CHALMERS, GÖTEBORGS UNIVERSITET

EXAM for
COMPUTATIONAL BIOLOGY A

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

Time:	March 21, 2019, at $14^{00} - 18^{00}$
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) Give an example of a biological system which is suitable to model using a time delay model.

b) What do we typically mean when we say a population size is 'small' or 'large'?

c) Assume a one-dimensional map $x_{n+1} = F(x_n)$ with a single stable fixed point x^* for $r < r_c$, where r is a system parameter. At $r = r_c$, the system undergoes a period-doubling bifurcation. Show that the eigenvalue of the second iterate of the map evaluated at the fixed point, $F(F(x^*))$, is equal to $+1$ at $r = r_c$.

d) In the first problem set you analyzed a time-delayed model with an Allee effect. Explain what the Allee effect is and give an example of a biological system where it may be important.

e) Consider the following chemical reaction

$$\mathrm{S} + \mathrm{E} \underset{\mathrm{k_{-1}}}{\overset{\mathrm{k_1}}{\rightleftharpoons}} \mathrm{SE} \xrightarrow{\mathrm{k_2}} \mathrm{P} + \mathrm{E}\,,$$

where k_{-1}, k_1, and k_2 are rate constants. Using the law of mass action, write down a dynamical system model for the change in concentrations of the chemicals.

f) Describe a possible mechanism that may explain morphogenesis such as patterns in animal coating.

g) Explain the difference between a quasi-steady state and a regular steady state. Give an example of a system with a quasi-steady state.

h) The Kuramoto model for N coupled oscillators with phases $\theta_1, \theta_2, \ldots \theta_N$ has the following time evolution

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

Here ω_i are random angular frequencies with a symmetric and unimodal (single peak) distribution $g(\omega)$. Discuss what is meant by drifting and phase-locked modes in a mean-field analysis of this model.

2. Interaction model with mutualism [2 points] A simple model for mutualistic interactions (symbiosis) between two species of sizes N_1 and N_2 is given by

$$\begin{aligned}
\frac{\mathrm{d}N_1}{\mathrm{d}t} &= r_1 N_1 \left(1 - \frac{N_1}{K} + \alpha \frac{N_2}{K}\right) \\
\frac{\mathrm{d}N_2}{\mathrm{d}t} &= r_2 N_2 \left(1 - \frac{N_2}{K} + \alpha \frac{N_1}{K}\right)
\end{aligned}$$

where r_1, r_2, K, and α are positive constants.

a) For the upper equation governing N_1, explain the role and meaning of the parameters r_1, K and α

b) Introduce dimensionless variables to reduce the number of parameters to a minimum. Write out your resulting dimensionless parameters in terms of the original parameters.

c) Consider the special case $\alpha = 1/2$ in this subtask. Locate the fixed point for which both population sizes are positive and investigate its stability. Discuss how the dimensional population sizes N_1^* and N_2^* at this fixed point compares to the positive steady state without interactions ($\alpha = 0$).

d) Investigate the long-term dynamics for the case $\alpha = 1$ and $r_1 = r_2$. Discuss what consequences your result has for the model.
Hint: It may be simpler to analyze the model by considering the coordinates $w_\pm = u_1 \pm u_2$, where u_1 and u_2 are the dimensionless population sizes.

3. Stochastic population model [2 points]

a) Write down an equation for how the probability $Q_N(t)$ to have a population of size N at time t changes in small time steps δt. Assume stochastic dynamics. At each time step δt any individual has the probability $b_1\delta t$ to give birth to one offspring and the probability $b_2\delta t$ to give birth to two offsprings.

b) By taking the limit $\delta t \to 0$, derive a differential equation in time (Master equation) for the probability in subtask a).

c) Show that in the limit of large N the average population size approaches a deterministic dynamics. What is the growth rate of the deterministic dynamics?

d) Explain the form of the growth rate you obtained in subtask c) in relation to the assumptions in subtask a).

e) Without doing any calculations, write down the growth rate in a model where, in addition to the conditions in subtask a), there are birth events with probability $b_3\delta t$ that result in three offsprings.

4. Reaction diffusion with density-dependent diffusion [2.5 points]
In spatial diffusion of insects, the diffusion sometimes depends on the density of the population. One example of a model taking this into account is

$$\frac{\partial n}{\partial t}(x,t) = rn(x,t)\left(1 - \frac{n(x,t)}{K}\right) + \frac{\partial}{\partial x}\left[D(n(x,t))\frac{\partial}{\partial x}n(x,t)\right] . \qquad (1)$$

Here $n(x,t)$ is the population density at position x and time t, r is a positive growth rate, K is the carrying capacity and $D(n(x,t))$ is a density-dependent diffusion coefficient. In what follows, assume $D(n(x,t)) = D_0 n(x,t)$, where D_0 is a positive constant.

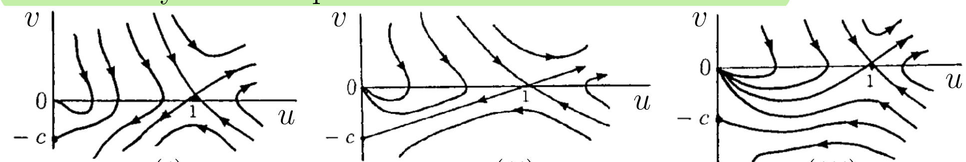
a) What is the dimensionality of D_0?

b) Introduce dimensionless units such that Eq. (1) can be written without any parameters.

c) Assume that n, x, t are the new dimensionless coordinates and that $n(x,t) = u(z)$ only depends on the combination $z = x - ct$. Starting from your dimensionless version of Eq. (1) derive an ordinary differential equation for $u(z)$.

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

e) The equations you derived in subtask d) should have a singularity at $u = 0$. This singularity can be regularized (you do not need to show nor consider this). The regularized dynamics has three fixed points at $(u^*, v^*) = (0, 0)$ (saddle point), $(u^*, v^*) = (1, 0)$ (saddle point) and $(u^*, v^*) = (0, -c)$ (stable non-linear node). Note that due to the singularity, trajectories reach the node $(u^*, v^*) = (0, -c)$ for finite values of z. The dynamics is plotted for three values of c below:



(i) (ii) (iii)

Discuss in which of the three cases travelling wave solutions are possible and sketch the wave profiles (as functions of z) for these cases.

5. Disease spreading with vaccination [2.5 points] A simple model for disease spreading is the following modified SIR model with the dynamics

$$\begin{aligned} \dot{S} &= (1-p)b(S+I+R) - \beta SI - dS \\ \dot{I} &= \beta SI - \alpha I - dI \\ \dot{R} &= pb(S+I+R) + \alpha I - dR\,. \end{aligned} \tag{2}$$

Here S is the number of susceptibles, I is the number of infectives, and R is the number of immune individuals (recovered or vaccinated individuals). The parameters b, d, β, α are positive, and p is the ratio of individuals that are vaccinated at birth, $0 \le p \le 1$.

a) Give brief explanations of the different terms in Eq. (2). Does the model apply to a disease that is likely to be transmitted from the mother to the baby upon birth? Does the model apply to a deadly disease?

b) Find a condition on the model parameters such that the total population size $N = S + I + R$ is constant.

c) In what follows, consider the special case $b = d = 1$ and $\alpha = 99$, leaving two model parameters β and p. Consider first the case of full vaccination, $p = 1$, and investigate the long-term behaviour of the system (2). Give an explanation of the result.

d) Use the parameters of subtask c) (with general p) to find a condition on the vaccination ratio p below which the disease may become endemic (non-zero number of infectives in the long run).