CHALMERS, GÖTEBORGS UNIVERSITET

EXAM for
COMPUTATIONAL BIOLOGY A

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

Time:	March 15, 2018, 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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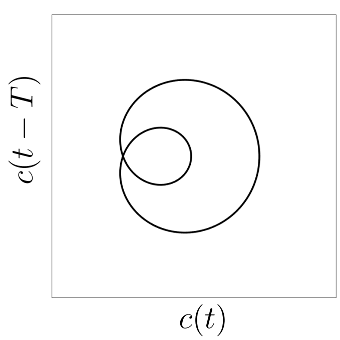
1. Short questions [3 points] For each of the following questions give a concise answer within a few lines per question.

a) When we analyze growth models we often use dimensionless units. Explain what the advantage of using dimensionless units is.

b) Consider a system with a single time delay T for the concentration c:

$$\dot{c} = f(c(t), c(t-T)) .$$

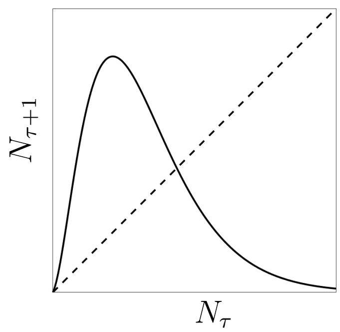
The delay embedding below shows an example of $c(t-T)$ against $c(t)$. But in one-dimensional dynamical systems without time delay, the existence and uniqueness theorem states that trajectories cannot cross. Explain why the curves may cross in the delay embedding below.



c) Consider a discrete growth model for a single species of population size N:

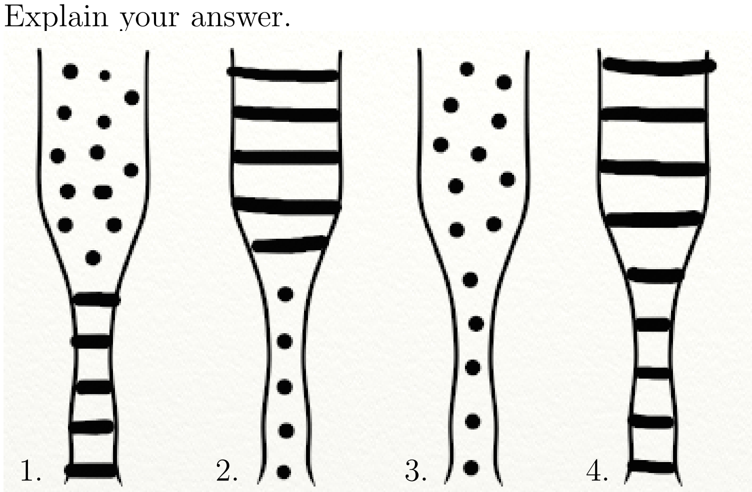
$$N_{\tau+1} = F(N_\tau)\,.$$

The figure below shows a particular choice of the map F (solid line) and the curve $N_{\tau+1} = N_\tau$ (dashed line). The scales of the axes are equal. Classify all fixed points in this system with respect to their stability and whether they show oscillations.



d) Explain what Brownian motion is. How does it differ from population diffusion of biological species?

e) Which (could be more than one) of the patterns below are consistent with being formed in a Turing instability (diffusion driven instability)? Explain your answer.



f) Explain what a metapopulation is. What is the rescue effect?
Note: The theory for this problem is not covered in the course this year

g) Consider a number N of coupled oscillators with phases $\theta_1, \theta_2, \ldots \theta_N$ with the following time evolution (Kuramoto model)

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

Explain the assumptions made to derive Eq. (1).

h) Discuss and contrast the effects of measurement noise and dynamical noise on a time series which is generated by linear (Malthus) decay (negative growth rate).

2. A model for competition with Neanderthals [2.5 points] Construct and analyze a mathematical model for competition between Neanderthal man (with population size N) and Early modern man (with population size E). Assume that the population sizes are large enough for a continuous model to apply. Assume further that no reproduction occurs between the two species. Assume that both species show linear (Malthus) growth for small population sizes, with equal birth rate, b, and with different death rates. The death rate of Neanderthal man is d (assume that $d < b$). Due to better survival rate, the death rate of Early modern man is sd, where s is a parameter taking a value in the range $0 < s < 1$.
Include competition for resources into the model. Assume that both species are equally competitive, i.e. assume that the per capita growth rates for both species are reduced proportional to the total number of competing individuals.

a) Using the assumptions above derive growth equations for the population sizes N and E.

b) Analyze your model by finding its biologically relevant fixed points and their linear stability. Discuss the possible long-term behaviours of the system.

c) By rewriting your growth model in terms of logarithmic derivatives:

$$\frac{\mathrm{d}}{\mathrm{d}t}\ln E = \dots$$
$$\frac{\mathrm{d}}{\mathrm{d}t}\ln N = \dots$$

it should be straightforward to find a solution for N in terms of E and t. Write down the relation you find between N, E and t.

d) Historical data from the time of Neanderthals show that the lifetime of an individual (both Neanderthal man and Early modern man) was approximately 35 years and that the time to extinction, $T_{\text{ext.}}$, of the Neanderthals upon contact with Early modern man was $T_{\text{ext.}} \approx 10500$ years.

Use these historical data in your model to roughly estimate the parameter s. Since the population never reaches zero in a continuous system, you can approximate $T_{\text{ext.}}$ as the time where N/E reaches five percent of its initial value (it may be helpful to approximate five percent by $0.05 \approx e^{-3}$). Interpret and discuss the value of s you find.

3. Harvesting strategies [2 points] A simple continuous growth model with harvesting is given by

$$\dot{N} = rN\left(1 - \frac{N}{K}\right) - Y(N)\,.$$

Here N is the size of the population, r and K are positive constants, and the yield $Y(N)$ denotes removal rate of the population due to harvesting. A good harvesting strategy (choice of $Y(N)$) is a strategy that gives a large yield Y in the long run, while also allowing the system to quickly recover from perturbations.

a) Consider the case $Y(N) = EN$, where $0 < E < r$ is a constant. Determine the long-term yield of the system. What is the maximal long-term yield?

b) Redo the analysis in subtask a) for the case $Y(N) = DN^2$, where D is a positive constant.

c) Discuss which of the two harvesting strategies in subtasks a) and b) is better. Explain which properties of this strategy makes it better. To come to a definite conclusion, it may be a good idea to, for each of the two strategies, consider the recovery time due to linear perturbations.

4. Spirals in reaction diffusion equations [2 points]

a) Give three examples where reaction-diffusion processes are of importance in mathematical models of biological systems.

b) Typical solutions to reaction-diffusion equations are travelling waves and spiral waves. A typical ansatz for the phase of a simple rotating spiral is

$$\phi(r, \theta, t) = \Omega t \pm m\theta + \psi(r)\,, \tag{2}$$

where ϕ is the phase, t is time, r and θ are the radial and angular coordinates in a polar coordinate system, Ω is a constant parameter, m is a positive integer, and $\psi(r)$ is some function of r.

Explain what is meant by a 'phase' and a 'wave front'.

Give interpretations of Ω, m and $\psi(r)$ in Eq. (2).

c) Sketch the wave fronts for the following set of parameters at $t = 0$:

$$\psi(r) = r\,, \qquad m = 2$$

d) Discuss how Eq. (2) could be applied in the context of reaction diffusion equations.

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

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

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

$$\begin{aligned} \dot{I} &= \beta I(1-I)e^{p} - \gamma I e^{-p} \\ \dot{p} &= -\beta(1-2I)(e^{p}-1) - \gamma(e^{-p}-1)\,. \end{aligned} \tag{3}$$

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. (3) 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. (3) 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 (3) 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 $p > 0$ (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. (3) for non-negative values of I.