Bioinformatics III

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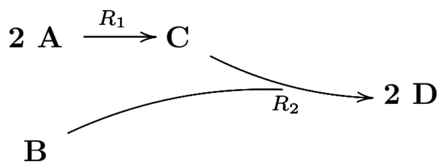
Exercise Sheet 10
Dynamics Simulation of Networks
Due: July 8, 2021 12:00

Submit your solutions to pratiti.bhadra@bioinformatik.uni-saarland.de with two attachments: (1) a PDF file containing your answers with plots (2) a compressed file (.zip / .tar) of your code. Subject of the email should be in the following format: *BI3 A10 LastName1 LastName2.*

Please feel free to contact me for any clarifications either via email or you can reach me in building E2.1, Room 3.01 (preferably between 3 pm and 4 pm).

Q1 Mass Action Kinetics(*25 points*)

A simple network



Two molecules of A associate to create one C, which is converted into D, when it encounters one molecule of B.

(a) Deterministic Model (*10 points*)

A convenient recipe to compile the (sometimes complicated) set of differential equations that describe a system is to start from the stoichiometric matrix.

i. Set up the stoichiometrix matrix.
ii. Derive the rates $\frac{dR_1}{dt}$ and $\frac{dR_2}{dt}$.
iii. List the rates for the changes of **A**, **B**, **C** and **D** in terms of the rates of R_1 and R_2.
iv. List the changes of the metabolites during a time step Δt.

(b) Deterministic Implementation (*10 points*)

With these differences per time step implement a differential equation model of the above network using the simple Euler-Forward Integrator.

Use: $\Delta t = 0.05$ s, $t_{final} = 500$,
$A_{t=0} = 10\ \mu\text{m}^{-3}$, $B_{t=0} = 5\ \mu\text{m}^{-3}$, $C_{t=0} = D_{t=0} = 0\ \mu\text{m}^{-3}$,
$k_{R_1} = 10^{-3}\ \frac{\mu m^{-3}}{s}$ and $k_{R_2} = 3 * 10^{-3}\ \frac{\mu m^{-3}}{s}$.

(c) Interpretation (*5 points*)

Describe the time traces and explain from their behavior the dynamics of the network.

Q2 Stochastic (*40 points*)

$\mathbf{2\ A + B \xrightarrow{R_1} 3\ A}$	$\emptyset \xrightarrow{R_2} \mathbf{A}$	$\emptyset \xleftarrow{R_3} \mathbf{A}$	$\emptyset \xrightarrow{R_4} \mathbf{B}$
$k_1 = 4 \cdot 10^{-5}\ \mathrm{s}^{-1}$	$k_2 = 50\ \mathrm{s}^{-1}$	$k_3 = 10\ \mathrm{s}^{-1}$	$k_4 = 25\ \mathrm{s}^{-1}$

(a) Rate Equations (10)

Set up the rate equations for the reactions and the metabolites and calculate the steady state.

(b) Implement the network using the Gillespie method. Plot the number of molecules of A and B, respectively, vs time . Initial state A(0) = 10 and B(0) = 10. $t_initial$ = 0 and t_final = 80 min. The number of molecules should be given on a logarithmic scale. Plot sould be implemented within python source code using matplotlib. (*30 points*)

Hints: Lecture V22, Slide no 36 "Gillespie Algorithm"

Q3 Enzyme kinetics (*35 points*)

(a) Derive equation of $\frac{1}{v_o}$ from Michalelis Menten Kinetic equation as a function of $\frac{1}{S}$ in form of straight line equation ($y = a.x + b$) (*10* points)

Michalelis Menten Kinetic equation: $v_o = \frac{V_{max}S}{K_M+S}$ *where* v_o *is the initial rate,* V_{max} *is the maximum rate of the reaction with substrate saturation, S is he substrate concentration at the start of the reaction.*

(b) The reaction between nicotineamide mononucleotide and ATP to form nicotineamideadenine dinucleotide and pyrophosphate is catalyzed by the enzyme nicotinamide mononucleotide adenylyltransferase. The following table provides typical data obtained at a pH of 4.95. The substrate, S, is nicotinamide mononucleotide and the initial rate, v, is the mol of nicotinamideadenine dinucleotide formed in a 3-min reaction period. Determine value of V_{max} and K_M. (*10* points)

S (mM)	v_o (μmol)
0.138	0.148
0.220	0.171
0.291	0.234
0.560	0.324
0.766	0.390
1.460	0.493

Hint:

- *The equation of* $\frac{1}{v_o}$ *which has been derived by you as answer of Q3(a).*
- *Plot* $\frac{1}{v_o}$ *Vs* $\frac{1}{S}$

(c) Is the equation of $\frac{1}{v_o}$has any advantage over Michalelis Kinetic equation? Justify your answer (*5* points)

(d) An solution initially contains a catalytic amount of an enzyme with $K_M = 1.5$ mM, 0.25 M of substrate, and no product. After 45 seconds, the solution contains 25 M of product. Find V_{max} and the concentration of product after 2.0 minutes. (*Hint:* $S >> K_M$) (*1*0 points)