frac{I}{S+I}$, of infected individuals among them. This frequency dependent model only deals with the latter by making the rate at which a susceptible individual is infected directly proportional to the fraction, f, of infected individuals. If one were to write that the expected number of individuals encountered per day should be a saturation function of the population density, e.g., $n = \frac{S+I}{h+S+I}$, and that the infection rate should be proportional the fraction of infected individuals encountered, i.e., $fn = \frac{I}{S+I}\,\frac{S+I}{h+S+I} = \frac{I}{h+S+I}$, we obtain from

$$\frac{\mathrm{d}I}{\mathrm{d}t} = \frac{\beta SI}{h + S + I} - (\delta + r)I = 0 \quad \text{that the nullcline,} \quad I = S(R_0 - 1) - h ,$$

is intersecting the horizontal axis at $S = \frac{h}{R_0 - 1}$ (see Panel (b)).

Question 6.6. Influenza virus infecting epithelial cells
Figures made with the model `epithelial.R`:



Assuming $\mathrm{d}V/\mathrm{d}t = \mathrm{d}F/\mathrm{d}t = 0$ in the first ODE for the virus and the factor leads to $V = \frac{p_V}{c_V} I$ and $F = \frac{p_F}{c_F} I$, showing that the QSSA-virus and QSSA-factor densities are both proportional to the infected cells. The QSSA model therefore becomes

$$\frac{\mathrm{d}E}{\mathrm{d}t} = bE(1-(E+I)/K) - dE - \beta' EI(1-I/h') \quad \text{and} \quad \frac{\mathrm{d}I}{\mathrm{d}t} = \beta' EI(1-I/h') - \delta I \ ,$$

where $\beta' = \beta p_V/c_V$ and $h' = hc_F/p_F$. For convenience, we drop the primes when performing the phase plane analysis. For the nullcline of the healthy cells one sets $\mathrm{d}E/\mathrm{d}t = 0$ giving $E = 0$ and

$$E = K(1-d/b) - I - \frac{K\beta}{b}\, I(1-I/h) = \kappa - I - \alpha I(1-I/h) \ ,$$

where κ is the carrying capacity of the healthy epithelium, and $\alpha = K\beta/b$. When the infection rate is very low, i.e., when $\alpha \to 0$, this is a declining straight line starting at $E = \kappa$ when $I = 0$, and ending at $I = \kappa$ when $E = 0$ (see the dotted line in Panel (a)). From that line one subtracts a parabola, $\alpha I(1-I/h)$, that is zero when $I = 0$ or $I = h$, and has a maximum, $\alpha h/4$, that is attained at $I = h/2$. Since one has to preclude negative infection rates by setting $(1-I/h)$ to zero whenever $I > h$, the $\mathrm{d}E/\mathrm{d}t = 0$ nullcline coincides with the dotted line whenever $I > h$ (see Panel (a) where we have set $h \simeq \kappa/2$). For the nullcline of the infected cells one sets $\mathrm{d}I/\mathrm{d}t = 0$ giving $I = 0$ and

$$E = \frac{\delta/\beta}{1-I/h} \quad \text{which starts at} \quad E^* = \frac{\delta}{\beta} \ ,$$

and approaches a vertical asymptote at $I = h$ (see the dashed line in Panel (a)). Around the origin $\mathrm{d}E/\mathrm{d}t \simeq (b-d)E > 0$, i.e., below the blue line the healthy epithelial cells grow. The infected cells increase above the red $\mathrm{d}I/\mathrm{d}t = 0$ nullcline because they require a minimum number, E^*, of target cells. The origin is an unstable steady state because the trivial nullclines intersect and $\mathrm{d}E/\mathrm{d}t > 0$ in its neighborhood. These nullclines will at least intersect in one non-trivial steady state (when $\kappa > \delta/\beta$, which is anyway required for successful infection), because the $\mathrm{d}I/\mathrm{d}t = 0$ nullcline starts below the $\mathrm{d}E/\mathrm{d}t = 0$ nullcline and approaches infinitely high values when $I \to h$. This intersection is the state approached by the trajectory corresponding to an infection in Panel (a), and is indeed a stable point because the vector field points towards it in all regions.

Next, consider an alternative model using a declining Hill function for the effect of interferon on the infection rate. The QSSA version of that model would look like

$$\frac{\mathrm{d}E}{\mathrm{d}t} = bE(1-(E+I)/K) - dE - \frac{\beta EI}{1+(I/h)^n} \quad \text{and} \quad \frac{\mathrm{d}I}{\mathrm{d}t} = \frac{\beta EI}{1+(I/h)^n} - \delta I \ ,$$

where we have already dropped the primes. This QSSA model readily reveals that choosing $n = 1$ would not allow for a large effect of interferon because the infection term would just become a saturation function of I, and not decline at maximum interferon levels. Choosing $n \geq 2$ would suffice because $x/(1+x^2)$ is a function with an optimum. Sketching the nullclines would follow a similar procedure because the non-trivial $\mathrm{d}E/\mathrm{d}t = 0$ nullcline now is the same dotted line minus this optimum function (see Panel (b)), i.e.,

$$E = K(1-d/b) - I - \frac{(K\beta/b)I}{1+(I/h)^n} = \kappa - I - \frac{\alpha I}{1+(I/h)^n} \ ,$$

giving $E = \kappa$ when $I = 0$ and $E = \kappa - I$ when $I \to \infty$ (see the dotted line in Panel (b)). For the nullcline of the infected cells one sets $\mathrm{d}I/\mathrm{d}t = 0$ giving $I = 0$ and

$$E = \frac{\delta}{\beta}\,(1+(I/h)^n) = \frac{1}{R_{0_I}}\,(1+(I/h)^n) \ ,$$

which is an increasing parabola starting at $E^* = \frac{\delta}{\beta} = \frac{1}{R_{0_I}}$ when $I = 0$ (see Panel (b)). The similarity between Panels (a) and (b) is reassuring as it suggests that these results do not depend on the shape of the function defining the effect of interferon of the infection rate. One can create more steady states by making this function steeper (which need not be realistic). For a high exponent, n, of the Hill function one can indeed obtain a stable steady state corresponding to an infection limited by the availability of target cells, and a saddle point separating the two basins of attraction (see Panel (c)).

Answers to Chapter 7

Question 7.1. Michaelis Menten

a. From the conservation equation one obtains that the concentration of freely available enzyme is given by $E = E_0 - C$. From the reaction scheme one derives for the complexes $\mathrm{d}C/\mathrm{d}t = k_1 ES - (k_{-1}+k_2)C$, which after substituting the conservation equation becomes

$$\frac{\mathrm{d}C}{\mathrm{d}t} = k_1(E_0 - C)S - (k_{-1}+k_2)C \ .$$

For the formation of product one simply writes $\mathrm{d}P/\mathrm{d}t = k_2 C$.

b. To solve $\mathrm{d}C/\mathrm{d}t = 0$ we first collect all the terms containing C,

$$\frac{\mathrm{d}C}{\mathrm{d}t} = k_1 E_0 S - (k_1 S + k_{-1} + k_2)C \ .$$

Because $\mathrm{d}C/\mathrm{d}t = 0$ we obtain $k_1 E_0 S = (k_1 S + k_{-1} + k_2)C$, and by solving for S

$$C = \frac{k_1 E_0 S}{k_1 S + k_{-1} + k_2} = \frac{E_0 S}{K_m + S} \quad \text{where} \quad K_m = \frac{k_{-1}+k_2}{k_1} \ .$$

Thus, C as a function of S looks like a standard Hill function $y = \frac{x}{h+x}$.

c. By defining K_m the simplification was already done. This means the the product equation can be written as $\mathrm{d}P/\mathrm{d}t = \frac{k_2 E_0 S}{K_m + S}$.

d. The beautiful trick of adding $\mathrm{d}C/\mathrm{d}t = 0$ to $\mathrm{d}S/\mathrm{d}t = -k_1 ES + k_{-1}C$ readily simplifies the substrate equation into $\mathrm{d}S/\mathrm{d}t = -k_2 C$. Filling in the quasi steady state expression for C gives $\mathrm{d}S/\mathrm{d}t = -\frac{k_2 E_0 S}{K_m + S}$.

e. This is indeed very similar, we just replaced k_1 by a and $k_{-1} + k_2$ by h.

Question 7.2. Parameters

The biological interpretation and dimension of the parameters are:

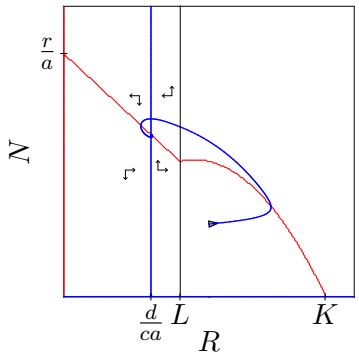
a. 1. a_1: Maximal *per capita* growth rate of the resource $(1/t)$
2. K: Carrying capacity (numbers or biomass).
3. b_1: Maximal amount of resource consumed per consumer per unit of time (R/t).
4. c_1: Population density R where N catches/feeds at its half maximal rate (numbers or biomass).
5. a_2: *per capita* death rate of the consumers $(1/t)$.
6. b_2: Maximum *per capita* birth rate of the consumers $(1/t)$.
7. c_2: Population R where the birth rate of N is at half its maximum value (numbers or biomass).

b. Yes, typically one obtains $b_2 = \alpha b_1$ where $\alpha < 1$ is the conversion factor. If population sizes are measured in biomass the normal trophic conversion factor is $\alpha = 0.1$, i.e., typically there is a 90% loss between tropic levels. If the population sizes are measured in numbers α could be anything because small consumers could feed on a large resource.

c. Choosing $c_1 = c_2$ means that the growth of the consumer is proportional to what it eats. Setting $c_1 > c_2$ means that the growth rate saturates earlier than the catching rate, which is to be expected when the birth rate of the consumer saturates as a function of its consumption; see Eq. (7.19). Setting $c_1 < c_2$ therefore seems strange because it means that the catching rate is saturated earlier than the birth rate.

Question 7.3. Type I functional response

Figure made with a previous version of Grind:



a. The nullcline of the consumer is only defined when $R < L$ because whenever $R > L$, one obtains $\mathrm{d}N/\mathrm{d}t = (caL - d)N$ with a *per capita* growth rate $\rho = caL - d$, which is either a positive or a negative constant, that can never switch sign. Considering $R < L$ and solving $\mathrm{d}N/\mathrm{d}t = caNR - dN = 0$ yields the familiar $R = \frac{d}{ca}$ nullcline. For the resource we consider both cases, i.e.,

$$\begin{cases} \mathrm{d}R/\mathrm{d}t = rR(1 - R/K) - aNR & \text{when } R < L \text{ and} \\ \mathrm{d}R/\mathrm{d}t = rR(1 - R/K) - aNL & \text{otherwise ,} \end{cases}$$

to obtain

$$\begin{cases} N = \frac{r}{a}\left(1 - \frac{R}{K}\right) & \text{when } R < L \text{ and} \\ N = \frac{rR}{aL}(1 - \frac{R}{K}) & \text{otherwise ,} \end{cases}$$

where the former is the straight line intersecting the vertical axis at $N = \frac{r}{a}$ and the horizontal axis at $R = K$, and the latter is a parabola intersecting the horizontal axis at $R = 0$ and $R = K$. Putting these together results in the picture shown above (where we ignore the case that $\frac{d}{ca} > K$). (Also note that if $L < \frac{d}{ca}$, the consumers would always decrease and $R = K$ would be the only attractor.)

b. The stability of the steady states has not changed in the model because nothing changed in the immediate neighborhood of the steady states of the model. Thus, the origin, $(0, 0)$, and

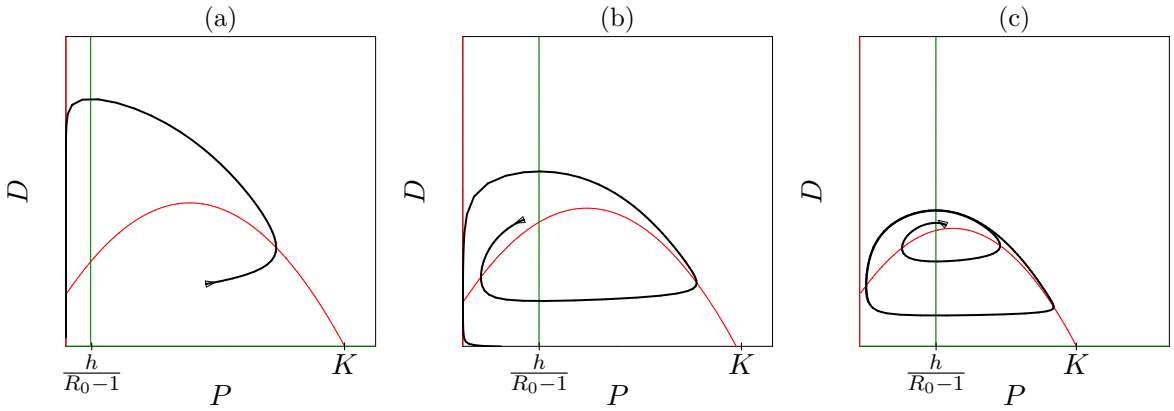
the carrying capacity, $(K, 0)$, remain saddle points, and the non-trivial point is stable like in the Lotka-Volterra model.

c. No, the consumer nullcline has to be located at a resource density where changing the resource density changes $\mathrm{d}N/\mathrm{d}t$.

d. No, the non-trivial steady state has to be located in the part where the resource nullcline is a declining straight line (see the answer in **b**), and there the steady state is stable.

Question 7.4. Luckinbill

Figures made with a previous version of Grind:



a. The oscillatory behavior suggests a Monod saturation

$$\frac{\mathrm{d}P}{\mathrm{d}t} = aP(1 - P/K) - \frac{bDP}{h + P} \quad \text{and} \quad \frac{\mathrm{d}D}{\mathrm{d}t} = \frac{cDP}{h + P} - dD \ .$$

b. Increasing the viscosity of the medium decreases the likelihood of meeting prey, which corresponds to increasing the h parameter; see Panel (b). Halving the concentration of food decreases the K parameter; see Panel (c).

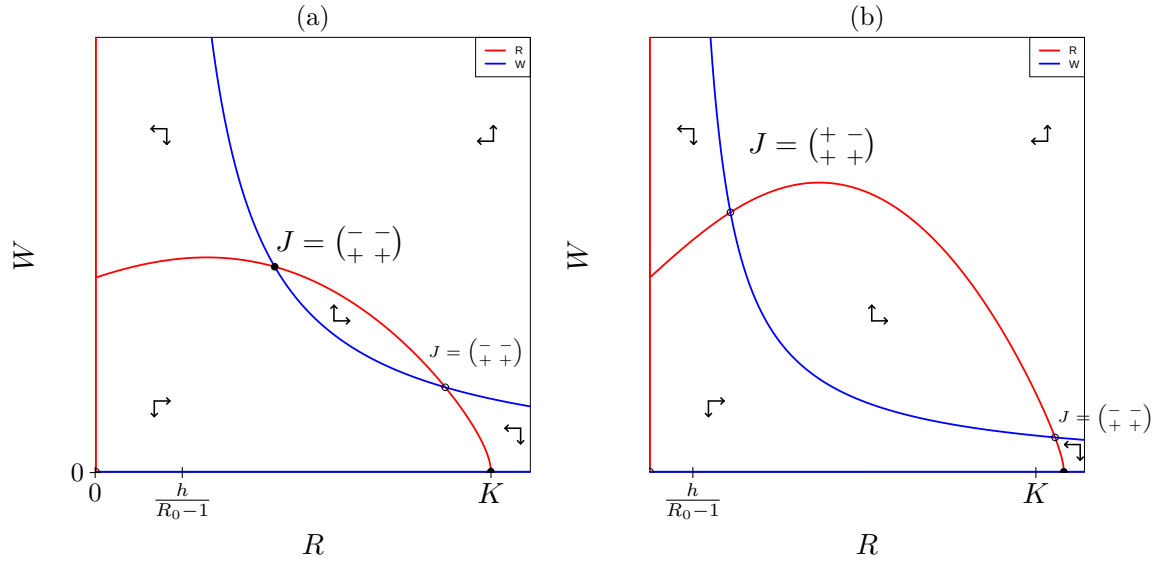
c. See Panels (a)–(c).

d. The agreement between model and data seems perfect; a Monod saturated functional response provides a good explanation.

e. Formally the populations cannot go extinct in the model; the noise in the data would require stochasticity in the model.

Question 7.5. Wolves

Figure made with the model `wolves.R`:



There are many different possibilities. For instance, let R be the prey, and W be the wolves:

a. One could define $\hat{R} = RW/(c+W)$ as the number of prey that can be caught, i.e., if there are enough wolves ($W \gg c$) all prey can be caught ($\hat{R} \to R$). Taking $\hat{R}$ through a normal Monod saturation gives

$$f(R,W) = \frac{\hat{R}}{h+\hat{R}} = \frac{RW}{hc+hW+RW}$$

$$\frac{\mathrm{d}R}{\mathrm{d}t} = rR(1-R/K) - \frac{aRW^2}{hc+hW+RW} \quad \text{and} \quad \frac{\mathrm{d}W}{\mathrm{d}t} = \frac{aRW^2}{hc+hW+RW} - dW \ ,$$

with $R_0 = a/d$.

b. To sketch the predator nullcline one solves

$$\frac{aRW}{hc+hW+RW} = d \quad \text{or} \quad W = \frac{hc}{R(R_0-1)-h} \ ,$$

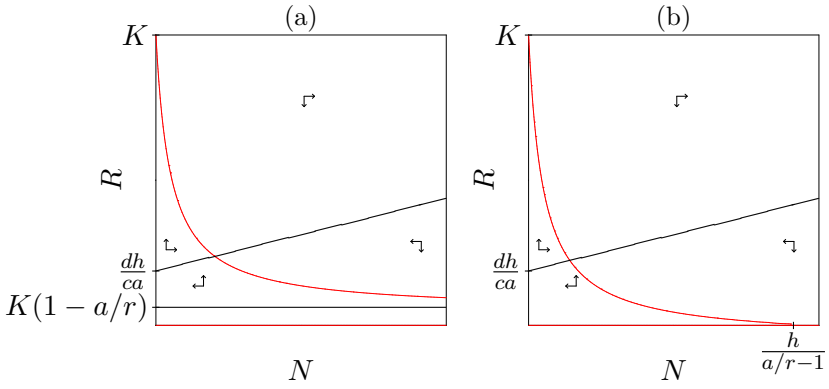
which has a vertical asymptote at $R = h/(R_0-1)$ and a horizontal asymptote at $W = 0$. The prey nullcline is not so easy to sketch. We have drawn it with Grind in the top panels above, where it looks like a upward parabola that can intersect the nullcline of the wolves in downslope, Panel (a), or in its upslope, Panel (b). From the vector field one can see that in both cases the carrying capacity op the prey is stable. This is an Allee effect because small numbers of wolves cannot invade when the prey is present at its maximum density. From the vector field we can also conclude that in both cases the lower intersection point is a saddle point, with a separatrix defining the Allee effect. Note that this cannot be inferred from the graphical Jacobian $J = \left(\begin{smallmatrix} - & - \\ + & + \end{smallmatrix}\right)$ of this point. The vector field does not allow us to infer the stability of the upper intersection point in Panel (a). The graphical Jacobian is the same, $J = \left(\begin{smallmatrix} - & - \\ + & + \end{smallmatrix}\right)$, as that of the saddle point, but numerically one can test that this can be stable; see the bullet in Panel (a) made with Grind's `newton()` function. The graphical Jacobian of the upper intersection point in Panel (b) has a positive trace, $J = \left(\begin{smallmatrix} + & - \\ + & + \end{smallmatrix}\right)$, meaning that this is an unstable point. This implies that in Panel (b) the model either approaches a stable limit cycle, or the carrying capacity.

Alternatively, one could use a mass action predation term and write a more phenomenological model,

$$\frac{\mathrm{d}R}{\mathrm{d}t} = rR(1-R/K) - \frac{aRW^2}{h+W} \quad \text{and} \quad \frac{\mathrm{d}W}{\mathrm{d}t} = \frac{aRW^2}{h+W} - dW \ .$$

One could also employ the Beddington functional response and define $f(R,W) = \frac{R}{h(1-cW)+R}$ as a functional response that decreases the saturation constant when the number of wolves increases (and use a maximum function to prevent that $h(1-cW)$ becomes negative).

Question 7.6. Saturation in consumers
Figure made with a previous version of Grind:



a. The non-trivial prey nullcline is solved from

$$r(1-R/K) = \frac{aN}{h+N} \quad \text{or} \quad R = K\left(1 - \frac{a/rN}{h+N}\right) ,$$

which is an inverse Hill function intersecting the vertical R-axis at $R = K$. If $a/r < 1$ one obtains a "limited predation" nullcline with a positive asymptote at $R = K(1-a/r)$; see Panel (a). If this is negative, i.e., if $a/r > 1$, the nullcline intersects the horizontal N-axis $N = h/(a/r-1)$; see Panel (b). The non-trivial consumer nullcline is solved from

$$\frac{caR}{h+N} = d \quad \text{or} \quad R = \frac{d}{ca}\,(h+N) ,$$

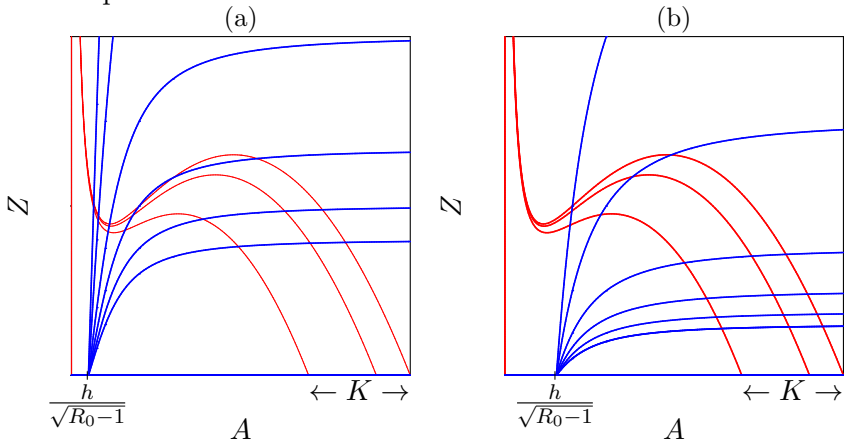
which is a straight line with slope $\frac{d}{ca}$ that intersects the vertical axis at $R = \frac{dh}{ca}$.

b. For the non-trivial steady states in both panels we derive the Jacobian

$$J = \begin{pmatrix} - & + \\ - & - \end{pmatrix} \quad \text{giving} \quad \mathrm{tr}J < 0 \quad \text{and} \quad \det J > 0 ,$$

i.e., they are stable. The origin is and carrying capacities are both unstable (saddle-points).

Question 7.7. Eutrophication
Figures made with a previous version of Grind:



a. For the algae, A, and the zooplankton, Z, one writes something like

$$\frac{\mathrm{d}A}{\mathrm{d}t} = rA(1-A/K) - bZ\frac{A^2}{h^2+A^2} \quad \text{and} \quad \frac{\mathrm{d}Z}{\mathrm{d}t} = cbZ\frac{A^2}{h^2+A^2} - dZ(1+eZ) \ ,$$

where e is the extra death due to intra-specific competition. The nullcline for the algae has been constructed in the text. For the zooplankton one obtains from $\mathrm{d}Z/\mathrm{d}t = 0$ that $Z = 0$ or

$$cb\frac{A^2}{h^2+A^2} - d - deZ = 0 \quad \text{or} \quad Z = \frac{cb}{de}\frac{A^2}{h^2+A^2} - \frac{1}{e} \ ,$$

which is a sigmoid function intersecting the vertical axis at $Z = -1/e$, and the horizontal axis at $A = h/\sqrt{R_0 - 1}$, where $R_0 = cb/d$. When $e = 0$ the Z-nullcline is a vertical line.

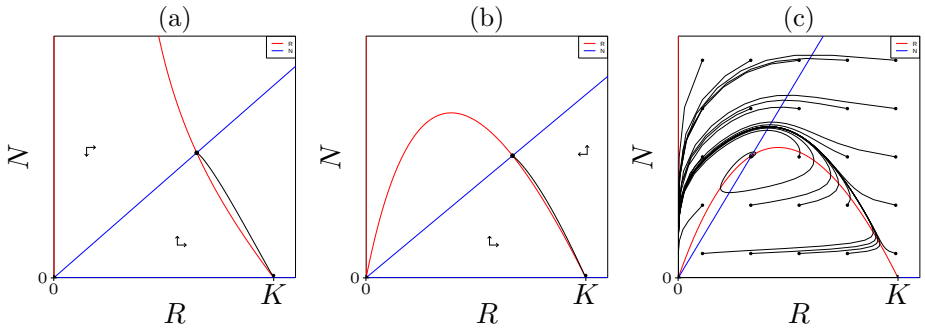
b. The carrying capacity, K, of the algae will depend on the total amount of nutrients that are available for the algae. Studying eutrophication therefore corresponds to increasing K.

c. There are many possibilities, see Panel (a) and (b). The effect of eutrophication corresponds to moving along a sigmoid zooplankton nullcline from the lowest to the highest algae nullcline. Steady states may stabilize or destabilize, and may appear or disappear.

d. Models suggest that changing a single parameter can have various different effects, depending on the precise initial circumstances. It is difficult to generalize, and reliable predictions are nearly impossible to make. A model plays the important role of suggesting various possible outcomes; possibly including undesired outcomes.

Question 7.8. Ratio-dependent predation

Figures made with `ratio.R`:



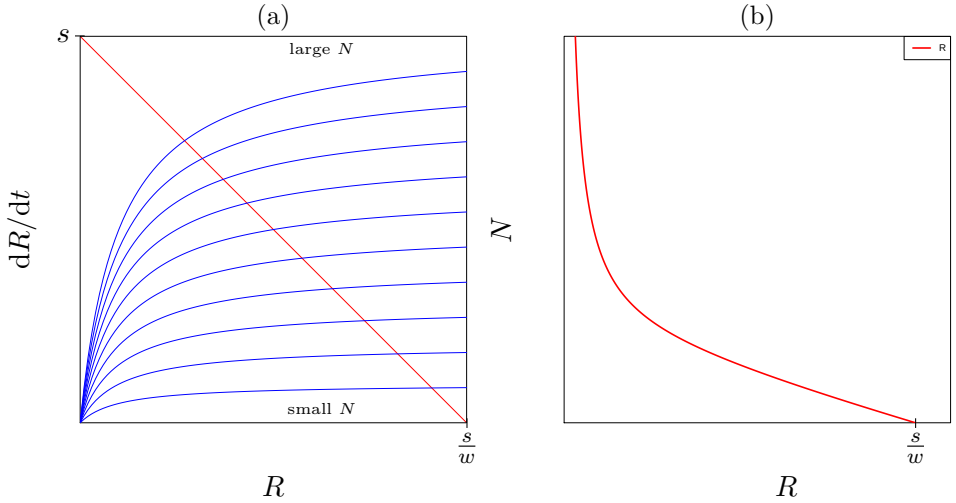
a. This model has the same two regimes as models based upon the Beddington functional response, with a limited-predation scenario in Panel (a), and a humped consumer nullcline with a stable steady state in Panel (b), and with an unstable steady state in Panel (c). Panel (c) reveals that the behavior of the model is problematic as all trajectories approach the origin, which is an unstable steady state. Like in the question on the SIR model, this is a consequence of the consumer nullcline going through the origin.

b. No, by increasing K in Panel (b) one will never find a Hopf bifurcation [9].

c. The functional response approaches infinity around the origin. The model better defines that very small predator populations still require a minimum prey density, e.g., because territory cannot become infinitely large.

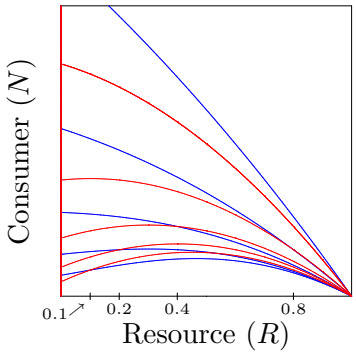
Question 7.9. Nullcline construction

Figures made with `chemoMonod.R`:



The red line in Panel (a) is the line $y = s - wR$ and the blue lines in depict the consumption term $y = \frac{aRN}{h+R}$ for various values of N. At all intersection points $\mathrm{d}R/\mathrm{d}t = 0$ because for the growth is perfectly balanced by the consumption. Copying the intersection points in Panel (a) for all values of N into a plot with N on the vertical axis gives the red nullcline depicted in Panel (b).

Question 7.10. Exponential functional response
Figure made with a previous version of Grind:



a. For $R \to \infty$ the functional response $(1 - \mathrm{e}^{-\ln[2]R/h}) \to 1$, which means that at high resource densities the consumption of a consumer is a per unit of time.

b. Since one can scale time by the natural rate of increase r, the resource density by its carrying capacity, and the consumer by the a parameter, the generic form of both models is:

$$\frac{\mathrm{d}R}{\mathrm{d}t} = R(1-R) - \frac{NR}{h+R} \quad \text{and} \quad \frac{\mathrm{d}R}{\mathrm{d}t} = R(1-R) - N(1 - \mathrm{e}^{-\ln[2]R/h}) \ ,$$

which has only one parameter h. Panel (a) shows the nullclines for $h = 0.1, 0.2, 0.4, 0.8$ and $h = 1.6$. The nullclines intersect when $R = h$ because the functional response then equals 0.5. Since there is no qualitative difference between the two sets of nullclines, we expect similar behavior for these two models.

Answers to Chapter 8

Question 8.1. Food chain

a. For $N = M = 0$ one finds $\bar{R} = s/r$. For $M = 0$ one solves $\bar{R} = d/b$ from $\mathrm{d}N/\mathrm{d}t = 0$ and then $\bar{N} = s/d - r/b$. When all three species are present, one solves $\bar{N} = e/c$ from $\mathrm{d}M/\mathrm{d}t = 0$, then $\bar{R} = \frac{s}{r+be/c}$ from $\mathrm{d}R/\mathrm{d}t = 0$, and finally $\bar{M} = (b\bar{R} - d)/c$ from $\mathrm{d}N/\mathrm{d}t = 0$.

b. Yes, the steady state of R only depends on its source when the length of the chain is odd.

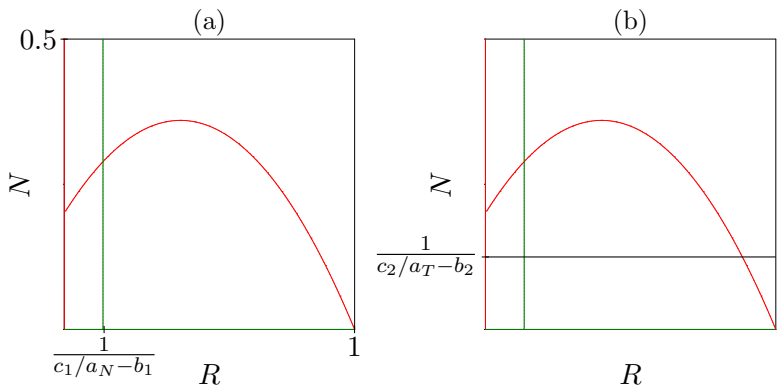
Question 8.2. Triangular Jacobian
Since $\mathrm{d}N_0/\mathrm{d}t$ only depends N_0, and $\mathrm{d}N_i/\mathrm{d}t$ only depends on N_{i-1} and N_i, the Jacobi matrix is of the triangular form

$$J = \begin{pmatrix} -(p+d) & 0 & 0 & 0 & \dots & \dots & 0 \\ 2p & -(p+d) & 0 & 0 & \dots & \dots & 0 \\ 0 & 2p & -(p+d) & 0 & \dots & \dots & 0 \\ & & \vdots & & & & \\ 0 & \dots & 0 & \dots & 0 & 2p & -d \end{pmatrix}, \tag{A.8.4}$$

with a characteristic equation corresponding to Eq. (8.11).

Question 8.3. Accumulating mutations
a. Mathematically this would seem appropriate, and it is similar to Eq. (8.9).
b. The problem with a cascade like this is that the variables described by ODEs are continuous, whereas actual cell numbers cannot become lower than a single cell. Solving this cascade, either mathematically or numerically, would immediately populate all the N_i equations, and hence yields very small densities into the equations for the senescent and leukemic cells at very early time points. For the senescent cells this is not a problem because they die and disappear, but since the leukemic cells have a growth rate that could be much faster than the division rate of the progenitor cells, they will start to expand much earlier than expected.
c. Note that the vector in the `leukemia.R` document is indexed from 1 to `ndiv` (and not from 0 to n), and that R allows one to write all the ODEs for $\mathrm{d}N_i/\mathrm{d}t$ as a single (fast) vector operation. The leukemic cells appear way too early in this model.
d. This model violates the constraint that size of a population of cells should be described by an integer number. When populations are large this is typically not a problem, but small populations should be described by stochastic models describing the behavior of individual cells. This problem is also known as the "atto-fox" problem (see Section 15.8). When $pN_i < 1$ one should define this term as the probability that a single cell divides forming exactly two daughter cells in the next generation. The formal procedure to do this is called a Gillespie simulation [6], in which every term of the model is translated into an event happening with a probability depending on the current population densities. If you like this question we could turn this model into a project.
e. No the Smith-Martin model would only delay the formation of the leukemic cells by $n \times \Delta$ days, i.e., by the total time spent in the B-phase division, which is short even if cells divide once per year.

Question 8.4. Chaos
Figures made with a previous version of Grind:



a. See Panel (a). Yes, for their values of b_1 the steady state is unstable.
b. See Panel (b). Yes, the unstable steady state around which the trajectory cycles is located above the nullcline of the top-consumer, and since the average consumer density is expected to be higher than this, we expect the top-consumer to invade.
c. Use Grind for the last 3 items.

Question 8.5. Detritus
A natural model would be

$$\frac{\mathrm{d}R}{\mathrm{d}t} = [bF - d_R - c_1 N]R \ , \quad \frac{\mathrm{d}N}{\mathrm{d}t} = [c_1 R - d_N - c_2 M]N \quad \text{and} \quad \frac{\mathrm{d}M}{\mathrm{d}t} = [c_2 N - d_M]M \ ,$$

where $F = K - R - N - M$. This shows that the $\mathrm{d}N/\mathrm{d}t$ and $\mathrm{d}M/\mathrm{d}t$ equations do not change. For $N = M = 0$ one now obtains $\bar{R} = K - d_R/b$, which increases linearly with the total amount of nutrients, K, in the system. When $N > 0$ and $M = 0$, one solves $\bar{R} = d_N/c_1$ from $\mathrm{d}N/\mathrm{d}t = 0$, and from $[b(K - \bar{R} - N) - d_R - c_1 N] = 0$ one solves that

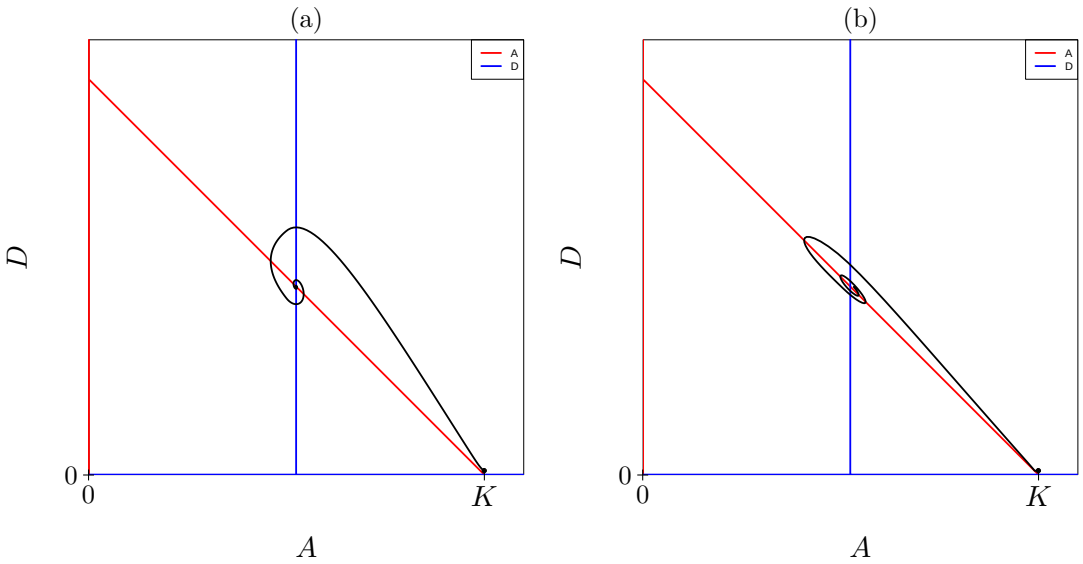
$$\bar{N} = \frac{c_1 bK - bd_N - c_1 d_R}{c_1(b + c_1)}$$

which increases linearly with K, and becomes positive when $K > (bd_N - c_1 d_R)/(c_1 b)$. When $N > 0$ and $M > 0$ one again solves $\bar{N} = d_M/c_2$ from $\mathrm{d}M/\mathrm{d}t = 0$, $\bar{M} = \frac{c_1 R - d_N}{c_2}$ from $\mathrm{d}N/\mathrm{d}t = 0$. After substitution of $\bar{N}$ and $\bar{M}$ one solves $\bar{R}$ from $\mathrm{d}R/\mathrm{d}t = 0$, i.e.,

$$\bar{R} = \frac{b(c_2 K + d_N - d_M) - c_1 d_M - c_2 d_R}{b(c_1 + c_2)} \ .$$

Thus, the steady state resource density again only depends on K when the food chain has an odd length.

Question 8.6. Maintenance and reproduction
Figures made with the model `daphnia.R`:



Making the QSSA

$$\frac{\mathrm{d}E}{\mathrm{d}t} = \frac{e(aA - k)D}{H + aA - k} - mE = 0 \quad \text{leads to} \quad E = \frac{(e/m)(aA - k)D}{H + aA - k} \ ,$$

and substituting this into the ODE for the adult *Daphnia*s gives

$$\frac{\mathrm{d}D}{\mathrm{d}t} = \frac{e(aA-k)D}{H+aA-k} - d_0 D - \frac{d_1 D}{1+aA/h} \ .$$

This looks complicated, but its nullcline solved by setting $\mathrm{d}D/\mathrm{d}t = 0$ corresponds to $D = 0$ and $A = c$, where c is a constant, because the ODE becomes independent of D when the $D = 0$ solution is factored out. Since the ODE for the algae was just a Lotka-Volterra prey equation, one obtains a classic Lotka-Volterra phase portrait. The nullclines of this QSSA model are depicted with a trajectory of the QSSA model in Panel (a) and with a trajectory of the full model in Panel (b). Note that the time scale of *Daphnia* is much slower in the full model and that the trajectory hence hovers around the nullcline, i.e., the quasi state state, of the algae.

Question 8.7. Kinetic proofreading
For receptors having n different phosphorylation sites one writes

$$\frac{\mathrm{d}C_0}{\mathrm{d}t} = k_1 F L - (k_{-1}+k_2)C_0 \ , \quad \frac{\mathrm{d}C_i}{\mathrm{d}t} = k_2 C_{i-1} - (k_{-1}+k_2)C_i \quad \text{and} \quad \frac{\mathrm{d}C_n}{\mathrm{d}t} = k_2 C_{n-1} - k_{-1} C_n \ ,$$

for $i = 1, 2, \ldots, n-1$, with the conservation equation $F = R - \sum_{i=0}^{n} C_i$. Summing these equations gives an ODE for the total amount of complexes,

$$\frac{\mathrm{d}\hat{C}}{\mathrm{d}t} = k_1 F L - k_{-1}\hat{C} = k_1 (R-\hat{C})L - k_{-1}\hat{C} \ ,$$

Setting $\mathrm{d}\hat{C}/\mathrm{d}t = 0$ reveals that

$$\hat{C} = \frac{k_1 R L}{k_{-1} + k_1 L} = \frac{RL}{K_m + L} \ ,$$

where $K_m = k_{-1}/k_1$, which is nothing more than the normal Michaelis Menten expression. This is a natural result because we are just counting the number of phosphorylation steps, and at each step we have the same off rate, k_{-1}. Setting all ODEs in the first equation to zero, one obtains

$$C_i = \left(\frac{k_2}{k_{-1}+k_2}\right)^i C_0 \quad \text{and} \quad C_n = \frac{k_2}{k_{-1}} \, C_{n-1} = \frac{k_2}{k_{-1}} \left(\frac{k_2}{k_{-1}+k_2}\right)^{n-1} C_0 \ ,$$

for $i = 0, 1, \ldots, n-1$. Since these ultimately all depend on C_0 we solve $\mathrm{d}C_0/\mathrm{d}t = 0$,

$$k_1(R-\hat{C})L - (k_{-1}+k_2)C_0 = \frac{k_1 K_m R L}{K_m + L} - (k_{-1}+k_2)C_0 = \frac{k_{-1} R L}{K_m + L} - (k_{-1}+k_2)C_0 = 0 \ ,$$

to obtain that

$$C_0 = \frac{k_{-1} R L}{(K_m + L)(k_{-1}+k_2)} = \frac{RL}{K_m + L} \, \frac{k_{-1}}{k_{-1}+k_2} = \frac{k_{-1}}{k_{-1}+k_2} \, \hat{C} \ .$$

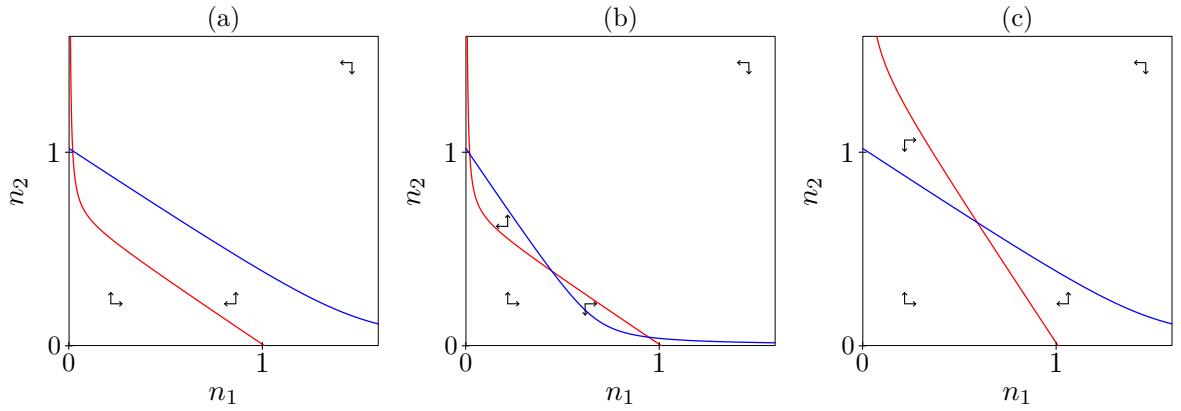
Hence

$$C_n = \hat{C} \, \left(\frac{k_2}{k_{-1}+k_2}\right)^n = \frac{RL}{K_m + L} \, \left(\frac{k_2}{k_{-1}+k_2}\right)^n \ ,$$

where the first term is the Michaelis-Menten function describing the saturation in the total number of complexes at large ligand concentrations, and the second term provides the fraction of C_n in this total. The final term introduces a novel dependence of C_n on the off-rate, k_{-1}, which becomes steep for large n (when k_{-1} is sufficiently large).

Answers to Chapter 9

Question 9.1. Migration
Figures made with the model `lotkaComp.R`:



a. A 2-dimensional Lotka-Volterra competition model with a small immigration term, ϵ, would be

$$\frac{\mathrm{d}N_1}{\mathrm{d}t} = \epsilon + r_1 N_1(1 - A_{11}N_1 - A_{12}N_2) \quad \text{and} \quad \frac{\mathrm{d}N_2}{\mathrm{d}t} = \epsilon + r_2 N_2(1 - A_{22}N_2 - A_{21}N_1) \ ,$$

with carrying capacities $\bar{N}_1 \simeq 1/A_{11}$ and $\bar{N}_2 \simeq 1/A_{22}$, as long as the immigration term is sufficiently small. To simplify this further we scale the populations such that their carrying capacity is close to one (see Section 15.4). By defining $n_i = A_{ii}N_i$ (and hence $N_i = n_i/A_{ii}$), we can rewrite this into

$$\frac{1}{A_{11}}\frac{\mathrm{d}n_1}{\mathrm{d}t} = \epsilon + \frac{r_1 n_1}{A_{11}}\left(1 - \frac{A_{11}n_1}{A_{11}} - \frac{A_{12}n_2}{A_{22}}\right) \quad \leftrightarrow \quad \frac{\mathrm{d}n_1}{\mathrm{d}t} = i_1 + r_1 n_1(1 - n_1 - \gamma_1 n_2) \ ,$$

where $i_1 = A_{11}\epsilon$ and $\gamma_1 = A_{12}/A_{22}$, and similarly

$$\frac{\mathrm{d}n_2}{\mathrm{d}t} = i_2 + r_2 n_2(1 - n_2 - \gamma_2 n_1) \ ,$$

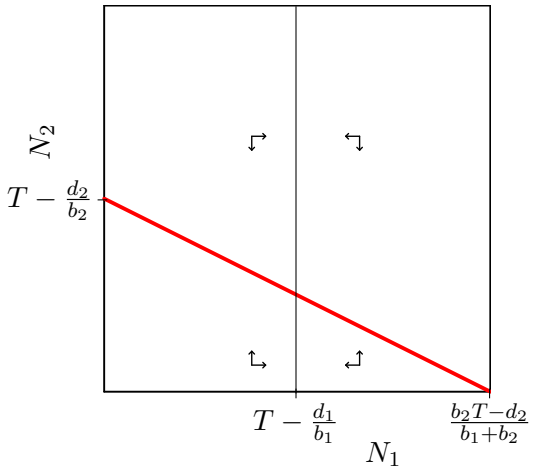
where $i_2 = A_{22}\epsilon$ and $\gamma_2 = A_{21}/A_{11}$. Note that once one has sufficient experience with scaling, one can just set $A_{ii} = 1$ in the first equation (like we did in the text).

b. For the four panels in Fig. 9.2, and small immigration terms, i_1 and i_2, one now obtains the nullclines in Panels (a)–(c) (where we collapse the first two cases with non-intersecting nullclines into Panel (a)).

c. From the vector field one can see that the steady states close to the carrying capacity are stable. The steady state in the middle of Panel (b) is unstable, whereas that in the middle of Panel (c) is stable.

d. In Panel (c) there is normal coexistence. In the other panels there is no true competitive exclusion, but since in the steady states near the carrying capacity the density of the rarest species is very low, one can consider it to be almost excluded.

Question 9.2. Equilibrium co-existence
Figure made with a previous version of Grind:



a. Since the trees can just overgrow the grass they experience areas occupied by grass as "empty space", and they do not suffer from the presence of the grass. The grass can only expand into true empty space, which is reflected by the $T - N_1 - N_2$ term, and suffers from the expansion of trees into grassy areas, which is reflected the $b_1 N_1 N_2$ term.

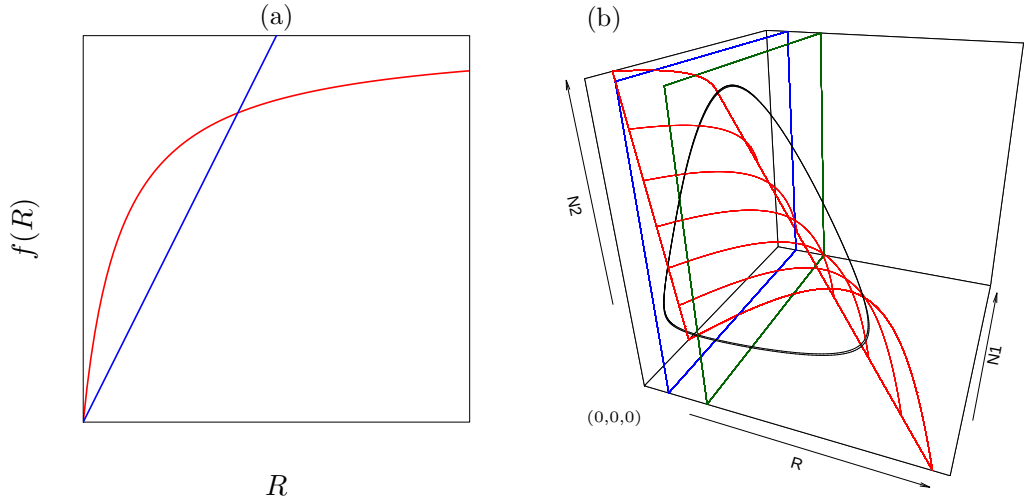
b. The $\mathrm{d}N_1/\mathrm{d}t = 0$ nullcline corresponds to the line $N_1 = T - \frac{d_1}{b_1} = T\big(1 - \frac{1}{R_{0_1}}\big)$. The $\mathrm{d}N_2/\mathrm{d}t = 0$ nullcline is given by $N_2 = T - \frac{d_2}{b_2} - N_1\big(1 + \frac{b_1}{b_2}\big)$. The vector field demonstrates that the non-trivial steady state is stable, and that the two carrying capacities, $\bar{N}_i = T - d_i/b_i$, are unstable when the nullclines intersect.

c. These lines will intersect, and give rise to the phase space shown above, when $\frac{b_2T-d_2}{b_1+b_2} > \frac{b_1T-d_1}{b_1}$, revealing that the maximum growth rate $r_{\max} = b_2T - d_2$ of the grass should at least be faster than that of the trees.

d. Yes, this is a counterexample. The reason is that the competition between these two species is not defined by their parameters, but by the structure of the model. Although the trees and the grass compete for the same resource, i.e., space, their competitive relationship is asymmetric just because trees are larger and can shadow the grass. One could argue that the trees and the grass (partly) belong to a different ecological guild, and that the model implicitly adds another resource dimension, i.e., light, allowing the trees to be superior over the grass with respect to this additional resource. For bacteria growing in a petri dish one could envision that N_1 produces a toxin killing N_2, which would enable the first species to overgrow the second one, irrespective of their respective birth and death rates. Again, the toxin would add another dimension allowing an independent ranking of competitive dominance. Finally, this deepens our understanding of the classical r-selected and K-selected species, as this model would allow K-selected species to invade into areas occupied by r-selected species, irrespective of their parameters.

Question 9.3. Non-equilibrium co-existence

Figure made with `noneqco.R` after finding appropriate parameters:



a. These are the standard phase planes of the Monod-saturated model, and the Lotka-Volterra model, respectively.

b. The initial slope of the saturated functional response should be steeper than that of the linear one (see Panel (a)).

c. The best approach is to first make a system where the Monod saturated consumer co-exists with the resource on a stable limit cycle. Then add the second consumer, and make sure that it can invade on this limit cycle. The nullcline of the Monod saturated consumer has to be located at a lower resource value than that of the linear consumer to enable the Monod saturated consumer to invade in the steady state of the linear consumer with the resource, i.e., $\frac{h}{a_1/d_1-1} < \frac{d_2}{a_2}$ (see Panel (b) made with the `cube.R` extension of Grind), where the black ellipse depicts a stable limit cycle.

d. Yes, one can always give the species with the linear functional response a saturation function with a large saturation constant.

Question 9.4. Larvae and adults

a. A natural model would be:

$$\frac{\mathrm{d}L}{\mathrm{d}t} = rA - dL(1+eL) - mL \quad \text{and} \quad \frac{\mathrm{d}A}{\mathrm{d}t} = mL - \delta A \ ,$$

where we assume density dependent death by competition between the larvae. The steady state can be solved by first setting $\mathrm{d}A/\mathrm{d}t = 0$ giving $A = mL/\delta$. Substituting this into $\mathrm{d}L/\mathrm{d}t = 0$ gives

$$\bar{L} = \frac{1}{e}\left[\frac{m}{d}\left(\frac{r}{\delta} - 1\right) - 1\right] \ , \bar{A} = \frac{m}{\delta}\,\bar{L} \ ,$$

which requires $\alpha = r/\delta > 1$ and $m(\alpha - 1)/d > 1$. The carrying capacity of this population would be defined as either $\bar{L}$ or $\bar{A}$.

b. Adding two predators changes to model into

$$\frac{\mathrm{d}L}{\mathrm{d}t} = rA - dL(1+eL) - mL - c_1 L N_1 \ , \quad \frac{\mathrm{d}A}{\mathrm{d}t} = mL - \delta A - c_2 A N_2 \ ,$$

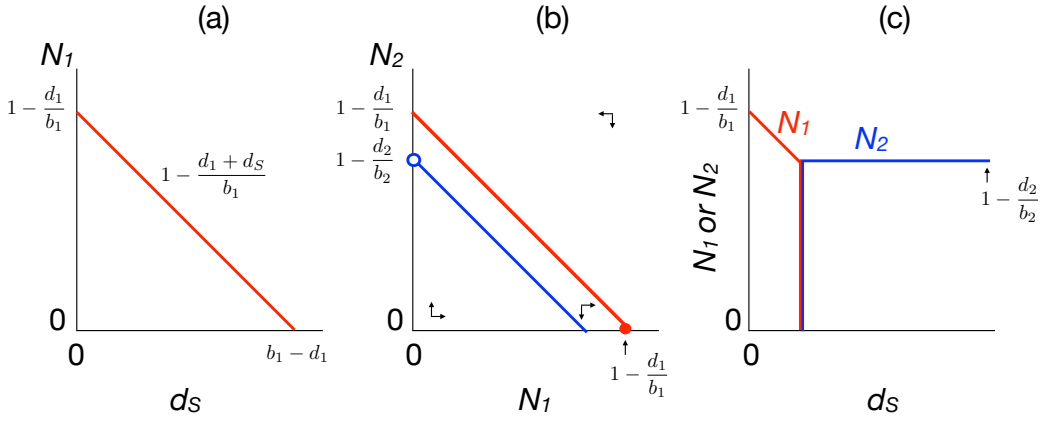
$$\frac{\mathrm{d}N_1}{\mathrm{d}t} = (c_1 L - d_1)N_1 \quad \text{and} \quad \frac{\mathrm{d}N_2}{\mathrm{d}t} = (c_2 A - d_2)N_2 \ .$$

Solving the steady state of the latter two gives $\bar{L} = d_1/c_1$ and $\bar{A} = d_2/c_2$. Substituting this into $\mathrm{d}L/\mathrm{d}t = 0$ and $\mathrm{d}A/\mathrm{d}t = 0$ gives

$$\bar{N}_1 = \frac{rd_2}{c_2 d_1} - \frac{m}{c_1} - \frac{d}{c_1}\left(1 + \frac{ed_1}{c_1}\right) \quad \text{and} \quad \bar{N}_2 = \frac{md_1}{c_1 d_2} - \frac{\delta}{c_2} \ .$$

Since one can always choose parameters such that $\bar{N}_1 > 0$ and $\bar{N}_2 > 0$ co-existence is possible.

Question 9.5. Gradients with sharp borders



a. Solving $\mathrm{d}N_1/\mathrm{d}t = N_1(b_1(1-N_1) - d_1 - d_S)$ gives the trivial $\bar{N}_1 = 0$ solution and the carrying capacity $\bar{N}_1 = 1 - \frac{d_1+d_S}{b_1} = 1 - 1/R_0$. This declines when the concentration of salt increases (because d_S increases with the salt).

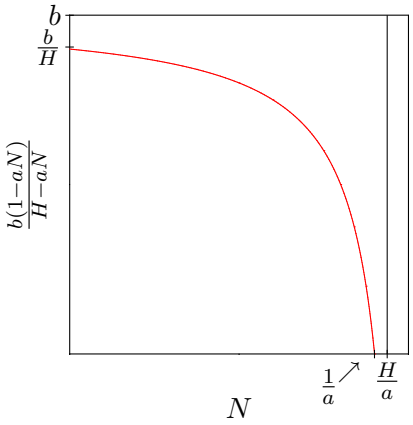
b. See Panel (a): $\bar{N}_1$ declines linearly with d_S. The species can no longer be maintained when $1 - \frac{d_1+d_S}{b_1} = 0$, i.e., when $d_S = b_1 - d_1$.

c. In the absence of salt the two nullclines are parallel lines with slope -1, $N_2 = 1 - \frac{d_1}{b_1} - N_1$ and $N_2 = 1 - \frac{d_2}{b_2} - N_1$, respectively. N_1 will outcompete N_2 because it has a higher R_0 at low concentrations of salt. See Panel (b). Along the gradient d_S will increase, and the $\mathrm{d}N_1/\mathrm{d}t = 0$ nullcline will be given by $N_2 = 1 - \frac{d_1+d_S}{b_1} - N_1$. The nullcline will shift downward and at some value of d_S overlap the $\mathrm{d}N_2/\mathrm{d}t = 0$ nullcline. Beyond that N_2 will outcompete N_1 and approach its carrying capacity $N_2 = 1 - \frac{d_2}{b_2}$.

d. See Panel (c). Along a smooth gradient we expect a sharp transition between the species due to competitive exclusion.

Question 9.6. Density dependent birth rate

Figure made with a previous version of Grind:



a. $R_0 = b/d$ or $R_0 = \frac{b}{d}\frac{a}{h+a}$, depending on its definition.

b. The QSS of the resource is $R = 1 - aN$ by substitution gives

$$\frac{\mathrm{d}N}{\mathrm{d}t} = \left[b\frac{a(1-aN)}{h+a(1-aN)} - d\right] N \ ,$$

which can be simplified into

$$\frac{\mathrm{d}N}{\mathrm{d}t} = \left[b\frac{1-aN}{H-aN} - d\right] N \ .$$

where $H = 1 + h/a$, which is larger than one.

c. The maximum birth rate is $\frac{ab}{a+h}$. Hence $R_0 = \frac{b}{d}\frac{a}{h+a}$, which is the same as the second answer in **a**.

d. To sketch the *per capita* birth rate as a function of N we need to consider the function $y = b\frac{1-aN}{H-aN}$ knowing that $H > 1$. For $N = 0$ this gives $y = b/H$, and for $y = 0$ we find $N = 1/a$. A horizontal asymptote is found by dividing numerator and denominator by N, i.e., $y = b\frac{1/N-a}{H/N-a}$, and letting $N \to \infty$ to find that $y \to b$. A vertical asymptote is located at $N = H/a$. Because $H > 1$ we know that the intersections with the horizontal and vertical axis fall below the asymptotes. See the sketch in the Figure above.

e. This concave shape is what we considered most realistic in Chapter 3. For instance see Fig. 3.3c and Fig. 3.5b.

f. The QSS now equals $R = 1/(1 + aN)$ which gives a *per capita* birth rate of $\frac{b}{1+h/a+hN}$ which is convex. Again the devil is in the details, as the shape of the consumers density dependence depends on the nature of the resource.

Question 9.7. Fitting Lotka-Volterra competition to the Gause data from 1934

a. Yes, by writing $A_{11} = 1/k_A, A_{22} = 1/k_C, A_{12} = \alpha/k_A$ and $A_{21} = \beta/k_C$, Eq. (9.20) becomes the same as Gause's handwritten model. The solitary data is well-described when $r_A = 1.11, k_A = 104.73, r_C = 0.916$, and $k_C = 60.277$.

b. For *Paramecium aurelia* we obtain $\alpha \simeq 1.05$ and for *P. caudatum* we obtain $\beta \simeq 0.64$. However, this does not mean that *P. aurelia* suffers more from *P. caudatum* than the other way around, because these parameters remain to be divided by the —quite different— carrying capacities.

c. Calling `plane(xmax=110,ymax=110)` for the estimated parameters, reveals that the nullclines fail to intersect, and that *P. aurelia* is the strongest competitor. Note that this probably the first time in your life that you sketch nullclines based upon measured parameters.

d. When *P. aurelia* suffers more from *P. caudatum* than from itself, it could be that the species are competing for more than one resource, and that *P. caudatum* consumes more from that resource than *P. aurelia*. However, this may not be required because $\alpha \simeq 1$, and that the standard error around its estimate includes $\alpha = 1$.

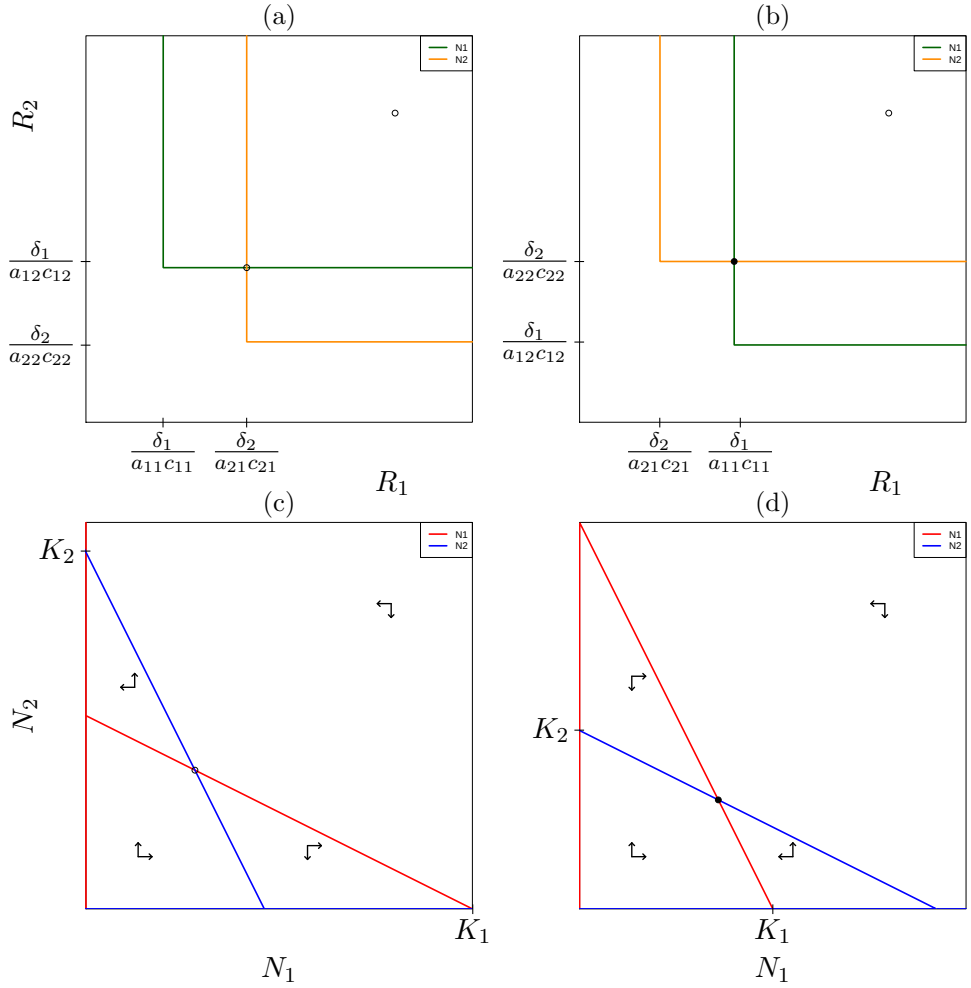
e. We indeed find similar results, but this is at least partly due to the fact that we have such a good initial guess of the parameter values (try other values to test how much this depends on the initial guess). Note that using all data we do obtain evidence that the two growth rates are truly different.

f. The confidence intervals for α and β overlap, and hence we cannot conclude that $\alpha > \beta$. Additionally the confidence interval for α includes $\alpha = 1$, so it would have been an over-interpretation to explain why $\alpha > 1$. The final call to `pairs()` depicts the relationships between all parameter estimates in the 100 bootstraps, e.g., depicts the positive correlation between α and β.

g. *P. aurelia* grows faster and has a higher carrying capacity than *P. caudatum*, and suffers about as much from the competition within its own species as from inter-specific competition. The parameter estimates suggest that *P. caudatum* suffers less from *P. aurelia* than from itself, which would suggest some niche differentiation.

Question 9.8. Tilman's competition model

Figure made with `tilmanMin.R`:



a. Solving $\alpha_{11}c_{11}R_1 + \alpha_{12}c_{12}R_2 - \delta_1 = 0$ gives $R^*_{11} = \frac{\delta_1}{\alpha_{11}c_{11}}$ and $R^*_{12} = \frac{\delta_1}{\alpha_{12}c_{12}}$. Similarly, solving $\alpha_{21}c_{21}R_1 + \alpha_{22}c_{22}R_2 - \delta_2 = 0$ gives $R^*_{22} = \frac{\delta_2}{\alpha_{22}c_{22}}$ and $R^*_{21} = \frac{\delta_2}{\alpha_{21}c_{21}}$.

b. In Fig. 9.5a $R^*_{11} < R^*_{21}$ and $R^*_{22} < R^*_{12}$, i.e., each consumer requires less than the other consumer of the resource it consumes most. In Fig. 9.5b this is the other way around, which leads to unstable steady state, corresponding to a founder controlled situation. (Note that Grind indicates the stability of the steady state by a bullet or a circle, and that the fact that the black production vector in Fig. 9.5b falls in between the two colored consumption vectors confirms that the 4-dimensional steady state exists (see the online tutorial)).

c. A consumer always needs both resources but is limited by the resource providing the lowest birth rate, $a_{ij}c_{ij}R_j$. If one of the resources were to decline it would ultimately become limiting.

d. To sketch these nullclines one first ignores the minimum function to find that the $\mathrm{d}N_1/\mathrm{d}t = 0$ nullcline is given by the vertical line $R^*_{11} = \frac{\delta_1}{\alpha_{11}c_{11}}$ and the horizontal line $R^*_{12} = \frac{\delta_1}{\alpha_{12}c_{12}}$ (see the green lines in Panel (a)). Only resource densities (R_1, R_2) larger than these two lines allow $\mathrm{d}N_1/\mathrm{d}t > 0$, i.e., N_1 can only grow in the region defined by the upper-right green square. Similarly, the $\mathrm{d}N_2/\mathrm{d}t = 0$ nullcline is constructed from the lines $R^*_{22} = \frac{\delta_2}{\alpha_{22}c_{22}}$ and $R^*_{21} = \frac{\delta_2}{\alpha_{21}c_{21}}$ (see the orange lines in Panel (a)). Note that the upper circle denotes the point $R_1 = R_2 = 1$ where both resources are at carrying capacity, s_i/d_i.

e. Apparently, the steady state is now stable when $R^*_{11} > R^*_{21}$ and $R^*_{22} > R^*_{12}$! In the stable situation of Panel (b) the steady state is located on the vertical part of the $\mathrm{d}N_1/\mathrm{d}t = 0$ nullcline, i.e., where N_1 is limited by R_1, and the horizontal part of the $\mathrm{d}N_2/\mathrm{d}t = 0$ nullcline, i.e., where N_2 is limited by R_2. Thus, this still corresponds to a situation where each consumer

is limited by the resource it consumes most. Note that in Panels (a) and (b)

$$\begin{pmatrix} \partial_{R_1} N_1' & \partial_{R_2} N_1' \\ \partial_{R_1} N_2' & \partial_{R_2} N_2' \end{pmatrix} = \begin{pmatrix} 0 & + \\ + & 0 \end{pmatrix} \quad \text{and} \quad \begin{pmatrix} \partial_{R_1} N_1' & \partial_{R_2} N_1' \\ \partial_{R_1} N_2' & \partial_{R_2} N_2' \end{pmatrix} = \begin{pmatrix} + & 0 \\ 0 & + \end{pmatrix} ,$$

respectively (see the online tutorial on tbb.bio.uu.nl/rdb/bm/clips/tilman).

f. The nullclines in Panels (c) and (d) were made the quasi steady state model in `tilmanMin.R`, and correspond to the Tilman diagrams of Panels (a) and (b), respectively. This confirms that the intersect in Panel (a) corresponds to the classical Lotka-Volterra competition situation with an unstable non-trivial state, and two stable carrying capacities on the axes.

Question 9.9. Co-existence by trade-offs?

a. No this is not an appropriate model for substitutable resources because the birth rate increases with every non-essential resource that is added to the ecosystem. Consumers are expected to approach their maximal birth rate at sufficiently high densities of just one resource if these are non-essential.

b. One could argue that this would become a model for essential resources when the birth rates, β_{ij}, on the individual resources are made smaller than the death rates, δ_i. Consuming a combination of resources then becomes essential, but this interpretation remains somewhat contrived.

c. One can define a trade-off by adding terms like $c_{12} = c - c_{11}, c_{21} = c - c_{22}$ and $c_{31} = c - c_{32}$ to the model, which defines a total consumption rate, c, that is the same for all consumers, and play with the other consumption rates. For substitutable resources defined by Eq. (9.22) (in the file `additive.R`), one indeed finds that the three consumer nullclines intersect in one steady state in a Tilman diagram spanned up by two resources, but this requires that all other parameters like the saturation constants and the death rates are also the same. For essential resources defined by Eq. (9.25) (in the file `essential.R`), defining this trade-off is not sufficient to let the three consumer nullclines intersect in one steady state. Thus, the result seems rather artificial: it is not based upon an appropriate model, and requires unreasonable parameter constraints. This would be a good project to study further.

Question 9.10. Fitness

a. Writing out Eq. (9.13) explicitly, and combining parameters

$$R_i^* = \frac{h_i}{b_i/d_i - 1} = \frac{h_i}{r_i - 1} , \tag{A.9.5}$$

where $r_i = b_i/d_i$, we have an expression for which species wins (i.e., the one with the lowest R_i^*). Writing

$$\hat{R}_{0_i} = \frac{b_i}{d_i} \frac{\bar{R}}{h_i + \bar{R}} = \frac{r_i}{h_i/\bar{R} + 1} ,$$

we can solve for r_i and write Eq. (A.9.5) in terms of $\hat{R}_{0_i}$:

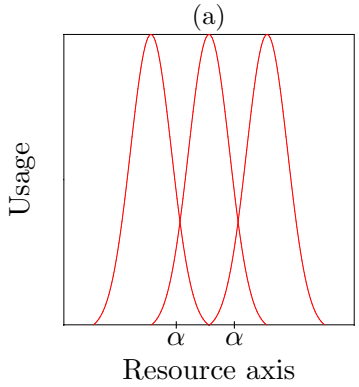
$$R_i^* = \frac{h_i}{\hat{R}_{0_i}(h_i/\bar{R} + 1) - 1} \quad \text{where} \quad \bar{R} = \frac{s}{d} .$$

The species with the lowest fitness $\hat{R}_{0_i}$ can therefore be the superior competitor when its h_i is sufficiently smaller than that of the other competitors. In conclusion, $\hat{R}_0$ does not uniquely identify the superior competitor, and the critical resource density, R^*, remains the best indicator.

b. The model `competition.R` provides an example where an r-selected species, with the lowest R_0 and carrying capacity, outcompetes a K-selected species.

Answers to Chapter 10

Question 10.1. Invasion criterion
Figure made with a previous version of Grind:



a. Since the diet of the two established species does not overlap, their resource usage curves should not overlap. The curve of the invading species should be located in the middle, and have an equal overlap with both species (here indicated by the α). See Panel (a).

b. Since N_1 and N_3 do not compete the model simplifies to

$$\frac{\mathrm{d}N_1}{\mathrm{d}t} = rN_1(1-N_1-\alpha N_2)\,, \frac{\mathrm{d}N_2}{\mathrm{d}t} = rN_2(1-N_2-\alpha N_1-\alpha N_3) \quad \text{and} \quad \frac{\mathrm{d}N_3}{\mathrm{d}t} = rN_3(1-N_3-\alpha N_2)\,,$$

where we have scaled all carrying capacities to one.

c. Because $N_2 \approx 0$ the steady state before invasion is $\bar{N}_1 = \bar{N}_3 = 1$, and hence $\mathrm{d}N_2/\mathrm{d}t \simeq rN_2(1-2\alpha)$. For invasion one requires $\mathrm{d}N_2/\mathrm{d}t > 0$, meaning that $1-2\alpha > 0$, giving that $\alpha < 1/2$. Since N_2 has an overlap of one with itself, the total overlap with the two other species should be less than the overlap with itself.

Question 10.2. Random Jacobian

a. At low connectivities the characteristic equation tends to be defined by the diagonal elements, i.e., $\lambda = -1$.

b. Running the script, and plotting the fraction of stable systems as function of the connectivity, P, confirms that Eq. (10.13) holds for large n. For small n the largest eigenvalue tends to be $\lambda = -1$.

c. When all diagonal elements are set to $A_{ii} = -c$, the condition for stability becomes $\sigma\sqrt{nP} < c$. Setting the diagonal elements to random values drawn from a random distribution readily destabilizes the system (e.g., uncomment the `diag(A) <- -abs(rnorm(n,mean=1,sd=0.5))` line). Thus, it appears to be a quite string assumption that all diagonal elements are equal and negative.

d. No answer provided: this would be good project.

Question 10.3. Roberts' random Lotka-Volterra model
Table made with the script `roberts.R`:

a. A piece of R-code for drawing $n \times n$ random positive and negative z-values and collecting these in an interaction matrix with ones on the diagonal is:

```
z <- rnorm(n*n,zmean,zmean/10)
k <- ifelse(runif(n*n)<0.5,1,-1)
A <- matrix(k*z,nrow=n,ncol=n)
diag(A) <- 1
```

Since all species survive when all off-diagonal A_{ij} elements are zero, one trivially finds maximal diversity when $\bar{z} \to 0$. Because the steady state computed algebraically is very different from the steady state approached by numerical integration whenever some species go extinct, we compute both states in the `roberts.R` script, and run many simulations to measure the

average diversity, $\bar{n}$, and the percentage of feasible systems, %F. To sweep parameters one should vary n and `zmean`. Since Eq. (10.13) derived from the analysis of random Jacobi matrices suggested that steady states tend to be stable when $\sigma\sqrt{nP} < 1$, and we here have a fully connected interaction matrix, i.e., $P = 1$, and an average interaction strength, $\bar{z}$ (instead of a standard deviation of off-diagonal elements in a Jacobi matrix), we hypothesize that the Roberts version of Eq. (10.13) would be something like $\bar{z}\sqrt{n} < c$, where c is an unknown constant. Running many simulations with $n = 16, 64$ and 144, while sweeping $\bar{z} = c/\sqrt{n}$ one indeed finds

n	$\bar{z} = \frac{0.2}{\sqrt{n}}$		$\bar{z} = \frac{0.25}{\sqrt{n}}$		$\bar{z} = \frac{0.3}{\sqrt{n}}$		$\bar{z} = \frac{0.4}{\sqrt{n}}$		$\bar{z} = \frac{0.5}{\sqrt{n}}$		$\bar{z} = \frac{1}{\sqrt{n}}$	
	$\bar{n}$	%F	$\bar{n}$	%F	$\bar{n}$	%F	$\bar{n}$	%F	$\bar{n}$	%F	$\bar{n}$	%F
16	16	100	16	100	16	100	15.8	80	15.5	65	11.2	0
64	64	100	64	100	63.9	100	62.5	40	61.3	10	42.8	0
144	144	100	143.9	100	143.7	85	142.1	15	136.5	0	98.9	0

where $\bar{n}$ is the number of species that remains present, and %F is the percentage of feasible systems in the simulations. Thus, increasing the average absolute interaction strength decreases the percentage of feasible systems, and scaling the interaction strength by $\sqrt{n}$ yields a similar critical interaction strength in systems markedly differing in the initial diversity, n. Moreover, a system classified as unfeasible can typically persist with the majority of the species being present.

To better understand the $\sqrt{n}$ in these conditions, it is important to realize that the total interspecific interaction strength of a species, $F_i = \sum_j A_{ij}\bar{N}_j$ for $i \neq j$, is the sum of a set of random numbers, i.e., random A_{ij} elements multiplied with their corresponding steady states $\bar{N}_j$. Since the variance of the sum of independent random variates is the sum of their variances, e.g., $\texttt{var}(\texttt{rnorm}(10000, 0, 1) + \texttt{rnorm}(10000, 0, 2)) \simeq 5$, the expected variance of all the F_is is proportional to n, and hence their expected standard deviation is proportional to $\sqrt{n}$. Eq. (10.13) and our hypothesized $\bar{z}\sqrt{n} < c$ therefore reflect that the F_is should be sufficiently similar for many species to co-exist. Moreover, because the statistical result on the sum of the variances is very general, and does not depend on the nature of the random distributions that are being summed, one expects similar results for any independent random filling of the interaction (or Jacobi) matrix (e.g., even after filling the A matrix with fixed values, $A_{ij} = \pm z$ like Roberts [11] did). Since many species are only expected to co-exist when they are sufficiently similar, these general results obtained with randomly created Lotka-Volterra systems resemble the ideas on neutral coexistence [8, 13].

b. Yes, because the replication rates, r_i, cannot be cancelled after setting $\mathrm{d}N_i/\mathrm{d}t = 0$ in Eq. (10.14), whereas they could in Eq. (9.20), variation in the growth rates decreases the diversity. By having faster growth rates some species will be better than others, i.e., the system is less neutral.

c. Yes, drawing the diagonal elements from a normal distribution with an average of one, decreases the diversity, and readily leads to integration errors because some populations become very large.

Question 10.4. Random Lotka-Volterra competition models

Table made with the script `randomCompetition.R`:

a. To model resource competition we draw symmetric off-diagonal elements, $0 < A_{ij} = A_{ji} < 2\bar{z}$, from a uniform distribution (such that the average is $\bar{z}$), in the model $\mathrm{d}N_i/\mathrm{d}t = b_i N_i(1 - \sum_j A_{ij}N_j) - d_i N_i$.

```
A <- matrix(0,nrow=n,ncol=n)
diag(A) <- 1
A[lower.tri(A)] <- runif((n*n-n)/2)*2*barZ
tA <- t(A)
A[upper.tri(A)] <- tA[upper.tri(tA)]
```

which uses general R functions to select the diagonal, and the lower and upper triangle of a matrix. The R-function `t()` computes the transpose of the interaction matrix. The b_i and d_i values can be set to fixed values, e.g., $b_i = 1$ and $d_i = 0$ for all i, to compare to the results of Roberts [11], or can be drawn from normal distributions, to allow the species to have different birth and death rates (while making sure that $b_i > d_i$, or $R_{0_i} > 1$, for every species i.

b. Repeating the analysis of Roberts [11] for a situation where all interactions are competitive, (and all species still have the same growth rate $b_i = 1$, and no death rate ($d_i = 0$)) yields very similar results:

	$\bar{z} = \frac{0.3}{\sqrt{n}}$	$\bar{z} = \frac{0.4}{\sqrt{n}}$	$\bar{z} = \frac{0.5}{\sqrt{n}}$	$\bar{z} = \frac{0.75}{\sqrt{n}}$	$\bar{z} = \frac{1}{\sqrt{n}}$
n	$\bar{n}$	$\bar{n}$	$\bar{n}$	$\bar{n}$	$\bar{n}$
16	16	16	15.9	13.1	10
64	64	64	63.8	56.9	39.1
144	144	144	143.3	128.5	88

For low average values of the off-diagonal A_{ij} elements, i.e., $\bar{z} \leq 0.4/\sqrt{n}$, most species tend to survive, otherwise a subset of species tends to go extinct. Because the critical average interaction strength, $\bar{z}$, at which a few species are excluded again scales with $\sqrt{n}$ when we increase n, this also resembles Eq. (10.13), which again suggests that the species have to be sufficiently similar (because the standard deviation of the total interspecific competition, $F_i = \sum_i^n A_{ij}\bar{N}_j$ for $i \neq j$, is expected to be proportional to $\sqrt{n}$).

c. Restricting $d_i = 0$ for all i, and allowing for different growth rates b_i does not change these results as the b_is cancel from the steady state when all $d_i = 0$. This can be checked by running the script. Allowing for death, and drawing birth and death rates from two normal distributions (while restricting $b_i > d_i$ or $R_{0_i} > 1$ for every species), species start to become excluded at somewhat lower interaction strengths (also shown by running the script).

d. The properties of the species that survive can be compared to those that were excluded by the code defined at the end of the script:

```
present <- (frun > 0.01)
meanN <- mean(frun[present])
meanR0present <- mean(b[present]/d[present])
meanR0absent <- mean(b[!present]/d[!present])
Apresent <- A[present,present]
Aabsent <- A[!present,!present]
meanApresent <- mean(Apresent[lower.tri(Apresent)])
meanAabsent <- mean(Aabsent[lower.tri(Aabsent)])
```

Running the script for an average interaction strength where a decent fraction of the species is excluded, e.g., $n = 32$ and $\bar{z} = 1/\sqrt{n}$ when allowing for random birth and death rates, reveals that surviving species on average have a higher R_0 and lower interaction coefficients, A_{ij}, which sounds very natural, but also implies that the model is selecting for neutrality.

e. When all species are present, the expected steady state of a population is obtained by solving

$$b(1 - (n-1)\bar{A}N - N) - d = 0 \quad \text{giving} \quad \bar{N} = \frac{1 - d/b}{1 + (n-1)\bar{A}} \ ,$$

where $\bar{A}$ is the average value of the off-diagonal A_{ij} elements. This in turn allows one to compute the expected strength of the intra-specific competition,

$$\bar{F} = (n-1)\bar{A}\bar{N} = \frac{(1 - d/b)(n-1)\bar{A}}{1 + (n-1)\bar{A}} \ .$$

Question 10.5. Control by parasites

a. Define $T = S + I$ as the total population size of susceptible and infected birds, and write

$$\frac{\mathrm{d}S}{\mathrm{d}t} = bT(1 - T) - dS - \beta SI \quad \text{and} \quad \frac{\mathrm{d}I}{\mathrm{d}t} = \beta SI - \delta I$$

b. The R_0 of the birds is b/d. The population size has been scaled such that the birth rate becomes zero at $T = 1$, and hence the scaled carrying capacity is obtained by solving $bT(1 - T) - dT = 0$ giving $\bar{T} = \frac{b-d}{b} = 1 - 1/R_0 = K$.

c. The R_0 of the parasites is $R_0' = \beta K/\delta$.

d. In the presence of the parasite the number of susceptibles is solved from $\mathrm{d}I/\mathrm{d}t$ which gives $S = \delta/\beta = K/R_0'$.

e. Defining O as the other species one could write

$$\frac{\mathrm{d}S}{\mathrm{d}t} = bT(1 - T - O) - dS - \beta SI \ , \quad \frac{\mathrm{d}I}{\mathrm{d}t} = \beta SI - \delta I \quad \text{and} \quad \frac{\mathrm{d}O}{\mathrm{d}t} = bO(1 - T - O) - d_0 O \ ,$$

with $d_0 > d$. Note that the other species can invade when $b(1 - T) - d_0 > 0$, or equivalently when the $R_0 = b(1 - T)/d_0 > 1$.

f. Thus, if the infection is sufficiently harmful, i.e., $\bar{T} \ll K$, the other species can invade despite its lower fitness.

g. If each species is sufficiently down-regulated by its parasite the resource density can stay high and many species can be maintained [13].

Question 10.6. Cross-feeding

a. Let the first species, N_1, feed on saccharose, R_1. The second resource, R_2 (fructose), will then be formed when N_1 consumes saccharose, splits it into glucose for its own growth and fructose as a metabolic by-product. Hence the equations for the two resources are

$$\frac{\mathrm{d}R_1}{\mathrm{d}t} = w(\hat{R}_1 - R_1) - b_1 R_1 N_1 \quad \text{and} \quad \frac{\mathrm{d}R_2}{\mathrm{d}t} = \alpha b_1 R_1 N_1 - b_2 R_2 N_2 - w R_2 \ ,$$

because $\hat{R}_2 = 0$. Since N_1 uses only half of the energy from each saccharose molecule, whereas N_2 uses all of the fructose, those for the bacteria are

$$\frac{\mathrm{d}N_1}{\mathrm{d}t} = \alpha b_1 R_1 N_1 - w N_1 \quad \text{and} \quad \frac{\mathrm{d}N_2}{\mathrm{d}t} = b_2 R_2 N_2 - w N_2 \ ,$$

where $\alpha = \alpha_1 = (1 - \alpha_1) = 0.5$, and $S_{21} = 1$ and all other elements of the stoichiometric matrix are zero. Note that if one were to scale by concentrations, rather than by energy, one can also set $\alpha = 1$.

b. The steady state is

$$\bar{R}_1 = \frac{w}{\alpha b_1} \ , \quad \bar{R}_2 = \frac{w}{b_2} \ , \quad \bar{N}_1 = \alpha \hat{R}_1 - \frac{w}{b_1} \quad \text{and} \quad N_2 = \bar{N}_1 - \frac{w}{b_2} \ ,$$

which means that N_1 will be present when $b_1/w > \hat{R}_1$, which is independent of the leakage rate, and N_2 is present when $b_2/w > \bar{B}_1$, which depends on α.

c. Following Eq. (10.20) one obtains the same, i.e.,

$$\frac{\mathrm{d}N_1}{\mathrm{d}t} = \alpha b_1 R_1 N_1 - w N_1 \quad \text{and} \quad \frac{\mathrm{d}N_2}{\mathrm{d}t} = b_2 R_2 N_2 - w N_2 \ ,$$

when $C = \begin{pmatrix} \alpha & 0 \\ 0 & 1 \end{pmatrix}$ and $A = \begin{pmatrix} b_1 & 0 \\ 0 & b_2 \end{pmatrix}$, and for the resources one again obtains

$$\frac{\mathrm{d}R_1}{\mathrm{d}t} = w(\hat{R}_1 - R_1) - b_1 R_1 N_1 \quad \text{and} \quad \frac{\mathrm{d}R_2}{\mathrm{d}t} = \alpha b_1 R_1 N_1 - b_2 R_2 N_2 - w R_2 \ ,$$

when $\hat{R}_2 = 0$, $S_1 = \begin{pmatrix} 0 & 0 \\ \alpha & 0 \end{pmatrix}$ and $S_2 = \begin{pmatrix} 0 & 0 \\ 0 & 0 \end{pmatrix}$. For this particular case both models therefore become identical.

Question 10.7. Neutral theory of biodiversity
The fact that a model can account for particular (sets of) data does not prove that the model provides the true mechanistic explanation for the data. Alternative models may also be able to account for the data. In this case the neutral model functions as a simple "null" model that is surprisingly good in explaining species-abundance distributions, even in cases where everyone would agree that the species do have different ecological properties. One should therefore not disprove the neutral model, but view it as a phenomenological null model, and keep trying to develop more mechanistic models that are better based upon established interactions and parameters.

Question 10.8. Huisman
Carefully read the `huisman.R` script to understand how this defines Eq. (10.15). Running simulations one finds the answers.

a. No, almost all systems approach a steady state.

b. No, running with $m = 3, 5$ or 10 resources one typically observes an approach to a steady state.

c. The standard deviation of the saturation constants, h_{ij}, of the consumers that are present at the end is somewhat smaller than that of all invaders that have been represent, and the variation of the successful invaders is markedly smaller than that of the consumers that were unable to invade. The model is therefore selecting for species with similar requirements for all resources, i.e., for neutrality. Additionally, the consumers that are present at the end tend to have higher maximum consumption rates, r_i, which was to be expected. For each new consumer the average h_{ij} is scaled to 0.5 and hence this cannot change.

Question 10.9. Scheffer
Carefully read the `scheffer.R` script to understand how this defines Eq. (10.16). Running simulations one should find the following answers.

a. No, it is hard to find situations when the number of consumers exceeds the number of resources.

b. Setting various values of `nr` and `nn`, even `nn>nr` in the `eps=0` regime, it appears to be difficult to have several more consumers than resources.

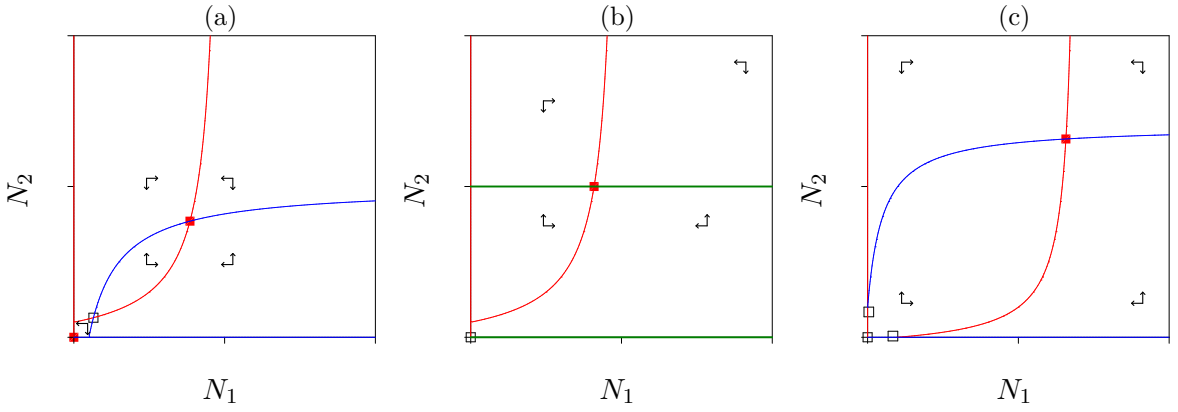
c. There is hardly any difference between the competition coefficients of resources that persist and those that go extinct. The consumers that persist tend do have higher consumption rates than those that go extinct.

Question 10.10. Monopolization

a. Yes, since most competition situations are "founder controlled" in the model of Yodzis, species that grow faster are more likely to outcompete the species that grow slower. Thus, the diversity of the communities would be somewhat lower when species have different birth and death rates.

b. No, one would still have that species with a low R_0 will survive in those patches were they arrived much earlier, or in greater numbers, than their competitors with a higher fitness.

Question 10.11. Symbiosis
Figures made with a previous version of Grind:



a. A natural model makes the birth rate a saturation function of the other species and assumes density dependent death:

$$\frac{\mathrm{d}N_1}{\mathrm{d}t} = N_1\left[\frac{b_1 N_2}{h+N_2} - d_1(1+e_1 N_1)\right] \quad \text{and} \quad \frac{\mathrm{d}N_2}{\mathrm{d}t} = N_2\left[\frac{b_2 N_1}{h+N_1} - d_2(1+e_2 N_2)\right] .$$

Note that it is quite natural that the symbiotic effect has some maximum. The $\mathrm{d}N_2/\mathrm{d}t = 0$ nullcline is given by

$$N_2 = \frac{1}{e_2}\left[R_{0_2}\frac{N_1}{h+N_1} - 1\right] ,$$

where $R_{0_2} = b_2/d_2$. This is a saturation function starting at $N_2 = -1/e_2$ when $N_1 = 0$. See Panel (a). The $\mathrm{d}N_1/\mathrm{d}t = 0$ nullcline is just the mirror image of this (Panel (a)). The nullclines intersect in three steady states. The origin and the system at "carrying capacity" are stable nodes, separated by a saddle point in the middle. The stable manifold of this saddle point defines the separatrix between the two stable steady states.

b. When N_1 is the saprophyte, one would write

$$\frac{\mathrm{d}N_1}{\mathrm{d}t} = N_1\left[\frac{b_1 N_2}{h+N_2} - d_1(1+e_1 N_1)\right] \quad \text{and} \quad \frac{\mathrm{d}N_2}{\mathrm{d}t} = N_2\left[b_2 - d_2(1+e_2 N_2)\right] .$$

The $\mathrm{d}N_1/\mathrm{d}t = 0$ nullcline stays the same (see Panel (b)), and the $\mathrm{d}N_2/\mathrm{d}t = 0$ nullcline is a horizontal line located at its carrying capacity.

c. The other species could merely increase the birth rate, e.g.,

$$\frac{\mathrm{d}N_1}{\mathrm{d}t} = N_1\left[b_1 + \frac{\beta_1 N_2}{h+N_2} - d_1(1+e_1 N_1)\right] \quad \text{and} \quad \frac{\mathrm{d}N_2}{\mathrm{d}t} = N_2\left[b_2 + \frac{\beta_2 N_1}{h+N_1} - d_2(1+e_2 N_2)\right] ,$$

where β_i is the maximum birth rate due to the presence of the symbiont, and b_i is the maximum birth rate in the absence of the symbiont. The nullclines have been depicted with Grind in Panel (c).

d. Yes, just make sure that $R_{0_i} = b_i/d_i < 1$ in the absence of the other species, and $(b_i+\beta_i)/d_i > 1$ to enable growth in the presence of the symbiont. Panel (c) depicts the typical phase space when $R_{0_i} > 1$.

Question 10.12. Infinite Niche-matrix

a. Every single ODE of this system is a function of all variables of the system, i.e., $\mathrm{d}N_i/\mathrm{d}t = f(\vec{N}) = N_i - \sum_j A_{ij}N_iN_j$, where $\vec{N}$ is a vector $(N_1, N_2, \ldots, N_i, \ldots, N_j, \ldots)$. For the off-diagonal elements of the Jacobi matrix we observe that for every $j \neq i$ the partial derivative, ∂_{N_j}, of $f(\vec{N})$ corresponds to $-A_{ij}N_i$. Further, because all populations have the same steady state, $N_i = \bar{N}$, these off-diagonal elements become $-\alpha\bar{N}$, $-\alpha^4\bar{N}$, $-\alpha^9\bar{N}$. For the partial

derivatives on the diagonal we write that the partial derivative, ∂_{N_i}, of $f(\vec{N})$ correspond to

$$1 - 2N_i - \sum_{j \neq i} A_{ij} N_j = 1 - 2\bar{N} - \sum_{j \neq i} A_{ij} \bar{N} \ ,$$

where we pull the $i = j$ term out of the sum term, and the factor two is due to the fact that $A_{ii} = 1$ and the partial derivative, ∂_{N_i}, of $-N_i^2$ equals $2N_i$. Hence the Jacobian is:

$$J = \begin{pmatrix} \dots & -\alpha\bar{N} & 1 - 2\bar{N} - \sum_{j\neq i} A_{ij}\bar{N} & -\alpha\bar{N} & -\alpha^4\bar{N} & -\alpha^9\bar{N} & \dots \\ \dots & -\alpha^4\bar{N} & -\alpha\bar{N} & 1 - 2\bar{N} - \sum_{j\neq i} A_{ij}\bar{N} & -\alpha\bar{N} & -\alpha^4\bar{N} & \dots \\ \dots & & & & & & \end{pmatrix}$$

Moving one of the $2\bar{N}$ on the diagonal into the sum we obtain

$$J = \begin{pmatrix} \dots & -\alpha\bar{N} & 1 - \bar{N} - \sum A_{ij}\bar{N} & -\alpha\bar{N} & -\alpha^4\bar{N} & -\alpha^9\bar{N} & \dots \\ \dots & -\alpha^4\bar{N} & -\alpha\bar{N} & 1 - \bar{N} - \sum A_{ij}\bar{N} & -\alpha\bar{N} & -\alpha^4\bar{N} & \dots \end{pmatrix}$$

Finally because $\bar{N} = 1/\sum A_{ij}$ all diagonal elements can be simplified as $-\bar{N}$, i.e.,

$$J = \begin{pmatrix} \dots & -\alpha\bar{N} & -\bar{N} & -\alpha\bar{N} & -\alpha^4\bar{N} & -\alpha^9\bar{N} & \dots \\ \dots & -\alpha^4\bar{N} & -\alpha\bar{N} & -\bar{N} & -\alpha\bar{N} & -\alpha^4\bar{N} & \dots \end{pmatrix}$$

b. The Jacobian is equal to $-\bar{N}A$, where A is the interaction matrix. The eigenvalues of the Jacobian are equal to those of the interaction matrix.

Answers to Chapter 11

Question 11.1. Geritz & Kisdi [5]
The quasi steady assumption for the resource gives $R = \mathrm{e}^{1-bA/r}$ and $\mathrm{d}E/\mathrm{d}t = cbA\mathrm{e}^{1-bA/r} - dE$ with solution

$$E(t) = \frac{cbA\mathrm{e}^{1-bA/r}}{d}\left(1 - \mathrm{e}^{-dt}\right) \quad \text{and} \quad A_{j+1} = \rho A_j \mathrm{e}^{-\beta A_j} \ ,$$

where $\rho = cb\mathrm{e}(1 - \mathrm{e}^{-d\tau})/d$ and $\beta = b/r$.

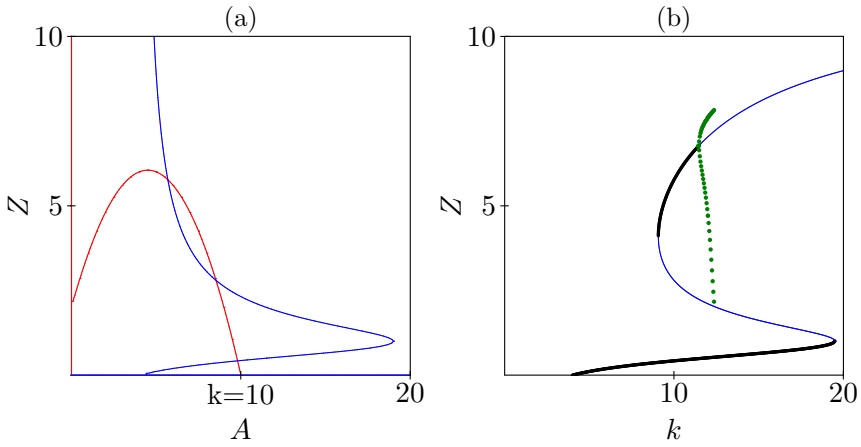
Question 11.2. Insect population
Since the death rate should increase when the amount of resource declines one could write for the *per capita* death rate

$$d = d_0 + \frac{d_1}{1 + r/h} \quad \text{such that} \quad \frac{\mathrm{d}n}{\mathrm{d}t} = -d_0 n - \frac{d_1 n}{1 + r/h} \ .$$

Question 11.3. Periodic forcing
Read the Scheffer *et al.* [12] paper and try to reproduce some of their results.

Answers to Chapter 12

Question 12.1. Biomanipulation
Figures made with a previous version of Grind:



a. For $F = 0.15, h = 1, k = 10, m = 0.4$ and $p = 0.5$ the phase space is given by Panel (a), which has three non-trivial steady states. By decreasing the carrying capacity the upper two states disappear.

b. Depleting the fish by setting $F = 0$ will transiently remove the lower two steady states from Panel (a), and the system will approach the attractor located near the top of the parabola. If the fish were to regrow to same $F = 0.15$ density, the two lower steady states would reappear, but the system would remain in the upper attractor because it is locally stable.

c. Changing the carrying capacity k yields the bifurcation diagram of Panel (b). The heavy solid line depicts stable steady states, the light solid line unstable steady states, and the green bullets denote the amplitude of a stable limit cycle. There is a transcritical bifurcation at $k = 4$, a saddle-node bifurcation at $k \simeq 9$, a Hopf bifurcation at $k \simeq 11.5$, and another saddle-node bifurcation at $k \simeq 19.5$. The stable limit cycle that is born at the Hopf bifurcation dies by a so-called "global bifurcation" around $k = 12$, when it "glues" with the stable manifold of the saddle point in the middle.

Question 12.2. Early warning signals
The script `warning.R` contains comments answering most of the questions.

a. Using `continue(state=s,x="c",y="X",xmin=0.1,xmax=3,ymax=10)` one obtains the classic picture with two saddle-node bifurcations.

b. Drawing normally distributed disturbances of the population size (with 10% standard deviation) one could run something like the following R-script, where the call to `plot()` depicts X_{t+1} as a function of X_t, and the call to `cor()` computes the correlation. One should do this for various values of c to test if the variation and the auto-correlation increases when the saddle-node bifurcation is approached:

```
noiseX <- "state[1]<-abs(state[1]*rnorm(1,1,0.1))"
data <- run(750,after=noiseX,table=TRUE)
plot(data$X[1:nrow(data)-1],data$X[2:nrow(data)],type="p")
cor(data$X[1:nrow(data)-1],data$X[2:nrow(data)])
```

c. The variance and the autocorrelation should increase when a critical value of c is approached.

d. Use `after="parms[1]<-abs(parms[1]*rnorm(1,1,0.1))"`.

e. Using the parameters in the model defined by `warning.R`, we basically get no early warning signal. We learn that one does not always receive an early warning signal when a saddle-node bifurcation is approached. This would then be absent from the return time and from the autocorrelation.

Answers to Chapter 13

Question 13.1. Cell division takes time

a. When $t < \Delta$ the cells in the A-stage disappear at rate $\mathrm{d}A/\mathrm{d}t = -(d+p)A$, whereas those in the B-phase obey $\mathrm{d}B/\mathrm{d}t = pA - dB$. Since the two pA terms cancel each other, summing both gives $\mathrm{d}N/\mathrm{d}t = -dN$, which is a natural results because the cells can only die before the first divided cells appear at $t = \Delta$. The model with a flexible delay gives very similar results because the $\frac{n}{\Delta}$ (B_i terms cancel each other when the $\mathrm{d}B_i/\mathrm{d}t$ equations are summed and n is sufficiently large such that $B_n \simeq 0$.

b. $\mathrm{d}A/\mathrm{d}t = -(p+d)A$ in the Smith-Martin model at early time points, i.e., the cells in the A-stage are declining until $t = \Delta$. Running the Smith-Martin model for a short period of time readily confirms this.

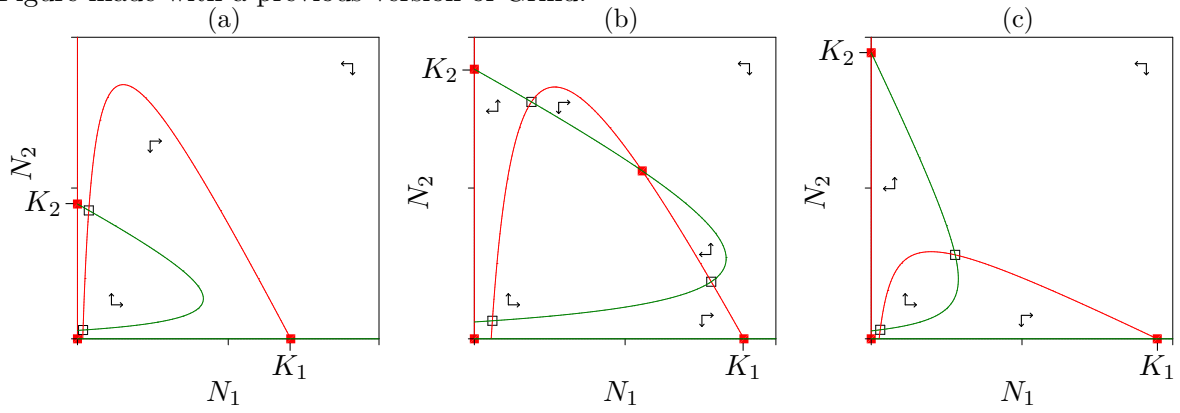
c. The expected time between divisions in the ODE model is $1/p'$, and in the Smith-Martin model it is the sum of the length of the A-stage and B-phase, i.e., $\frac{1}{p} + \Delta$. To compute the corresponding division rate, p', in the simplest ODE model, $\mathrm{d}N/\mathrm{d}t = (p' - d)N$, we take the inverse of division time in the Smith-Martin model, i.e., $p' = \frac{1}{1/p+\Delta}$.

d. No, cells dividing according to the Smith-Martin model will expand slower because they have a minimum interdivision time Δ. Consider for simplicity that the cells do not die, i.e., $d = 0$. Cells in the ODE will then expand at a rate $r' = p'$, which for $p = 1$ and $\Delta = 0.5$ gives $r' = 1/(1 + 0.5) = 2/3$. The ultimate growth rate, r, of cells in the Smith-Martin model is given by Eq. (13.3). Evaluating this numerically for $d = 0, p = 1$ and $\Delta = 0.5$, we obtain $r = 0.53$, which is slower than $r' = 2/3$. When cells die, those in the ODE also grow faster those in the Smith-Martin model (just test a few examples with $d > 0$).

e. The Smith-Martin model approaches the exponential growth model $\mathrm{d}N/\mathrm{d}t = rN$, which is not different from the $\mathrm{d}N/\mathrm{d}t = (p' - d)N$ model when the parameters are set by Eq. (13.3). When the B-phase is short compared to the length of the A-stage the models will be very similar. The Smith-Martin model is therefore most appropriate for rapidly dividing cells with a division time dominated by the length of the B-phase. An example would be proliferating tumor cells, or lymphocytes during their clonal expansion phase [2].

Question 13.2. Sexual reproduction

Figure made with a previous version of Grind:



A model with density dependent death rates would be something like

$$\frac{\mathrm{d}N_1}{\mathrm{d}t} = N_1\left[\frac{b_1 N_1}{h+N_1} - d_1(1 + e_1 N_1 + c_1 N_2)\right] \quad \text{and} \quad \frac{\mathrm{d}N_2}{\mathrm{d}t} = N_2\left[\frac{b_2 N_2}{h+N_2} - d_2(1 + e_2 N_2 + c_2 N_1)\right]$$

This model is available as the file `sexual.R`. Note that one has to separate birth from death because the sexual reproduction should only affect reproduction, and not the death. Assuming that the chance to find a mate approaches one when the population is close to its carrying capacity, i.e., assuming $h \ll K$, the carrying capacity is approximately $K_i \simeq (R_{0_i} - 1)/e_1$. In

the absence of sexual reproduction, i.e., when $h \to 0$, the nullclines are solved from $b_i - d_i(1 + e_i N_i + c_i N_j) = 0$ giving the normal straight lines

$$N_2 = \frac{R_{0_1} - 1}{c_1} - \frac{e_1}{c_1} N_1 \quad \text{and} \quad N_2 = \frac{R_{0_2} - 1}{e_2} - \frac{c_2}{e_2} N_1 \ ,$$

which may or may not intersect, intersect in a stable state when there is resource competition, and intersect in an unstable steady state when there is interference competition. From these three situations one can sketch the three Panels depicted above. For instance, the $\mathrm{d}N_1/\mathrm{d}t = 0$ nullcline is given by

$$N_2 = \frac{1}{c_1} \left[R_{0_1} \frac{N_1}{h + N_1} - 1 \right] - \frac{e_1}{c_1} N_1 \ ,$$

which resembles the straight line with slope $-e_1/c_1$ for $N_1 \gg h$, and which gives $N_2 = -1/c_1$ when $N_1 = 0$. Panel (a) would correspond to non-intersecting nullclines, Panel (b) to resource competition (i.e., $c_i < e_i$), and Panel (c) to resource competition (i.e., $c_i > e_i$). Note that sexual reproduction implies an Allee effect, and that (0,0), and the two carrying capacities are always stable (stable states are marked by closed boxes, unstable states by open boxes).

Question 13.3. Paradox of enrichment

a. We could scale the density of the algae at which the birth rate vanishes to $k = 2$ and scale time by their expected life span such that $d_1 = 1$ (which implies a time scale of about one week). We could give the algae a maximum rate of increase of $b - d_1 = 1$ per week by setting $b = 2$ per week. Because the carrying capacity $K = k(1-1/R_0)$ (see Table 3.1) we then obtain that $K = 1$. (An even simpler alternative approach would be to let the algae be described by logistic growth by setting $d_1 = 0$, then set $b = 1$ for the weekly time scale, and $K = k = 1$ to scale the density, as this leads to the same model, i.e., $2R(1 - R/2) - R = R(1 - R)$). Because the saturation of the functional response probably occurs at prey densities below the carrying capacity, it seems wise to set $h \ll K$, e.g., $h = 0.1$. We could scale the predator biomass such that its attack rate becomes $e = 1$, and let us give the predators a 2-fold longer life span, i.e., $d_2 = 0.5$. To give the predator an $R_0 = ce/d_2 = c/0.5 > 1$ we could set $c = 0.6$ such that the initial growth rate of the predator at high prey densities is about 0.1, i.e., 10-fold slower than the algae. For these values the predator nullcline is located at $h/(R_0 - 1) = 0.1/(0.6/0.5 - 1) = 0.5$, which is just at the right hand side of the maximum of the prey nullcline at $(K - h)/2 = 0.45$.

b. Different possibilities for the location of the predator nullcline, without changing that of the prey, can be made by changing the death rate of the predator.

c. The carrying capacity can be changed by altering the density k at which the birth rate of the algae vanishes.

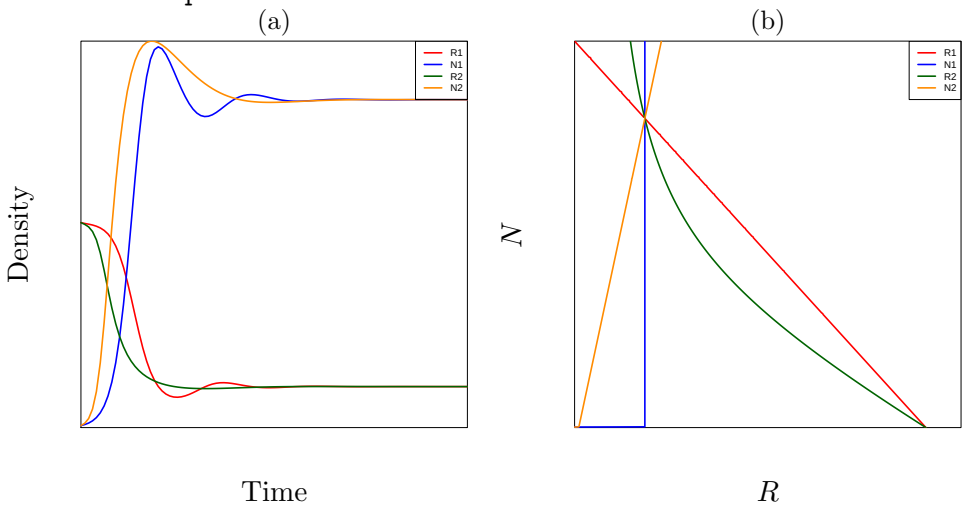
d. First settle into a non-trivial steady state by giving proper initial values and then issuing the `f<-newton(s)` command. Then call `continue(f,x="k",xmin=0.1,xmax=5,y="N")` to define a horizontal axis (where we avoid $k = 0$ because the model is dividing by k), and we keep the predator on the vertical axis.

e. Replace the death rate of the predators by $d_2(1 + \epsilon N)$.

f. This indeed gives a phase plane resembling that of consumer-resource model with a sigmoid functional response.

Question 13.4. Dampened oscillations

Figures made with `dampen.R`:



a. Time was scaled such that the growth rate of the resource is one, and the resource was scaled such that the carrying capacity is one.

b. For high value of h the time plots of the Lotka-Volterra model and the Beddington model coincide (not shown), which was to be expected. For low values of h, e.g., $h = 0.1$, the behavior of the Lotka-Volterra model has faster oscillations than the Beddington model (see Panel (a)). The phase plane in Panel (b) confirms that both models have the same steady state.

c. When both populations are small their encounters should be proportional to the product of their densities, and in this regime the Beddington term approaches the mass-action term. When only one of the populations is large the Beddington term approach a normal saturation function, whereby the process is limited by the smallest population. All of this seems quite reasonable.

d. The return time of both models is the same because the real part of the eigenvalues are identical. The real part of the eigenvalues is therefore also not changing when h is changed. The imaginary part of the eigenvalues is larger in the Lotka-Volterra model, which corresponds to a shorter wave length of the dampened oscillations. Therefore, the trajectory of the Beddington model completes fewer cycles before the steady state is approached. On a more critical note, we observe in the example shown in Panel (a) that the resource (R2) obeys an almost perfect monotonic curve, but that the consumer (N2) has a higher peak than the consumer (N1) of the Lotka-Volterra model.

Question 13.5. Stem cell renewal

a. When on average half of the stem cell divisions gives a new stem cell, their cell division is not changing the density of stem cells, and on average gives a single daughter cell into the population of differentiated cells:

$$\frac{\mathrm{d}S}{\mathrm{d}t} = -d_S S \quad \text{and} \quad \frac{\mathrm{d}D}{\mathrm{d}t} = p_S S - d_D D \ ,$$

where p_S is the fixed division rate of the stem cells, and the d parameters are death rates. This illustrates that the stem cell population will go extinct and that more than half of their divisions have to be asymmetric to compensate for their death rate (many models therefore set $d_S = 0$). Thus, if f is the fraction of asymmetric divisions, and one needs to solve

$$\frac{\mathrm{d}S}{\mathrm{d}t} = -p_S S + 2fpS - d_S S = p_S(2f-1)S - d_S S = 0 \quad \text{with} \quad \frac{\mathrm{d}D}{\mathrm{d}t} = 2p_S(1-f)S - d_D D \ ,$$

to derive that the stem cells will be at steady state when $f = \frac{1}{2} + \frac{d_S}{2p_S}$ (which indeed approaches $f \to 1/2$ when $d_S \ll p_S$). Note that it is very unlikely that stem cells "know" this parameter

expression for f, which strongly suggests that the fraction of asymmetric divisions has to regulated by the (local) environment.

b. The previous equation was already written with a free parameter, f, for the fraction of asymmetric divisions, and we only need to rewrite that into a function, $0 < f(D) \leq 1$, that should should decline with the density D. A general choice would be a Hill function, e.g.,

$$\frac{\mathrm{d}S}{\mathrm{d}t} = p_S[2f(D)-1]S - d_S S = 0 \quad \text{and} \quad \frac{\mathrm{d}D}{\mathrm{d}t} = 2p_S[1-f(D)]S - d_D D \quad \text{with} \quad f = \frac{1}{1+D/h_f} \, .$$

c. To allow for a density dependent division rate of the stem cells one multiplies the parameter p_S with another function, $g(D)$ for growth rate, also declining as a function of D:

$$\frac{\mathrm{d}S}{\mathrm{d}t} = p_S g(D)[2f(D)-1]S - d_S S = 0 \quad \text{and} \quad \frac{\mathrm{d}D}{\mathrm{d}t} = 2p_S g(D)[1-f(D)]S - d_D D \, ,$$

with $f = \frac{1}{1+D/h_f}$ and $g = \frac{1}{1+D/h_g}$. We have now arrived at the full, and quite complicated terms of the Lander *et al.* [10] model. Note that reading this equation is almost more difficult than deriving it.

d. If differentiated cells also divide we can add a similar growth term to $\mathrm{d}D/\mathrm{d}t$:

$$\frac{\mathrm{d}S}{\mathrm{d}t} = p_S g(D)[2f(D)-1]S - d_S S = 0 \quad \text{and} \quad \frac{\mathrm{d}D}{\mathrm{d}t} = 2p_S[1-f(D)]g(D)S + p_D G(D) - d_D D \, ,$$

where $G = \frac{1}{1+D/h_G}$. There will be two dynamical regimes because the differentiated cells only strictly depend on the stem cells when $p_D < d_D$, i.e., if their maximal self-renewal rate cannot fully compensate for their death rate. Note that Lander *et al.* [10] also allow for asymmetric division in the early stages of the differentiated cells.

e. Yes in that model the fraction of asymmetric divisions depended almost linearly on the stem cell density.

Question 13.6. Lymphocyte migration

a. Because the total number of cells is not changing the number of cells in the blood can be described with a conservation equation. The ODE would have been $\mathrm{d}B/\mathrm{d}t = e_S S + e_L L - (i_S + n i_L)B$, and replacing the conservation equation with this ODE gives exactly the same model. Numerically, the version with the conservation equation is more stable because small numerical errors could make $\mathrm{d}B/\mathrm{d}t + \mathrm{d}S/\mathrm{d}t + \mathrm{d}L/\mathrm{d}t \neq 0$.

b. The steady state is $\bar{S} \simeq 22$, $\bar{D} \simeq 1.9$, and $\bar{L} \simeq 72.4$ cells, and hence there will be $B \simeq 3.7$ cells in the blood. Every lymph node is expected to contain $72.4/38 = 1.9$ cells, which is also revealed by $\bar{D} \simeq 1.9$.

c. The only term missing in the denominator is the $e_L e_S$ term, and hence $\bar{B} = \frac{e_L e_S}{e_L e_S + e_L i_S + e_S n i_L}$ The recurrent pattern in the expression is that $\bar{S}$ and $\bar{L}$ increase with their own influx times the efflux of the other compartment. It makes sense that increasing the rate of efflux from the lymph nodes increases the number of cells in the spleen (and similarly in the blood).

d. Running the model for several days reveals that one needs 20 days of capturing cells to exceed $D(t) = 50$. Waiting for almost three weeks to recruit just 50% of the cognate naive T cells would be dangerously long.

e. Adding on a $f_i = 9$-fold increase in the influx to the draining lymph nodes reveals that it would take about 2.5 days to accumulate 50% of the cells. Note that this still requires that cognate cells do not egress from the draining lymph node: otherwise a new steady state is established where most of the cells reside in the other lymph nodes (because $f_i < n - 1$).

f. To model infection with a gradual angiogenesis, one could replace the $f_i i_L B$ term by $\frac{t}{h+t}\,(f_i - 1)i_L B + i_L B$ to define that at $t = 0$ the influx is $i_L B$, at $t = h$ the influx is $\frac{(f_i-1)i_L B}{2} + i_L B$, and that when $t \to \infty$ the influx approaches the previous $f_i i_L B$.

Answers to Chapter 14

Question 14.1. Seedlings over-shadowed by adult plants
Start by assuming that the density of seeds, seedlings and adult plants is distributed evenly over the field. This allows one to write ODEs for the change in the number of seedlings and the number of adult plants in the field. Call them J for juveniles and A for adults, respectively. Because the time scale at which the number of seeds in the seed bank changes is so slow, we can define a constant, S, for the number (or the density) of seeds in the seed bank underlying the field. Seedlings can only be produced when a seed sprouts. Seedlings do not replicate, they can only mature or die. For the production of seedlings we therefore write a term, pS, where p is the probability that a single seed sprouts. For the death of the seedlings and the adults plants one could write $d_1 J$ and $d_2 A$, respectively, whereby we assume that these death rates remain independent of the plant densities. Since the maturation rate of the seedlings depends on the adult plant densities, we need a term like $mJf(A)$ for the flux of seedlings from the juvenile to the adult population (where $f(A)$ is a declining function of A). Combining these four terms we arrive at the following model

$$\frac{\mathrm{d}J}{\mathrm{d}t} = pS - d_1 J - mJf(A) \quad \text{and} \quad \frac{\mathrm{d}A}{\mathrm{d}t} = mJf(A) - d_2 A \ ,$$

composed of the processes sprouting, death and maturation. Finally, we need to define how the maturation rate declines with the number of adult plants, i.e., we need to sketch $mf(A)$ as a function of A. Defining m as the maximum maturation rate, one can define a non-dimensional function, $f(A)$, that equals one when $A = 0$ and declines when A increases (one may sketch a few alternatives). The most simple choice would be a linear decline, e.g., $f(A) = 1 - A/k$, where k is the adult density where the maturation rate becomes zero. Another natural choice would be a declining Hill function, $f(A) = \frac{1}{1+(A/k)^n}$, where h defines the adult density at which the maturation rate is $m/2$, and n can be used to define a sigmoid decline (when maturation only slows down at high adult densities). The linear choice would lead to the simplest model

$$\frac{\mathrm{d}J}{\mathrm{d}t} = s - d_1 J - mJ(1 - A/k) \quad \text{and} \quad \frac{\mathrm{d}A}{\mathrm{d}t} = mJ(1 - A/k) - d_2 A \ ,$$

where $s = pS$. Because $1 - A/k$ can be interpreted as the probability that a seedling is growing at spot not covered by an adult plant, this linear interaction function may actually be the most natural one.

Question 14.2. Whales
To develop a proper model for the whales we have to consider three biological processes: birth, death, and the likelihood of finding a male. One could write a model for the number of females, N, in the population, and assume that there is a similar number of males (the true population size would then be similar to $2N$). The probability that an individual female finds a male should increases with the number of males, and approach one at large densities of males. We here opt for a saturation function, $p(N) = \frac{N}{h+N}$, where $p(N)$ is the probability, and h is the population size at which there is a 50% probability of finding a male. This (daily) probability, $p(N)$, needs to be multiplied with the birth rate (that itself could also be a density dependent function). Indeed, to allow for a carrying capacity we have to include negative density dependence in either the birth or the death terms. Starting with the latter, one could define a minimum death rate, d, defining their maximum life span, $1/d$, of several decades, and let the death rate increase with the whale density, and write $d(1 + (N/k_d)^n)$ for the *per capita* death rate. When $N = k_d$ the death rate has doubled, and when $n = 1$ the death rate increases linearly with the density N. This increase can be made steeper than linear by setting $n > 1$, or slower than linear by choosing $n < 1$. If the birth rate were to be density dependent, e.g., because the probability that calves survive and mature is low when food (krill) availability is low, we could pick one of the declining density-dependent functions, e.g., $f(N) = \frac{1}{1+(N/k_b)^n}$, where k_b defines the whale

density at which the birth rate has halved, and $n > 1$ can be used to make this function sigmoid. Combining these three functions, one obtains

$$\frac{\mathrm{d}N}{\mathrm{d}t} = \Big[\frac{b}{1+(N/k_b)^n}\ \frac{N}{h+N} - d(1+(N/k_d)^n)\Big]N\ ,$$

where one could let $k_b \to \infty$, or let $k_d \to \infty$, to only consider density-dependent birth, or density-dependent death, respectively. Note that by treating each process independently we were able to write three fairly simple terms, that together form a quite complicated ODE.

PS. Our choice of a saturation function, $p(N) = \frac{N}{h+N}$, is somewhat phenomenological here, but a sigmoid Hill function would have been inappropriate because at low densities this probability should increase linearly with the density. Puristically, an exponential function, $p(N) = 1 - \mathrm{e}^{-aN}$, would have the best choice, because the probability of finding at least one male whale in a particular area can be described as a Poisson process that can be approximated with an exponential function.

Question 14.3. Kingfishers
Since the density of kingfishers in the area is assumed to be constant, we define B_T as the total number of birds in the area. Defining B as the number kingfishers at the lake, we obtain that there should be $B_E = B_T - B$ kingfishers elsewhere. Since these fly in at a rate depending on the fish density in the lake, one would obtain $iB_Ef(F)$ for the immigration of birds at the lake, where $f(F)$ is an increasing function of the density of fish, F, in the lake. One could sketch a few functions for the *per capita* immigration rate, $if(F)$, of kingfishers elsewhere into the lake surroundings. For simplicity, we could choose for a linear increase, $if(F) = iF$, and hence write a mass-action $iB_EF = i(B_T - B)F$ term to define the immigration. The maximum *per capita* immigration rate would then be iK, where K is the carrying capacity of the fish in the lake, which is bounded, and therefore seems fine. Alternatively, one could assume that the immigration rate is a saturation function of the local fish density, and write $if(F) = \frac{iF}{h+F}$, where i would be the maximum *per capita* immigration rate, and then write $\frac{i(B_T-B)F}{h+F}$ for the immigration term in the model. For the emigration rate of birds from the lake we read that they leave after catching fish. If we were to write a mass-action predation term, i.e., aFB in the fish equation, the emigration term in the bird equation would also be aFB, because we loose both a fish and a bird when a kingfisher catches a fish. However, this would lead to the strange situation that birds never leave if there is no fish at the lake, which implies that one has to define an additional emigration term, e.g., eB, allowing birds to give up and leave anyway after some time. Arbitrarily choosing for the simplest immigration term, and adding both emigration terms to $\mathrm{d}B/\mathrm{d}t$, one obtains

$$\frac{\mathrm{d}F}{\mathrm{d}t} = rF(1-F/K) - aFB \quad \text{and} \quad \frac{\mathrm{d}B}{\mathrm{d}t} = i(B_T - B)F - aFB - eB\ ,$$

which also adopts the logistic growth given by the story for the fish. Note the birds leaving the lake immediately arrive "elsewhere" thanks to the conservation equation $B_E = B_T - B$.

Question 14.4. Influenza virus infecting epithelial cells
Consider a tissue of a certain size by defining K as the maximum of cells that can be packed in this tissue. Uninfected epithelial cells, E, will divide when they find empty space, S, around them, i.e., $S = K - E - I$, where I is the number of infected cells. The probability of finding empty space would then be $S/K = 1 - (E+I)/K$. Defining a maximum division rate, b, and a death rate, d (such that $1/d$ corresponds to a few weeks), one would start by writing $\mathrm{d}E/\mathrm{d}t = bES - dE = bE(1-(E+I)/K) - dE$. Epithelial cells are infected by virus, which

could be modeled with a mass-action term, βEV (where V represent virus). The infection rate declines when there is interferon, F. If the effect of interferon on the infection rate is modeled with a declining Hill function one would write $f(F) = \frac{1}{1+(F/h)^n}$, where h is the interferon concentration at which the infection rate is halved. If the effect of interferon were modeled with a declining linear function one would write $f(F) = 1 - F/h$, where h is the interferon concentration at which the infection rate becomes zero. Multiplying the infection term, βEV, with either of these two non-dimensional functions, allows interferon to reduce the infection rate, where β remains the maximum mass-action infection rate. Arbitrarily choosing for the linear function, one obtains

$$\frac{\mathrm{d}E}{\mathrm{d}t} = bE(1-(E+I)/K) - dE - \beta EV(1-F/h) \ ,$$

and since infected cells appear by successful infection and die at a faster rate, one readily writes for the infected cells, I,

$$\frac{\mathrm{d}I}{\mathrm{d}t} = \beta EV(1-F/h) - \delta I \ ,$$

where $\delta \gg d$, and we assume that infected cells do not divide. Finally, infected cells produce virus and interferon, which both should decay, e.g.,

$$\frac{\mathrm{d}V}{\mathrm{d}t} = p_V I - c_V V \quad \text{and} \quad \frac{\mathrm{d}F}{\mathrm{d}t} = p_F I - c_F F \ ,$$

where the p parameters are production rates, the c parameters clearance rates. For completeness one could allow virus and interferon to be absorbed to the healthy cells,

$$\frac{\mathrm{d}V}{\mathrm{d}t} = p_V I - c_V V - a_V VE \quad \text{and} \quad \frac{\mathrm{d}F}{\mathrm{d}t} = p_F I - c_F F - a_F FE \ ,$$

where the a parameters are mass-action absorption rates.

Question 14.5. DNA circles
First write a model for the number of cells, N, and the total number of circles C, i.e.,

$$\frac{\mathrm{d}N}{\mathrm{d}t} = s + (b-d)N \quad \text{and} \quad \frac{\mathrm{d}C}{\mathrm{d}t} = s - dC \ ,$$

where we have omitted the division rate, b, from the second equation because cell division does not affect the number of circles. The steady state of this model would be $\bar{N} = \frac{s}{d-b}$ and $\bar{C} = s/d$. The fraction of cells containing a circle would be defined as $F = C/N$. Hence the ODE for F needs to be written as a quotient of the two derivatives, i.e.,

$$\frac{\mathrm{d}F}{\mathrm{d}t} = \frac{C'}{N} - \frac{CN'}{N^2} = \frac{s-dC}{N} - \frac{C(s+(b-d)N)}{N^2} = \frac{s}{N} - dF - \frac{sF}{N} - (b-d)F = \frac{s}{N} - \frac{sF}{N} - bF$$

or,

$$\frac{\mathrm{d}F}{\mathrm{d}t} = \frac{s}{N} - F(s/N+b) \ ,$$

which is an equation that would be very difficult to write from scratch.

Interestingly, the quasi steady state (quasi because it still depends on N) for this fraction,

$$F = \frac{s/N}{s/N+b} = \frac{s}{s+bN} \ ,$$

has been used to better interpret experimental data on these circles in circulating T cells [3, 7]. Since bN corresponds to the daily production of cells by division, and s to the daily production

by the thymus, the observed fraction of circles is expected to approach the fraction of cells produced in the thymus. Increasing the division rate, b, would decrease F by dilution. Note that a transient increase of the death rate, d, of the cells will decrease N, which hence would increase the fraction of cells containing a circle. Finally, one can obtain the full steady state of the fraction from $\bar{N} = \frac{s}{d-b}$ and $\bar{C} = s/d$, i.e.,

$$\bar{F} = \frac{\bar{C}}{\bar{N}} = \frac{s}{d}\,\frac{d-b}{s} = \frac{d-b}{d} \ .$$

This also reveals that $\bar{F}$ corresponds to the fraction produced by the thymus (because the total *per capita* production at steady state is d, and b reflects the part produced by cell division), and confirms that $\bar{F}$ increases when d increases (at high death rates $F \to 1$).

Question 14.6. Maintenance and reproduction
Since we learn little about the algae in this system, one could assume a mass-action consumption rate, and conventional logistic growth for the algae, to write

$$\frac{\mathrm{d}A}{\mathrm{d}t} = rA(1 - A/K) - aAD \ ,$$

where aA is the *per capita* consumption rate of *Daphnia*, D. Since the death rate of the zooplankton declines as a function of their *per capita* consumption, we could sketch a declining Hill function $f(aA)$ starting at a maximum death rate, $d_1 + d_0$, when $aA = 0$, and approaching a minimum death rate, d_0, when $aA \to \infty$, e.g.,

$$f(aA) = d_0 + \frac{d_1}{1 + aA/h} \ .$$

Since the production of eggs should only start at consumption levels at which the organisms become long-lived, i.e., when $aA > h$, one could sketch an increasing Hill function, $g(aA)$, with a saturation constant, k, exceeding h. One could even choose for a sigmoid function to define that virtually no eggs are produced at low consumption levels, e.g.,

$$g(aA) = \frac{e(aA)^n}{k^n + (aA)^n} \ ,$$

where e is maximum rate at which eggs can be produced, $k > h$, and $n > 1$. An alternative would be a shifted Hill function,

$$g(aA) = \frac{e(aA - k)}{H + aA - k} \ ,$$

where k is the consumption level at which eggs begin to be produced, and H is a saturation constant. Arbitrarily choosing for the latter, one would write for the eggs, E, and the *Daphnia*, D,

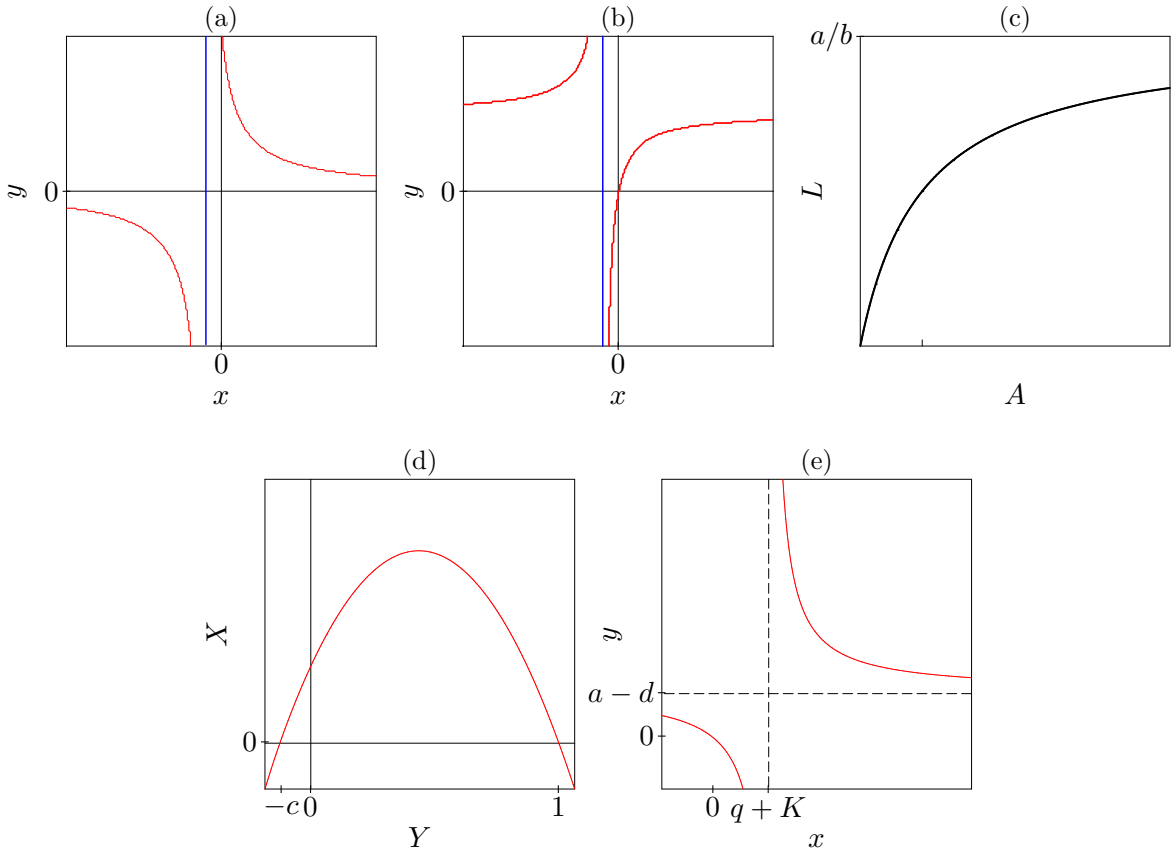
$$\frac{\mathrm{d}E}{\mathrm{d}t} = \frac{e(aA-k)D}{H + aA - k} - mE \quad \text{and} \quad \frac{\mathrm{d}D}{\mathrm{d}t} = mE - d_0 D - \frac{d_1 D}{1 + aA/h} \ ,$$

where m is the rate at which eggs hatch to form novel *Daphnia*s. Note that this remains a phenomenological model because we are not distributing the consumed resources over the maintenance and reproduction processes in a conserved manner, and note that one should make sure that $aA - k \geq 0$ when analyzing the model.

Answers to Chapter 15

Question 15.1. Sketch a few functions

Figures made with a previous version of Grind:



a. First note that $y = \frac{h}{h+x} = 1$ when $x = 0$. Second, we see that for $x \to \infty, y \to 0$, and similarly that for $x \to -\infty, y \to 0$. There is a vertical asymptote at $x = -h$. See Panel (a).

b. First note that $y = \frac{x}{h+x} = 0$ when $x = 0$. Second, we see that for $x \to \infty, y \to 1$, and similarly that for $x \to -\infty, y \to 1$. There is a vertical asymptote at $x = -h$. See Panel (b).

c. Plotting $L = \frac{aA}{c+bA}$ we first rewrites this into $L = \frac{a}{c/A+b}$, to see that there is a horizontal asymptote at $L = a/b$ (see Panel (c)). If we were to plot $A = \frac{cL}{a-bL}$ this would become a vertical asymptote at $L = a/b$ (not shown).

d. Remove the $Y = 0$ solution and observe that $X = (a/b)(1-Y)(c+Y)$ is the parabola shown in Panel (d).

e. The intersection with the x-axis corresponds to $x = \frac{ak-dq-dk}{a-d}$, and that with the y-axis to $y = \frac{ak}{q+k} - d$. Rewriting the function as $y = a\frac{k/x-1}{q/x+k/x-1} - d$ and sending $x \to \infty$ we see that $y \to a - d$, meaning that there is a horizontal asymptote at $y = a - d$. There is a vertical asymptote at $x = q + k$. See Panel (e), where the dashed lines denote the two asymptotes.

Question 15.2. Linearization

a. The derivative is $\partial_x x^2 = 2x$.

b. Filling in $f(x) \simeq f(\bar{x}) + \partial_x f(\bar{x})\,(x - \bar{x})$ we obtain that $f(3.1) = 9 + 0.1 \times 2 \times 3 = 9.6$. The true value is $3.1^2 = 9.61$.

Question 15.3. Linear models

The steady state is $x = y = 0$ and the Jacobian, $J = \begin{pmatrix} a & b \\ c & d \end{pmatrix}$, is the same as the interaction matrix. Use Fig. 15.6 to create an interaction matrix with the eigenvalues corresponding to the different types of steady states.

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