CHALMERS, GÖTEBORGS UNIVERSITET

EXAM for
COMPUTATIONAL BIOLOGY A

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

Time:	June 8, 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) Explain what a period-doubling bifurcation is. In what kind of biological models do you find them?

b) The Lotka-Volterra model is given by

$$\dot{N} = N(a - bP)$$
$$\dot{P} = P(cN - d)$$

where a, b, c, and d are positive constants. Discuss the limitations of this model and how it can be improved.

c) Explain the difference between stochastic and deterministic growth models. Under which circumstances is it better to use a stochastic model?

d) In the law of diffusion for Brownian motion the mean-square displacement is given by $\langle (x - x_0)^2 \rangle = 2Dt$. Discuss whether the diffusion constant D increases, decreases, or remains unchanged upon an increase of the system temperature, or upon an increase of the particle size.

e) Explain what a travelling wave is.

f) A simple model for disease spreading is the SIR model

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

Explain what it means to have an epidemic in this model.

g) Can the SIR model describe an endemic disease, i.e. a disease with a non-zero number of infectives in the long run? If not, suggest a model that may describe an endemic.

h) Explain how one can use linear filters to remove linear trends in a time series.

2. Discrete model for harvesting [2.5 points] Consider the following discrete model for a population of density u_τ at discrete times $\tau = 0, 1, 2, \ldots$

$$u_{\tau+1} = \frac{bu_\tau^2}{1+u_\tau^2} - Eu_\tau\,,$$

with $b > 2$ and $E > 0$.

a) Interpret the two terms on the right-hand side from the viewpoint of a model that describes regular harvesting of the population. Does the population show a linear growth rate? What is the stability of the steady state $u = 0$?

b) Show that there exists a threshold E_{m} such that when $E > E_{\mathrm{m}}$ no harvest can be obtained in the long run.

c) Determine the bifurcation that is obtained when E passes E_{m}, for example by sketching a cobweb plot.

d) For $0 < E < E_{\mathrm{m}}$, the model only has positive stable steady states u between two positive values $u_- < u^* < u_+$. Find analytical expressions for u_- and u_+. Hint: To simplify the calculation, it may be useful to sketch a cobweb plot.

3. Hypercycles [2.5 points] One example of a so called *hypercycle* for n molecules with concentrations $x_i(t)$, with $i = 1, 2, \dots, n$ is given by

$$\dot{x}_i = x_i \left(x_{i-1} - \sum_{j=1}^{n} x_j x_{j-1} \right) . \tag{1}$$

Assume periodic indices so that $x_0(t) = x_n(t)$ and assume $x_i(t) > 0$ for all i.

a) Consider the case $n = 2$ in Eq. (1). Derive the explicit equations for $\dot{x}_1$ and $\dot{x}_2$ in terms of x_1 and x_2.

b) Determine all relevant fixed points and their stability for $n = 2$.

c) Determine the long-term fate for all relevant initial conditions when $n = 2$. Hint: To come to a definite conclusion, it may simplify to change to the coordinates $x_\pm = x_1 \pm x_2$.

d) Now consider a general value of n. What is the long-term fate of the sum $N = \sum_{i=1}^{n} x_i$?

e) Explain the effect of the two terms $x_i x_{i-1}$ and $-x_i \sum_{j=1}^{n} x_j x_{j-1}$ in Eq. (1). Explain how the hypercycle may model molecules that are connected in a cyclic, autocatalytic manner.

4. Turing instability [2 points] Consider the following reaction-diffusion equation in one spatial dimension for two reactants $N_1(x, t)$ and $N_2(x, t)$:

$$\begin{aligned} \frac{\partial N_1}{\partial t} &= k_1 - k_2 + k_4 \frac{N_1}{N_2} + D_1 \frac{\partial^2 N_1}{\partial x^2} \\ \frac{\partial N_2}{\partial t} &= k_4 N_1^2 - k_3 N_2 + D_2 \frac{\partial^2 N_2}{\partial x^2} \end{aligned} . \tag{2}$$

a) Discuss a mechanism which may cause the reaction-diffusion system in Eq. (2) to form spatial patterns if $D_2 > D_1$.

b) Make Eq. (2) dimensionless by introduction of suitable dimensionless variables u, v, x', t' such that the dimensionless reaction-diffusion system becomes

$$\begin{aligned} \frac{\partial u}{\partial t'} &= \alpha + \frac{u}{v} + d \frac{\partial^2 u}{\partial x'^2} \\ \frac{\partial v}{\partial t'} &= u^2 - v + \frac{\partial^2 v}{\partial x'^2} \end{aligned} . \tag{3}$$

What are the expressions for α and d?

c) Find the condition on α for which the homogeneous steady state of Eq. (3) is stable.

Let $\delta u(x,t) \equiv u(x,t) - u^*$ and $\delta v(x,t) \equiv v(x,t) - v^*$ be small perturbations from the homogeneous steady state. In the lectures we showed that the ansatz

$$\begin{pmatrix} \delta u \\ \delta v \end{pmatrix} = e^{\lambda t + \mathrm{i}kx} \begin{pmatrix} \delta u_0 \\ \delta v_0 \end{pmatrix}$$

in Eq. (3) with small δu and δv gives rise to the following equation:

$$0 = [\lambda - \mathbb{K}] \begin{pmatrix} \delta u_0 \\ \delta v_0 \end{pmatrix} , \text{ where } \mathbb{K} = \mathbb{J}(u^*, v^*) - k^2 \begin{pmatrix} d & 0 \\ 0 & 1 \end{pmatrix} .$$

Here $\mathbb{J}$ is the Jacobian of the homogeneous system.

d) Assume that $\alpha = 1/2$. Analytically find the bifurcation point $d_\mathrm{c}(k_\mathrm{c})$ for which space-dependent perturbations first become unstable, i.e. for $d > d_\mathrm{c}$ all space-dependent perturbations are stable and for $d < d_\mathrm{c}$ at least one wave number k_c corresponds to unstable perturbations.

5. Kuramoto model [2 points] Consider a large 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

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

b) Give interpretations of the order parameters r and ψ in subtask a). Illustrate the distribution of oscillators when $r \approx 0$ and $r \approx 1$.

c) Consider the limit where $K \to \infty$ and assume that $0 < r < 1$ initially. What is the long term fate of the Kuramoto model in this limit? Which value does r approach?

d) What does it mean to do a mean field analysis of the Kuramoto model? What can the results of the mean-field analysis be used for?