Physical Modelling of Complex Systems: Assignment 3

Thibeau Wouters

March 20, 2021

Contents

1 Linear example of quasi steady-state approximation

When dealing with N coupled first-order differential equations, one can use the so-called *quasi-steady-state approximation* (QSSA). This approximation can be applied if one variable evolves much faster than the others. Let us suppose that $x_1(t)$ is this 'fast' variable. We take then $\dot{x}_1 = 0$, from which one obtains $x_1(t)$ as function of the other $N-1$ variables. The procedure is known in mathematics as singular perturbation theory.

As an example of this method, we consider the following system of linear differential equations

$$\begin{cases} \dot{x} &= -3x + y \\ \dot{y} &= 100(2x - y) \end{cases}, \tag{1.1}$$

with initial conditions $x(0) = 1$ and $y(0) = 0$. The fast variable can be identified by looking at a plot of the solutions, obtained via numerically solving the above set of differential equations as in the previous assignment. Figure 1.1 below shows the solutions for the given initial conditions. It is clear that y is the fast changing variable in this scenario.

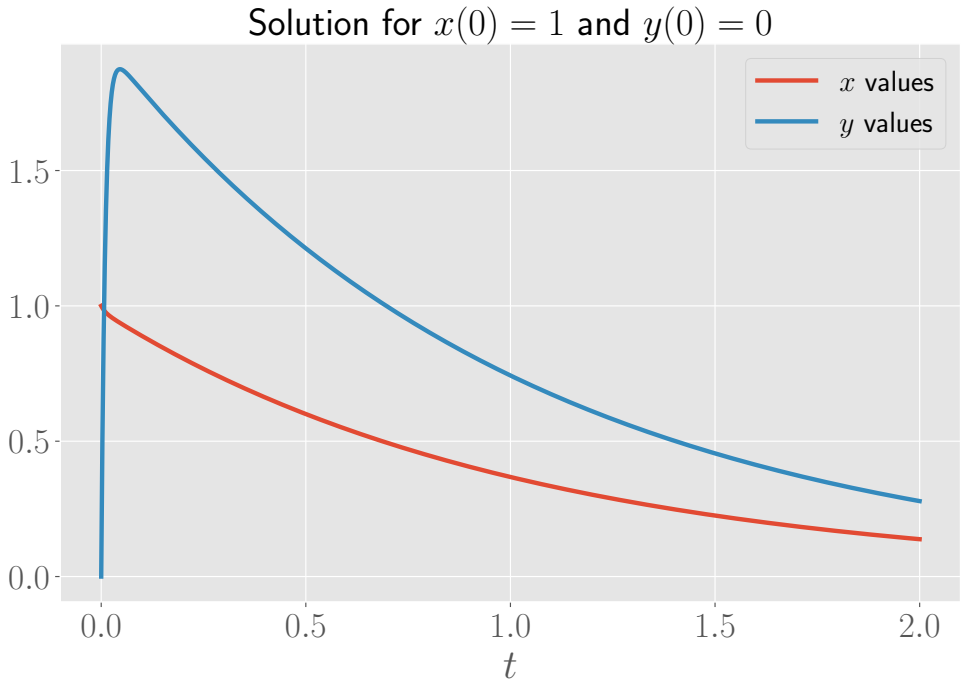

Figure 1.1: Solution to the set of differential equations (1.1) for initial conditions $x(0) = 1$ and $y(0) = 0$. From this, we can identify that y is the fast variable.

We now rewrite the system of differential equations in a matrix form

$$\dot{\Omega}(t) = M\Omega(t)\,, \quad \Omega(t) = \begin{pmatrix} x(t) \\ y(t) \end{pmatrix}\,, \tag{1.2}$$

where M is a 2×2 matrix. The system can be solved exactly, and the solution can be expressed in terms of the eigenvectors and eigenvalues of M. to do (facultative)

We now apply the QSSA to the set of differential equations, by setting $\frac{\mathrm{d}y}{\mathrm{d}t} = 0$. This allows us to express $y(t)$ in function of $x(t)$, as was our claim above. Indeed, from equation (1.1) we see that in the QSSA we have $y = 2x$. We can reproduce the Figure 1.1, but with an additional plot sowing the curve $y_{QSSA}(t) = 2x(t)$. The result is shown in Figure 1.2 below, with the QSSA shown as a grey dashed line.

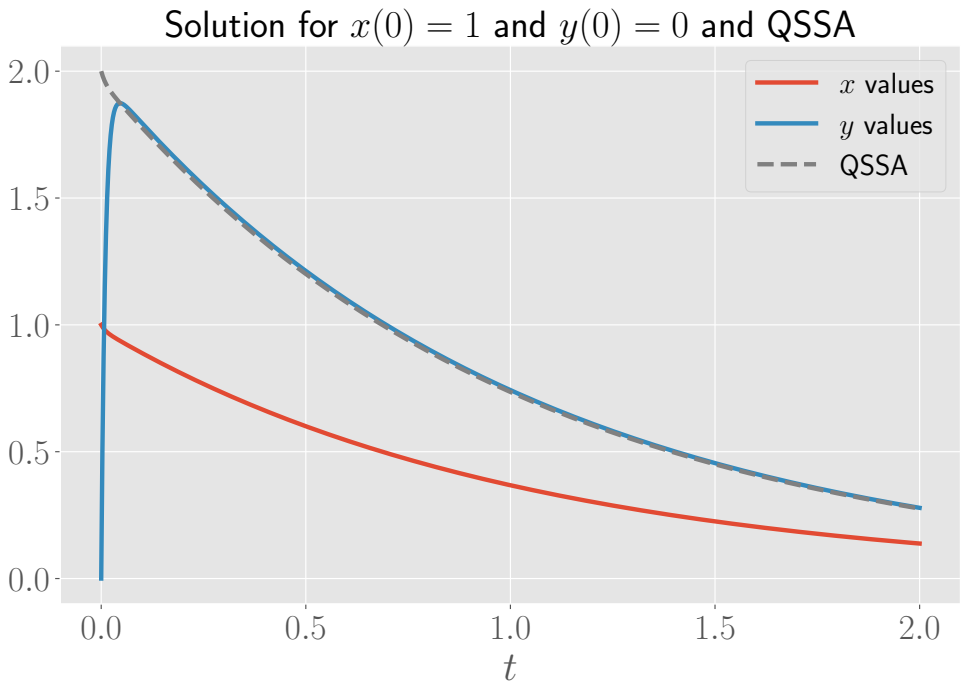

Figure 1.2: Solution to the system of differential equations (1.1) for initial conditions $x(0) = 1$ and $y(0) = 0$, along with the curve showing the QSSA $y = 2x$.

We see that approximation is very close to the exact (i.e., without the QSSA) solution for almost all values of t. However, for small t, the fast variable is varying much, and the approximation is not close at all. Hence we can conclude that the QSSA is a method to deduce the long time behaviour of fast variables and does not provide an accurate description for times $t \approx 0$.

2 Enzymatic degradation

In many situations a chemical X is degradated, meaning that it breaks into fragments which do not participate to the reactions anymore. Spontaneous degradation of X, i.e. a reaction $X \to \emptyset$ is described in the mass action kinetics by a term $-\alpha x$, where x is the concentration of X, and α the degradation rate. Synthesis and degradation of a chemical are described by the equation

$$\frac{\mathrm{d}x}{\mathrm{d}t} = \beta - \alpha x\,, \tag{2.1}$$

where β is the creation rate, which can eventually depend on other chemical concentrations. For the time being, we take β as a constant.

We consider here a different type of degradation due to the effect of an enzyme E on X. The enzymatic degradation is described by the following reactions

$$E + X \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} EX \xrightarrow{k'} E\,, \tag{2.2}$$

which describe binding of X to the enzyme E and formation of a complex EX, through a reversible reaction, followed by the irreversible degradation of X. Once degradation has occured, the free enzyme is released. For clarity, we will from now on write C (for 'complex') instead of EX.

We will first write down the system of differential equations corresponding to the above scenario. For this, we write the chemical reactions in equation (2.2) in separate chemical reactions.

$$E + X \xrightarrow{k_1} C \tag{2.3}$$

$$C \xrightarrow{k_{-1}} E + X \tag{2.4}$$

$$C \xrightarrow{k'} E\,. \tag{2.5}$$

To find the differential equations governing these chemical reactions, we use mass action kinetics. Define

$$x \equiv [x]\,, \quad e \equiv [e]\,, \quad c \equiv [c]\,. \tag{2.6}$$

Then we find

$$\begin{cases} \dot{e} &= -k_1 ex + (k_{-1} + k')C \\ \dot{x} &= -k_1 ex + k_{-1} c \\ \dot{c} &= k_1 ex - (k_{-1} + k')c \end{cases}\,. \tag{2.7}$$

As expected, not all these differential equations are independent. Indeed, since X is the only chemical which exhibits degradation, the sum of the concentration of E and C should be fixed. This is verified by looking at equation (2.7), which shows that

$$\frac{\mathrm{d}(e+c)}{\mathrm{d}t} = 0\,. \tag{2.8}$$

Therefore, we can write $e + c = e_0 \equiv e(0)$ and eliminate e from the above equations. This gives the equivalent set of differential equations

$$\begin{cases} \dot{x} &= -k_1 e_0 x + (k_1 x + k_{-1})c \\ \dot{c} &= k_1 e_0 x - (k_1 x + k_{-1} + k')c \\ e + c &= e_0 \end{cases}\,. \tag{2.9}$$

We will now apply the QSSA, assuming that the complex is rapidly formed and hence c is the fast variable. Therefore, we are allowed to put $\dot{c} = 0$. Then we find that

$$c = \frac{k_1 e_0}{k_1 x + k_{-1} + k'} x = \frac{e_0}{x + K_m}, \quad K_m \equiv \frac{k_{-1} + k'}{k_1}\,, \tag{2.10}$$

where K_m is the so-called Michaelis-Menten constant. Substituting this result for c back into the equation of $\dot{x}$, and doing some straightforward algebraic manipulations, we find

$$\dot{x} = \frac{-k' e_0 x}{x + K_M} \,. \tag{2.11}$$

We see that in this approximation, the equation for $\dot{x}$ containts a degradation term which is different from the degradation term in equation (2.1), and can be called *enzymatic degradation*. In Figure 2.1 below, we make a plot of this enzymatic degradation curve. As is already clear from the equation in (2.11), this curve has saturation and becomes approximately constant for large x. The concentration of the complex has the same feature and also has a plateau for large x, as seen from equation (2.10). The explanation is that for a large concentration of x, all enzymes are bound to the substrate chemicals X. Since the reaction needs an enzyme to occur, there are no additional reactions occurring unless an enzyme becomes free again and available to link with another substrate chemical. Hence the formation of complexes does not speed up beyond this point.

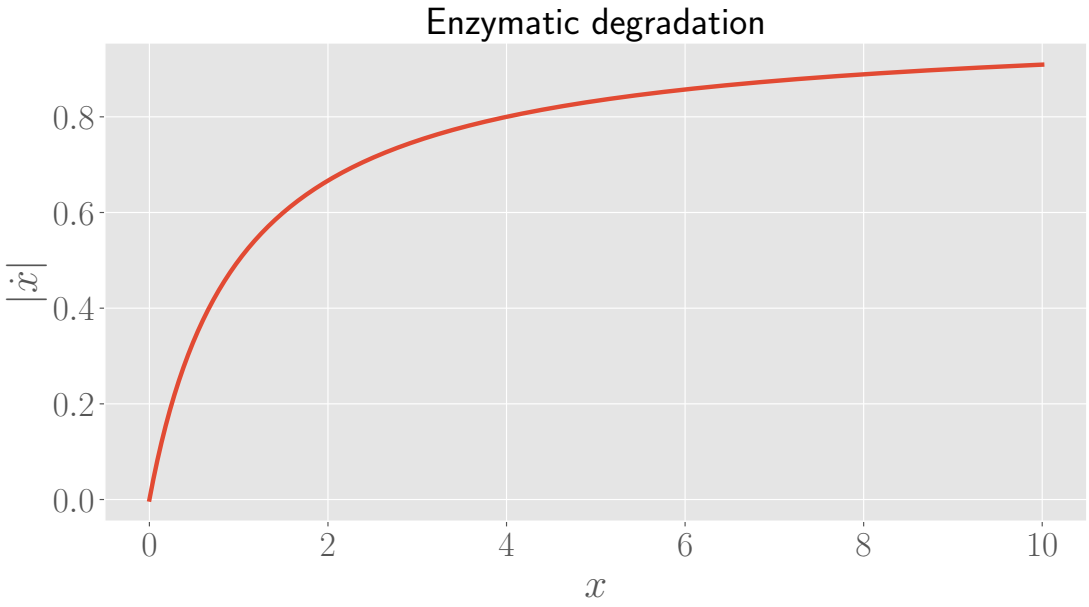

Figure 2.1: Plot of the absolute value of the enzymatic degradation curve, defined in equation (2.11), for $k' = e_0 = K_m = 1$.

3 Two subunit enzyme

We consider an enzyme which is formed by two subunits and which we denote as EE. Each subunit is capable of transforming a substrate S into a product P. The reactions are

$$EE + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} EES \tag{3.1}$$

$$EES \xrightarrow{k_3} EE + P \tag{3.2}$$

$$EES + S \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} SEES \tag{3.3}$$

$$SEES \xrightarrow{k_4} EES + P\,. \tag{3.4}$$

For notational simplicity, we will denote the complex EES by C_1 and the complex SEES by C_2. Define $s \equiv [s]$, $e \equiv [e]$, $c_1 \equiv [EES]$, $c_2 \equiv [SEES]$ and $p = [P]$. The system of equations governing the reactions is

$$\begin{cases} \dot{s} &= -k_1 es + k_{-1} c_1 + k_{-2} c_2 - k_2 c_1 s \\ \dot{e} &= -k_1 es + (k_{-1} + k_3) c_1 \\ \dot{c}_1 &= k_1 es - (k_{-1} + k_3) c_1 - k_2 c_1 s + (k_{-2} + k_4) c_2 \\ \dot{c}_2 &= k_2 c_1 s - (k_{-2} + k_4) c_2 \\ \dot{p} &= k_3 c_1 + k_4 c_2 \end{cases}\,. \tag{3.5}$$

As before, we have a conservation equation

$$\frac{\mathrm{d}(e + c_1 + c_2)}{\mathrm{d}t} = 0\,, \tag{3.6}$$

from which we find $e + c_1 + c_2 = e_0$, and this again allows us to eliminate e from the above equations. The system of equations then becomes

$$\begin{cases} \dot{s} &= -k_1 e_0 s + (k_1 s + k_{-1}) c_1 + (k_1 s + k_{-2}) c_2 - k_2 c_1 s \\ \dot{c}_1 &= k_1 e_0 s - (k_{-1} + k_3) c_1 - (k_1 + k_2) c_1 s + (k_{-2} + k_4 - k_1 s) c_2 \\ \dot{c}_2 &= k_2 c_1 s - (k_{-2} + k_4) c_2 \\ \dot{p} &= k_3 c_1 + k_4 c_2 \end{cases}\,. \tag{3.7}$$

We apply the QSSA for c_1 and c_2, and hence set $\dot{c}_1 = 0 = \dot{c}_2$.

Now, we consider the rates to be

$$k_{\pm 1} = 2k_{\pm 1}, \quad k_4 = 2k_3\,. \tag{3.8}$$

This corresponds to the situation where the two subunits of the enzyme work independently from each other. Indeed, these rates tell us that reactions (3.1) and (3.4) are twice as strong

compared to the similar reactions (3.3) and (3.2), respectively. Hence, for example in reaction (3.1), the substrate S can bind itself to either side of the enzyme, and both possibilities are equally likely since the two subunits work independently, such that the reaction is twice as likely to occur compared to the situation where one of the two subunits is already bounded to a substrate. Similarly, in reaction (3.4), either of the two bounded substrates can form a product particle, and hence this is also twice as likely to occur compared to reaction (3.2). nalezen