

Systems Biology Tutorial 2: Non-enzyme catalyzed kinetics

Passive diffusion

Consider the passive diffusion of ethanol across a yeast cell membrane described in terms of concentrations by

$$\frac{dEtOH_{in}(t)}{dt} = v_1, \quad (1)$$

$$\frac{dEtOH_{out}(t)}{dt} = -\frac{V_i}{V_o}v_1, \quad (2)$$

$$v_1 = \frac{P \cdot A}{V_i} \cdot (EtOH_{out}(t) - EtOH_{in}(t)), \quad (3)$$

where

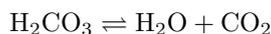
- the permeability coefficient P of ethanol is given by 1.8×10^{-3} dm/min,
- the membrane area A and cell volume V_i are respectively 5.02655×10^{-9} dm² and 3.35103×10^{-14} dm³
- and $V_i / V_o = 1/50$.

1. What are the units of the constant $k = P \cdot A / V_i$ and the rate as a whole if the concentrations are in mM?
2. For a fixed external ethanol concentration $EtOH_{out} = 5$ mM, plot this rate as a function of internal concentration 0 - 10 mM.
 - (a) In what direction will the reaction proceed and what will happen to the internal ethanol concentration (explain) if
 - i. $0 \leq EtOH_{in} < EtOH_{out}$?
 - ii. $EtOH_{in} = EtOH_{out}$?
 - iii. $EtOH_{in} \geq EtOH_{out}$?
3. Plot the internal ethanol concentration as a function of time ($0 \leq t \leq 0.05$ min) given that the external concentration is fixed at 5 mM and $EtOH_{in}(t = 0) = 10$ mM (use NDSolve).
 - (a) What is the final value of the internal ethanol concentration and why?
 - (b) Plot the rate as a function of time by substituting the solution of NDSolve into the expression for v_1 .
 - (c) Take the derivative of the solution for internal ethanol concentration (i.e. obtain the rate) and plot it as a function of time. Compare to the plot obtained in (b).
4. Plot the internal and external ethanol concentrations as functions of time ($0 \leq t \leq 0.05$ min) given that $EtOH_{in}(t = 0) = 5$ mM and $EtOH_{out}(t = 0) = 0$ mM (both concentrations are variables).
 - (a) What is the final value of the internal ethanol concentration and why?
 - (b) Calculate the change in external and internal concentrations. Why are they not the same?
 - (c) Check if the amount of ethanol is conserved.
5. Use the data set provided (i.t.o. initial transport rates for different internal ethanol concentrations in Q5_Internal_EtOH.dat) and fit the function $v_1 = k \cdot x$ to obtain a value for k .
 - (a) How well does your value for k agree with that used in Question 1?

6. Repeat Questions 2 and 3 for the passive diffusion of glucose where $P \approx 1 \times 10^{-9}$ dm/min (let $0 \leq t \leq 30000$ min).
- What are your conclusions about the diffusion rate of glucose when compared to that of ethanol?
 - Considering how the permeability is calculated and the fact that the diffusion coefficients D of glucose and ethanol are of similar magnitude, what factor and therefore what property of glucose and ethanol makes the diffusion characteristics of these two so different? ($P = \frac{D \cdot C}{r}$, with C the partition coefficient and r the thickness of the membrane.)
 - Would passive transport be an efficient way of getting glucose into the cytosol?

Decarboxylation of carbonic acid

Consider the reaction



The change in carbonic acid concentration is described by

$$\frac{d\text{H}_2\text{CO}_3(t)}{dt} = -v_1 \quad (4)$$

$$v_1 = k_f \cdot \text{H}_2\text{CO}_3(t) - k_r \cdot \text{H}_2\text{O}(t) \cdot \text{CO}_2(t) \quad (5)$$

- What must the units of k_f and k_r be (if time is measured in seconds and concentration in M)?
- Given that $k_f = 23$ and $k_r = 0.039$, write Eq. 5 in the form

$$v = k_f \cdot \left(A - \frac{B \cdot C}{K_{eq}} \right) \quad (6)$$

- What are the units of K_{eq} ?
 - For fixed $\text{H}_2\text{CO}_3 = 5$ M, $\text{H}_2\text{O}(t = 0) = 0$ and $\text{CO}_2(t = 0) = 0$, what is the initial value of the mass action ratio? Plot the concentration of CO_2 as a function of time ($0 \leq t \leq 10$ sec). Also plot the mass action ratio as function of time. To what value does this ratio strive and how long does it take to attain this value? Why?
 - For fixed $\text{H}_2\text{CO}_3 = 5$ M, $\text{H}_2\text{O}(t = 0) = 50$ and $\text{CO}_2(t = 0) = 50$, what is the initial value of the mass action ratio? Plot the concentration of CO_2 as a function of time ($0 \leq t \leq 10$ sec). Also plot the mass action ratio as function of time. To what value does this ratio strive and how long does it take to attain this value? Why? How does this compare to (b)?
 - How does this behaviour change if you increase the value of k_r (and therefore decrease the value of K_{eq})?
- Use the data set provided (i.t.o. initial rates as a function for different concentrations of A in Q3_H2CO3.dat and initial rates as a function for different concentrations of B and C in Q3_H2O_CO2.dat) and fit a function of the form given by Eq. 6 to obtain values for k_f and k_r .