

## Exercise 1

The purpose of this exercise sheet is to revise some of the basics that are needed for spatio-temporal modelling. Here, we will focus on the formulation of reaction kinetics for biological networks.

a) Recall the definition, the rate of a reaction  
 $\propto$  the probability of reactants collision  
 $\propto$  the concentration of the reactants.

### 1. Review Material from the Lecture

Note the assumption for  $n$  and the limitation for  $K$  [ must be finite ]

- Describe the concept of mass action!
- What are Michaelis-Menten and Hill kinetics?
- How can activator and inhibitory action be represented in mathematical models of biological regulatory networks?

b) MM: The model that accounts for the enzymatic reaction



In this case, the compound C is first synthesized in a reversible way and later turns into the products and the enzymes, completing the enzymatic reaction.

### 2. Basic biochemical reaction mechanisms.

- Complete Table 1. Assume mass action kinetics for all six reaction mechanisms.
- For each mechanism of 2.a implement in Matlab the corresponding ordinary differential equations (ODEs). As rate constants set all to the value 1 and initial conditions to 0.1. Set the integration time to 10 and plot all the state variables over that time span for each mechanism.

Hill:

Hill kinetics better models the reactions involving a series of reactants that are dependent upon each's predecessors. If the first/init. has a low affinity to the compound X. This rate of reaction can be estimated as

$$\frac{d[P]}{dt} = V_{max} \frac{[X]^n}{K^n + [X]^n}$$

where  $K = \left( \prod_{i=1}^n K_i \right)^{1/n}$

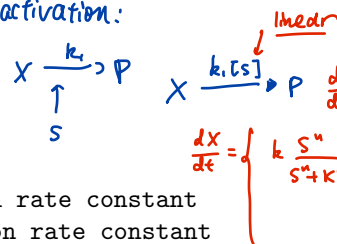
$$\text{where } K_i = \frac{k_{-i(i-1)} + k_{-i}}{k_{i-1}}$$

Hint: To solve each system of ODEs numerically you can use the function ode45. Recall, that you have to code the right-hand side of the system of ODEs as a separate function with time t, state vector x and parameter vector k as input arguments and the derivatives of the state vector dxdt as an output argument. Those functions can be either distinct files in the same folder (name.m) as the function that calls them, or simply contained within your main function. To integrate these functions you can call them from the main function with: [t,x] = ode45(@name,[t0 tend],x0,[],k). A template example for mechanism 1.a.a is given below. Create a new .m file (exercise1b.m) and complete the example script given above to include all mechanisms.

### MATLAB Template:

```
% The main function:
function exercise1b
%% Mechanism (a)
p(1) = 1; % k1: production rate constant
p(2) = 1; % k2: degradation rate constant
x0 = 0.1; % set initial condition for A
tspan = [0 10]; % define time span of integration
% Call matlab integrator ode45 to solve the ODEs for (a)
```

activation:



activation?

Inhibition:

i) By competition



See page 15.

ii) constant degradation

Assuming MM:

$$i) \quad \frac{d[X]}{dt} = V_{max} \frac{[X]}{[X] + K_m (1 + \frac{[I]}{K_i})}$$

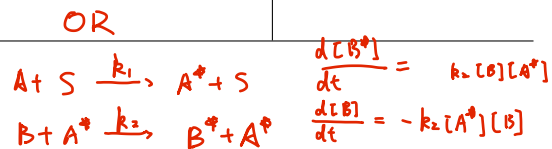
$$ii) \quad \frac{d[X]}{dt} = \frac{V_{max} [X]}{(1 - \frac{[I]}{K_i}) [X] + K_m}$$

$$V_{max} \frac{[S]}{[S] + K_m}$$

Table 1: REACTION NETWORKS

	Interaction Graph	Rate equation scheme	ODE
a)		$\begin{aligned} & \xrightarrow{k_1} A \\ A & \xrightarrow{k_2} \emptyset \end{aligned}$	$\dot{[A]} = k_1 - k_2 [A]$
b)		$\begin{aligned} C & \xrightarrow{k_1} B + A \\ A & \xrightarrow{k_2} C \end{aligned}$	$\begin{aligned} \dot{[A]} &= -k_2 [A] + k_1 [C] \\ \dot{[B]} &= k_1 [C] \\ \dot{[C]} &= k_2 [A] - k_1 [C] \end{aligned}$
c)		$A + A \xrightarrow{k} C$	$\begin{aligned} \dot{[A]} &= -2k [A][A] \\ \dot{[C]} &= k [A][A] \end{aligned}$
d)		$A + B \xrightarrow{k_1} C + A$	$\begin{aligned} \dot{[A]} &= 0 \\ \dot{[B]} &= -k_1 [A][B] \\ \dot{[C]} &= k_1 [A][B] \end{aligned}$
e)		$\begin{aligned} A + A & \xrightleftharpoons[k_{-1}]{k_1} AA \\ A + AA & \xrightleftharpoons[k_{-1}]{k_1} AAA \end{aligned}$	$\begin{aligned} \dot{[A]} &= k_{-1} [AA][AAA] - k_1 [A][A][A][AA] \\ \dot{[AA]} &= -k_{-1} [AA] - k_1 [A][AA] \\ & \quad + k_1 [A][A] + k_{-1} [AAA] \\ \dot{[AAA]} &= k_1 [A][AA] - k_{-1} [AAA] \end{aligned}$
f)		$\begin{aligned} A & \xrightarrow{k_1 [S]} A^* \\ B & \xrightarrow{k_2 [A^*]} B^* \end{aligned}$	$\begin{aligned} \frac{d[A]}{dt} &= -k_1 [S] \cdot [A] \\ \frac{d[S]}{dt} &= -k_1 [S] \cdot [A] \end{aligned}$

Is it a enzymatic or reaction in a cooperative manner?



```

[t_a,x_a] = ode45(@mech_a,tspan,x0,[],p);
clear p x0
%%% Mechanism (b)
...
figure
subplot(2,3,1)
plot(t_a,x_a)
...
end

% The function for the right-hand side of 1.a.a:
function dxdt_a = mech_a(t,x,p)
k1 = p(1);
k2 = p(2);
dxdt_a = zeros(size(x));
dxdt_a(1) = k1-k2*x(1);
end

% The function for the right-hand side of 1.a.b:
...

```