CHALMERS, GÖTEBORGS UNIVERSITET

EXAM for
COMPUTATIONAL BIOLOGY A

COURSE CODES: **FFR 110, FIM740GU, PhD**

Time:	Test exam
Place:	
Teachers:	
Allowed material:	Mathematics Handbook for Science and Engineering
Not allowed:	any other written material, calculator

Maximum score on this exam: 12 points (need 5 points to pass).
Maximum score for homework problems: 18 points (need 7 points to pass).
CTH $\geq$15 grade 3; $\geq$20 grade 4; $\geq$25 grade 5,
GU $\geq$15 grade G; $\geq$ 23 grade VG.

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1. Short questions [2 points] For each of the following questions give a concise answer within a few lines per question.

a) Consider the two growth equations below

$$\frac{\mathrm{d}N}{\mathrm{d}t}(t) = rN(t)$$
$$\frac{\mathrm{d}N}{\mathrm{d}t}(t) = rN(t-T)\,.$$

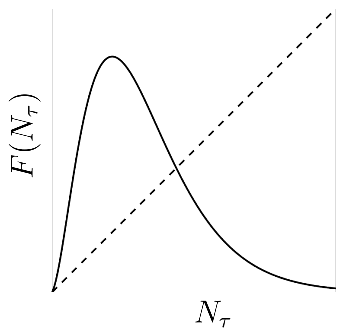
with $r > 0$ and $T > 0$. Both these equations can be solved using the following ansatz $N(t) = \sum_i A_i e^{\lambda_i t}$. Without doing any calculations, explain the difference in the spectrum of allowed λ_i for the two equations and what this difference implies in terms of oscillations of the solutions.

Solution
Without the time delay, λ_i takes a single value for the first equation and the resulting exponential solution cannot exhibit oscillations. For the second equation the allowed values λ_i form an infinite number of complex pairs. Choosing coefficients A_i such that the solution is real, the solution show either damped, marginal or growing oscillations depending on the real parts of λ_i.

b) Consider a discrete growth model for a single species of population size N

$$N_{\tau+1} = F(N_\tau)\,.$$

The figure below shows a particular choice of the map F (solid line) and the curve $N_{\tau+1} = N_\tau$ (dashed line). The scales of the axes are equal. On your answer sheet, sketch this map and mark a minimal upper bound $N_{\max}$ and a maximal lower bound $N_{\min}$ for the long-term dynamics. Explain your answer.



Solution

From the form of $N_{\tau+1} = F(N_\tau)$, $N_{\tau+1}$ becomes larger than N_τ in the region where $F > N_\tau$. Thus, the largest value $N_{\max}$ is obtained from the map of the maximum of F. Similarly, $N_{\tau+1}$ becomes smaller than N_τ in the region where $F < N_\tau$. Since $N_{\max}$ is the maximal long-term value of N, the smallest long term value of F in this region is obtained at the value $N_{\max}$ and therefore the smallest value becomes $N_{\min} = F(N_{\max})$.

c) What does the law of mass action state? Explain the form of the law of mass action.

Solution

The law of mass action states that reaction rates of chemical reactions are proportional to the product of the concentrations of the reactants. The reason for this is that the rate at which the reactants encounter each other in a well mixed environment is proportional to the number of pairs of the reacting entities, which in turn is proportional to the product of concentration of reactants.

d) What is the dimensionality of the diffusion coefficient? The characteristic law of diffusion describes how the mean squared displacement of diffusing particles grows with time for large times in an infinite domain. How does this growth depend on the diffusion coefficient and on time?

Solution

The dimensionality of the diffusion coefficient is length squared over time. The law of diffusion states that the mean squared displacement $\langle (x(t) - x_0)^2 \rangle$ grows as $\sim Dt$ for large times.

e) What is meant by the phase of oscillation? Why is it useful?

Solution

The phase characterises the state of an oscillator (which fraction of its full oscillation cycle it has traversed). In reaction-diffusion equations it is possible to have local oscillatory reactions that are coupled spatially via diffusion. This results in a spatial distribution of oscillators with different phases. Using contour lines of the phase, we can describe how wave fronts propagate through the coupled oscillators (e.g. travelling waves, spiral waves or other waves).

f) Explain what the difference is between measurement noise and dynamical noise in a time series obtained from experimental measurements of a biological process.

Solution
The measurement noise corresponds to fluctuations in an observable due to inaccuracies in a measurement device. The dynamical noise on the other hand corresponds to inherent fluctuations in the evolution of the underlying dynamics, for example due to imperfections of the model or due to stochastic fluctuations.

2. Competition and hunting [2.5 points] Rabbits, being very rapidly reproducing and invasive herbivores, are introduced into a land patch where it comes to compete with a species of native herbivores. One possible model for this situation is:

$$\begin{aligned}\dot{N} &= r_1 N \left(1 - \frac{N + b_{12} R}{K_1}\right) \\ \dot{R} &= r_2 R \left(1 - \frac{b_{21}}{K_2} N\right) ,\end{aligned} \tag{1}$$

where N is the population size of the native species of herbivores and R is the population size of rabbits. Assume that all parameters r_1, r_2, b_{12}, b_{21}, K_1, and K_2 are positive.

a) Explain the different parameters and the assumptions used to derive Eq. (1). Explain why Eq. (1) is a suitable model for the situation described above.

Solution
Eq. (1) is on the form of competition between the natural herbivore and rabbits, where the carrying capacity of rabbits is neglected. The parameters r_1 and r_2 are the growth rates of the native herbivores and of the rabbits, the parameter K_1 is the carrying capacity of N in absence of R. The intrusion of rabbits adds to the population that is limited by the carrying capacity K_1 by a fraction b_{12} of the rabbit population (competition). Similarly, the population N limits the growth of rabbits by the interaction b_{21}/K_2. Eq. (1) is a suitable model for the invasion of rabbits as long as the rabbit population is small enough not to be affected by its carrying capacity.

b) Change to suitable dimensionless parameters and population sizes such that Eq. (1) takes the form:

$$\begin{aligned}\frac{\mathrm{d}u}{\mathrm{d}\tau} &= u\,(1-u-v) \\ \frac{\mathrm{d}v}{\mathrm{d}\tau} &= \rho v\,(1-a_{21}u)\end{aligned}\,. \tag{2}$$

What expressions do you obtain for ρ and a_{21}?

Solution

We change to dimensionless variables $t = A\tau$, $N = Bu$, $R = Cv$

$$\begin{aligned}\frac{B}{A}\frac{\mathrm{d}}{\mathrm{d}\tau}u &= Br_1u\left(1-\frac{Bu+b_{12}Cv}{K_1}\right) \\ \frac{C}{A}\frac{\mathrm{d}}{\mathrm{d}\tau}v &= Cr_2v\left(1-\frac{b_{21}}{K_2}Bu\right)\,,\end{aligned}$$

Choose $A = 1/r_1$, $B = K_1$, $C = K_1/b_{12}$ to get the dimensionless equations

$$\begin{aligned}\frac{\mathrm{d}u}{\mathrm{d}\tau} &= u\,(1-u-v) \\ \frac{\mathrm{d}v}{\mathrm{d}\tau} &= \rho v\,(1-a_{21}u)\end{aligned}\,, \tag{3}$$

where we defined $\rho = r_2/r_1$ and $a_{21} = b_{21}K_1/K_2$.

c) In what follows, assume that $a_{21} < 1$. Sketch the phase-plane dynamics (you can use the null-clines as guide lines) and explain the long-term fates of the two populations.

Solution

Eq. (3) has three fixed points: $(u_1^*, v_1^*) = (0,0)$, $(u_2^*, v_2^*) = (1,0)$, $(u_3^*, v_3^*) = (1, a_{21}-1)/a_{21}$. The Jacobian becomes

$$\mathbb{J} = \begin{pmatrix} 1-2u-v & -u \\ -a_{21}\rho v & \rho(1-a_{21}u)\end{pmatrix}\,.$$

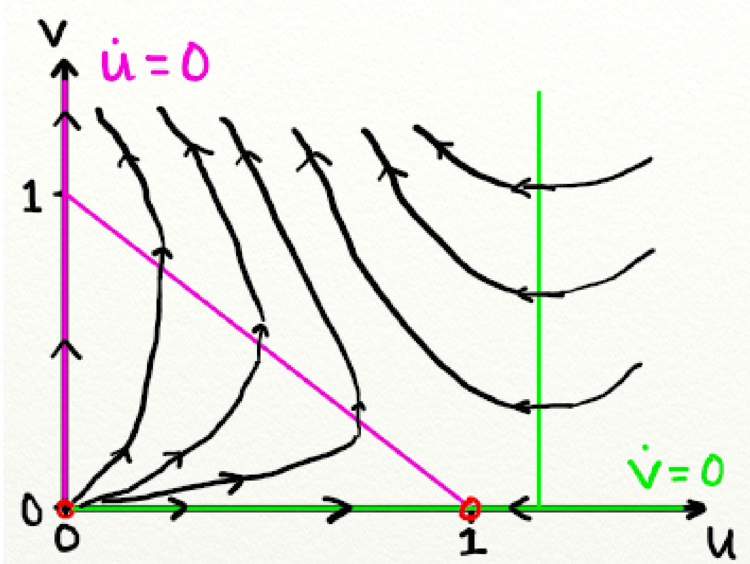
The first fixed point is an unstable node for all parameters.
The second fixed point is a stable node if $a_{21} > 1$ and a saddle point if $a_{21} < 1$.
The third fixed point is only biologically relevant if $a_{21} > 1$, where it is a saddle point.

The null-clines of the dimensionless system Eq. (3) are:

- Case $\dot{u} = 0$:
  $u = 0$, flow $\dot{v} = \rho v > 0$
  $v = 1-u$, flow $\dot{v} = \rho v\,(1 - a_{21} + a_{21}v)$

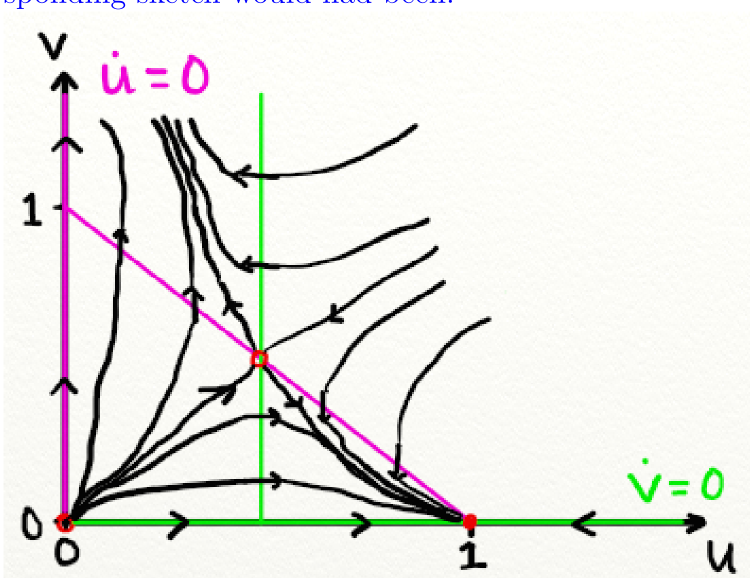
- Case $\dot{v} = 0$:
  $v = 0$, flow $\dot{u} = u\,(1-u)$
  $u = 1/a_{21}$, flow $\dot{u} = 1/a_{21}\,(1 - 1/a_{21} - v)$

For the case $0 < a_{21} < 1$ considered here, we draw the flow at the nullclines and fill in the details from that:



The long-term fate is that the natural herbivores goes extinct and the number of rabbits approach infinity.

As a side remark, for the case $a_{21} > 1$ not considered here, the corresponding sketch would had been:



For this case, depending on the initial condition, either the natural herbivores or the rabbits goes extinct. Which one is decided by whether the initial condition lies below or above the unstable manifold of the saddle point.

d) After some time it is decided that the rabbit population must decrease and rabbits are hunted with a population-dependent hunting rate $h(v)$. Modify the equations to take this into account. Find a hunting strategy that result in the rabbit population going extinct within the model.

Solution

The modified equations take the form

$$\frac{\mathrm{d}u}{\mathrm{d}\tau} = u\,(1-u-v) \tag{4}$$

$$\frac{\mathrm{d}v}{\mathrm{d}\tau} = \rho v\,(1-a_{21}u) - h(v)\,, \tag{5}$$

This system has fixed points where $u^* = 0$ and v^* solves $\rho v^* - h(v^*) = 0$, and where $u^* = 1 - v^*$ and v^* solves $\rho v^*\,(1 - a_{21}(1-v^*)) - h(v^*) = 0$. The choice $h(v) = \text{const.}$ results in a fixed point with $u = 0$ and finite v. We want to avoid this. Therefore, try $h(v) = h_0 v$ with constant h_0. The fixed points then becomes $(u^*, v^*) = (0, 0)$, $(u^*, v^*) = (1, 0)$, and $(u^*, v^*) = (-(h_0 - \rho)/(a_{21}\rho), 1 + (h_0 - \rho)/(a_{21}\rho))$. Choosing $h_0 > \rho$ makes the third steady state negative and irrelevant (the dynamics outside of the upper right quadrant cannot attract trajectories from the upper right quadrant due to the nullclines $\dot{u} = 0$ and $\dot{v} = 0$ acting along the axes).

The Jacobian becomes

$$\mathbb{J} = \begin{pmatrix} 1 - 2u - v & -u \\ -a_{21}\rho v & \rho(1 - a_{21}u) - h_0 \end{pmatrix}.$$

For the fixed point $(u^*, v^*) = (1, 0)$ we have (use $h_0 > \rho$ to determine the signs of the trace and determinant)

$$\begin{aligned} \mathbb{J} &= \begin{pmatrix} -1 & -1 \\ 0 & \rho(1 - a_{21}) - h_0 \end{pmatrix} \\ \mathrm{tr}\mathbb{J} &= -1 + \rho(1 - a_{21}) - h_0 < 0 \\ \det \mathbb{J} &= -\rho(1 - a_{21}) + h_0 + 1 > 0\,. \end{aligned}$$

Since $\mathrm{tr}\mathbb{J} < 0$ and $\det \mathbb{J} > 0$ this fixed point is stable. For the fixed point $(u^*, v^*) = (0, 0)$ we have

$$\begin{aligned} \mathbb{J} &= \begin{pmatrix} 1 & 0 \\ 0 & \rho - h_0 \end{pmatrix} \\ \mathrm{tr}\mathbb{J} &= 1 + \rho - h_0 \\ \det \mathbb{J} &= \rho - h_0 < 0\,. \end{aligned}$$

Since $\det \mathbb{J} < 0$ this is a saddle point with stable/unstable manifolds along the coordinate axes.

In conclusion, a hunting strategy that drives the rabbits extinct is to hunt them proportionally to their population size with a rate that is larger than $\rho = r_2/r_1$.

3. Stochastic models [1.5 points]

a) Write down a gain-loss equation (Master equation) for the probability $Q_N(t)$ to have a population of size N at time t. Assume stochastic dynamics where the population can change in a small time interval δt either due to a birth with probability $b\delta t$, or due to a death with probability $d\delta t$.

Solution

The change in probability $Q_N(t)$ during one time step is given by one-step transitions due to births or deaths from or to N individuals. These are

- $N-1 \to N$ due to birth
- $N \to N+1$ due to birth
- $N \to N-1$ due to death
- $N+1 \to N$ due to death

The Master equation taking all of these transitions into account is

$$\begin{aligned} Q_N(t+\delta t) - Q_N(t) = b\delta t(N-1)Q_{N-1}(t) - b\delta t N Q_N(t) \\ + d\delta t(N+1)Q_{N+1}(t) - d\delta t N Q_N(t) \,. \end{aligned}$$

b) Show that in the limit of large N the average population size approaches a deterministic dynamics. Which growth model does the deterministic dynamics correspond to?

Solution

Dividing the Master equation in subtask a) by δt and taking the limit $\delta t \to 0$ we obtain the following differential equation

$$\frac{\mathrm{d}}{\mathrm{d}t} Q_N(t) = b(N-1)Q_{N-1}(t) - (b+d)NQ_N(t) + d(N+1)Q_{N+1}(t) \,.$$

Multiply this equation by N and sum over N

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t} \sum_{N=0}^{\infty} NQ_N &= b\sum_{N=0}^{\infty} N(N-1)Q_{N-1} - (b+d)\sum_{N=0}^{\infty} N^2 Q_N + d\sum_{N=0}^{\infty} N(N+1)Q_{N+1} \\
&\text{[Change of variables } N = N'+1 \text{ in the first sum, } N = N'-1 \text{ in the last sum]} \\
&= b\sum_{N'=-1}^{\infty} (N'+1)N'Q_{N'} - (b+d)\sum_{N=0}^{\infty} N^2 Q_N + d\sum_{N'=1}^{\infty} (N'-1)N'Q_{N'} \\
&\text{[The lower limits of the } N'\text{-sums can be changed to zero without changing the result.]} \\
&= b\sum_{N'=0}^{\infty} (N'+1)N'Q_{N'} - (b+d)\sum_{N=0}^{\infty} N^2 Q_N + d\sum_{N'=0}^{\infty} (N'-1)N'Q_{N'} \\
&= \sum_{N=0}^{\infty} \left[b(N+1)N - (b+d)N^2 + d(N-1)N\right] Q_N \\
&= \sum_{N=0}^{\infty} [b-d]\, NQ_N \,.
\end{aligned}$$

The average population size N at time t is

$$\langle N(t)\rangle = \sum_{N=0}^{\infty} N Q_N(t)$$

which gives the deterministic dynamics

$$\frac{\mathrm{d}}{\mathrm{d}t}\langle N(t)\rangle = r\langle N(t)\rangle\,.$$

This is a Malthus growth with birth rate b and death rate d.

c) What are the fundamental differences between the stochastic and deterministic models if the initial population size N_0 is small? What are the differences when N_0 is large?

Solution
We expect the relative error between a stochastic model and a deterministic counterpart to go as $\sim N_0^{-1/2}$ for large times, where N_0 is the initial population size. Therefore, a small initial population will show large fluctuations around the deterministic population, and there is a large probability that the population goes extinct. A larger initial population evolves closer to the deterministic model and the probability for the population to go extinct is small, but always finite as long as the population size N_0 is finite.

4. Travelling waves [2 points] Consider a reaction-diffusion equation in one spatial dimension

$$\frac{\partial n}{\partial t}(x,t) = f(n(x,t)) + D\frac{\partial^2 n}{\partial x^2}n(x,t)\,. \tag{6}$$

a) In a few lines give interpretations of the two terms on the right-hand side of Eq. (6).

Solution
The function n can for example be a population density or the concentration of a chemical.

The first term on the right-hand side is a reaction term. It describes the local production/destruction of n, for example due to a growth process or a chemical reaction.

The second term is a diffusion term, in the absence of the first term its effect is to smoothen concentration gradients (Fick's law). In combination with the first term its effect become richer, allowing for structural solutions (travelling waves, spiral waves, spatial patterns, etc).

b) Assume that $n(x,t) = u(z)$ only depends on the combination $z = x - ct$. Starting from Eq. (6) derive an ordinary differential equation for $u(z)$.

Solution

For this coordinate change partial derivatives transform as

$$\frac{\partial n}{\partial t} = -c\frac{\mathrm{d}u}{\mathrm{d}z}$$
$$\frac{\partial n}{\partial x} = \frac{\mathrm{d}u}{\mathrm{d}z}$$

and Eq. (6) gives the ordinary differential equation

$$-c\frac{\mathrm{d}}{\mathrm{d}z}u(z) = f(u(z)) + D\frac{\mathrm{d}^2}{\mathrm{d}z^2}u(z)\,, \tag{7}$$

c) Give an interpretation of c. What changes if the value of c is changed?

Solution

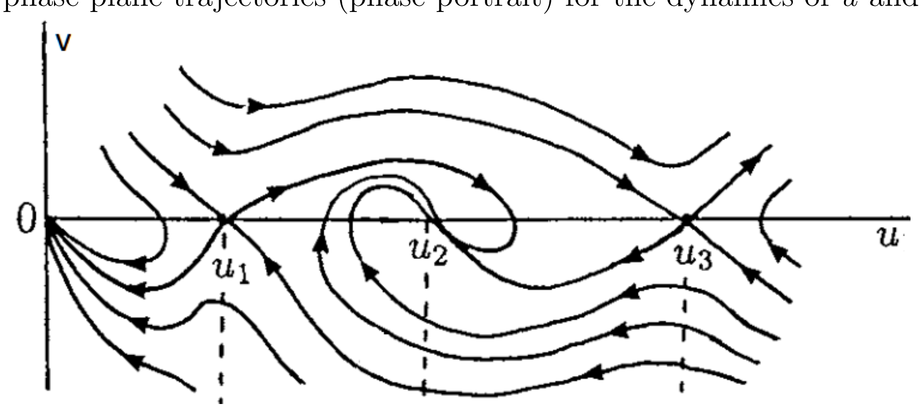
The solution $u(z)$ to Eq. (7) is on the form of a travelling wave. The constant c in $z = x - ct$ is the speed of the travelling wave. Depending on the value of c we may get different solutions to Eq. (7). The initial and boundary conditions of Eq. (6) determine if the system approaches a travelling wave solution and which of the allowed values of c is obtained.

d) Rewrite the ordinary differential equation for $u(z)$ obtained in subtask b) in terms of a first order system for $u(z)$ and $v(z) = u'(z)$.

Solution

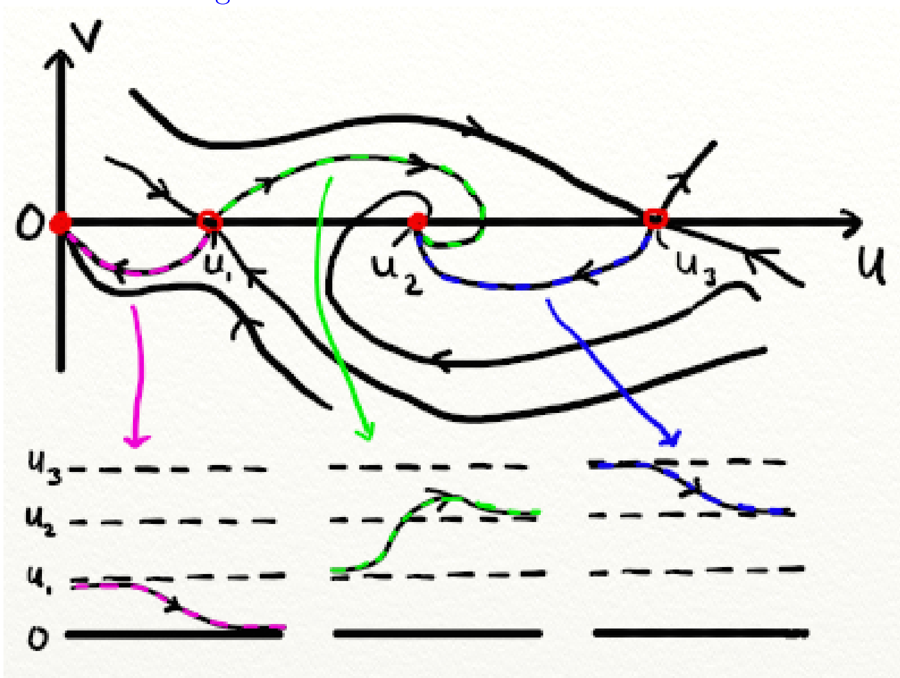
$$\frac{\mathrm{d}u}{\mathrm{d}z} = v(z)$$
$$\frac{\mathrm{d}v}{\mathrm{d}z} = \frac{-f(u(z)) - cv(z)}{D}$$

e) Assume that a particular combination of $f(u)$ and c gives the following phase-plane trajectories (phase portrait) for the dynamics of u and v:



Here $(0,0)$, $(u_1,0)$, $(u_2,0)$, and $(u_3,0)$ are the fixed points (u^*,v^*) of the system. Sketch the allowed travelling wave solution(s) $u(z)$ of Eq. (6) as function(s) of the z coordinate.

Solution
Travelling-wave solutions are orbits in the phase-plane connecting fixed points. For the phase-plane shown above, the travelling-wave solutions are the following:



5. Disease spreading [2 points] A simple model for disease spreading is the SIR model with the following dynamics

$$\begin{aligned}\dot{S} &= -rSI \\ \dot{I} &= rSI - \alpha I \\ \dot{R} &= \alpha I\,.\end{aligned} \tag{8}$$

a) Give brief explanations of the different population sizes S, I and R, and the parameters r and α.

Solution
Susceptibles S denotes individuals that have not been effected but that are susceptible to the disease. Infectives I denotes individuals that have been affected and who are able to spread the disease to the susceptible individuals. Removed R denotes individuals that have been infected by the disease, but have been removed (recovered and immune, isolated, or dead) since they are no longer able to spread the disease.

The parameter r is the infection rate and the parameter α is the removal rate of infectives ($1/\alpha$ is the mean infective period). These parameters enter the equations similar as rate constants for the law-of mass action.

b) By solving the system (8) find the maximal value $I_{\max}$ of I and the final value S_∞ of S as $t \to \infty$.

Solution
The last equation in Eq. (8) is slave to the other two, it is therefore enough to solve the first two equations. Divide these equations

$$\frac{\mathrm{d}I}{\mathrm{d}S} = \frac{\dot{I}}{\dot{S}} = \frac{rSI - \alpha I}{-rSI} = \frac{\alpha}{rS} - 1$$

and integrate

$$I(S) - I_0 = \frac{\alpha}{r}(\ln S - \ln S_0) - (S - S_0)\,. \tag{9}$$

Find maximal value by differentiation with respect to S:

$$I'(S) = \frac{\alpha}{rS} - 1$$
$$I''(S) = -\frac{\alpha}{rS^2} < 0\,.$$

This, we have a maximum at $S_{\text{opt.}} = \frac{\alpha}{r}$:

$$I_{\max} = I(S_{\text{opt}}) = I_0 + S_0 + \frac{\alpha}{r}\left(\ln\left(\frac{\alpha}{rS_0}\right) - 1\right)\,.$$

Eq. (8) has fixed points where $I = 0$. Since we have shown that the system has a maximum at $I = I_{\max}$, trajectories must decay towards the fixed point $I = 0$ as $t \to \infty$. The final value S_∞ is obtained as the solution to Eq. (9) with $I(S) = 0$:

$$-I_0 - S_0 = \frac{\alpha}{r}\ln\left(\frac{S_\infty}{S_0}\right) - S_\infty\,.$$

This equation can be solved by the Lambert W function, but that is not necessary (for the real exam I will check that all calculations can be carried out to the end).

c) Discuss why the values $I_{\max}$ and S_∞ are important in an epidemic.

Solution
The value of $I_{\max}$ estimates the maximal number of infectives at one time. This may be important to estimate the maximal number of individuals needing hospital places or medicine, or to estimate a decrease in the work ability of a population due to illness.

The value of S_∞ is important because it tells how many individuals were not infected by the epidemic.

6. The Kuramoto model [2 points] Consider a number N of coupled oscillators with phases $\theta_1, \theta_2, \ldots \theta_N$ with the following time evolution

$$\dot{\theta}_i = \omega_i + \frac{K}{N}\sum_{j=1}^{N}\sin(\theta_j - \theta_i)\,. \tag{10}$$

a) In the Kuramoto model the frequencies ω_i are drawn from a symmetric distribution $g(\omega)$ with one maximum. Explain the reason $g(\omega)$ is symmetric. What would be the difference if it was not?

Solution
The symmetry in $g(\omega)$ is used to simplify the evaluation of the self-consistency condition for the order parameter. If $g(\omega)$ were not symmetric, the contribution to the order parameter from drifting oscillators would not necessarily vanish.

b) The order parameter r satisfies

$$1 = K \int_{-\pi/2}^{\pi/2} \mathrm{d}\theta \cos^2(\theta) g(Kr \sin\theta)\,.$$

Determine for which value of $K = K_\mathrm{c}$ the system shows a phase transition if

$$g(\omega) = \frac{\gamma}{\pi} \frac{1}{\omega^2 + \gamma^2}\,.$$

Solution
Evaluating the integral with Lorenzian $g(\omega)$ gives

$$\begin{aligned}
1 &= K \int_{-\pi/2}^{\pi/2} \mathrm{d}\theta \cos^2(\theta) \frac{\gamma}{\pi} \frac{1}{[Kr\sin\theta]^2 + \gamma^2} \\
&= [X = \sin\theta,\, \mathrm{d}X = \cos\theta \mathrm{d}\theta] \\
&= \frac{\gamma K}{\pi} \int_{-1}^{1} \mathrm{d}X \frac{\sqrt{1 - X^2}}{K^2 r^2 X^2 + \gamma^2} \\
&= \frac{K}{\gamma + \sqrt{\gamma^2 + K^2 r^2}}\,.
\end{aligned}$$

Solve this equation for r

$$\begin{aligned}
\gamma^2 + K^2 r^2 &= (K - \gamma)^2 \\
\Rightarrow r &= \pm\sqrt{\frac{K - 2\gamma}{K}}\,.
\end{aligned} \tag{11}$$

Thus, the system shows a phase-transition when the order parameter r becomes non-zero. Neglecting the negative solution, the order parameter takes the form $r = \sqrt{(K - K_\mathrm{c})/K}$, where $K_\mathrm{c} = 2\gamma$.

c) What would happen if the distribution g was replaced by a Dirac delta function $g(\omega) = \delta(\omega)$ in subtask b)?

Solution
Evaluating the integral with dirac delta distributed $g(\omega)$ gives

$$1 = K \int_{-\pi/2}^{\pi/2} \mathrm{d}\theta \cos^2(\theta) \delta(Kr \sin\theta) = K \frac{1}{Kr} = \frac{1}{r}\,.$$

The integral becomes $1/r$, the order parameter becomes r=1

d) Explain how the result in subtask c) can be obtained from subtask b).

Solution

The Lorentzian

$$g(\omega) = \frac{\gamma}{\pi}\frac{1}{\omega^2+\gamma^2}\,.$$

approaches a dirac delta function as $\gamma \to 0$. This means that the order parameter for a Dirac delta function is given by Eq. (11) with $\gamma = 0$, i.e. $r = 1$.