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T VI: Nonlinear Dynamics and Pattern formation

(Prof. E. Frey)

Problem set 1: From models to dynamic equations; bifurcations

Aufgabe 1 *Dilution of proteins due to cell growth*

A single bacteria at time $t = 0$ has a volume V_0. After a time interval T_D, the doubling time, the cell grows and devides into two cells, each of volume V_0; after another interval T_D, there are four cells, and so on.

a) Show that the combined volume of cells at time t may be written as: $V(t) = V_0 \exp(\gamma t)$. Derive γ in terms of T_D.

b) The protein P is created at some production rate $\kappa(t)$, so the total number of proteins n_p of the protein P satisfies: $\dot{n}_p = \kappa(t)$. Show that the protein's concentration $c_p = n_p/V$ satisfies: $\dot{c}_p = V^{-1}\kappa(t) - \gamma c_p$.
Discuss the origin of the decay term.

c) Extend the equation above for a term which accounts for the activity of proteinases; these are molecules destroying the proteins. Their impact on the systems is equal to the following effective chemical reaction: $P \to \phi$.

Nevertheless, proteins are constructed from mRNA, which is in turn replicated from the DNA.
DNA $\to$ mRNA $\to$ Proteins .

d) Ignoring backwards reactions, which assumption is required to ignore the fact that proteins are embedded in a reaction chain?

Aufgabe 2 *A model of a fishery*

a) Recall the logistic growth equation:

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

Explain the meaning of each term. What is the biological assumption of a constant carrying capacity?

Consider a population of N fishes that is assumed to grow logistically with growth rate r and carrying capacity K.

b) Extend the logistic growth by a term which accounts for a constant harvesting denoted by H which is independent of the population size N. The following equation provides an extremely simple model of a fishery.

c) Show that the system can be rewritten in dimensionless form as

$$\frac{dx}{d\tau} = x(1-x) - h,$$

for suitably defined dimensionless quantities x, τ, and h.

d) Find the fixed points and plot the velocity fields for different values of h.

e) Show that a bifurcation occurs at a certain value h_c, and classify this bifurcation.

f) Discuss the long-term behavior of the fish population for $h < h_c$ and $h > h_c$, and give the biological interpretation in each case.

A constant harvesting rate is unrealsitic.

g) Think of a modification of the harvesting term concerning the following 3 respects:
i.) $N = 0$ should be a fixpoint independent of the parameters, ii.) harvesty should be harder if fishes are rare, iii.) for quasi-infinite fishes, the harvesty rate approaches the constant H (only a limited amount of ships are available).

Problem 3 *Michaelis-Menten equation with reversible inhibition*

The kinetics of the following simple enzymatic reaction (E: enzyme, S: substrate, ES: enzyme-substrate complex, P: product)

$$E + S \underset{\lambda_b}{\overset{\lambda_f}{\rightleftarrows}} ES \overset{\lambda_p}{\to} E + P \tag{1}$$

is captured by the Michaelis-Menten equation

$$\frac{d[P]}{dt} = \frac{[S]}{K_M + [S]}\, v_{\max}, \tag{2}$$

which relates the rate of production $d[P]/dt$ to the amount of available substrate $[S]$. Here square brackets denote concentrations.

a) Assuming the total amount of enzymes to be constant (*i.e.* $[E_T] = [E] + [ES] = \text{const.}$), as well as $d[ES]/dt = 0$ (both assumptions are justified if $\lambda_f, \lambda_b \gg \lambda_p$), derive the Michaelis-Menten equation and determine $v_{\max}$ and K_M as functions of the rates λ_i ($i \in \{f, b, p\}$) and the total total amount of enzymes $[E_T]$.

In realistic cases the presence of inhibitors (I) may alter the kinetics of enzymatic reactions. Irreversible inhibitors combine with or destroy a functional group of an enzyme that is essential for the enzyme's activity or for a particular stable noncovalent association. In contrast reversible inhibitors can be removed so that the enzyme's function is fully recovered. Among different kinds of reversible inhibitors we shall focus on so called *competitive* and *uncompetitive* inhibitors, whose actions are described by the chemical equations

$$E + I \rightleftharpoons EI$$

for competitive and

$$ES + I \rightleftharpoons ESI$$

for uncompetitive inhibitors. Here K_I and K_I' are given by

$$K_I = \frac{[E][I]}{[EI]}, \quad K_I' = \frac{[ES][I]}{[ESI]}.$$

Either of these two reactions takes place simultaneously with the actual enzymatic reaction (1).

b) Derive the Michaelis-Menten equation for competitive and for uncompetitive inhibition. For the sake of greater clarity abbreviate $\alpha \equiv (1 + [I]/K_I)$ and $\alpha' \equiv (1 + [I]/K_I')$.

c) Make sure to bring the corresponding Michaelis-Menten equations to the form (2) and discuss the effect of competitive and uncompetitive inhibition on the constants K_M and $v_{\max}$.

d) Write down $(d[P]/dt)^{-1}$ as a function of $[S]^{-1}$ (Lineweaver-Burke equation) and use it to illustrate the effect of competitive and uncompetitive inhibition graphically.

Problem 4 *Model of an epidemic*

In pioneering work in epidemiology, Kermack and McKendrick proposed the following simple model for the evolution of an epidemic. Suppose that the population can be divided into three classes: $x(t) =$ number of healthy people, $y(t) =$number of sick people, $z(t) =$number of dead people. Assume that the total population remains constant in size, except for death due to the epidemic. Hence, we assume that the epidemic evolves so rapidly that we can ignore the slower changes in the population due to birth, emigration or death by other causes. Then the model is:

$$\dot{x} = -kxy, \tag{3}$$

$$\dot{y} = kxy - ly, \tag{4}$$

$$\dot{z} = ly, \tag{5}$$

where k and l are positive constants. The equations are based on two assumptions:

1. Healthy people get sick at a rate proportional to the product of x and y. This would be true if healthy and sick people encounter each other at a rate proportional to their numbers, and if there were a constant probability that each such encounter would lead to transmission of the disease.

2. Sick people die at a constant rate l.

The goal of this problem is to reduce the model, which is a *third-order system* to a first-order system that can be analyzed by the methods introduced so far.

a) Show that $x + y + z = N$, where N is constant.

b) Use the $\dot{x}$ and $\dot{z}$ equation to show that $x(t) = x_0 \exp(-kz(t)/l)$, where $x_0 = x(0)$.

c) Using the results derived in a) and b) show that z satisfies the first-order equation $\dot{z} = l[N - z - x_0 \exp(-kz/l)]$ and that this equation can be nondimensionalized to

$$\frac{du}{d\tau} = a - bu - e^{-u},$$

by appropriate choice of u, τ, a and b.

d) Determine the number of fixed points $u^\star$ graphically and classify their stability. What kind of bifurcation do you observe?

e) Show that the maximum of $\dot{u}(t)$ occurs at the same time as the maximum of both $\dot{z}(t)$ and $y(t)$. Hence, at the peak of the epidemic there is a maximum of sick people and the highest daily death rate.

f) Show that if $b < 1$, then $\dot{u}(t)$ is increasing at $t = 0$, reaching a maximum at some time and eventually decreasing to 0. In an epidemic things get worse before they get better. On the other hand show that no peak exists for $b > 1$. Hence, $b = 1$ is a *threshold* for an epidemic to occur. Give a biological interpretation of this condition.