Mathematical Methods in Biology

Exercises

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EXERCISES 1-6: GRAPHING FUNCTIONS

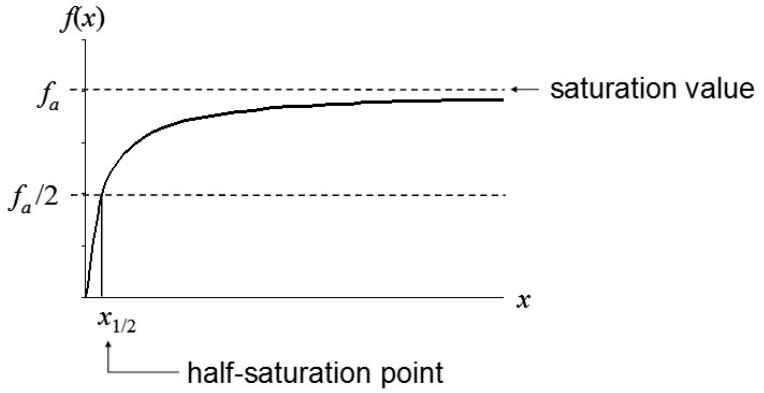
The aim of these exercises is to get familiar with the functions one encounters most often in mathematical modelling and statistical analysis. Although at this point we are not yet addressing biological questions directly, these functions we shall use over and over again, so it is worthwhile to know them well.

Exercise 1. *Hyperbolas.* Plot the hyperbola

$$f(x) = \frac{\beta x}{1 + ax}$$

with $\beta = 2$ and $a = 1$ using any software (e.g. Excel). Then plot this hyperbola with other values of its parameters (β, a) and compare with the original. What happens if β is greater (e.g. $\beta = 3, a = 1$)? What happens if a is greater? And what happens if both β and a are greater, but such that we preserve the ratio $\beta/a = 2$ as in the original (take e.g. $\beta = 10, a = 5$)?

Convince yourself that $f(x)$ is approximately β/a when x is very large, i.e., this gives the saturation (or asymptotic) value f_a shown in the figure below. Calculate the half-saturation point $x_{1/2}$ where the function attains $f_a/2$. Use these results to explain how the shape of the hyperbola changes with the parameter values.



Exercise 2. *Exponential and logarithmic functions.*

(a) Plot the exponential function

$$f(x) = ce^{kx}$$

with both positive and negative values of k. Is the function increasing (exponential growth) or decreasing (exponential decay)? Is it convex or concave? How does the shape change if k is greater in absolute value (i.e., if k is greater positive or more negative)? What if $k = 0$? What happens if we change c?

(b) Plot the logarithmic function

$$f(x) = c\ln(kx)$$

and study the effects of parameter changes as above.

Exercise 3. *The Gaussian function.* The Gaussian function

$$f(x) = \alpha \exp\left(-\frac{(x-m)^2}{2\sigma^2}\right)$$

is often used in modelling and, with the choice $\alpha = 1/\sqrt{2\pi\sigma^2}$, it defines the famous normal distribution, which is exceedingly important in both probability theory and statistics. Plot the Gaussian function with $\alpha = 1$ and study how its shape depends on m and σ^2. Next, substitute $\alpha = 1/\sqrt{2\pi\sigma^2}$ and investigate again how the shape of the function changes with the parameters m and σ^2.

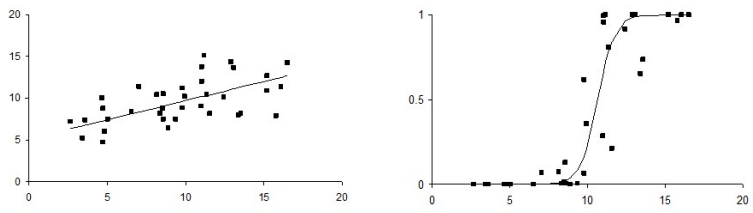
Exercise 4. *A sigmoidal function.* Another commonly used function is the sigmoidal function

$$f(x) = \frac{1}{1 + \exp[-(\alpha + \beta x)]}$$

with α and β positive or zero.

(a) Plot this function and study how its shape depends on α and β.
(b) How should we modify this function if we want
- a decreasing, sigmoidal-shaped function
- a sigmoidal function that spans the interval (0,2)
- a sigmoidal function that spans the interval (-1,1)?

Exercise 5. *Logistic regression.* In ordinary linear regression, we seek a straight line that fits the data best as shown in the left panel of the figure below. There are many statistical software packages that can find the regression line. However, linear regression is not appropriate if the variable plotted on the vertical axis is a fraction or a probability (for example the fraction of animals dead in a drug safety test, at different dosages of the drug). This is because the fraction (or probability) must remain between 0 and 1 even if the variable on the horizontal axis (e.g. dosage) takes a very small or very large value. In this case, we want to fit a sigmoidal curve to the data as shown in the right panel of the figure.



To this end, we first transform the probability p with the so-called logit function

$$\text{logit}(p) = \ln\left(\frac{p}{1-p}\right)$$

and then perform the linear regression analysis with $\text{logit}(p)$ on the vertical axis and an explanatory variable (e.g. drug dosage) x on the horizontal axis.

(a) Plot the logit function and check that $\text{logit}(p)$ can take any positive or negative value with p between 0 and 1.

(b) Suppose that using linear regression, we find the relationship $\text{logit}(p) = \alpha + \beta x$. Show that in this case, p depends on x according to the sigmoidal function given in exercise 4.

Exercise 6. *Log-log plots.* In an experiment, we measure two quantities, x and y, and plot $\ln y$ against $\ln x$. Suppose that in this so-called "log-log" plot, the data fit a straight regression line. What is the relationship between the original variables, x and y? Draw a figure with x and y on the axes.

EXERCISES 7-12: EXPONENTIAL GROWTH AND DECAY

Exercise 7. *Bacterial growth.* Under ideal conditions, a bacterium can divide every 15 minutes. How long would it then take that a single bacterium produces $2 \cdot 10^{35}$ descendants? (They would weight about as much as the Earth!)

Exercise 8. *Radioactive decay.* How many times the half-life of a radioactive material we have to wait until only 1% of the original activity is left? Until 1 ppm (part per million, 10^{-6}) is left? Calculate these waiting times for caesium-137, a radioactive isotope that polluted Europe after the Chernobyl accident and still contaminates mushrooms and fishes. The half-life of Cs-137 is 30 years.

Exercise 9. *Carbon dating.* Carbon dating cannot be used for very old samples, because the remaining activity of C^{14} is too small to measure reliably. In practice, the minimum activity required for measurement is about 0.05 decays per minute per gram carbon.

(a) Calculate the activity (number of decays per minute per gram carbon) of a carbon sample extracted from living tissue. Recall that 1 g carbon is 1/12 mole and hence contains $5 \cdot 10^{22}$ carbon atoms, in living tissue a fraction 10^{-12} of carbon atoms is C^{14}, the half-life of C^{14} is 5730 years, and 1 year is approximately 526,000 minutes.

(b) How old is a sample when its activity is at the minimum measurable level? Can we use carbon dating for archaeological samples, for the first hominids, or for dinosaurs?

Exercise 10. *The habitable zone of algae.* In water, light intensity decreases with depth as water absorbs and scatters the photons. The chance that a photon is absorbed in the

next infinitesimal layer of water is constant.

(a) Argue that light intensity must decrease exponentially, i.e.,

$$I(z) = I(0)e^{-\alpha z}$$

where $I(z)$ is the intensity of light at depth z ($z = 0$ at the surface). The coefficient α is called the vertical attenuation coefficient. Is α greater or smaller when the water is more opaque?

(b) To measure α, a simple method is to drop a standardized white disk, called a Secchi-disk, in the water and measure the depth where it disappears from sight. This happens when the light reaching the eye from the disk is about 1% of the surface light intensity. What is the attenuation coefficient of a lake where the Secchi-depth is 10m? (Remember that light must cross the water column twice: once to reach the disk, once to come up to the observer.)

(c) Algae can live in water to the depth where the light intensity is at least 1% of the surface intensity: Below this so-called compensation level, photosynthesis is so ineffective that the respiratory loss exceeds the photosynthetic product. Calculate the compensation level in a lake where the attenuation coefficient is $\alpha = 0.5/m$.

Exercise 11. *Plant growth.* Under ideal conditions (no resource limitation etc.) and with constant illumination, the weight of algae (w) grows exponentially according to the equation

$$\frac{dw}{dt} = rw$$

(a) Calculate the time, expressed in terms of the growth rate r, when the weight of the algae hits 10-fold of the initial weight.

(b) At night, there is no photosynthesis. The weight decreases due to respiration at rate μ, i.e., the equation

$$\frac{dw}{dt} = -\mu w$$

applies during the night. Suppose that at the beginning of daytime on day 1, the algae weigh 1g. Daytime lasts 14h and the night 10h. At what time will the weight of the algae first hit 10g if $r = 0.1/h$ and $\mu = 0.02/h$?

Exercise 12. *Exponential decay with influx.* The equation

$$\frac{dx}{dt} = c - ax$$

is similar to the equation of exponential decay, except the constant c on the right hand side.

(a) Argue that this equation describes a process where a substance is provided at a constant rate c and is decaying exponentially at the *per capita* rate a. Examples include proteins that are synthesised at a constant speed in a cell and decay spontaneously; a medicine infused at a constant speed and removed by metabolism; an empty chemostat where the nutrient is supplied at a constant rate and lost with the outflow; a population in an unsuitable habitat that is maintained by immigration but mortality exceeds local reproduction.

(b) Show that the function

$$x(t) = \frac{c}{a} - \left(\frac{c}{a} - x(0)\right) e^{-at}$$

is the solution to the differential equation above.

(c) To interpret the solution, plot $x(t)$ as a function of time for different initial values of the variable, $x(0)$ (choose arbitrary positive values for the parameters a, c). How does x change in time if $x(0)$ is small relative to c/a? What if $x(0)$ exceeds c/a? And if $x(0) = c/a$? Describe in words how x changes in time relative to c/a, and demonstrate that a affects the speed of this change.

EXERCISES 13-15: DIFFERENTIATION

Exercise 13. *Maximum frequency of heterozygotes.* Use the standard technique of differentiation to show that the frequency of heterozygotes in Hardy-Weinberg equilibrium, $H = 2p(1-p)$, is maximal when the two alleles have the same frequency, i.e., when $p = 0.5$.

Exercise 14. *The shape of the Gaussian function.* Use the standard technique of differentiation to show that the Gaussian function given in exercise 3 has its maximum at $x = m$. Use the second derivative to find which parts of the Gaussian function are concave and which parts are convex.

Exercise 15. *Mode of the lognormal distribution.* The function

$$f(x) = \frac{1}{\sqrt{2\pi}\,\sigma x} \exp\left(-\frac{(\ln(x) - m)^2}{2\sigma^2}\right)$$

defines the so-called lognormal distribution. Find the value of x where $f(x)$ is maximal (you may skip checking the sign of the second derivative). This value of x is called the *mode* of the distribution.

EXERCISES 16-18: OPTIMIZATION PROBLEMS

Exercise 16. *Optimal harvest.* The most common model to describe the growth of a population is the so-called logistic equation,

$$\frac{dN}{dt} = rN\left(1 - \frac{N}{K}\right)$$

where N is the number of individuals and r, K are positive parameters. If the population has size $N = K$, then the expression in the parentheses is zero, and therefore $\frac{dN}{dt}$ is zero. This means that the size of the population constant in time, i.e., the population is at equilibrium. If N is less than K, then N/K is less than 1, so that the expression in the parentheses is positive, and therefore $\frac{dN}{dt}$ is positive. This means that the size of the population increases with time. Find the value of N where the speed of growth, $\frac{dN}{dt}$, is the highest. This value is important for a sustainable economy: If we want to harvest the population, we can remove as many individuals per unit of time as natural population growth can compensate for. Hence if we keep the size of the populaion, N, at its optimal value, then we can harvest the most individuals in a sustainable manner.

Exercise 17. *Iteroparity vs semelparity.* If a mother produces more offspring, this jeopardizes her own physiological condition and therefore decreases the probability that she survives to the next year. Let $p(x)$ denote the probability of survival of a mother with x offspring, and let s be the (constant) probability that an offsping survives till the next year. One mother thus leaves sx surviving offspring plus herself with probability $p(x)$, i.e., a total of $f(x) = sx + p(x)$ descendants by the next year (cf. lecture notes, optimal fecundity 2). The optimal fecundity, x_{opt}, maximizes the number of descendants, $f(x)$. For the trade-off function $p(x)$, consider two variants: (i) $p(x) = p_0 - cx^2$; (ii) $p(x) = ce^{-\alpha x} - b$ (where we assume $0 < c - b < 1$ so that the probability of survival of a non-reproducing female, $p(0) = c - b$, is between 0 and 1).

(a) The probability of survival, $p(x)$, cannot be negative. Plot the two trade-off functions and determine the maximal value x_{max} such that this condition is satisfied. We assume that the mother cannot produce more than x_{max} offspring.

(b) Find the optimal fecundity for each trade-off function. (Remember to check the second derivative.) Does the optimum correspond to an iteroparous population (the mother may survive and reproduce several times) or a semelparous population (the mother reproduces only once because she never survives)?

Exercise 18. *Optimal age at maturation.* Many animals grow only until maturation. A large body size is advantageous because it correlates with high fecundity, but delaying maturation in order to grow large means a higher risk that something kills the animal before it could reproduce. The optimal maturation strategy is the best compromise between a large enough size and short enough time before reproduction.

(a) Suppose that before maturation, individuals die at a constant rate μ. Let $s(T)$ denote the fraction of individuals who survive from birth to maturation if maturation occurs at age T. Calculate $s(T)$.

(b) The growth of an individual is commonly described by the Von Bertalanffy function,

$$L(t) = a - be^{-kt}$$

where $L(t)$ is the length of the body at age t and a, b, k are positive parameters. Assume that an individual follows this growth curve until age T, when it matures and does not grow any more. Fecundity is proportional to body volume, so that an individual who matures at age T has $B(T) = cL(T)^3$ offspring in her adult life.

If a newborn is to mature at age T, then with probability $s(T)$ she will survive till maturation and produce $B(T)$ offspring, and with probability $1 - s(T)$ she will die before reproduction. On average, a newborn thus expects $R(T) = s(T)B(T)$ offspring. Find the optimal age at maturation, at which $R(T)$ is the highest[1].

(c) Calculate the optimal size at maturation, $L(T)$.

(d) Suppose that the environment gets worse such that the death rate of juveniles, μ, increases. How does the optimum change; will the animals mature earlier and at a smaller size, or later and at a larger size?

Exercise 19. *Optimal virulence of a pathogen.* The virulence of a pathogen is the rate at which it kills the host. Suppose that infected hosts die at a rate α (the virulence) and recover at a rate ν, so that they disappear at a total rate $\alpha + \nu$ (for simplicity, we assume that natural death is negligible). The average length of an infection is then $1/(\alpha + \nu)$ time units (see lecture notes, exponential decay). An infected host infects β other hosts in each unit of time, and therefore one infected host infects

$$R_0(\beta) = \frac{\beta}{\alpha + \nu}$$

other hosts during the entre infection. R_0 is called the *basic reproduction number* of the disease.

Pathogens that can transmit from host to host more agressively (and hence have higher β) are also more harmful to the host. Alizon and Van Baalen (2005, The American Naturalist) argue that virulence is related to transmission according to the function

$$\alpha(\beta) = a\beta^2 + b\beta + c$$

[1] *Hint:* Checking the second derivative to see if we indeed got the maximum (and not the minimum) of $R(T)$ is rather cumbersome. Instead of taking the second derivative, check whether the derivative of $R(T)$ is positive at $T = 0$. Argue that if the derivative is positive at $T = 0$ and there is only one point where the derivative is zero, then this zero derivative must correspond to a maximum and not a minimum.

where $a > 0$ and $b, c \geq 0$.

(a) Find the optimal value of β and calculate the corresponding optimal virulence, $\alpha(\beta)$.

(b) Suppose that by treating the disease, we increase the rate of recovery, ν. Show that in this case, the optimal virulence *increases*. This means that if we treat the disease, it evolves to be more dangerous!

(c*) The pathogen evolving to be more virulent is bad news, but what we may be most interested in is the probability that an infected person dies because of the disease. Higher virulence means that the disease kills faster, but higher recovery rate means that the infected person gets free of the disease faster, so has shorter time while at risk. The probability of dying of the disease is given by $p = \alpha/(\alpha+\nu)$ (see lecture notes, alternative modes of decay). Show that the probability of death due to the disease, p, decreases if the recovery rate increases and the virulence assumes its optimal value corresponding to the increased recovery rate (use the result of (a))[2]. This means that, fortunately, treatment is beneficial even after the pathogen has increased its virulence in response to the faster recovery rate achieved by the treatment.

EXERCISES 19-21: CONSTRUCTION OF DYNAMICAL MODELS

Exercise 20. *Enzyme reactions.* Write down the differential equations modelling the following processes, and note any conservation law. Can you point out weaknesses of the models described below?

(a) *An enzyme with two substrates (e.g. ligase, kinase).* The enzyme E binds the substrate S_1 and thereby forms an enzyme-substrate complex X_1. This complex, in turn, binds substrate S_2 to make X_{12}. The enzymatic catalysis takes place in the complex X_{12} and produces the product P, plus releases the free enzyme E. Alternatively, each complex can decay into its progenitors (backwards reactions).

$$E + S_1 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} X_1, \quad X_1 + S_2 \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} X_{12} \overset{k_3}{\rightarrow} E + P$$

(b) *Competitive inhibition of an enzyme with an exponentially decaying inhibitor.* There is a single substrate S that is bound by the enzyme E to make the enzyme-substrate complex X. The complex either decays into its progenitors (backwards reaction) or the catalytic reaction takes place and the complex decays into the product P and free enzyme E. The enzyme can also bind an inhibitor I to become an inactive enzyme E^*, which

[2] *Hint:* taking the derivative of p with respect to ν when α also depends on ν is very cumbersome. Instead, use the following trick: (i) convince yourself that if $1/(1-p)$ decreases then p must decrease, too; (ii) express $1/(1-p)$ with α and ν; (iii) differentiate the resulting formula to show that $1/(1-p)$ decreases when ν increases.

cannot bind the substrate. This inhibition is reversible, the inhibited enzyme E^* decays back into the free enzyme plus the inhibitor. The free inhibitor decays exponentially.

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} X \overset{k_2}{\to} E + P, \quad E + I \underset{\nu}{\overset{\mu}{\rightleftharpoons}} E^*, \quad I \overset{\alpha}{\to} \varnothing$$

Exercise 21. *The SIR model of epidemics.* Let S, I, and R denote respectively the number of susceptible, infected, and recovered individuals in a population of total size $N = S + I + R$. All individuals give birth to susceptible offspring at the same density-dependent rate $b(N)$ and die a natural death at a constant rate μ. Susceptible and infected individuals encounter each other according to mass action with rate β, and when such an encounter happens, the susceptible individual contracts the infection. Infected individuals die because of the disease (i.e., in addition to natural death) at a rate α and recover at a rate ν. Recovered individuals are immune and cannot contract the disease any more. Write the differential equations for the dynamics of S, I, and R.

Exercise 22. *A simple predator-prey model.* Denote the number of prey and predator with N and P, respectively. When the predator is absent, the prey population grows according to the logistic model. A predator captures a prey individual according to mass action with rate β. From each captured prey, the predator makes γ offspring. The predators die at a constant rate δ. Construct differential equations for the change of prey and predator population size. This is a very simplistic model of a predator-prey system: which assumptions are unrealistic? Can you propose a better model?

EXERCISES 23-26: ANALYSIS OF DYNAMICAL MODELS

Exercise 23. *Numerical solution of a differential equation.* Solve the differential equation of logistic growth numerically, and plot $N(t)$ as a function of time. *Hint:* see section 3.3 of the lecture notes. First use the following parameter values: $r = 2.5, K = 1, N(0) = 0.01, \Delta t = 0.1$. Next, experiment with changing the parameters: What happens if K is higher? if r is lower? Interpret the results. Furthermore, experiment with increasing r or increasing Δt. There will be weird results; to understand these, make sure to plot invididual data points (not only a smooth line connecting them). We shall discuss the weird results in the exercise class.

Exercise 24. *Alcohol metabolism.* Let x denote the concentration of alcohol in the blood (since alcohol concentration equilibrates in all tissues within minutes after ingestion, we can treat the entire body as a single unit). Alcohol is broken down in the liver. The higher the alcohol concentration is in the blood, the harder the liver works to remove it; as a result, the amount of alcohol removed, $f(x)$ grams per litre per hour, increases with the concentration of alcohol, x. $f(x)$ can however not become arbitrarily high, as the liver cannot remove more than a certain amount of alcohol. Therefore, f(x) must

be a saturating function. As an approximation, we can use the familiar hyperbolically saturating function

$$f(x) = \frac{cx}{k+x}$$

Assume that there is a constant intake of u grams of alcohol per litre of body fluids per hour (this approximates an evening of bar-hopping). The concentration of alcohol thus increases by $u\Delta t$ and decreases by $f(x)\Delta t$ in Δt time, i.e., we have

$$\frac{dx}{dt} = u - f(x) = u - \frac{cx}{k+x}$$

(a) Show that if $u > c$, the concentration of alcohol increases without bound. Interpret this result verbally.

(b) Calculate the equilibrium alcohol concentration for the case $u < c$, and plot it as a function of alcohol intake, u.

(c) In a heavily intoxicated person, alcohol concentration initially decreases by 1 g/litre in 4 hours (this gives you the maximum speed of the liver). An adult of average size has approximately 45 litres of body fluids. A standard drink (e.g. 100 ml wine) contains 10 g alcohol. How many drinks per hour lead to serious intoxication?

Exercise 25. *Allee effect in population growth.* According to the logistic model, the growth rate, $r(1 - N/K)$, is a decreasing function of population size, N; i.e., an individual reproduces best when population size is small and resources are plentiful. In reality, however, there may be factors not considered in the derivation of the logistic model, which hinder the growth of small populations. An obvious example is mating (it is difficult to find a mate and therefore to reproduce when few others are around), but other types of cooperative behaviour such as cooperative defense and niche construction are also less efficient when the population is small, and this has a negative effect on the growth rate. All mechanisms that decrease the growth rate as the population becomes smaller (i.e., increase the growth rate with increasing N) are called Allee-effects.

The Wikipedia article on Allee effects proposes the equation

$$\frac{dN}{dt} = rN\left(\frac{N}{A} - 1\right)\left(1 - \frac{N}{K}\right)$$

with parameters $r > 0$, $K > A > 0$ to model an Allee effect in the dynamics of the population. This is a *phenomenological* model: it is not derived from underlying processes, but behaves qualitatively as we expect a population with an Allee effect to behave[3].

Find all equilibria of this model and investigate their stability.

[3]The use of phenomenological models is discouraged. Here this model serves only as an exercise to practice the analysis of equilibria and stability.

Exercise 26. *Environmental pollution of bacteria.* A population of bacteria produces a toxic substance that pollutes their environment and increases their death rate. Denote the size of the bacterial population by N and the concentration of the toxin by T. The bacteria reproduce at a rate b and die at a rate $\mu + \rho T$, where μ is the death rate in a toxin-free environment and the coefficient ρ tells how fast the death rate increases with increasing the concentration of the toxin, T. The population of bacteria therefore grows according to the differential equation

$$\frac{dN}{dt} = bN - (\mu + \rho T)N$$

The toxin is produced by the bacteria at a rate α per bacterium per time, and decays exponentially at a rate δ. This yields the differential equation

$$\frac{dT}{dt} = \alpha N - \delta T$$

for the toxin.

We assume that the production and decay of the toxin is much faster than the reproduction and death of the bacteria. In other words, the change in N is negligible during the time the toxin concentration T needs to attain its equilibrium. If we follow the system only for a short while, then we see that T equilibrates as if N were constant.

(a) Find the equilibrium toxin concentration $\hat{T}(N)$ at a fixed bacterium density N. (Obviously, the equilibrium we find in this step depends on at what value we fix for N, and therefore we denote the equilibrium with $\hat{T}(N)$.)

(b) Show that this equilibrium is stable: If we perturb T (but hold N fixed), then T returns to $\hat{T}(N)$.

(c) Now we want to follow the growth of the bacterial population over a long time. Since the toxin equilibrates quickly, we can approximate T in the equation for dN/dt with $\hat{T}(N)$. Show that with this approximation, the bacteria follow the logistic model of population growth with parameters $r = b - \mu$ and $K = (b - \mu)\delta/(\rho\alpha)$.

Exercise 27. *Consumer dynamics with constant resource influx.* At the bottom of the sea, resources arrive by sinking from the sunlit, productive layers of water. Suppose that a resource R arrives at a rate c (i.e., the amount of resource that arrives in Δt time is $c\Delta t$), and it decays exponentially at a rate α (e.g. due to decomposition by bacteria). A consumer captures the resource at a *per capita* rate β. With N consumers present, the resource dynamics is then given by

$$\frac{dR}{dt} = c - \alpha R - \beta N R$$

The consumer produces γ offspring from each unit of resource consumed and dies at a constant rate μ, yielding

$$\frac{dN}{dt} = \gamma\beta NR - \mu N$$

(a) Assume that the resource dynamics is much faster than the dynamics of the consumer, i.e., R attains a (quasi-)equilibrium before N would change. From the equation describing the resource dynamics, find the equilibrium of $\hat{R}$ for N fixed, and check that this equilibrium is stable.

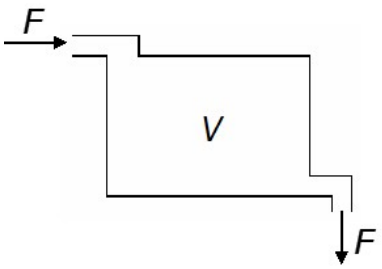
(b) Now we want to follow the slow dynamics of the consumer over a long time. At any point in time, we can approximate R with $\hat{R}$ calculated for the current consumer population size N. Verify that this approximation leads to the consumer dynamics

$$\frac{dN}{dt} = \left(\frac{\gamma\beta c}{\alpha + \beta N} - \mu\right) N$$

(c) A population is said to be *viable* if it can grow when its population size is very small. Suppose we start with a very small consumer population (N is near zero). Such a population enjoys a high resource density, but still may fail to grow e.g. if its death rate, μ, is too high. Under what condition is the consumer population viable?

(d) Find the equilibria of the consumer and investigate their stability. Check whether the equilibrium population size is positive. Compare the results with (c), and summarize them by drawing the biologically possible equilibria as a function of the consumer death rate, μ.

Exercise 28. *Chemostat dynamics.* Bacteria are often cultured in continuous-flow chemostats with a constant inflow of nutrients and a constant outflow of bacteria. The set-up is as follows. The chemostat has volume V, and the speed of inflow is F units of volume per unit of time. Obviously, the outflow must also be F (otherwise the chemostat is either emptied or overfilled).



The inflow is a solution of a nutrient with concentration c_0. Within the chemostat, the concentration of the nutrient is c and the concentration of bacteria is x. The aim of the model is to predict how c and x change with time, and how these quantities equilibrate ((a)-(b)). Having done that, we can determine how we can optimize the chemostat to our

purposes (see (c)).

When working with flows, it is strongly recommended to set up the model in terms of the *number* of particles (molecules of nutrient, bacteria), not in terms of concentrations (=number/volume). This is because the number of particles is conserved in the flow (i.e., with a flow from A to B, as many particles come in B as many left A). The concentrations are however not conserved. (Just think of a flow from a small vessel A of concentrated syrup into a big tank B of pure water; the outflow from the small vessel has high concentration, but in the big tank, the same number of particles corresponds to a low concentration.)

The number of bacteria in the chemostat is the concentration (=number/volume) times the volume of the tank, i.e., xV.. Similarly, the number of nutrient particles is cV. With the inflow, there are c_0F nutrient particles arriving per unit of time, and with the outflow, cF nutrient particles and xF bacteria leave per unit of time.

Inside the tank, the bacteria grow at a *per capita* growth rate $r(c)$. The more nutrient there is, the faster the bacteria can grow; yet the bacteria cannot divide arbitrarily fast even if there is plenty of nutrient. Hence $r(c)$ must be an increasing but saturating function. The hyperbolic function

$$r(c) = \frac{\rho c}{a + c}$$

satisfies these biological requirements (verify this statement!).

Each new bacterium incorporates k particles of the nutrient, i.e., when one bacterium is born, k nutrient particles are taken away.

(a) Construct a model to describe how the number of bacteria (xV) and of nutrient particles (cV) changes in time. Then rewrite these equations to obtain differential equations for the concentrations (x and c). [Since the rest of this exercise builds on these equations, you may want to check the solution before proceeding.]

(b) Find the equilibria of the model. Investigate the conditions under which the equilibrium concentrations ($\hat{c}$ and $\hat{x}$) are positive (it is best to rearrange inequalities such that you obtain conditions that F/V should satisfy). What happens if these conditions are not met?

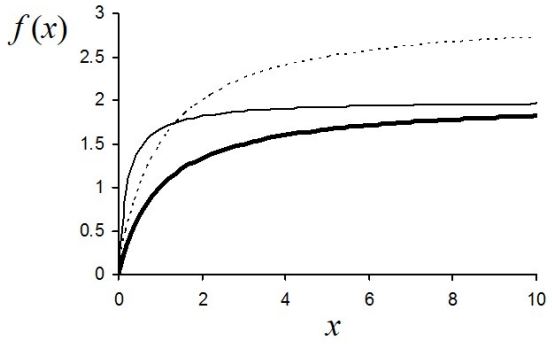
(c) Suppose we maintain the chemostat in order to harvest a substance that is produced by the bacteria (e.g. antibiotics), and we want to optimise the set-up such that we can harvest the most product per unit of time in equilibrium. The amount of product in the outflow is proportional to the number of bacteria in the outflow, so we simply maximize the number of bacteria that leave the chemostat per unit of time, $\hat{x}F$.

The model has six parameters, ρ, a, k, c_0, F and V, of which ρ, a and k are properties of the bacterium. Assume that c_0 and V are also given (for example, there is a nutrient solution of a given concentration c_0 available in the shop, and we have bought a chemostat of volume V). We are however free to choose the flow F (by turning a knob on the chemostat). Determine the optimal value of F, which maximizes the number of bacteria harvested from the outflow per unit of time[4]. In particular, see (i) if, and how, the optimal flow F depends on the volume of the chemostat, and (ii) if we have a more concentrated nutrient solution as inflow, should we increase or decrease the flow.

[4] *Hint:* You get a quadratic equation. This is no problem to solve; however, the solution does not look nice. Instead of solving this equation for the optimal value of F, you can solve it for c_0, and plot the solution as a function of F. The points of this graph represent optima: if you are given the value of c_0, you can read the optimal value of F from the graph. This trick is often used when the equation cannot be solved, or when the solution would be too ugly, yet we would like to visualize the solution.

SOLUTIONS

1. The following figure shows the shape of the hyperbola $f(x) = \frac{\beta x}{1+ax}$ with $\beta = 2, a = 1$ (thick line, "original"), $\beta = 3, a = 1$ (dotted line), and $\beta = 10, a = 5$ (thin line).



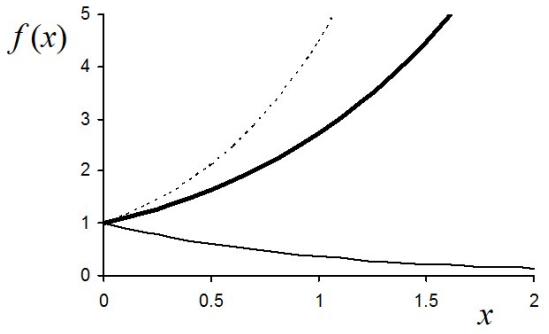
If x is very large, then adding 1 to ax does not really matter, i.e., $1 + ax \approx ax$. Taking ax instead of $1 + ax$ in the denominator, $f(x) \approx \frac{\beta x}{ax} = \frac{\beta}{a}$. Hence the hyperbola saturates to $f_a = \beta/a$. The half-saturation value $x_{1/2}$ is the value of x where $f(x) = f_a/2$, i.e., where $\frac{\beta x}{1+ax} = \frac{\beta}{2a}$. Solving this last equation yields $x_{1/2} = 1/a$.

If β is greater, then the function saturates to a higher asymptotic value but the half-saturation point remains the same. At every x the value of the function is multiplied by the same factor (e.g. by 3/2 when increasing β from 2 to 3), and therefore the function is simply stretched vertically (compare the thick and the dotted lines).

If both β and a are greater but their ratio β/a remains the same, then the saturation value remains the same but $x_{1/2} = 1/a$ becomes smaller: the function saturates faster to its asymptote. If e.g. both β and a are multiplied by 5, then the function assumes the same value already at $x/5$ what the original function assumed at x (the products βx and ax are the same, and hence $f(x) = \frac{\beta x}{1+ax}$ is the same). The function is thus "compressed" horizontally towards the y-axis.

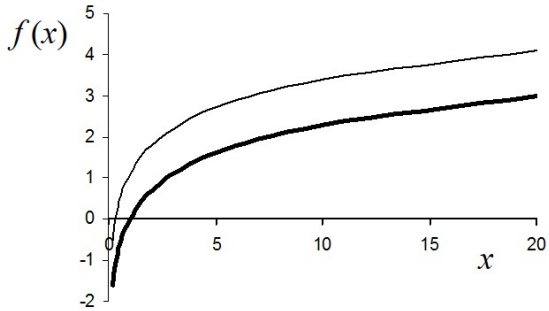
If only the value of a is greater with no change in β, then the function saturates to a smaller value (since $f_a = \beta/a$) is smaller but saturates faster than the original ($x_{1/2} = 1/a$ is closer to the y-axis).

2. (a) The exponential function is increasing when $k > 0$, decreasing when $k < 0$ and constant ($f(x) = c$ for every value of x) when $k = 0$. Except the constant case, the function is convex. The figure below shows $f(x) = ce^{kx}$ with $c = 1$ and $k = 1$ (thick line), $k = 1.5$ (dotted line) and $k = -1$ (thin line).

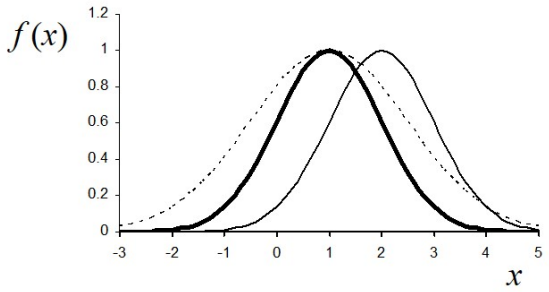


When k is greater in absolute value, then the value of the function remains the same at $x = 0$ ($f(0) = ce^0 = c \cdot 1 = c$ irrespectively of k), but changes "faster" elsewhere. If k is multiplied with a factor m (e.g. k is doubled, $m = 2$), then the function attains the same value already at x/m what the original attained at x, since the product kx is then the same. A smaller change on the x-axis therefore implies the same change on the y-axis, and the function is horizontally "compressed" towards the y-axis.

(b) The figure below shows $f(x) = c\ln(kx)$ with $c = 1$ and $k = 1$ (thick line) and $k = 3$ (thin line). Multiplying k with a factor m ($m = 3$ in the figure) means that the function is horizontally "compressed", for the same reason as above. For the logarithmic function, we also have $\ln(mkx) = \ln(m) + \ln(kx)$. Hence the same change in the shape of the function can also be seen as the function simply shifted vertically (the number $\ln m$ added to the function at each point). Compression and shift are the same only for the logarithmic function.

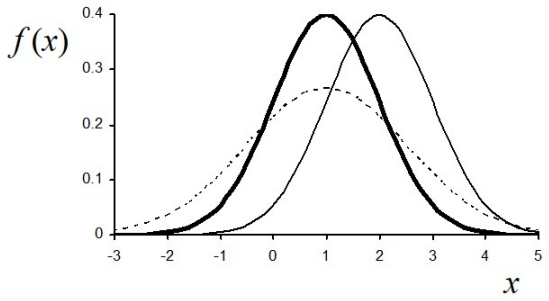


3. With $\alpha = 1$, the Gaussian function $f(x) = \alpha \exp\left(-\frac{(x-m)^2}{2\sigma^2}\right)$ is shown in the figure below for $m = 1, \sigma = 1$ (thick line), $m = 1, \sigma = 1.5$ (dotted line) and $m = 2, \sigma = 1$ (thin line).



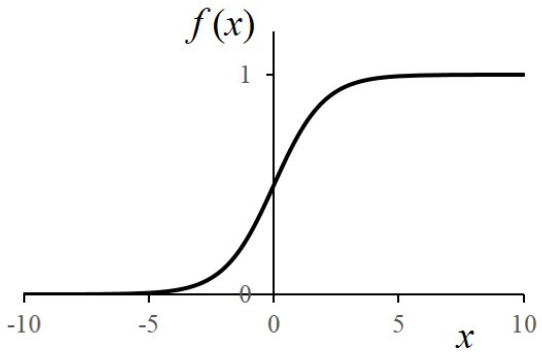
The value of m sets where the maximum of the function is: For higher m, a higher value of x is necessary to make the same difference $x - m$, and therefore the whole function shifts horizontally to the right. σ controls how broad the function is. When σ is higher, the fraction $(x-m)/\sigma$ is correspondingly smaller [this fraction is squared in the Gaussian function)], so that a greater difference $(x-m)$ is necessary to obtain the same value of the function. The function thus becomes wider by "expanding" around m when σ is increased.

With $\alpha = 1/\sqrt{2\pi\sigma^2}$ (normal distribution), the same parameters yield the plot



(notice that the vertical scale is different from the previous figure). Multiplying with the number $\alpha = 1/\sqrt{2\pi\sigma^2}$ instead of 1 stretches the function vertically (every point on the y-axis is multiplied with the same number). When σ increases, then $\alpha = 1/\sqrt{2\pi\sigma^2}$ decreases, and therefore the width and the height of the function change in a concerted way; the function becomes wider as above and also lower because α is smaller. With the specific choice $\alpha = 1/\sqrt{2\pi\sigma^2}$, changing σ does not change the area below the function; it can be proven that the area is then always 1. This fact is important in probability theory, where the areas below some parts of the function represent probabilities, and these probabilities must always add up to 1 (or 100%) for the area below the entire function. Changing m only shifts the function horizontally for the same reason as above, and does not affect the area below the function.

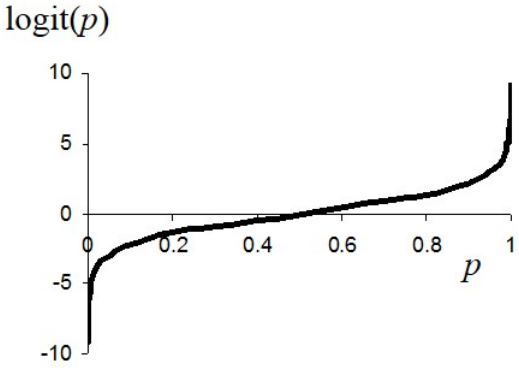
4. (a) The graph of $f(x) = \frac{1}{1+\exp[-(\alpha+\beta x)]}$ is shown below for $\alpha = 0$ and $\beta = 1$.



Increasing α shifts the function to the left, because then a smaller value of βx makes the same value of $\alpha + \beta x$. Increasing β makes the function steeper, because a smaller change in x makes then the same change in βx.

(b) To get a decreasing sigmoidal function, replace βx with $-\beta x$, i.e., take $f(x) = \frac{1}{1+\exp[-(\alpha-\beta x)]}$. To get an increasing sigmoidal function that spans the interval $(0, 2)$ instead of $(0, 1)$, multiply the original function with 2, i.e., take $f(x) = \frac{2}{1+\exp[-(\alpha+\beta x)]}$. To get an increasing sigmoidal function that spans the interval $(-1, 1)$, subtract 1 from the previous, i.e., take $f(x) = \frac{2}{1+\exp[-(\alpha+\beta x)]} - 1$.

5. (a) The graph of $\text{logit}(p) = \ln\left(\frac{p}{1-p}\right)$ is



Notice the two vertical asymptotes at $p = 0$ and at $p = 1$: at these points, the function goes to minus and plus infinity, respectively, and hence takes every possible value on the vertical axis.

(b) The equation $\text{logit}(p) = \alpha + \beta x$ can be rearranged into $p(x) = \frac{1}{1+\exp[-(\alpha+\beta x)]}$, the sigmoidal function in exercise 4. The detailed steps are

$$\begin{aligned} \ln\left(\frac{p}{1-p}\right) &= \alpha + \beta x \\ \frac{p}{1-p} &= e^{\alpha+\beta x} \\ \frac{1-p}{p} = \frac{1}{p} - 1 &= e^{-(\alpha+\beta x)} \\ \frac{1}{p} &= 1 + e^{-(\alpha+\beta x)} \\ p &= \frac{1}{1+e^{-(\alpha+\beta x)}} \end{aligned}$$

6. The log-log regression line is $(\ln y) = a + b(\ln x)$. Rearrange this equation to express y as a function of x:

$$y = e^{a+b\ln x} = (e^a)(e^{b\ln x}) = k(e^{b\ln x}) = kx^b$$

where I wrote $k = e^a$ (a positive number). y is thus proportional to x^b.

7. In one period of 15 min, there are two descendants; in n such periods, there are 2^n descendants. Solving the equation $2^n = 2 \cdot 10^{35}$ yields $n = 117.26$ periods of 15 min each, i.e., 29.32 hours: In little more than a day, the descendants of a single bacterium would outweigh the Earth! Of course there is no way to maintain ideal conditions for all this time. As these numbers aptly illustrate, population growth must be limited by shortage of food and other factors, which slow and eventually stop population growth.

8. The half-life is the length of time during which the activity decays to 1/2 times the original. After n half lives, the remaining activity is $(1/2)^n$. If we seek n such that the remaining activity is only 1%, then we need to solve the equation $(1/2)^n = 0.01$, which gives $n = 6.64$ half-lives. Repeating the same with 1 ppm ($= 10^{-6}$) instead of 0.01 gives $n = 19.93$ half-lives. For Cs-137, $n = 6.64$ half lives are 199 years and $n = 19.93$ half lives are 598 years.

9. (a) 11.5/min/g carbon; (b) ca 45 000 years old.

10. (a) α is greater for more opaque water; (b) $\alpha = 0.23/m$; (c) 9.21 m

11. (a) $t = \frac{\ln 10}{r}$

(b) At the end of the first daytime period, the weight of the algae is $w(0)e^{14r} = 1 \cdot e^{1.4} = 4.055$g, i.e., the algae do not reach 10g in the first day. At the end of the night, there remains $4.055 \cdot e^{-10\mu} = 4.055 \cdot e^{-0.2} = 3.320$g. By the end of the second daytime period, the algae grow by a factor 4.055 again, i.e., they reach $3.320 \cdot 4.055 = 13.46$g. Since this

is more than 10g, it should happen during the second daytime period that the algae hit 10g. Let t denote the time in hours since the beginning of the second day. The weight of the algae during the second day is $w(t) = 3.32e^{rt} = 3.32e^{0.1t}$ in grams, and from the equation $3.32e^{0.1t} = 10$, we obtain $t = 11.03$h. Hence the weight of the algae reaches 10g at 11.03 hours of the second daytime period.

12. (b) To check whether the proposed function $x(t) = \frac{c}{a} - \left(\frac{c}{a} - x(0)\right) e^{-at}$ is indeed the solution, take its derivative:

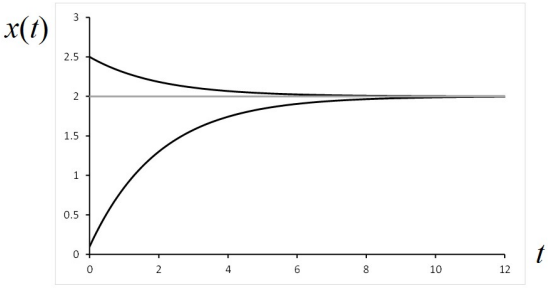
$$\frac{dx(t)}{dt} = -\left(\frac{c}{a} - x(0)\right) e^{-at} \cdot (-a) = (c - ax(0))e^{-at}$$

Substitute the proposed solution also into the right hand side of the differential equation:

$$c - ax(t) = c - a\left(\frac{c}{a} - \left(\frac{c}{a} - x(0)\right) e^{-at}\right) = (c - ax(0))e^{-at}$$

The two sides of the differential equation are indeed equal when the proposed solution is substituted, i.e., the proposed solution is indeed the solution of the differential equation.

(c) The figure below shows $x(t) = \frac{c}{a} - \left(\frac{c}{a} - x(0)\right) e^{-at}$ with parameters $c = 1$ and $a = 0.5$ for different initial values $x(0)$. As time increases, $x(t)$ tends towards $c/a = 2$ because in $x(t) = \frac{c}{a} - \left(\frac{c}{a} - x(0)\right) e^{-at}$, the difference $\frac{c}{a} - x(0)$ is multiplied with an increasingly small factor e^{-at}, such that for large t, $x(t)$ is approximately $\frac{c}{a}$. If $x(0) = c/a$, the solution is a constant line (grey line in the figure).



13. $H'(p) = 2[(1 - p) + p(-1)] = 2[1 - 2p]$ is zero when $p = 0.5$. The second derivative $H''(p) = -4$ is negative, hence H has a maximum rather than a minimum at $p = 0.5$.

14. The first derivative is

$$f'(x) = \alpha e^{-\frac{(x-m)^2}{2\sigma^2}} \left[-\frac{(x - m)}{\sigma^2}\right]$$

which is zero at $x = m$. The second derivative

$$f''(x) = \alpha e^{-\frac{(x-m)^2}{2\sigma^2}} \left[\frac{(x - m)^2 - \sigma^2}{\sigma^4}\right]$$

is negative when $(x-m)^2 < \sigma^2$, i.e., when $|x-m| < \sigma$; the middle part of the Gaussian function is therefore concave. This middle part includes $x = m$, which means that the function has indeed a maximum, not a minimum. The second derivative is positive, and hence the Gaussian function is convex when $|x-m| > \sigma$. In other words, the Gaussian function is concave for x between $m-\sigma$ and $m+\sigma$, and convex outside this interval.

15. The mode of the lognormal distribution is at $x = e^{m-\sigma^2}$.

16. The first derivative of $rN(1-N/K)$ is $r(1-2N/K)$, which is zero at $N = K/2$. The second derivative is $-2r/K < 0$. Hence $N = K/2$ yields the fastest population growth.

17. (a) The maximum fecundity is (i) $x_{max} = \sqrt{p_0/c}$ and (ii) $x_{max} = \frac{1}{\alpha}\ln\frac{c}{b}$.
(b) For the case (i), $f'(x)$ is zero at $x = \frac{s}{2c}$ and the second derivative is $f''(x) = -2c < 0$. $\frac{s}{2c}$ is therefore the optimal fecundity, provided that it is less than the maximum fecundity, i.e., provided that $\frac{s}{2c} < \sqrt{p_0/c}$; in this case, the mother survives with some positive robability and the population is iteroparous. If $\frac{s}{2c}$ is greater than the maximum fecundity, then $f(x)$ increases for all x between zero and the maximum, and therefore the maximum fecundity is the best. In this case, the mother's survival probability is zero (each mother reproduces only once), and the population is semelparous.

For the case (ii), one finds that $f'(x)$ is zero at $x = \frac{1}{\alpha}\ln\frac{\alpha c}{s}$, but since the second derivative $f''(x) = \alpha^2 c e^{-\alpha x}$ is positive, this point is a minimum, not a maximum. If $\frac{1}{\alpha}\ln\frac{\alpha c}{s}$ is greater than the maximum fecundity $\frac{1}{\alpha}\ln\frac{c}{b}$, then $f(x)$ is decreasing for all x between zero and the maximum, and therefore zero fecundity is the best (but this means that the population goes extinct since realistically $p(x)$ must be less than 1 even at $x = 0$). In the opposite case, $f(x)$ has a minimum between zero and x_{max}, and either zero or the maximum fecundity may be the best; to decide which of the two, see whether $f(0) = p(0) = c - b$ is greater or smaller than $f(x_{max}) = sx_{max} = \frac{s}{\alpha}\ln\frac{c}{b}$. With trade-off function (ii), the population cannot be iteroparous.

18. (a) $s(T) = e^{-\mu T}$
(b) The optimal age at maturation is $T_{opt} = \frac{1}{k}\ln\frac{(3k+\mu)b}{a\mu}$. Note that this is negative if $(3k+\mu)b < a\mu$; in this case, the best is to mature at birth without growth, i.e., with size $L(0) = a-b$. $R'(0) = (a-b)^2 c[(3k+\mu)b - a\mu]$ is positive whenever T_{opt} is positive. Hence every positive T_{opt} corresponds to a maximum of $R(T)$.
(c) The size at the optimal maturation age is $L(T_{opt}) = \frac{3ak}{3k+\mu}$.
(d) If μ increases, $L(T_{opt})$ decreases: the juveniles mature at a smaller size (and younger age).

19. (a) $\beta_{opt} = \sqrt{\frac{c+\nu}{a}}$; $\alpha(\beta_{opt}) = \nu + 2c + b\sqrt{(\nu+c)/a}$
(b) If ν increases, β_{opt} increases; and since $\alpha(\beta)$ is an increasing function of β, $\alpha(\beta_{opt})$ also increases.
(c) Decreasing p is equivalent to increasig $1-p$ and therefore to decreasing $1/(1-p)$. The derivative of $1/(1-p) = (\alpha/\nu) - 1$ with respect to ν (using $\alpha = \nu + 2c + b\sqrt{(\nu+c)/a}$) is

$$-\frac{(b/2a)(\nu+2c) + 2c\sqrt{(c+\nu)/a}}{\nu^2\sqrt{(c+\nu)/a}}$$

which is negative. Increasing ν therefore decreases $1/(1-p)$, and this is equivalent to decreasing p, the probability of dying of the disease.

20. For brevity, I use the "dot" notation for the time derivative: $\dot{x}$ means $\frac{dx}{dt}$.

(a)
$$\dot{s}_1 = -k_1 e s_1 + k_{-1} x_1$$
$$\dot{s}_2 = -k_2 x_1 s_2 + k_{-2} x_{12}$$
$$\dot{x}_1 = k_1 e s_1 - k_{-1} x_1 - k_2 s_2 x_1 + k_{-2} x_{12}$$
$$\dot{x}_{12} = k_2 s_2 x_1 - (k_{-2} + k_3) x_{12}$$
$$e = e_0 - (x_1 + x_{12}) \quad \text{and} \quad p = s_{1_0} - (s_1 + x_1 + x_{12}) = s_{2_0} - (s_2 + x_{12})$$

where e_0, s_{1_0} and s_{2_0} are the initial (total) amounts of the enzyme and of the substrates S_1 and S_2, respectively.

(b)
$$\dot{s} = -k_1 e s + k_{-1} x$$
$$\dot{x} = k_1 e s - (k_{-1} + k_2) x$$
$$\dot{e}^* = \mu e i - \nu e^*$$
$$\dot{i} = -\mu e i + \nu e^* - \alpha i$$
$$e = e_0 - (x + e^*) \quad \text{and} \quad p = s_0 - (s + x)$$

where e_0 and s_0 are the initial (total) amounts of the enzyme and of the substrate, respectively. Think about possible weaknesses or alternatives of these models before checking the footnote[5]!

21. SIR-model:
$$\frac{dS}{dt} = b(N)N - \mu S - \beta SI$$
$$\frac{dI}{dt} = \beta SI - (\mu + \alpha + \nu) I$$
$$\frac{dR}{dt} = \nu I - \mu R$$

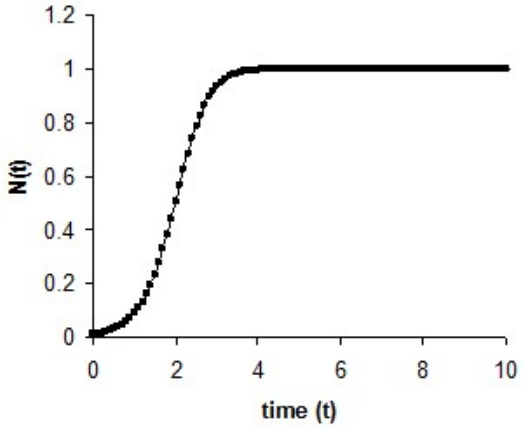
22. Predator-prey model:
$$\frac{dN}{dt} = rN(1 - N/K) - \beta NP$$
$$\frac{dP}{dt} = \gamma \beta NP - \delta P$$

Think of weaknesses of this model before checking the footnote[6]!

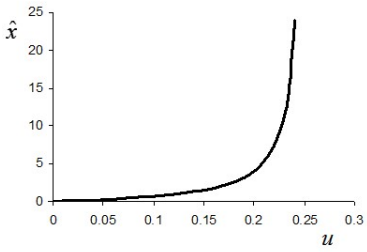
[5](a) Can S_2 bind to the enzyme before S_1 binds? For some enzymes, the order of binding is fixed, but for others, it is not. Can S_1 be released from the complex X_{12} without releasing S_2? Isn't the last reaction reversible? (b) Would not I decay also when bound to the enzyme? In the present model, the inhibitor eventually runs out; would not it be supplied by another process in the cell?

[6]The predator puts all the resources it gains from the prey into reproduction, how does it maintain its own body? Shouldn't also the death rate of the predator depend on the food intake or on energy reserves? You might include also the handling time a predator must spend on each prey, i.e., include the Holling II functional response.

23. Using the parameter values $r = 2.5$, $K = 1$, $N(0) = 0.01$ and $\Delta t = 0.1$, one obtains the figure below:



24. (a) Since c is the asymptotic value of $f(x)$, the removal is never faster than c. If $u > c$, then the right hand side of the differential equation is always positive, i.e., the alcohol keeps accumulating and eventually would go to infinitely high concentration if the person did not die.
(b) $\hat{x} = ku/(c-u)$. The figure below shows the equilibrium concentration as the function of the intake u for $c = 0.25$ g/l/h and $k = 1$ g/l.



Notice the vertical asymptote at $u = c = 0.25$ g/l/h: If u exceeds c, there is no (non-negative) equilibrium concentration. Instead, x increases indefinitely (leading to serious alcohol-poisoning or death).
(c) 1.125 drinks per hour[7]

25. The model has three equilibria, $\hat{N}_1 = 0$ (the trivial equilibrium), $\hat{N}_2 = A$ (the so-called Allee threshold), and $\hat{N}_3 = K$ (as in the logistic model). The derivative of $f(N) = rN(N/A-1)(1-N/K)$ is $f'(N) = r(N/A-1)(1-N/K)+rN(1/A)(1-N/K)+rN(N/A-1)(-1/K)$. Evaluating the derivative at the equilibria, we obtain

[7]One can drink more in a bar-hopping evening, but the evening fortunately does not last long enough for the alcohol concentration to reach equilibrium or infinity.

$f'(0) = -r < 0$, i.e., the trivial equilibrium $\hat{N}_1 = 0$ is stable
$f'(A) = r(1 - A/K) > 0$ (recall that $A < K$), i.e., the equilibrium $\hat{N}_2 = A$ is unstable
$f'(K) = -r(K/A - 1) < 0$, i.e., the equilibrium $\hat{N}_3 = K$ is stable

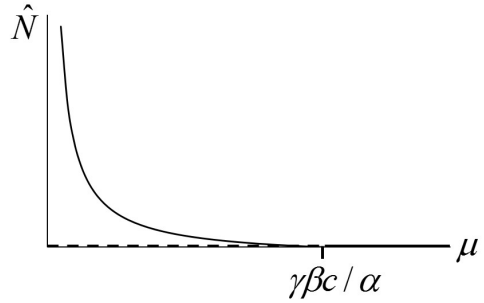
Since the trivial equilibrium is stable, small populations go extinct. The initial population size must be above the Allee threshold, i.e., above the unstable equilibrium $\hat{N}_2 = A$ for the population to grow and attain the positive stable equilibrium $\hat{N}_3 = K$ (sketch $f(N)$ to see this).

26. (a) $\hat{T}(N) = \alpha N/\delta$ (b) If $T < \alpha N/\delta$, then dT/dt is positive, i.e., T increases towards $\alpha N/\delta$. If however $T > \alpha N/\delta$, then dT/dt is negative, i.e., T decreases towards $\alpha N/\delta$. In both cases, T moves towards $\hat{T}(N) = \alpha N/\delta$, i.e., $\hat{T}(N)$ is stable.
(c) Substituting $T = \alpha N/\delta$ into the differential equation dN/dt yields

$$\frac{dN}{dt} = bN - \left(\mu + \rho\frac{\alpha N}{\delta}\right) N = (b-\mu)N\left(1 - \frac{N}{(b-\mu)\delta/(\rho a)}\right)$$

which is the logistic equation with $r = b - \mu$ and $K = (b-\mu)\delta/(\rho a)$. Note that K is positive if $r = b - \mu$ is positive, i.e., if the bacteria can grow in a toxin-free environment. K becomes infinite if α or ρ goes to zero. If the toxin is not produced ($\alpha = 0$) or it is not harmful ($\rho = 0$), then in this model there is nothing that would limit the bacteria, and exponential growth continues at the rate $r = b - \mu$ ad infinitum. In reality, of course, food limitation or other factors would influence the rates of reproduction and death, but this model considered only the effect of the toxin.

27. (a) $\hat{R} = \frac{c}{\alpha + \beta N}$, stable
(c) The consumer is viable if the *per capita* growth rate at $N = 0$ is positive, i.e., if $\frac{\gamma\beta c}{\alpha} > \mu$.
(d) The consumer has the trivial equilibrium $N = 0$ and the nontrivial equilibrium $\hat{N} = \frac{\gamma\beta c - \alpha\mu}{\mu\beta}$. When the population is viable, then the nontrivial equilibrium is positive and stable. When the population is not viable, the trivial equilibrium is the only biologically possible equilibrium and it is stable. The figure below shows the equilibria and their stability (thick line: stable, dashed line: unstable) as a function of μ. There is a transcritical bifurcation at $\mu = \gamma\beta c/\alpha$.



28. (a) The equations for the numbers of particles are

$$\begin{aligned} \frac{dxV}{dt} &= r(c)xV - xF \\ \frac{dcV}{dt} &= c_0F - kr(c)xV - cF \end{aligned}$$

and for the concentrations

$$\begin{aligned} \frac{dx}{dt} &= r(c)x - x(F/V) \\ \frac{dc}{dt} &= c_0(F/V) - kr(c)x - c(F/V) \end{aligned}$$

Notice that the dynamics of concentrations depends only on the ratio F/V and not on F or on V separately. This is because the concentrations remain the same if we use a larger chemostat (V higher) *and* adjust the flow proportionally (F proportionally higher).

(b) Trivial equilibrium: $\hat{c} = c_0$, $\hat{x} = 0$ (there are no bacteria, the nutrient flows through the chemostat without change)

Nontrivial equilibrium: $\hat{c} = a(F/V)/(\rho - (F/V))$, $\hat{x} = (c_0 - \hat{c})/k$. $\hat{c}$ is less than c_0 such that $\hat{x}$ is positive if $(F/V) < c_0\rho/(a + c_0)$; this condition also guarantees that (F/V) is less that ρ and therefore $\hat{c}$ is positive. The nontrivial equilibrium is therefore biologically meaningful if

$$(F/V) < \frac{c_0\rho}{a + c_0}$$

If this condition is violated, then there is no positive equilibrium; the flow F is too high for the volume of the chemostat V, and the culture is flushed out.

(c) The optimal flow is determined by the equation

$$c_0 = a(F/V)\frac{2\rho - (F/V)}{(\rho - (F/V))^2}$$

The figure below shows c_0 as a function of (F/V), i.e., the points of the curve are the pairs of c_0 values and the corresponding optimal flow per volume. Hence (i) the optimal flow F is proportional to the volume V; and (ii) the optimal flow increases (!) with the nutrient concentration of the inflow, c_0.