

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 ≥ 15 grade 3; ≥ 20 grade 4; ≥ 25 grade 5,

GU ≥ 15 grade G; ≥ 23 grade VG.

1. Short questions [3 points] For each of the following questions give a concise answer within a few lines per question.

- Give an example of a biological system which is suitable to model using a time delay model.
- What do we typically mean when we say a population size is ‘small’ or ‘large’?
- 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 $r = r_c$.
- 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.
- Consider the following chemical reaction



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 $\theta_1, \theta_2, \dots, \theta_N$ 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

$$\begin{aligned} \frac{dN_1}{dt} &= r_1 N_1 \left(1 - \frac{N_1}{K} + \alpha \frac{N_2}{K} \right) \\ \frac{dN_2}{dt} &= r_2 N_2 \left(1 - \frac{N_2}{K} + \alpha \frac{N_1}{K} \right) \end{aligned}$$

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 $\delta t \rightarrow 0$, 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]

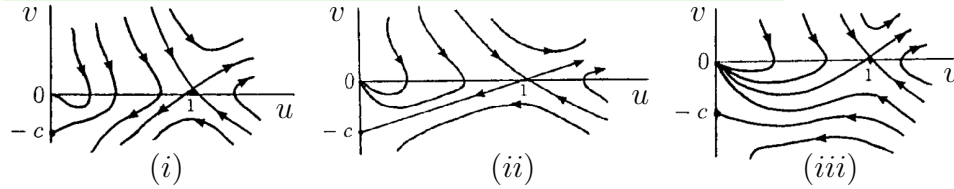
In spatial diffusion of insects, the diffusion sometimes depends on the density of the population. One example of a model taking this into account is

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

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:



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, $0 \leq p \leq 1$.

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