CHALMERS, GÖTEBORGS UNIVERSITET

EXAM for
COMPUTATIONAL BIOLOGY A

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

Time:	August 29, 2018, at $08^{30} - 12^{30}$
Place:	Johanneberg
Teachers:	Kristian Gustafsson, 070-050 2211 (mobile), visits once around 10^{00}
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 [3 points] For each of the following questions give a concise answer within a few lines per question.

a) Give two examples of how discrete dynamical systems can be obtained from continuous ones.

b) Explain how a discrete dynamical system of dimensionality one can be visualised using a cobweb plot. Sketch the cobweb plot for a system that in the long run show oscillations with period 2.

c) Explain the difference between the microscopic view of diffusion (Brownian motion) and a macroscopic view (Fick's law).

d) Explain why travelling wave solutions of reaction-diffusion equations (for example Fisher's equation) typically spread quicker than pure diffusive spread (law of diffusion) in the diffusion equation.

e) Sketch the wave fronts of the spiral wave with the phase

$$\phi(r, \theta) = 4\theta + r^2 \,,$$

where r and θ are radial and angular coordinates.

f) Explain the long-term behaviour of the SIR model:

$$\dot{S} = -rSI\,, \qquad \dot{I} = rSI - \alpha I\,, \qquad \dot{R} = \alpha I\,.$$

How does an epidemic die out in the SIR-model? You do not need to do/show any calculations for this problem.

g) Explain the difference between stochastic and deterministic models for disease spreading. Under which circumstances is it better to use a stochastic model?

h) Give two examples of systems for which the Kuramoto model may be a reasonable model.

2. Delay differential model for whales [2.5 points] The following delay equation is a model for the population $N(t)$ of sexually mature blue whales

$$\frac{\mathrm{d}N}{\mathrm{d}t} = -dN(t) + N(t-T)\left[d + b\left\{1 - \left(\frac{N(t-T)}{K}\right)^z\right\}\right]. \tag{1}$$

Here d is a death rate, b a birth rate, K a carrying capacity, z models a non-linear per capita growth rate, and T is a delay time. Assume that all parameters are positive, $d > 0$, $b > 0$, $K > 0$, $z > 0$, and $T > 0$.

a) For the case $z = 1$, give a plausible motivation of the delay time T and the forms of the two terms on the right-hand side in Eq. (1). Why are there two terms proportional to the death rate, $-dN(t) + dN(t-T)$?

Solution
The delay time T is introduced to model the time between birth and sexual maturity. At time t, the number of sexually mature blue whales, $N(t)$, decreases due to deaths with linear rate d and increases due to whales born at time $t-T$ becoming mature. At time $t-T$ the rate of individuals being born is given by logistic growth, $N(t-T)b\left\{1 - \left(\frac{N(t-T)}{K}\right)^z\right\}$. One may argue that if the death rate at time $t-T$ is high, the probability of survival of the baby whales is increased due to reduced competition and this could be modelled by adding the positive contribution $+dN(t-T)$.

b) Find all steady states ($N(t) = \text{const.}$) of the delay equation (1).

Solution
There are two steady states when $N^* = 0$ and when $N^* = K$.

c) Show that close to the most positive steady state, the dynamics of a small perturbation η can be approximated by

$$\frac{\mathrm{d}\eta}{\mathrm{d}t} \approx -d\eta(t) + (d - bz)\eta(t-T)\,. \tag{2}$$

Solution
The most positive steady state is $N^* = K$. Write $N = K + \eta$ and expand the dynamics (1) to first order in η:

$$
\begin{aligned}
\frac{\mathrm{d}\eta}{\mathrm{d}t} &= -d(K+\eta(t)) + (K+\eta(t-T))\left[d + b\left\{1 - \left[\frac{K+\eta(t-T)}{K}\right]^z\right\}\right] \\
&\approx -d(K+\eta(t)) + K\left[d + b\left\{1 - \left[1 + z\frac{\eta(t-T)}{K}\right]\right\}\right] + d\eta(t-T) \\
&= -d\eta(t) + (d - bz)\eta(t-T)\,.
\end{aligned}
$$

d) Using the ansatz $\eta(t) = Ae^{\lambda t}$ in Eq. (2), derive an equation for λ.

Solution
Inserting the ansatz gives

$$
\begin{aligned}
\lambda A e^{\lambda t} &= -dAe^{\lambda t} + Ae^{\lambda(t-T)}(d-bz)\,. \\
\Rightarrow \lambda &= -d + (d-bz)e^{-\lambda T}\,.
\end{aligned}
$$

e) By analyzing the equation for λ, contrast the dynamics for the two special cases $T = 0$ and very large T (compared to all other time scales of the problem). Explain the relevant time scale of the dynamics in the two cases.

Solution
When $T = 0$ we have

$$\lambda = -bz\,,$$

i.e. we have a linearly decaying stable solution without oscillations (regular one-dimensional system).

When T is very large we have

$$\lambda = -d + (d-bz)e^{-\lambda T}\,,$$

Assuming $\mathrm{Re}[\lambda] > 0$ and taking $T \to \infty$ we obtain $\lambda = -d$ which is smaller than zero, i.e. a contradiction. Assuming instead $\mathrm{Re}[\lambda] < 0$ and $\lambda \sim A/T$ for large T we find that $\mathrm{Re}[A] = \log[1 - bz/d]$ and we have a consistent solution with $\mathrm{Re}[\lambda] < 0$ if $d > bz$.

For the $T = 0$ case, the decay rate $1/(bz)$ is the relevant time scale of the dynamics: When the delay is removed from Eq. (1), the population shows regular logistic growth with growth rate b which gives the decay rate towards the steady state $N^* = K$ (the extra factor z is a consequence of the non-linear modification).

For the case of very large T, the decay rate T/A is the relevant time scale of the dynamics: it approaches infinity and a small perturbation from the steady state $N^* = K$ therefore does not recover.

3. Effect of spruce budworms on a forest [2.5 points] A model for the effect of a constant spruce budworm population of size P on a forest with average tree size $S(t)$ (surface area of brances) and 'energy reserve' $E(t)$ (health of the trees) is given by

$$\begin{aligned}\dot{S} &= r_S S\left(1-\frac{S}{K_S}\frac{K_E}{E}\right)\\ \dot{E} &= r_E E\left(1-\frac{E}{K_E}\right)-P\frac{B}{S}\end{aligned}, \tag{3}$$

where r_S, r_E, K_S, K_E, and P are positive parameters.

a) Interpret all the terms in Eq. (3) from a biological viewpoint.

Solution

The tree size grows logistically with a carrying capacity that is proportional to the energy reserve: in times of stress the surface area may decline by death of branches or whole trees, and in good times E will be close to its capacity K_E.

The energy reserve also grows logistically with constant carrying capacity, but is reduced proportional to B/S, the budworm concentration on the trees.

b) Change to suitable dimensionless units and rewrite the system (3) in terms of two dimensionless parameters.

Solution

Let $t=\tau t_0$, $S=xS_0$, $E=yE_0$ to obtain

$$\begin{aligned}\frac{\mathrm{d}x}{\mathrm{d}\tau} &= t_0 r_S x\left(1-\frac{S_0 s}{K_S}\frac{K_E}{E_0 y}\right)\\ \frac{\mathrm{d}y}{\mathrm{d}\tau} &= t_0 r_E y\left(1-\frac{E_0 y}{K_E}\right)-\frac{t_0}{E_0}P\frac{B}{S_0 x}\end{aligned}.$$

Choose $t_0=1/r_S$, $E_0=K_E$ $S_0=K_S$ to obtain

$$\begin{aligned}\frac{\mathrm{d}x}{\mathrm{d}\tau} &= x\left(1-\frac{x}{y}\right)\\ \frac{\mathrm{d}y}{\mathrm{d}\tau} &= \rho y\left(1-y\right)-\frac{\alpha}{x}\end{aligned}.$$

where two dimensionless parameters $\rho=r_E/r_S$ and $\alpha=PB/(r_S K_S K_E)$ have been introduced.

c) Using a graphical method, show that your dimensionless system in subtask b) has two biologically relevant fixed points if B is small and no relevant fixed point if B is large.

Solution

The condition $\dot{x}=0$ implies that either $x=0$ or $x=y$. The former solution is not valid in $\dot{y} = 0$, implying that any fixed points must have $x^* = y^*$. The condition $\dot{y} = 0$ becomes

$$\frac{\alpha}{\rho} = x^2(1-x)\,.$$

The right-hand side increases from $\alpha/\rho = 0$ at $x = 0$, reaches a maximum and crosses $\alpha/\rho = 0$ at $x = 1$. Thus, if α/ρ is small enough (small B), the system has two fixed points. When α/ρ is large (large B), the system has no fixed points.

d) What is the critical level of B (in terms of the other dimensional parameters) above which no biologically relevant steady state exists.

Solution
A saddle-node bifurcation occurs at x_c for which $x^2(1-x)$ is maximal:

$$0 = \frac{\mathrm{d}}{\mathrm{d}x}x^2(1-x) = 2x - 3x^2 \qquad \Rightarrow \qquad x_c = 2/3$$

At this value $\alpha/\rho = 4/27$, i.e. the critical value becomes $B_c = 4/27 r_E K_S K_E/P$.

e) Given that one of the biologically relevant fixed points is stable if it exists, discuss possible effects of refuge and outbreaks of spruce budworms on the forest.

Solution
As discussed in the course, spruce budworms essentially have two modes of refuge (small B) and outbreak (large B). Upon refuge, the system moves towards the stable fixed point if the initial average tree size is large enough. During the outbreak, if the spruce budworm population becomes large enough, no fixed points exists and the average tree size is driven towards zero.

As a side remark it can be noted that even if the tree size does not go to zero within the time of outbreak, the trees may not recover if the size is too small. This is because a separatrix from the second fixed point (saddle) bounds the basin of attraction of the stable fixed point.

4. A linear reaction-diffusion equation [2.5 points] Consider the reaction-diffusion equation

$$\begin{aligned} \frac{\partial u}{\partial t} &= u + 3v - 4 + \frac{\partial^2 u}{\partial x^2} \\ \frac{\partial v}{\partial t} &= -u - 2v + 3 + 8\frac{\partial^2 v}{\partial x^2} \end{aligned}\,. \tag{4}$$

a) Find the homogeneous steady state (u^*, v^*) of the system (4) and determine its stability.

Solution
The steady state is given by

$$\begin{aligned} 0 &= u + 3v - 4 \\ 0 &= -u - 2v + 3 \end{aligned}$$

i.e. it is located at $(u^*, v^*) = (1, 1)$.

The stability matrix becomes

$$\begin{aligned} \mathbb{J} &= \begin{pmatrix} 1 & 3 \\ -1 & -2 \end{pmatrix} \\ \mathrm{tr}\mathbb{J} &= -1 \\ \det \mathbb{J} &= 1 \end{aligned}$$

i.e. the fixed point is stable.

b) By making an ansatz $(u, v) = (u^*, v^*) + e^{\lambda t + \mathrm{i}kx}(\delta u_0, \delta v_0)$ where $(\delta u_0, \delta v_0)$ are (possibly complex) constants, show that λ is related to k by

$$\lambda(k) = \frac{1}{2}\left(-1 - 9k^2 \pm \sqrt{49k^4 + 42k^2 - 3}\right) .$$

Solution
Inserting the ansatz into Eq. (4) gives

$$\begin{aligned} \lambda e^{\lambda t + \mathrm{i}kx}\delta u_0 &= e^{\lambda t + \mathrm{i}kx}\delta u_0 + 3e^{\lambda t + \mathrm{i}kx}\delta v_0 - k^2 e^{\lambda t + \mathrm{i}kx}\delta u_0 \\ \lambda e^{\lambda t + \mathrm{i}kx}\delta v_0 &= -e^{\lambda t + \mathrm{i}kx}\delta u_0 - 2e^{\lambda t + \mathrm{i}kx}\delta v_0 - 8k^2 e^{\lambda t + \mathrm{i}kx}\delta v_0 \\ \Rightarrow 0 &= -[\lambda - 1 + k^2]\delta u_0 + 3\delta v_0 \\ 0 &= -\delta u_0 - [\lambda + 2 + 8k^2]\delta v_0 \, . \end{aligned}$$

The second eguation gives $\delta u_0 = -[\lambda + 2 + dk^2]\delta v_0$ which when inserted into the first equation gives

$$\begin{aligned} 0 &= [\lambda - 1 + k^2][\lambda + 2 + 8k^2] + 3 = \lambda^2 + (1 + 9k^2)\lambda + 1 - 6k^2 + 8k^4 \\ \Rightarrow \lambda &= \frac{1}{2}(-1 - 9k^2 \pm \sqrt{49k^4 + 42k^2 - 3}) \end{aligned}$$

Solutions corresponding to the positive sign in λ are unstable if $\lambda > 0$.

c) Show that the homogeneous steady state becomes unstable to linear perturbations for a range of wave numbers $k^2_{\mathrm{min}} < k^2 < k^2_{\mathrm{max}}$. Determine k^2_{min} and k^2_{max}.

Solution
Search for the limiting solutions where $\lambda = 0$:

$$\begin{aligned} 0 &= -1 - 9k^2 + \sqrt{49k^4 + 42k^2 - 3} \\ &\Rightarrow (1 + 9k^2)^2 = (49k^4 + 42k^2 - 3) \\ &\Rightarrow k^4 - 6/8k^2 + 1/8 = 0 \\ &\Rightarrow k^2 = \frac{1}{4} \text{ or } k^2 = \frac{1}{2} \end{aligned}$$

It is straightforward to show that λ is positive for k^2 between $k^2_{\text{min}} = 1/4$ and $k^2_{\text{max}} = 1/2$.

d) Assume that the spatial part of the system (4) is constrained to zero at $x = 0$ and $x = 3\pi$. Which k-values in the ansatz in subtask b) are relevant for this constrained dynamics? Sketch how a small perturbation in this system evolves in time.

Solution

The spatial part of the ansatz in subtask b) consists of $\cos(kx)$ and $\sin(kx)$ (real solutions can be obtained by superposition of positive and negative modes with suitable complex prefactors δu_0 and δv_0).

Since the solution is zero at $x = 0$, we use $\sin(kx)$. The additional constraint that the solution is zero at $x = 3\pi$ gives allowed values of k: $k = n/3$ with integer n. Consequently $k^2 = 0, 1/9, 4/9, 1, \ldots$. Only $k^2 = 4/9$ lies in the interval of unstable solutions.

The solution looks like a sine wave ($n = 2$) on the interval from zero to 3π and is proportional to $e^{\lambda t}$, i.e. a small perturbation will increase the concentration in the left half of the interval and reduce it on the right half (or the opposite if the prefactor is negative).

5. Noise in time series [1.5 points] Consider a general time series x_0, x_1, ... generated by a map F:

$$x_{n+1} = F(x_n)\,.$$

Measurement noise in a time series is defined as an error in the observations of the values of x_n. Dynamical noise is defined as an inherent disturbance to the dynamics: at each time step an error is added to the map. In what follows, you can assume the measurement and dynamical noises to be Gaussian white noise with variance σ^2.

a) Discuss and contrast the effects of measurement noise and dynamical noise on a time series which is generated by linear (Malthus) decay (negative growth rate).

Solution

Lecture notes 14.2

b) Assume that you are given noisy time series data and that you know that the data is generated by an underlying linear (Malthus) decay map. Discuss how the (negative) growth rate of the underlying map can be recovered from the time series for the two cases of measurement noise and of dynamical noise. For which case is it easier to reconstruct the underlying growth rate?

Solution

Lecture notes 14.3