Universität Bielefeld

Mathematical Biology

Faculty of Technology, Biomathematics and Theoretical Bioinformatics

Exercises

Ellen Baake, Luigi Esercito, Enrico Di Gaspero

Summerterm 2019

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Mathematical Biology 1

Submission of your solutions: 12.04.2019 (in the lecture)

Mathematical Biology

Faculty of Technology, Biomathematics and Theoretical Bioinformatics

Summerterm 2019

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Presence exercise

Exercise 1.1 IVP $\dot{x} = x(t) \cdot f(t),\ x(0) = x_0$

As a generalisation of the differential equation defined in the lecture, consider now the initial value problem

$$\dot{x}(t) = x(t) \cdot f(t),\ x(0) = x_0$$

(with a *time dependent* function f!). Its solution reads

$$x(t) = x_0 e^{\int_0^t f(\tau)\mathrm{d}\tau}.$$

Subtask 1.1.1 Verification of the statement

Verify the statement.

Subtask 1.1.2 Derivation/separation of variables

Derive the solution in a constructive way
(by using separation of variables, which will be explained by the tutor).
[Hint: $\frac{\dot{x}(t)}{x(t)} = \frac{\mathrm{d}}{\mathrm{dt}} \log x(t)$*]* [!]

Exercise 1.2 Check solution of a 2nd order ODE

Let the function $g:\ \mathbb{R} \to \mathbb{R}$ be twice differentiable with $g'(x) \neq 0$ for all $x \in \mathbb{R}$. Furthermore, let the function $f:\ \mathbb{R} \to \mathbb{R}$ be defined by $f(x) = \cos(kg(x))$, where $k \in \mathbb{R}$. Show that

$$f'' - f' \frac{g''}{g'} + (kg')^2 f = 0.$$

Home exercise

Exercise 1.3 Spreading of a disease

We want to describe the spreading of an infectious disease, which is transmitted at rate α if an infected individual meets a noninfected one, and from which infected individuals recover at rate μ. Let p be the proportion of infected individuals in a population; then $1-p$ is the proportion of noninfected ones. Since infections require contact between infected and noninfected individuals, the increase of the proportion of infected individuals is proportional to both p and $1-p$; the constant of proportionality is α. The loss of infected individuals is only proportional to p with constant of proportionality μ. Altogether, p changes at rate

$$\dot{p} = \alpha p(1-p) - \mu p$$

Subtask 1.3.1 Phase line diagrams, 1 point

Draw the phase line diagrams for $\alpha < \mu$ and $\alpha > \mu$. What follows for the qualitative behavior (equilibria, stability)? Sketch selected solutions.

Subtask 1.3.2 Discussion state of health, 1 point

Discuss what the two cases mean for the state of 'health' of the population and the spreading of the disease?

Exercise 1.4 Logistic ODE: Check solution of IVP, 1 point

Consider the logistic differential equation, this time in the form

$$\dot{x} = \lambda x \frac{K-x}{K}$$

Verify that the function

$$x(t) = \frac{Kx_0}{x_0 + (K-x_0)e^{-\lambda t}}$$

is the solution of this differential equation with initial value x_0.
[Hint: Differentiate and have a sharp look at the resulting expression. Don't expand in any case!] [!]

Exercise 1.5 Solution $x(t) = 2e^t - 1$ given: find IVP, 1 point

Find the initial value problem that is solved by $x(t) = 2e^t - 1$

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Mathematical Biology 2

Submission of your solutions: 18.04.2019 (in the lecture)

Mathematical Biology

Faculty of Technology, Biomathematics and Theoretical Bioinformatics

Summerterm 2019

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Presence exercise

Exercise 2.1 Calcute eigensystem

Calculate the eigenvalues and (right) eigenvectors of the following matrices:

$$A = \begin{pmatrix} 1 & 1 \\ 0 & 2 \end{pmatrix} \quad \text{and} \quad B = \begin{pmatrix} 1-\alpha & \beta \\ \alpha & 1-\beta \end{pmatrix}$$

Home exercise

Exercise 2.2 Carrion eater-hyena-model

Consider the behaviour of two competing species, i.e. carrion eater and hyenas. The population size of the carrion eater at timepoint t is denoted by $A(t)$, those of the hyenas by $H(t)$. Both species compete more or less for the same ressource. The following equations may serve to describe the dynamic of the population sizes:

$$\frac{\mathrm{d}A}{\mathrm{dt}} = A - (A^2 + \alpha AH)$$
$$\frac{\mathrm{d}H}{\mathrm{dt}} = H - (H^2 + \alpha HA)$$

with the additional condition that $0 < \alpha$.

Subtask 2.2.1 Equlibria, 1 point

Calculate all equilibria.

Subtask 2.2.2 Graphical analysis, 1 point

Draw the nullisoclines as well as the vector field sketch in the case $\alpha = 2$. Sketch the trajectories in the case $\alpha = 2$ for an initial value (A_0, H_0) with $A_0 < H_0$. Conclude the stability of the equilibria for this α with the help of your sketch.

Subtask 2.2.3 Analysis via Jacobian, 3 points

Validate the stability of the equilibria for an arbitrary $\alpha \neq 1$ by using the Jacobian matrix. Which case distinction is necessary? What can you conclude for the long time development of both species from your results?

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Mathematical Biology 3

Submission of your solutions: 26.04.2019 (in the lecture)

Mathematical Biology

Faculty of Technology, Biomathematics and Theoretical Bioinformatics

Summerterm 2019

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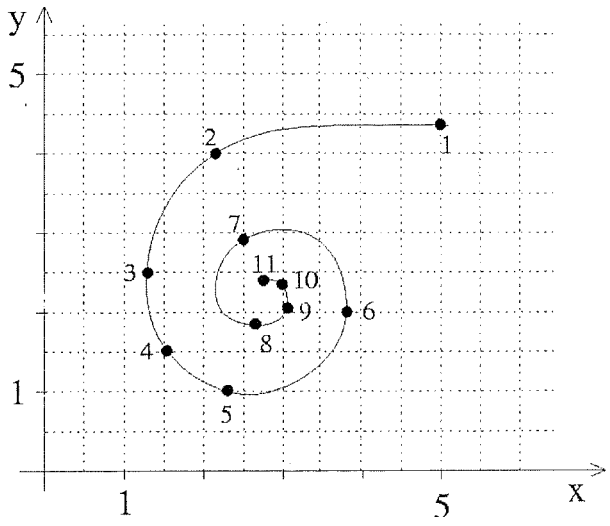
Presence exercise

Exercise 3.1 Solution in the plane

Consider the following solution of a differential equation in the plane:



Subtask 3.1.1 Coordinates as functions of t, 1 point

Draw the corresponding time courses $x(t)$, $y(t)$, as precisely as possible. The 11 time points are equidistant.

Subtask 3.1.2 Possible nullisoclines and ODE system, 3 points

Draw possible nullisoclines in the picture and set up an associated possible system of differential equations.

Home exercise

Exercise 3.2 Generalised logistic ODE

Consider the following differential equation, which describes the size of a population:

$$\dot{x} = -rx\left(1 - \frac{x}{T}\right)\left(1 - \frac{x}{K}\right)$$

with $0 < T < K$.

Subtask 3.2.1 Phase lines, equilibria, stability, 2 points

First draw the phase line diagram and use it to conclude the stability of the equilibria. Then verify the stability properties by analysing the derivative of the right-hand side at equilibrum.

Subtask 3.2.2 Time course of solutions, long time behaviour, 1 point

Sketch the time course of the solution for $0 < x_0 < T$, $T < x_0 < K$, and $x_0 > K$, and draw conclusions about the long-term behaviour of the size of the population. Interpret the meaning of the parameter T.

Exercise 3.3 System of ODEs

Consider the ODE system

$$\begin{aligned}\dot{x} &= g(x, y) = 5 - x - xy + 2y\\ \dot{y} &= h(x, y) = xy - 3y.\end{aligned}$$

Subtask 3.3.1 Equilibria , 1 point

Calculate the equilibra. (Hint: factorise h and insert its solutions (individually) into g (g cannot be factorised)).

Subtask 3.3.2 Nullisoclines, 1 point

Solve g for y to obtain the x nullisocline as a function of x. This function has a vertical and a horizontal asymptote; which ones? What kind of function is the x nullisocline?

Draw both nullisoclines as well as the equilibria.

Subtask 3.3.3 Vector field sketch, 1 point

Determine the signs of $\dot{x}$ and $\dot{y}$ in the positive quadrant (i.e. for $x, y > 0$). (Hint: A case distinction is required.)

Sketch the corresponding vector field. Can you conclude the stability of the equilibrium in the positive quadrant?

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Mathematical Biology 4

Submission of your solutions: 03.05.2019 (in the lecture)

Mathematical Biology

Faculty of Technology, Biomathematics and Theoretical Bioinformatics

Summerterm 2019

Ellen Baake, Luigi Esercito, Enrico Di Gaspero

Presence exercise

Exercise 4.1 SI-model

Consider the following infection model:

$$\begin{aligned} \dot{I} &= \alpha IS - \mu I \\ \dot{S} &= -\alpha IS + \rho S\Big(1 - \frac{I+S}{K}\Big) \end{aligned}$$

Here I denotes the number of infected, S the number of susceptible individuals.

Subtask 4.1.1 Description of the model

Which situation ist described by the model? What meaning do the parameters α, μ, ρ, K have?

Subtask 4.1.2 Nullisoclines, equilibria, vector field, stability

Calculate and draw the nullisoclines and the equilibria and sketch the vector field in the positive quadrant. Can you infer the stability of the internal equilibrium (that is, the one with both components positive)?

Home exercise

[TODONächstes Mal: $N(t)$ schon in Aufgabenstellung definieren.] **[!!!]**

Exercise 4.2 SIR-model

Let $S(t)$ be the number of individuals that can be infected with a disease (suspectibles), $I(t)$ be the number of those that are already infected (infecteds) and $R(t)$ be the number of those that were infected and are recovered now (recovered). β, ν and γ are positive parameters. The interplay of the three groups may be described by a simple epidemiological model

$$\begin{aligned}\frac{\mathrm{dS}}{\mathrm{dt}} &= -\beta S\frac{I}{N} + \gamma R\\ \frac{\mathrm{dI}}{\mathrm{dt}} &= \beta S\frac{I}{N} - \nu I\\ \frac{\mathrm{dR}}{\mathrm{dt}} &= \nu I - \gamma R.\end{aligned}$$

Subtask 4.2.1 constant population size, 1 point

Show that the total population size,

$$N(t) := S(t) + I(t) + R(t),$$

is constant over time.

Subtask 4.2.2 Assumptions and reduction, 1 point

Interpret the equations in terms of the basic assumptions of the model; in particular, describe the meaning of the parameters. Then, reduce the model to a system of *two* coupled differential equations. For this purpose, use the additional condition in the form $R = N - I - S$.

Subtask 4.2.3 Equilibria, stability, 3 points

Calculate the equilibria of the reduced model. Use the Jacobian matrix to examine the equilibrium $(\bar{S}, \bar{I}) = (N, 0)$ with respect to stability. Under which condition is it attractive? Interpret your result.

Subtask 4.2.4 Enhancement to birth-death process, 1 point

The above model is unrealistic in various ways. Generalise the system of equations by including births and deaths of individuals. Use μ as a constant rate of birth and death per individual. Which assumption do you make?

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Mathematical Biology 5

Submission of your solutions: 10.05.2019 (in the lecture)

Mathematical Biology

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Summerterm 2019

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Presence exercise

Exercise 5.1 Blood-cell model

Most types of blood cells are formed from primitive bone marrow stem cells. Until today, the exact production process of blood cells has not yet been sufficiently understood. However, it is known that the production rate depends on the cell density $y(t)$. A model that has very well described the measured cell density is based on the equation

$$\dot{y} = \frac{b\theta^n y}{\theta^n + y^n} - cy = p(y) - cy,$$

where b, θ, c, $n > 1$ are positive parameters with $b \neq c$ and $p(y) = \frac{b\theta^n y}{\theta^n + y^n}$ indicating the production rate of blood cells.

Subtask 5.1.1 Transformation of the differential equation

Show that, via the subtitution $y = u\theta$, the equation above may be transformed into:

$$\dot{u} = \frac{bu}{1 + u^n} - cu. \tag{1}$$

Subtask 5.1.2 Equilibria, stability

Find all equilibria and calculate their stability.

Home exercise

Exercise 5.2 Diploid selection equation

Consider the following differential equation

$$\dot{x} = \gamma x^2(1-x) - ux = g(x)$$

with parameters $u, \gamma > 0$.
(This is the so-called diploid selection equation for a recessive allele.)

Subtask 5.2.1 , 1 point

Determine the equilibra; distinguish the cases $u < \frac{1}{4}\gamma$ and $u > \frac{1}{4}\gamma$ (you need not consider the case $u = \frac{1}{4}\gamma$).

Subtask 5.2.2 , 1 point

Sketch the phase line diagram and determine the stability of the equilibria, individually for the two cases in 5.2.1. (*Hint:* Since g is a polynomial, 5.2.1 already gives you the required information; no further calculation is needed.)

Subtask 5.2.3 , 1 point

Represent the equilibria and their stabilities graphically as a function of u.

Exercise 5.3 BRN SIR

Subtask 5.3.1 , 1 point

Consider again the SIR model of Exercise 4.2.

Calculate its basic reproduction number, that is, the mean number of secondary cases induced by a single infected individual introduced into an otherwise susceptible population.

Subtask 5.3.2 , 1 point

Consider now the following modified version of the SIR model

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI + \gamma R \\ \frac{dI}{dt} &= \beta SI - \nu I \\ \frac{dR}{dt} &= \nu I - \gamma R\,, \end{aligned}$$

again with $N(t) := I(t) + S(t) + R(t) \equiv N$.

Calculate R_0 for this model. What is different, and why?

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Mathematical Biology 6

Submission of your solutions: 17.05.2019 (in the lecture)

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Faculty of Technology, Biomathematics and Theoretical Bioinformatics
Summerterm 2019

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Presence exercise

Exercise 6.1 IVP $\dot{y} = cy^2$, determine solution and validate it

Solve the initial value problem

$$\dot{y} = cy^2, \ y(t_0) = y_0 > 0, \ c > 0$$

via separation of variables. Does the solution exist for all $t > t_0$?

Home exercise

Exercise 6.2 Vaccination , 1 point

Consider some infection model with a given R_0. Consider now the case that at the beginning a share v of the population is vaccinated. What is the value of the new reproduction number, R_v? How big must v be to avoid an outbreak? Calculate the proportion of vaccinated people necessary to prevent the spread of the disease. Evaluate this proportion explicitly for the case of measles ($R_0 = 15$ without vaccination) and smallpox ($R_0 = 6$ without vaccination).

Exercise 6.3 Exponential transformation , 4 points

Consider the differential equation

$$\dot{y} = -sy(1-y) + u(1-y) - vy, \quad y \in [0,1]\,.$$

Consider now the following quantities obtained from y via

$$\begin{array}{rcll} z_0(t) & := & \big(1-y(t)\big) & f(t) \\ z_1(t) & := & y(t) & f(t) \end{array}$$

where $f(t) = e^{\int_0^t s(1-y(\tau))d\tau}$.

Find the system of differential equations that is satisfied by $z(t) = \big(z_0(t), z_1(t)\big)$.

Interpret this system in terms of a population model with two types of individuals that reproduce and mutate.

Express $y(t)$ and $1-y(t)$ as functions of $z(t)$. So what is the meaning of $y(t)$ and $1-y(t)$ in terms of thte population model?

Also give an interpretation of $f(t)$ in terms of the population model.

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Mathematical Biology 7

Submission of your solutions: 24.05.2019 (in the lecture)

Mathematical Biology

Faculty of Technology, Biomathematics and Theoretical Bioinformatics

Summerterm 2019

Ellen Baake, Luigi Esercito, Enrico Di Gaspero

Presence exercise

Exercise 7.1 Fitzhugh–Nagumo model with additional coefficients

Consider again the Fitzhugh–Nagumo model, that is

$$\begin{aligned} \frac{d}{dt}v &= -v(v-a)(v-1) - w \\ \frac{d}{dt}w &= \varepsilon(v - \gamma\, w). \end{aligned} \tag{2}$$

In the right-hand side of the equation for v, the coefficients seem to be missing; it may seem more appropriate to formulate the model as

$$\begin{aligned} \frac{d}{d\tau}\tilde{v} &= -\tilde{\beta}\,\left[\tilde{v}(\tilde{v}-a)(\tilde{v}-1) - \tilde{\alpha}\,\tilde{w}\right], \\ \frac{d}{d\tau}\tilde{w} &= \tilde{\varepsilon}(\tilde{v} - \tilde{\gamma}\,\tilde{w}). \end{aligned} \tag{3}$$

Here, $\tau = u\,t$ is a new time variable, and $\tilde{\alpha}$ and $\tilde{\beta}$ are additional parameters. Starting from (3), we want to obtain (2) for $v(t) = \tilde{v}(\tau)$ and $w(t) = \tilde{\alpha}\,\tilde{w}(\tau)$. How do we have to choose $u, \tilde{\varepsilon}$, and $\tilde{\gamma}$?

Home exercise

Exercise 7.2 Fishing , 3 points

Consider a fish population that grows logistically (with reproduction rate $r > 0$ and competition paramter $\gamma > 0$) and is fished at rate μ with $0 < \mu < r$, so its size evolves according to

$$\dot{x} = rx - \gamma x^2 - \mu x\,.$$

Determine the equilibria and their stability. Then determine the fishing rate μ^* that maximises the yield at the stable equilibrium. What is the equilibrium population size at $\mu = \mu^*$? Compare it with the equilibrium size of the population without fishing, that is, for $\mu = 0$. Why does the result make sense?

Exercise 7.3 Original Fitzhugh model

The original model by Fitzhugh was a bit different from the one presented in the lecture, namely:

$$\begin{aligned} \frac{dx}{dt} &= c\left(y + x - \frac{1}{3}x^3 - I\right), \\ c\frac{dy}{dt} &= a - x - by. \end{aligned}$$

Here, x is the membrane potential (analogous to v in the lecture), and y is a 'relaxation variable', such as the opening state of the potassium channel. I is the input (current, taken to be constant), and a, b, and c are positive parameters with $b < c, b < 1, b < c^2$.

Subtask 7.3.1 2 points

Calculate the Jacobian at an equilibrium point $(\bar{x}, \bar{y})$. (Assume $\bar{x}, \bar{y}$ as parameters, without calculating the equilibrium explicitly.) Show that the equilibrium is stable if

$$\frac{b}{c} - c\left(1 - (\bar{x})^2\right) > 0, \quad 1 - b\left(1 - (\bar{x})^2\right) > 0.$$

Subtask 7.3.2 1 point

Show that the equilibrium is unstable if and only if$-\gamma < \bar{x} < \gamma$, where $\gamma = \sqrt{1 - \frac{b}{c^2}}$.

Subtask 7.3.3 1 point

Show that, due to the condition in 7.3.2, for any unstable equilibrium $(\bar{x}, \bar{y})$, $\bar{x}$ must be between the local minimum and the local maximum of the x-nullisocline.

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Mathematical Biology 8

Submission of your solutions: 31.05.2019 (in the lecture)

Mathematical Biology

Faculty of Technology, Biomathematics and Theoretical Bioinformatics

Summerterm 2019

Ellen Baake, Luigi Esercito, Enrico Di Gaspero

Presence exercise

Exercise 8.1 Luria-Delbrück: variance

Verify the statement made in the lecture:
For the Luria-Delbrück experiment, one has

$$\mathbb{V}(Z) = \sum_{t=1}^{T} \mathbb{V}(Y(t)) = (2^T - 1)Np(1-p).$$

[Hint: geometric series] [!]

Home exercise

Exercise 8.2 Equilibria of simple infection model , 1 point

Consider again the simple infection model of Exercise 1.3, that is,

$$\dot{p} = \alpha p(1-p) - \mu p\,.$$

You already know its equilibria and their stability. Represent them graphically as a function of μ.

Exercise 8.3 Finite number of replicates, 3 points

In the lecture, we considered expectation and variance of the number of mutation events and the number of mutated cells in the Luria-Delbrück model.

Expectation and variance are theoretical quantities, which would be observed if the experiment were repeated an infinite number of times. In the true experiment, however, only a finite number of replicates can be performed.

Let us therefore consider the effect of a finite number of replicates.

1. Assume that we have C parallel cultures. Under the hypothesis of spontaneous mutations, calculate the probability that the first mutation event (over all C cultures) happens in generation t.
2. Plot the resulting distribution of time points for $p = 10^{-7}$ and $C = 10,\ 100,\ 1000,\ 10000$.
3. Discuss your result in terms of the evaluation of the Luria-Delbrück experiment.
   [Hint: Remember, that $\mathbb{E}[Y(t)] = Np$ is indenpendent of t.] [!]

Exercise 8.4 Voltage clamp, 3 points

Consider the voltage-clamp experiment, where the membrane potential is stepped from the resting potential $\nu_r = 0$ to some given value $\bar{\nu}$ and fixed there (via a feedback amplifier). Show that, under the original Hodgkin–Huxley model, the probability $p(t)$ of a gating-particle to be "on" is given by

$$p(t) = \bar{p} - \big(\bar{p} - p(0)\big)\, e^{-\left(\alpha_p(\bar{\nu}) + \beta p(\bar{\nu})\right) t}\,, \tag{4}$$

where $p \in \{m, n, k\}$. It is assumed that the voltage step has happened at $t = 0$. Furthermore, $p(0)$ and $\bar{p}$ are given by $p(0) = \frac{\alpha_p(0)}{\alpha_p(0)+\beta_p(0)}$ and $\bar{p} = \frac{\alpha_p(\bar{\nu})}{\alpha_p(\bar{\nu})+\beta_p(\bar{\nu})}$.

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Mathematical Biology 9

Submission of your solutions: 07.06.2019 (in the lecture)

Mathematical Biology
Faculty of Technology, Biomathematics and Theoretical Bioinformatics
Summerterm 2019

Ellen Baake, Luigi Esercito, Enrico Di Gaspero

Presence exercise

Exercise 9.1 Expectation and variance: new assumptions concerning mutation

Calculate $\mathbb{E}(Z)$ and $\mathbb{V}(Z)$ in the Luria-Delbrück model if

1. mutated cells only divide every second generation
2. mutated cells do not divide at all any more.

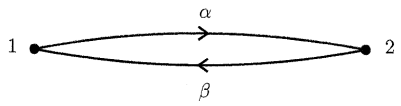
Home exercise

Exercise 9.2 n-step transition probability

The most general two-state Markov chain has transition matrix of the form

$$P = \begin{pmatrix} 1-\alpha & \alpha \\ \beta & 1-\beta \end{pmatrix}, \qquad \alpha, \beta \geqslant 0\,,$$

as represented by the transition graph



Subtask 9.2.1 , 2 points

Show that $(P^n)_{11} = \mathbb{P}(X_n = 1 \,|\, X_0 = 1)$ satisfies the recursion

$$(P^{n+1})_{11} = (1-\alpha-\beta)(P^n)_{11} + \beta,\ (P^0)_{11} = 1\,. \tag{5}$$

[Hint: $P^{n+1} = P^n P$ for $n \geqslant 0$.] [!]

Subtask 9.2.2 , 2 points

Show that the (unique) solution of (5) is given by

$$(P^n)_{11} = \begin{cases} \frac{\beta}{\alpha+\beta} + \frac{\alpha}{\alpha+\beta}(1-\alpha-\beta)^n, & \alpha+\beta > 0\,, \\ 1, & \alpha+\beta = 0\,. \end{cases} \tag{6}$$

Exercise 9.3 virus mutation , 2 points

Suppose a virus can exist in N different strains and in each generation either stays the same, or with probability $\alpha > 0$ mutates to another strain, which is chosen at random. What is the probability that the strain in the nth generation is the same as in the 0th?

To approach the problem, use the symmetry present in the mutation model to describe the process via two-state Markov chain (with states "initial" and "other"), so that you can then use part (9.2.2).

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Mathematical Biology 10

Submission of your solutions: 14.06.2019 (in the lecture)

Mathematical Biology

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Summerterm 2019

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Presence exercise

Exercise 10.1 Competition model

The following system of differential equations

$$\dot{x} = x(1 - 2x - y)$$
$$\dot{y} = y(2 - y - x)$$

describes the competition between two populations.

Subtask 10.1.1 Explanation, ODE for symbiosis

First, explain why this is a competition model. Next, write down a differential equation system that describes the *symbiosis* of two populations.

Subtask 10.1.2 Geometrical analysis and biological interpretation

Consider now your symbiosis model. Calculate and draw the nullisoclines and equilibria. Indicate the directions of the vector field and draw conclusions about the stability of the equilibria. Draft some solutions in the x-y plane. Also draft the time course for an initial value of your choice.
Finally, interpret your results biologically.

Home exercise

Exercise 10.2 n-step transition matrix , 2 points

Consider again the two-state Markov chain of Ex. (9.2) and calculate its n-state transition matrix P^n (ignore the trivial cases $\alpha = \beta = 0$ and $\alpha = \beta = 1$). What is $\lim_{n\to\infty} P^n$? What can you conclude about the long-term behaviour of the chain?

Exercise 10.3 diagonalisation of Markov transition matrix , 4 points

Consider the Markov transition matrix

$$P = \begin{pmatrix} 1 & 0 & 0 \\ \frac{1}{2} & 0 & \frac{1}{2} \\ \frac{1}{2} & \frac{1}{2} & 0 \end{pmatrix}.$$

Calculate its eigenvalues and eigenvectors and use them to diagonalise P, that is, to write P in the form

$$P = U \Lambda U^{-1}, \tag{7}$$

Λ a diagonal matrix that holds the eigenvalues. Use (7) to calculate P^n explicitly; write out the intermediate steps. Read off the long-term behaviour.

Universität Bielefeld

Mathematical Biology 11

Submission of your solutions: 21.06.2019 (in the lecture)

Mathematical Biology

Faculty of Technology, Biomathematics and Theoretical Bioinformatics

Summerterm 2019

Ellen Baake, Luigi Esercito, Enrico Di Gaspero

Presence exercise

Exercise 11.1 Luria-Delbrück, start with M cells

Let us go back once more to the Luria-Delbrück experiment, more precisely to its initial condition. Indeed it could never be guaranteed that the culture started with *exactly one* sensitive cell. It was rather a culture of a small (but unknown) number M of cells, of whom one or more may have been resistant.

Subtask 11.1.1

Assume that the culture starts with M *sensitive* cells. Calculate $\mathbb{E}[Z]$ and $\mathbb{V}[Z]$ for the case of directed and the case of spontaneous mutation.

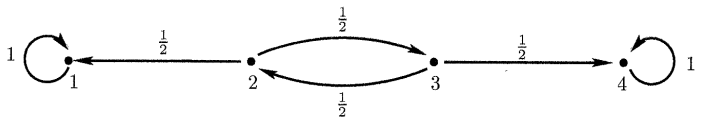
Subtask 11.1.2

What can we say about Z (again for the 'directed' and the 'spontaneous' case each)? (There is no need to do a calculation here; a qualitative statement is sufficient.)

Home exercise

Exercise 11.2 warm-up absorption probabilities Markov chain , 2 points

Consider the Markov chain $(X_n)_{n\geqslant 0}$ with the following transition graph:



Calculate the absorption probabilities

$$a_i := \mathbb{P}\big((X_n)_{n\geqslant 0} \text{ absorbs in } 4 \,|\, X_0 = i\big)$$

[Hint: Write down the first-step decomposition together with the boundary conditions, and solve the resulting linear system.] [!]

Exercise 11.3 Absorption probabilities , 4 points

Calculate the absorption probabilities of the random walk $(Z_j)_{j\geqslant 0}$ with increments $+1$ and -1 with probabilities $0 < p < 1/2$ and $q = 1 - p$, respectively, and absorbing states -1 and $y > 0$. Namely, calculate the probabilities

$$a_i := \mathbb{P}\big((Z_j)_{j\geqslant 0} \text{ absorbs in } y \mid Z_0 = i\big), \quad -1 \leqslant i \leqslant y\,,$$

via a first-step analysis (and taking into account the boundary conditions). In particular, verify that

$$a_0 = \frac{1 - (q/p)^{-1}}{(q/p)^y - (q/p)^{-1}}$$

as stated in the lecture.

[Hint: Use the first-step equation to express $a_{i+1} - a_i$ as a function of $a_i - a_{i-1}$ and thus of a_0. Then use a telescopic sum to express a_i in terms of a_0. Finally, use the boundary condition at y to find a_0.] [!]

Universität Bielefeld

Mathematical Biology 12

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Faculty of Technology, Biomathematics and Theoretical Bioinformatics

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Ellen Baake, Luigi Esercito, Enrico Di Gaspero

Presence exercise

Exercise 12.1 Mulitype Wright–Fisher model

Up to now we have only considered genetic drift for two types (for example A, a). Consider now the Wright–Fisher model with K types. Let $X_n^{(i)}$ be the number of individuals of type i in generation $n, i = 1, \ldots, K$ such that $\Sigma_{i=1}^K X_n^{(i)} = N$. The next generation is then constructed as follows: Each individual draws (with replacement) its parent from the previous generation and inherits its type. Find the probability, that the next generation consists of j_1' individuals of type $1, \ldots, j_K'$ individuals of type K, where $(\Sigma_i j_i' = \Sigma_i j_i = N)$. Thus give the probability

$$\mathbb{P}(X_{n+1} = \boldsymbol{j}' \mid X_n = \boldsymbol{j})$$

with $X_n = (X_n^{(1)}, \ldots, X_n^{(K)}), \boldsymbol{j} = (j_1, \ldots, j_K)$, and accordingly for $\boldsymbol{j}'$.

Home exercise

Exercise 12.2 Typefrequency under genetic drift

Subtask 12.2.1 2 points

Genetic drift in a population of size 1 corresponds to repeated self-fertilisation. Consider a population that consists of self-fertile heterozygote plants that all start with genotype Aa in generation 0. In every generation, one offspring is chosen at random from every parental plant. The vector $p^{(n)} = p_{AA}^{(n)}, p_{Aa}^{(n)}, p_{aa}^{(n)}$ contains the frequencies of the genotypes in the n-th (discrete!) generation. How does the transition matrix P read for the number of A alleles in a given line (that is, every given population of size 1)? Use P to calculate $p^{(1)}, p^{(2)}, andp^{(3)}$. Conclude the general expression for $p^{(n)}$.

Subtask 12.2.2 1 point

Calculate the expected time until a given line is homozygous.

[Hint: The offspring of a heterozygous individual is homozygous with probability 1/2. What is the distribution of the number of generations until a homozygous state is achieved?] [!]

Exercise 12.3 Two-state Markov chain in continuous time, 3 points

Consider the Markov chain in continuous time characterised by the transition graph $1 \underset{\lambda}{\overset{\mu}{\rightleftarrows}} 2$. Write down the rate matrix Q and calculate the corresponding Markov semigroup $P(t)$.