CHALMERS, GÖTEBORGS UNIVERSITET

EXAM for
COMPUTATIONAL BIOLOGY A

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

Time:	August 28, 2019, at $08^{30} - 12^{30}$
Place:	Johanneberg
Teachers:	Anshuman Dubey, 072-190 6469 (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) Discuss why we study mathematical models of biological systems. What are the advantages and disadvantages compared to other approaches such as computer models or experimental models?

Solution
Lecture notes 1.1

b) Explain what a cobweb plot is and how it is generated. Illustrate using an explicit example.

Solution
Lecture Notes 2.1

c) Show that the Ricker map

$$N_{\tau+1} = \rho N_\tau e^{-N_\tau}$$

with $\rho > 0$ has a period-doubling bifurcation at a critical value ρ_c.

Solution
The map has fixed points at $N_1^* = 0$ and $N_2^* = \ln \rho$. Evaluate

$$\frac{\partial N_{\tau+1}}{\partial N_\tau} = \rho e^{-N_\tau}(1 - N_\tau)$$

$$\Lambda_1 = \left.\frac{\partial N_{\tau+1}}{\partial N_\tau}\right|_{N_\tau = N_1^*} = \rho$$

$$\Lambda_2 = \left.\frac{\partial N_{\tau+1}}{\partial N_\tau}\right|_{N_\tau = N_1^*} = 1 - \ln \rho$$

We have a period-doubling bifurcation when Λ_2 passes -1, i.e. when $\rho = \rho_c = e^2$.

d) 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.

e) The following is a stochastic model for Malthus growth:

$$Q_N(t) = Q_N(t - \delta t) + r\delta t(N-1)Q_{N-1}(t-\delta t) - r\delta t N Q_N(t - \delta t)\,.$$

Here $Q_N(t)$ is the probability to have a population of size N at discrete time steps separated by δt. Explain the meaning of r and the form of the different terms in this equation.

Solution

Lecture Notes 5.1

f) Discuss similarities and differences between molecular diffusion and population diffusion.

Solution

Lecture Notes 6.1

g) Consider a generic reaction diffusion equation in one spatial dimension

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

where f only implicitly depends on t and x through $n(x,t)$. Explain why the solutions to $f(n) = 0$ are important for travelling wave solutions of the reaction diffusion equation.

Solution

Lecture notes 6.3

h) Write down the SIR model for spreading of diseases and explain all involved variables and parameters.

Solution

Bernhard's lecture notes

2. Delay model for white blood cells [2.5 points] White blood cells are produced in the bone marrow to be released in the body. Since it takes several days to produce white blood cells in response to a deficit, the number of white blood cells N in the blood stream at time t can be modeled using

$$\frac{\mathrm{d}N}{\mathrm{d}t} = -\gamma N(t) + \frac{\beta N(t-T)\theta^m}{\theta^m + N(t-T)^m}\,. \tag{1}$$

Here $0 < \gamma < \beta$, $\theta > 0$ and $T > 0$. m is a positive integer.

a) Assuming N has dimension 'size' and t has dimension 'time', what are the dimensions of the parameters γ, β, θ and T? Explain the roles of T, γ, β and θ in the model.

Solution
The dimensions are $[\gamma] = [\beta] = \text{time}^{-1}$, $[\theta] = \text{size}$ and $[T] = \text{time}$. T is a time delay modeling the time delay of producing the blood cells. γ is the decay rate of blood cells in the blood stream. The second term models (delayed) production of blood cells. For population sizes that have been small (compared to θ) on the times scale T, we have linear production with growth rate β, for population sizes that have been larger that θ on the times scale T, the production is small (or constant if $m = 1$) and the population decays due to $-\gamma N$. We can therefore think of θ as proportional to a target cell population size (similar to a carrying capacity).

b) Introduce dimensionless units and write Eq. (1) in terms of m, a dimensionless delay time, and one additional dimensionless parameter.

Solution
Let $t = t_0\tau$ and $N(t) = N_0 u(\tau)$

$$\frac{\mathrm{d}u}{\mathrm{d}\tau} = \frac{1}{N_0}\frac{\mathrm{d}N}{\mathrm{d}\tau} = \frac{1}{N_0}\frac{\mathrm{d}N}{\mathrm{d}t}\frac{\mathrm{d}t}{\mathrm{d}\tau} = \frac{t_0}{N_0}\left[-\gamma N_0 u(\tau) + \frac{\beta N_0 u(\tau - T/t_0)\theta^m}{\theta^m + N_0^m u(\tau - T/t_0)^m}\right]$$
$$= -t_0\gamma u(\tau) + \frac{\beta t_0 u(\tau - T/t_0)\theta^m}{\theta^m + N_0^m u(\tau - T/t_0)^m} = -u(\tau) + \alpha\frac{u(\tau - D)}{1 + u(\tau - D)^m}$$

where we chose $t_0 = 1/\gamma$, $N_0 = \theta$ and defined the dimensionless parameter $\alpha = \beta/\gamma > 1$ and dimensionless delay time $D = \gamma T$ in the last step.

c) Find all steady states ($N(t) = \text{const.}$) of the dimensionless system in subtask b) [if you failed subtask b) you can use Eq. (1) in what follows]. Verify that the steady states are biologically relevant for the parameter constraints given below Eq. (1).

Solution
There are two steady states solutions to $0 = -u + \alpha\frac{u}{1+u^m}$, when $u^* = 0$ and $u^* = (\alpha - 1)^{1/m}$. Since $\alpha > 1$ by the constraints, both fixed points are non-negative and thus biologically relevant.

d) To simplify, consider the case $m = 1$ in this subtask. Derive the dynamics of a small time-dependent perturbation $\eta(t)$ close to the most positive steady state.

Solution

The most positive steady state is $u^* = (\alpha-1)^{1/m}$. Write $u(t) = (\alpha-1)^{1/m} + \eta(t)$ and expand the dimensionless dynamics to first order in η

$$\begin{aligned}
\frac{\mathrm{d}\eta}{\mathrm{d}\tau} &= -[(\alpha-1)^{1/m} + \eta(t)] + \alpha\frac{(\alpha-1)^{1/m} + \eta(\tau - D)}{1 + [(\alpha-1)^{1/m} + \eta(\tau-D)]^m} \\
&= -(\alpha-1)^{1/m} - \eta(t) + \alpha\frac{(\alpha-1)^{1/m} + \eta(\tau-D)}{1 + (\alpha-1)[1 + (\alpha-1)^{-1/m}\eta(\tau-D))]^m} = [\text{Beta}] \\
&\approx -(\alpha-1)^{1/m} - \eta(t) + \alpha\frac{(\alpha-1)^{1/m} + \eta(\tau-D)}{1 + (\alpha-1)[1 + m(\alpha-1)^{-1/m}\eta(\tau-D)]} \\
&= -(\alpha-1)^{1/m} - \eta(t) + \frac{(\alpha-1)^{1/m} + \eta(\tau-D)}{1 + m(\alpha-1)^{1-1/m}\eta(\tau-D)/\alpha} = [\text{Beta}] \\
&\approx -(\alpha-1)^{1/m} - \eta(t) + [(\alpha-1)^{1/m} + \eta(\tau-D)][1 - m(\alpha-1)^{1-1/m}\eta(\tau-D)/\alpha] \\
&\approx -\eta(t) + \frac{\alpha(1-m)+m)}{\alpha}\eta(\tau-D)
\end{aligned}$$

Using $m = 1$ as suggested would simplify the calculation and give $\frac{\mathrm{d}\eta}{\mathrm{d}\tau} \approx -\eta(t) + \eta(\tau-D)/\alpha$.

e) It can be shown (you do not need to show this) that the ansatz $\eta(t) = e^{\lambda t}$ has solutions with positive real part of λ for certain parameter values, while for other parameters all solutions have negative real part of λ. Discuss possible long-term behaviours of the system (1).

Solution

If all λ are negative, the system approaches the fixed point $\eta(t)$, possible oscillating if the imaginary part of λ is non-zero. When any λ has positive roots, the small perturbations will grow and one will obtain periodic or chaotic motion depending on the nature of the non-linear terms.

3. Plants in dry environments [2.5 points] In dry environments plant growth is mainly limited by the access to water. Assuming a small constant supply of water, the population size N of plants and amount W of accessible water can be modeled by the following system

$$\begin{aligned}
\dot{N} &= aNW - bN \\
\dot{W} &= S - cW - dNW
\end{aligned} \tag{2}$$

where a, b, c, d and S are positive parameters.

a) Give plausible interpretations of the different terms in Eq. (2).

Solution

The number of plants grow with a rate aW, i.e. proportional to the amount of available water. $-bN$ is a linear death rate of plants. S is the constant supply of water, cW is linear decrease (for example due to evaporation or runoff) of water and $-dNW$ is decrease of water due to plant uptake.

b) Introduce dimensionless units in Eq. (2). Choose units such that the dimensionless growth rate of W does not depend on any parameter. Which parameter combinations govern the dimensionless growth of N?

Solution

Let $N = uN_0$, $W = vW_0$ and $t = \tau t_0$ to obtain

$$\frac{\mathrm{d}u}{\mathrm{d}\tau} = \frac{t_0}{N_0}[aN_0W_0uv - bN_0u]$$
$$\frac{\mathrm{d}v}{\mathrm{d}\tau} = \frac{t_0}{W_0}[S - cW_0v - dN_0W_0uv]$$

Choose $t_0 = 1/c$, $W_0 = S/c$ and $N_0 = c/d$ to get

$$\frac{\mathrm{d}u}{\mathrm{d}\tau} = \alpha u[\beta v - 1]$$
$$\frac{\mathrm{d}v}{\mathrm{d}\tau} = 1 - v - uv$$

with $\alpha = b/c$ and $\beta = aS/(bc)$ the governing parameter combinations.

c) Find all steady states of the dimensionless system [or (2) if you failed subtask b)] and determine conditions for which they are biologically relevant. Discuss the biological meaning of the different steady states.

Solution

The fixed points are $(u_1^*, v_1^*) = (0, 1)$ and $(u_2^*, v_2^*) = (\beta - 1, \beta^{-1})$. The first steady state is a desert state without plants ($v = 1$ corresponds to $W = W_0 = S/c$, i.e. the balance state between water supply and loss). The second steady state is positive (biologically relevant) if $\beta > 1$.

d) Determine the stability of the fixed points as a function of the system parameters. Discuss the possible long-term states of the system for different parameters.

Solution

Stability

$$\mathbb{J} = \begin{pmatrix} \alpha[\beta v - 1] & \alpha\beta u \\ -v & -1 - u \end{pmatrix}$$
$$\mathrm{tr}\mathbb{J}(u_1^*, v_1^*) = \alpha[\beta - 1] - 1$$
$$\mathrm{tr}\mathbb{J}(u_2^*, v_2^*) = -\beta$$
$$\det\mathbb{J}(u_1^*, v_1^*) = \alpha[1 - \beta]$$
$$\det\mathbb{J}(u_2^*, v_2^*) = \alpha[\beta - 1]$$

If $0 < \beta \leq 1$ the system has a single stable fixed point (u_1^*, v_1^*) and the system becomes desertified. If $\beta > 1$ the system has two fixed points, where (u_1^*, v_1^*) is unstable and (u_2^*, v_2^*) is stable, the long term behavior is a system with plants.

4. A linear reaction-diffusion equation [2 points] Consider the reaction-diffusion equation in two spatial dimensions

$$\begin{aligned}\frac{\partial u}{\partial t} &= 2 - u + \frac{\partial^2 u}{\partial x^2} + \frac{\partial^2 u}{\partial y^2} \\ \frac{\partial v}{\partial t} &= u - 2v + 4 + 3\left(\frac{\partial^2 v}{\partial x^2} + \frac{\partial^2 v}{\partial y^2}\right)\end{aligned} \tag{3}$$

a) Find the homogeneous steady state (u^*, v^*) of the system (3) and determine its stability.

Solution

The steady state is given by

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

i.e. it is located at $(u^*, v^*) = (2, 3)$.

The stability matrix becomes

$$\begin{aligned}\mathbb{J} &= \begin{pmatrix} -1 & 0 \\ 1 & -2 \end{pmatrix} \\ \text{tr}\mathbb{J} &= -3 \\ \det \mathbb{J} &= 2\end{aligned}$$

i.e. the fixed point is stable.

b) By making an ansatz $(u, v) = (u^*, v^*) + e^{\lambda t + \mathrm{i}(k_x x + k_y y)}(\delta u_0, \delta v_0)$ where $(\delta u_0, \delta v_0)$ are (possibly complex) constants, find all solutions λ as functions of $k = \sqrt{k_x^2 + k_y^2}$.

Solution

Inserting the ansatz into Eq. (3) gives

$$\begin{aligned}\lambda e^{\lambda t + \mathrm{i}(k_x x + k_y y)}\delta u_0 &= -e^{\lambda t + \mathrm{i}(k_x x + k_y y)}\delta u_0 - k^2 e^{\lambda t + \mathrm{i}(k_x x + k_y y)}\delta u_0 \\ \lambda e^{\lambda t + \mathrm{i}(k_x x + k_y y)}\delta v_0 &= e^{\lambda t + \mathrm{i}(k_x x + k_y y)}\delta u_0 - 2e^{\lambda t + \mathrm{i}(k_x x + k_y y)}\delta v_0 - 3k^2 e^{\lambda t + \mathrm{i}(k_x x + k_y y)}\delta v_0 \\ \Rightarrow 0 &= -[\lambda + 1 + k^2]\delta u_0 \\ 0 &= \delta u_0 - [\lambda + 2 + 3k^2]\delta v_0\end{aligned}$$

The first equation gives $\lambda_1 = -1 - k^2$ or $\delta u_0 = 0]$. For the first case the second equation simply gives a relation between δv and δu. For the second case, the second equation becomes $0 = -[\lambda + 2 + 3k^2]\delta v_0$ with solution $\lambda_2 = -2 - 3k^2$

c) An observation in nature is that there is (almost) no animal with striped body and spotted tail, but there is animal with spotted body and striped tail. Give one possible explanation (without calculations) for this observation.

Solution

Lecture notes 8

5. 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

$$\dot{\theta}_i = \omega_i + \frac{K}{N} \sum_{j=1}^{N} \sin(\theta_j - \theta_i) \,. \tag{4}$$

a) Introduce the order parameters $r(t)$ and $\psi(t)$

$$r e^{\mathrm{i}\psi} = \frac{1}{N} \sum_{j=1}^{N} e^{\mathrm{i}\theta_j} \tag{5}$$

and show that Eq. (4) can be written on the following form

$$\dot{\theta}_i = \omega_i + K r \sin(\psi - \theta_i) \,. \tag{6}$$

Solution
Multiplication of Eq. (5) with $e^{-\mathrm{i}\theta_i}$ and evaluation of the imaginary part gives

$$\mathcal{I}m[r e^{\mathrm{i}(\psi - \theta_i)}] = \mathcal{I}m\left[\frac{1}{N}\sum_{j=1}^{N} e^{\mathrm{i}(\theta_j - \theta_i)}\right]$$
$$\Rightarrow r \sin(\psi - \theta_i) = \frac{1}{N}\sum_{j=1}^{N} \sin(\theta_j - \theta_i) \,.$$

Inserting this relation into Eq. (4) gives the sought form:

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

b) What is the significance of r and ψ? Explain the significance of Eq. (6), what is gained compared to Eq. (4)?

Solution
r quantifies the phase coherence (unity if all phases are equal and zero if phases are uniformly distributed)

ψ is the arithmetic mean, $\overline{e^{\mathrm{i}\theta}}$, over all oscillators, i.e. a measure of the average phase of the oscillators.

In Eq. (4) all oscillators are coupled to each other, while in Eq. (6) each oscillator is instead only implicitly coupled to the other oscillators through the average phase.

c) In the limit of $N \to \infty$ we may, for each ω, interpret the oscillators as a continuum on the interval $-\pi < \theta < \pi$. Denote by $n(\theta, t)$ the concentration of oscillators with angle θ at time t. Use the dynamics of individual oscillators (6) to derive a continuity equation for $n(\theta, t)$.

Solution

The change of total concentration in a small interval $\delta\theta$ is given by the net flux $j(\theta, t) - j(\theta + \delta\theta, t)$ of concentration through the interval.

$$\frac{\partial}{\partial t} \int_{\theta}^{\theta+\delta\theta} \mathrm{d}\theta' n(\theta', t) = j(\theta, t) - j(\theta + \delta\theta, t) .$$

$$\Rightarrow \frac{\partial}{\partial t} n(\theta, t) = -\frac{\partial}{\partial \theta} j(\theta, t)$$

Here $j(\theta, t)$ is given by advection using the flow (6), $j = [\omega + Kr \sin(\psi - \theta)] n(\theta, \omega, t)$. Using this expression for j gives

$$\frac{\partial}{\partial t} n(\theta, t) = -\frac{\partial}{\partial \theta} [\omega + Kr \sin(\psi - \theta)] n(\theta, \omega, t)$$

d) Find a steady state solution (by setting $\frac{\partial n}{\partial t} = 0$) to the continuity equation you derived in subtask c) for the case of $r = 0$. Does your result correspond to your expectations?

Solution

When $r = 0$ and $\frac{\partial n}{\partial t} = 0$ we have

$$0 = -\omega \frac{\partial}{\partial \theta} n(\theta, \omega, t) ,$$

i.e. $n(\theta) = \text{const.} = N_\omega/(2\pi)$ where N_ω is the total number of oscillators with natural frequencey ω. A uniform distribution of angles is indeed what we expect for the incoherent state of oscillators when $r = 0$.