

# Mathematical Models, Analysis and Simulation

## Part I, Fall 2009.

November 3, 2009

### Homework 5, Enzymatic Reactions, Max. Score: 6 or 7, Deadline Sun, Nov. 8

Most chemical reactions in biology are catalyzed by enzymes. A catalyst is a chemical substance which influences the speed of chemical reactions by either accelerating or slowing down the reaction by changing activation energies. Even if the catalyst is involved in the reactions, at the end it neither did change nor is it part of the reaction products. In inorganic chemistry the catalyst is often neglected when describing catalytic reactions. The situation is different in bio-chemical reactions because the number of enzyme molecules is restricted as well as their chemical activity. Therefore, one has to include the kinetics of the catalyst when mathematically modelling enzymatic reactions. A more detailed description can be found in the accompanying excerpt from C.C. Lin, L.A. Segel, *Mathematics Applied to Deterministic Problems in the Natural Sciences*.

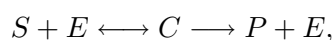
**1. (1.5)** Let us start with a simple problem in order to repeat the basics. Consider the scalar initial value problem

$$\varepsilon \dot{x} = (t - 1)x, \quad x(0) = 1.$$

- a) Find the exact solution  $x(t, \varepsilon)$ .
- b) Show that the outer solution  $X(t, \varepsilon)$  for  $0 < t < 1$  is asymptotically trivial.
- c) Determine  $x(1, \varepsilon)$  and its asymptotic size.
- d) Explain, on symmetry grounds, why  $x(2, \varepsilon) = 1$ .
- e) Show that  $x(t, \varepsilon)$  becomes exponentially large for  $t < 0$  and  $t > 2$ .

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Schematically, an enzymatic reaction can be described by,



where  $S$  is some substrate,  $E$  the enzyme, and  $C$  the enzyme-substrate molecule, or complex.  $P$  is the product. Let  $s$  and  $c$  denote the scaled concentrations of  $S$  and  $C$ , respectively.

After a careful scaling of the chemical parameters (cf. the provided copies), the kinetics of the system can be described by

$$\dot{s} = -s + (s + \kappa - \lambda)c, \quad (1)$$

$$\varepsilon \dot{c} = s - (s + \kappa)c, \quad (2)$$

where  $\kappa$  and  $\lambda$  are positive constants of order 1 while  $\varepsilon$  fulfills  $0 < \varepsilon \ll 1$ . Here,  $\dot{s} = ds/dt$  and  $\dot{c} = dc/dt$ . The initial values at  $t = 0$  are given by

$$s(0) = 1, \quad c(0) = 0. \quad (3)$$

This is a singular perturbation problem. Your task will be to compute a uniform  $O(\varepsilon)$  approximation to the solution of the problem (1), (2), (3).

The reduced problem is

$$\dot{S}_0 = -S_0 + (S_0 + \kappa - \lambda)C_0, \quad (4)$$

$$0 = S_0 - (S_0 + \kappa)C_0. \quad (5)$$

Since  $0 \leq c(t) \leq 1$  for all  $t \geq 0$ , (4) indicates that we should expect an initial layer near  $t = 0$ . Therefore, the following ansatz for asymptotic expansion is justified:

$$s(t, \varepsilon) = S(t, \varepsilon) + \varepsilon \xi(\tau, \varepsilon), \quad (6)$$

$$c(t, \varepsilon) = C(t, \varepsilon) + \eta(\tau, \varepsilon), \quad (7)$$

where  $\tau = t/\varepsilon$  is the stretched time. Moreover,

$$S(t, \varepsilon) \sim S_0(t) + \varepsilon S_1(t) + \varepsilon^2 S_2(t) + \dots, \quad C(t, \varepsilon) \sim C_0(t) + \varepsilon C_1(t) + \varepsilon^2 C_2(t) + \dots$$

are the regular expansions of the outer solutions  $S(t, \varepsilon)$  and  $C(t, \varepsilon)$ , respectively, while

$$\xi(t, \varepsilon) \sim \varepsilon \xi_1(t) + \varepsilon^2 \xi_2(t) + \dots, \quad \eta(t, \varepsilon) \sim \eta_0(t) + \varepsilon \eta_1(t) + \varepsilon^2 \eta_2(t) + \dots$$

are the asymptotic expansions of the inner solutions  $\varepsilon \xi(\tau, \varepsilon)$  and  $\eta(\tau, \varepsilon)$  which vanish exponentially for  $\tau \rightarrow \infty$ .

**2. (1.0)** Show that the solution of the reduced problem (4), (5) will fail to satisfy the initial condition  $C_0(0) = 0$ !

*Note:* The reaction rate in the differential equation for  $S_0$  has an important chemical interpretation. This reaction rate includes saturation effects. In the bio-chemical literature, it is known as the *Michaelis-Menten kinetics*.

**3. (1.0)** Because of

$$\frac{ds}{dt} = \frac{dS}{dt} + \frac{d\xi}{d\tau}, \quad \frac{dc}{dt} = \frac{dC}{dt} + \frac{1}{\varepsilon} \frac{d\eta}{d\tau}$$

it holds

$$\begin{aligned} \frac{d\xi}{d\tau} &= \frac{ds}{dt} - \frac{dS}{dt} = -(S + \varepsilon\xi) + (S + \varepsilon\xi + \kappa - \lambda)(C + \eta) + S - (S + \kappa - \lambda)C, \\ \frac{d\eta}{d\tau} &= \varepsilon \left( \frac{dc}{dt} - \frac{dC}{dt} \right) = S + \varepsilon\xi - (S + \varepsilon\xi + \kappa)(C + \eta) - S + (S + \kappa)C. \end{aligned}$$

By letting  $\varepsilon \rightarrow 0$  show that  $\eta_0$  fulfils

$$\frac{d\eta_0}{d\tau} = -(1 + \kappa)\eta_0, \quad \eta_0(0) = -C_0(0) = \frac{-1}{1 + \kappa}.$$

Solve this equation!

**4. (2.0)** If your computations are correct, then it holds

$$\begin{aligned} s(t, \varepsilon) - S_0(t) &= O(\varepsilon), \\ c(t, \varepsilon) - (C_0(t) + \eta_0(t/\varepsilon)) &= O(\varepsilon) \end{aligned}$$

uniformly on every bounded interval. Perform numerical computations, e.g. in `Matlab`, for  $\varepsilon = 0.1$  and  $\varepsilon = 0.01$  on, say  $t \in [0, 1]$ , and compare  $s(t, \varepsilon)$  with  $S_0(t)$  and  $c(t, \varepsilon)$  with  $C_0(t) + \eta_0(t/\varepsilon)$ , respectively.

**5. (0.5)** It is interesting to look at the asymptotic behaviour for very small and very large values of  $t$ . For very small values of  $t$ ,  $S_0(t)$  can be approximated by a Taylor expansion,

$$S_0(t) = S_0(0) + t\dot{S}_0(0) + \dots$$

Do it!

**6.\* (1.0)** How does  $S_0(t)$  behave for very large times?