CHALMERS, GÖTEBORGS UNIVERSITET

EXAM for
COMPUTATIONAL BIOLOGY A

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

Time:	June 12, 2019, at $08^{30} - 12^{30}$
Place:	Johanneberg
Teachers:	Kristian Gustafsson, 070-050 2211 (mobile), visits once around 15^{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) Consider the logistic equation for a population of size $N(t)$ with a time delay T:

$$\frac{\mathrm{d}N}{\mathrm{d}t}(t) = rN(t)\left(1 - \frac{N(t-T)}{K}\right).$$

Without doing any calculations, discuss the nature of the possible solutions to this equation i) without delay ($T = 0$), ii) with a small delay ($T \ll r^{-1}$), and iii) with a large delay ($T \gg r^{-1}$).

b) Consider a process where a substrate forms a product. How is this process different in a spontaneous reaction compared to an enzyme reaction?

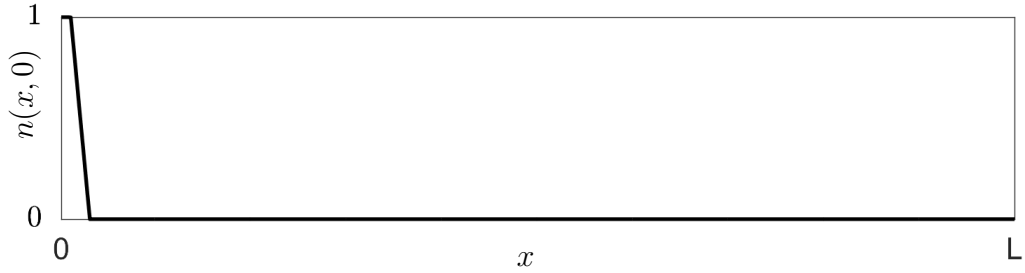
c) Explain the difference between stochastic and deterministic growth models. When is it better to use a stochastic model?

d) Explain what is meant by a Turing (diffusion driven) instability.

e) Why is it common to treat the total population size N as constant in the SIR model for disease spreading? For which types of diseases do you think a constant N is relevant?

f) What is meant by the 'order parameters' in the Kuramoto model? What do they quantify?

For subtasks g) and h), consider a concentration $n(x,t)$ in a bounded domain $0 \leq x \leq L$. At $t = 0$, $n(x,0)$ is unity at $x = 0$, decreases linearly to zero for small x, and stays at zero up to $x = L$, as illustrated below:



Assume that the concentration is governed by Fisher's equation:

$$\frac{\partial n}{\partial t}(x,t) = rn(x,t)(1 - n(x,t)) + D\frac{\partial^2 n}{\partial x^2}(x,t)\,,$$

with constant boundary condition at $x = 0$ and no-flux condition at $x = L$:

$$n(0,t) = 1\,, \qquad \frac{\partial n}{\partial x}(L,t) = 0\,.$$

Consider the following three cases for the parameters r and D:
i) $D = 0$ and $r = 1$; ii) $D = 1$ and $r = 0$; iii) $D = 1$ and $r = 1$.

g) Without doing any calculations, sketch the concentrations as $t \to \infty$ for the three cases i), ii) and iii).

h) Without doing any calculations, explain the difference in the dynamics for the cases with $D = 1$, i.e. cases ii) and iii).

2. Discrete and continuous logistic growth model [2 points] The discrete logistic growth model is given by

$$N_{\tau+1} = aN_\tau \left(1 - \frac{N_\tau}{C}\right) \tag{1}$$

where a, C are positive parameters and $\tau = 0, 1, 2, \ldots$ denotes discrete time.

a) Discuss how the model above is related to a time discretisation of a continuous logistic growth equation. How is a and C related to the growth rate r, carrying capacity K and the discretisation time step δt of the continuous model?

b) For which values of a and C is the discretised model a good approximation of the continuous model?

c) Find the positive fixed point of the discrete logistic map (1) and determine for which range of a the fixed point is stable.

d) Make a cobweb plot illustrating the dynamics of Eq. (1) for $2 < a < 3$.

3. Lotka-Volterra model [2 points] A simple model for predator prey interaction between two species of sizes N and P is the Lotka-Volterra model:

$$\begin{aligned} \dot{N} &= aN - bNP \\ \dot{P} &= cNP - dP \end{aligned}, \tag{2}$$

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

a) Explain the forms of the different terms in the Lotka-Volterra model (2).

b) Consider $a = b = c = d = 1$ in Eq. (2) and sketch the solution starting from $N(0) = 2$ and $P(0) = 1$ in the N-P plane. Also plot the solutions $N(t)$ and $P(t)$ against time t in a separate plot. You do not need to find an analytical solution, but the qualitative behavior of prey and predator sizes should be clear. Briefly explain the dynamics.

c) Identify one weakness of the Lotka-Volterra model in modelling a biological system.

d) One way to improve the Lotka-Volterra model is to modify the growth rate $\dot{N}$ in Eq. (2) to

$$\dot{N} = aN\left(1 - \frac{N}{K}\right) - \frac{bNP}{1 + N/B}\,,$$

where K and B are positive parameters. Explain the form of these modifications. What are the significance of K and B?

4. Model with spatially regulated fishing [2.5 points] Assume that fishing is regulated in a zone of width H from a country's shore (taken to be a straight line) and that outside of this zone over-fishing makes the population vanish. Consider the following model for the fish concentration $n(x,t)$:

$$\frac{\partial n}{\partial t} = rn\left(1 - \frac{n}{K}\right) - En + D\frac{\partial^2 n}{\partial x^2}\,, \tag{3}$$

where r,K and D are positive parameters, $0 < E < r$, and with boundary conditions

$$n(x = H, t) = 0\,, \qquad \frac{\partial n}{\partial x}(x = 0, t) = 0\,.$$

a) Briefly explain the different terms and parameters in this model. In particular explain the significance of the boundary conditions.

b) Introduce dimensionless variables $\tau = t/t_0$, $u = n/n_0$, $\xi = x/x_0$ and determine t_0, n_0 and x_0 such that Eq. (3) does not depend on any parameters in the dimensionless variables. What are the boundary conditions in these units?

c) Investigate the linear stability of the homogeneous steady state $u^* = 0$ by making a small perturbation $u(\xi, \tau) \approx 0 + \delta u(\xi, \tau)$ and keeping only first-order terms in δu. Using the ansatz $\delta u(\xi, \tau) = A \cos(k\xi) e^{\lambda \tau}$ with real parameters A, k and λ, find a condition on k such that the boundary conditions are satisfied.

d) Show that if $H < H_c = \frac{\pi}{2}\sqrt{\frac{D}{r-E}}$ the fishing zone is not sustainable, i.e. $u(\xi, \tau) = 0$ is stable.

5. Disease spreading in large but finite populations [2.5 points] Assume that a population consists of N (constant in time) individuals. Each individual is either infected by, or susceptible to a disease. Assume that recovered individuals once again become susceptible (SIS model).

a) In the lecture notes and the hand-ins a Master equation was derived that describes the probability ρ to observe n infected individuals. Discuss what it means that this Master equation has a 'quasi-steady state'.

An approximate solution for the quasi-steady state that is valid for large N can be found by an ansatz

$$\rho(I) = \exp\left[-NS_0(I) - S_1(I) - 1/NS_2(I) - \dots\right] ,$$

where $I = n/N$ is the ratio of infected individuals. To lowest order in N^{-1}, the dynamics of $I(t)$ and $p(t) = S_0'(I)$ was shown to follow Hamilton's equations

$$\begin{aligned} \dot{I} &= \beta I(1-I)e^p - \gamma I e^{-p} \\ \dot{p} &= -\beta(1-2I)(e^p - 1) - \gamma(e^{-p} - 1) . \end{aligned} \tag{4}$$

Here β and γ are positive parameters.

b) A disease is said to be endemic if it can sustain a finite number of infected individuals in the long run. Find a condition on the parameters β and γ for which the disease described by Eq. (4) is endemic in the limit $N \to \infty$ (corresponding to $p \to 0$).

c) In the endemic limit found in subtask b), find all biologically relevant fixed points of Eq. (4) that lies on either of the axes $I = 0$ or $p = 0$ and determine their stability. To speed up this calculation, it may be helpful to first evaluate the trace of the stability matrix (Jacobian) for general points (I, p) and to think about how the flow behaves along the axes $I = 0$ and $p = 0$.

d) In the endemic limit found in subtask b), the dynamics (4) has one additional biologically relevant fixed point (I^*, p^*) with $I^* > 0$ and $p^* < 0$. You can assume that this fixed point is a center.

Contrast the case $p = 0$ (corresponding to $N \to \infty$) and $p \neq 0$ (corresponding to large but finite N). In particular, discuss the implications of a finite population size for endemic diseases. It could be helpful to sketch the phase portrait for the dynamics in Eq. (4) for non-negative values of I.