

Basics of Chemical Kinetics - 1



- Rate of reaction = rate of disappearance of A = $r_A = -d[A]/dt =$
of moles of A reacting (“disappearing”) per unit time per unit volume

[A] = concentration of A = (# moles/volume) ; 1 mole = 6.023×10^{23} molecules

- Reaction rate law is an algebraic equation involving concentrations
(not a differential equation)

$$r_A = -k [A]$$

$$r_A = -k [A]^2$$

$$r_A = -k_1 [A]/(1+k_2[A])$$

- For a given reaction, the rate law is determined **experimentally**
- Measure [A] as a function of time and calculate slope ($d[A]/dt$) at various time points.

Basics of Chemical Kinetics - 2



➤ In general : $r_A = -k(T) \cdot f([A],[B],\dots)$

**Temperature
dependence**

Rate Constant

**Concentration
dependence**

Other factors impacting
rate constant

- Catalyst
- Pressure
- Ionic strength (pH)
- Solvent

(Not really “constant”, just
independent of concentration)

➤ Reaction Order (power):

$$r_A = -k \cdot [A]^\alpha \cdot [B]^\beta$$

The reaction is of order α with respect to A and of order β with respect to B

➤ Reaction order can be fractional

$$r_A = -k \cdot [A]^1 \cdot [B]^{0.5}$$

➤ Not every reaction has an order!

$$r_A = -k_1 \cdot [A] / (1 + k_2 \cdot [B])$$

(Temperature and concentration dependence not separable)

Basics of Chemical Kinetics - 3

- **Elementary Reaction:** Reaction order of each species is identical with the stoichiometric coefficient of that species



- Elementary reactions hypothesized to happen exactly how they are written!

(One molecule of A colliding with 2 molecules of B to produce C)

- Elementary reactions are typically 1st or 2nd order

(Probability of three molecules colliding very low)

- Reversible reactions:



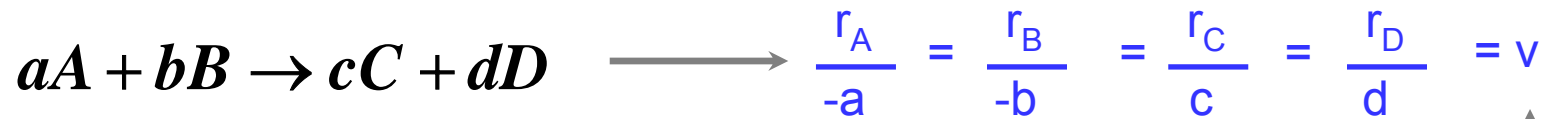
Forward Reaction



Backward Reaction

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➤ Reaction Stoichiometry + Law of Conservation of Mass



(Irrespective of whether reaction is elementary or not)

Reaction flux

Specify rate law

$$d[A] / dt = -a \cdot v$$

$$d[B] / dt = -b \cdot v$$

$$d[C] / dt = c \cdot v$$

$$d[D] / dt = d \cdot v$$

$$v = -k \cdot [A]^a \cdot [B]^b \text{ or}$$

$$v = -k \cdot [A] \cdot [B]$$

Specify initial conditions

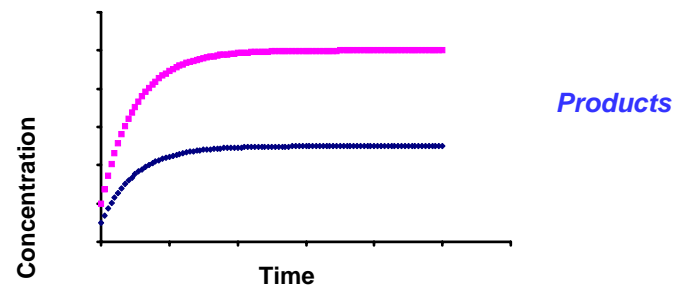
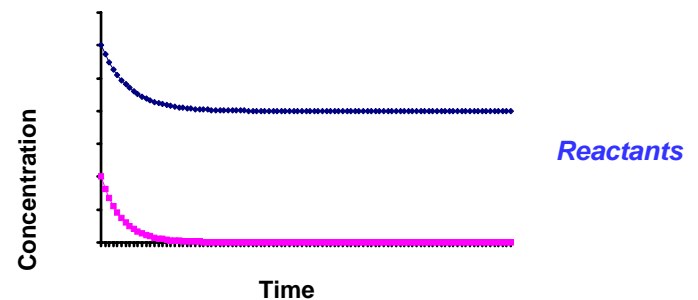
$$[A]_{(t=0)} = [A]_0$$

$$[B]_{(t=0)} = [B]_0$$

$$[C]_{(t=0)} = [C]_0$$

$$[D]_{(t=0)} = [D]_0$$

Concentration Time Course





Determine the relation between the reaction rates and the reaction flux.

Assume the reaction is elementary. Determine the rate of change of [A], [B], [C]



Determine the relation between the reaction rates and the reaction flux.

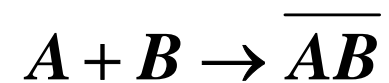
Assume the reaction is elementary. Determine the rate of change of [A], [B], [C]

$$\frac{d[A]}{dt} = \frac{d[B]}{dt} = -k[A][B] \quad \frac{d[C]}{dt} = k[A][B]$$

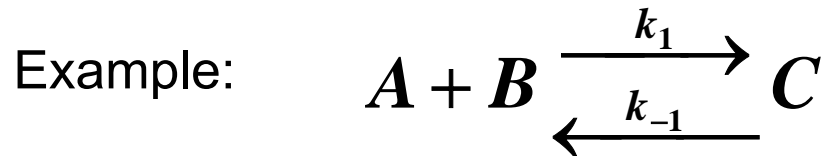
Ex. 2

Write the condition(s) of mass conservation.

Hint: think of the reaction as a complex formation



Reversible reactions



For simplicity, we'll leave off the brackets from $[A]$, ..

$$\frac{dA}{dt} = \frac{dB}{dt} = -k_1 AB + k_{-1} C$$

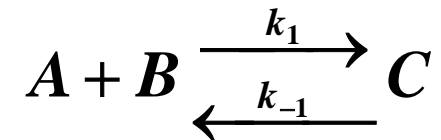
$$\frac{dC}{dt} = k_1 AB - k_{-1} C$$

Mass conservation: $A + C = A_0$ $B + C = B_0$

Units: $k_1 - (\text{mol}/\text{volume}/\text{time})^{-1}$, $k_{-1} - (\text{time})^{-1}$

Steady states

If the rates of the forward and backward reactions are equal, the system is able to reach a steady state where the concentrations do not change in time



$$\frac{dA}{dt} = \frac{dB}{dt} = \frac{dC}{dt} = 0 \quad \text{if} \quad k_1 AB - k_{-1} C = 0$$

$$C_{ss} = \frac{k_1}{k_{-1}} A_{ss} B_{ss} = \frac{k_1}{k_{-1}} (A_0 - C_{ss})(B_0 - C_{ss})$$

Solve for C_{ss}

Enzyme-catalyzed reactions

Most reactions in biological systems would not take place at perceptible rates in the absence of **enzymes**.

Enzymes are specialized proteins that bind specific reactants, get them close together, and by this, accelerate the reaction up to a million times.

In this context, the reactants are called **substrates**.

In enzyme-catalyzed reactions the rate of product synthesis depends **nonlinearly** on the concentration of the substrate.

Michaelis-Menten model of enzymatic reactions

Leonor Michaelis, Maud Menten (1913)

1. A specific enzyme-substrate complex is a necessary intermediate in catalysis
2. The product does not revert to the original substrates



Ex. Draw two possible network representations of this process.

Michaelis-Menten kinetics



$$\frac{dS}{dt} = -k_1 E S + k_{-1} \overline{ES} \quad \frac{dE}{dt} = -k_1 E S + k_{-1} \overline{ES} + k_2 \overline{ES}$$

$$\frac{d\overline{ES}}{dt} = k_1 E S - k_{-1} \overline{ES} - k_2 \overline{ES} \quad \frac{dP}{dt} = k_2 \overline{ES}$$

Mass conservation: $E_T = E + \overline{ES}$

Assumption: the enzyme-substrate complex is in quasi-steady-state

$$\frac{d\overline{ES}}{dt} = 0, \quad \overline{ES} = ES \frac{k_1}{k_{-1} + k_2}$$

Michaelis-Menten kinetics (cont.)



Goal: express the rate of product synthesis as a function of substrate concentration

$$\frac{dP}{dt} = k_2 \overline{ES}$$

$$\left. \begin{aligned} \overline{ES} &= ES \frac{k_1}{k_{-1} + k_2} \\ E_T &= E + \overline{ES} \\ K_M &= \frac{k_{-1} + k_2}{k_1} \end{aligned} \right\} \frac{dP}{dt} = k_2 E_T \frac{S}{K_M + S}$$

Michaelis-Menten kinetics (cont.)



$$\frac{dP}{dt} = k_2 E_T \frac{S}{K_M + S} \quad K_M = \frac{k_{-1} + k_2}{k_1}$$

Ex. 1

Draw the dependence of the rate of product synthesis on the substrate concentration. Characterize three limits/points on the curve.

Ex. 2

What is the upper limit for k_2/K_M ?

Enzyme-catalyzed reactions

$$\frac{dP}{dt} = k_2 E_T \frac{S}{K_M + S}$$

K_M is equal to the substrate concentration at which the reaction rate is half its maximal value.

Limit 1 $S \gg K_M \Rightarrow \frac{dP}{dt} \approx k_2 E_T$

$k_2 E_T$ is the number of substrate molecules converted in a unit time when the enzyme is fully saturated with substrate.

Limit 2 $S \ll K_M \Rightarrow \frac{dP}{dt} \approx \frac{k_2}{K_M} E_T S$

The efficiency of an enzyme can be described by k_2 / K_M

The ultimate limit for enzyme efficiency is the diffusion-limited encounter of enzyme and substrate, or $10^9 s^{-1} mol^{-1}$

Chemical kinetics-like models of cellular processes

Assumption: cellular synthesis and degradation processes can be described as simple or enzyme-catalyzed reactions

Ex.: receptor - ligand binding

methylation reactions – catalyzed by methylating enzymes,

phosphorylation - catalyzed by kinases

dephosphorylation – spontaneous or catalyzed by phosphatases

protein synthesis –catalyzed by mRNA,

protein degradation – spontaneous or catalyzed

[J. Tyson, K. Chen, B. Novak, Curr. Opin. Cell Biology 15, 221 \(2003\)](#)

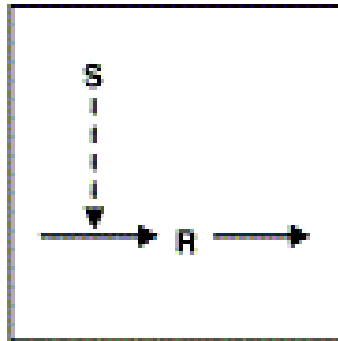
Protein synthesis and degradation

Protein synthesis: mRNA \rightarrow protein (sufficient supply of amino-acids)

Protein degradation: protein \rightarrow

[Notations in Tyson et al 2003](#): The source element (here the mRNA) is denoted S (for signal). One component (here the protein) is designated as the response.

Network diagram:



Solid edge: mass flow
Dashed edge: regulation

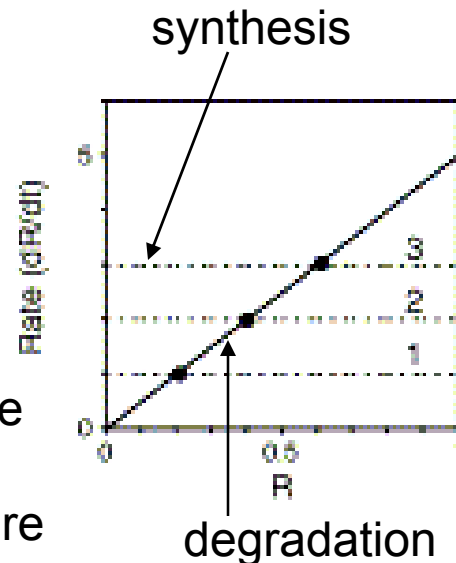
Q: Draw an alternative network, more in line with what we have seen before, where edges connect two nodes and signify regulation.

Kinetics of protein synthesis and degradation

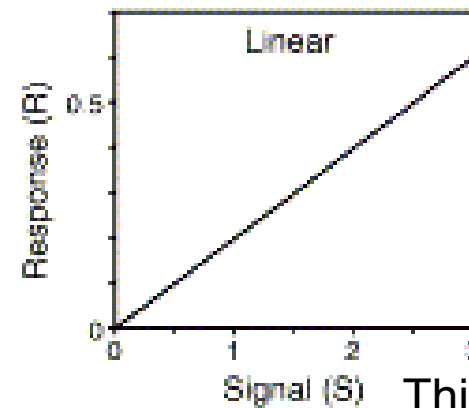
Protein synthesis: mRNA \rightarrow protein (sufficient supply of amino-acids)

Protein degradation: protein \rightarrow

$$\frac{dR}{dt} = k_1 S - k_2 R \quad \text{Steady state:} \quad R_{ss} = \frac{k_1 S}{k_2}$$



The points where the synthesis and degradation terms are equal indicate the steady states.



This is the input-output characteristic of the system.

Kinetics of phosphotransfer

Phosphorylation: protein \rightarrow phospho-protein

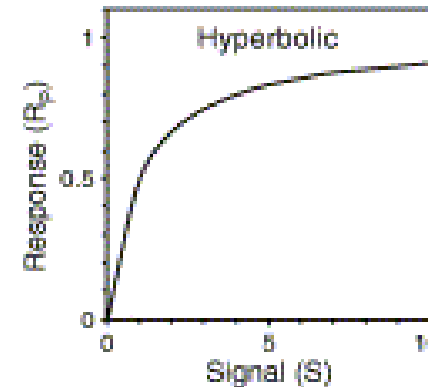
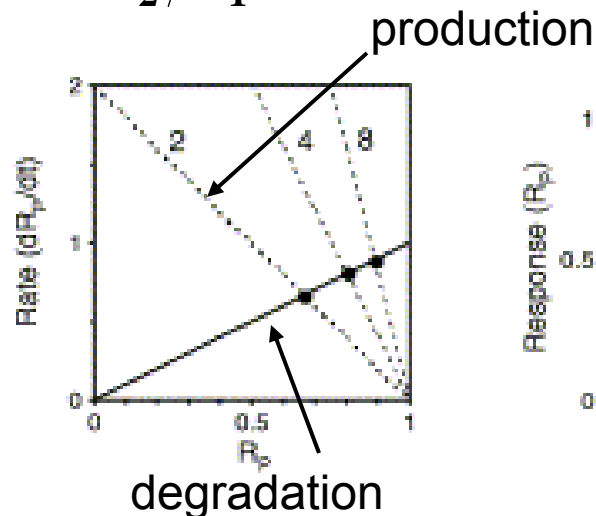
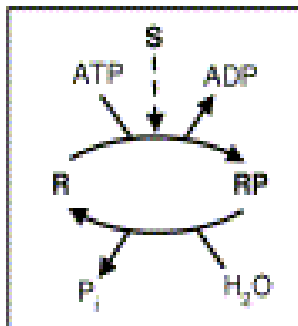
Dephosphorylation: phospho-protein \rightarrow protein

The first reaction is catalyzed by a kinase, **assume** first –order kinetics

$$\frac{dR_P}{dt} = k_1SR - k_2R_P \quad R_T = R + R_P$$

Steady state: $R_{P_{ss}} = R_T \frac{S}{k_2/k_1 + S}$

(b)

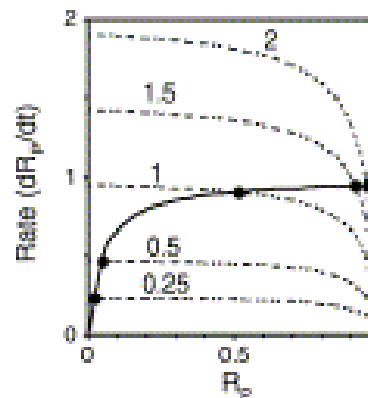
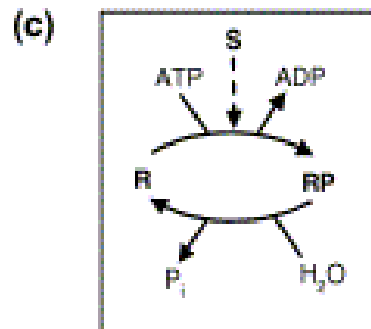


Phosphotransfer with Michaelis-Menten kinetics

Assume that the phosphorylation and dephosphorylation reactions follow Michaelis-Menten kinetics



$$\frac{dR_P}{dt} = k_1 S \frac{R_T - R_P}{K_{M1} + R_T - R_P} - \frac{k_2 R_P}{K_{M2} + R_P}$$



Phosphotransfer with Michaelis-Menten kinetics

$$\frac{dR_P}{dt} = k_1 S \frac{R_T - R_P}{K_{M1} + R_T - R_P} - \frac{k_2 R_P}{K_{M2} + R_P}$$

Steady state: $R_{P_{ss}} = R_T G\left(k_1 S, k_2, \frac{K_{M1}}{R_T}, \frac{K_{M2}}{R_T}\right)$

G - Goldbeter-Koshland function

