Modelling Biochemical Reaction Networks

Lecture 3: Overview of chemical kinetics

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Elementary reactions

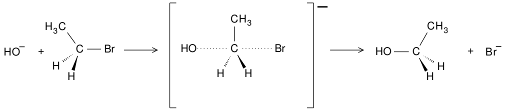
- Occurs as written, without any intervening steps
- Examples:
  - Binding of two molecules to form a complex:

$$\mathrm{A} + \mathrm{B} \rightarrow \mathrm{AB}$$

  - Dissociation of a complex:

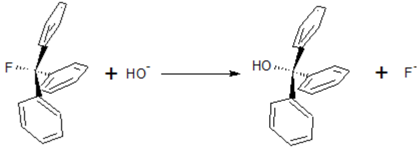
$$\mathrm{AB} \rightarrow \mathrm{A} + \mathrm{B}$$

  - A chemical transformation that occurs in a single step, such as an S_N2 nucleophilic substitution:

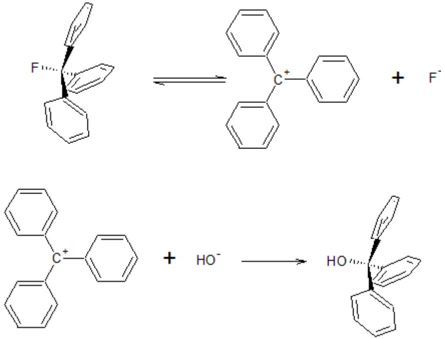


Complex reactions

- Composed of several elementary reactions
- The list of elementary reactions making up a complex reaction is a mechanism.
- Example: S_N1 nucleophilic substitution
  Overall reaction:



S_N1 mechanism:



Rate of reaction

Convention: The rate of reaction is the rate of change of the concentration of a product with a stoichiometric coefficient of 1.

Convention: The rate of reaction is usually denoted v.

Example: For the reaction $\mathrm{A} + 2\mathrm{B} \rightarrow \mathrm{P} + 2\mathrm{Q}$, $v = d[\mathrm{P}]/dt$.

- Other rates are related by stoichiometry, so in this example, $d[\mathrm{A}]/dt = -v$, $d[\mathrm{B}]/dt = -2v$ and $d[\mathrm{Q}]/dt = 2v$.

The rate law tells us how v for a reaction depends on the concentrations of species in the system.

Law of mass action

- The rate of an elementary reaction is proportional to the product of the concentrations of its reactants.
- The proportionality constant is called a rate constant, and usually denoted k.
- Example: For the elementary S_N2 reaction $C_2H_5Br + OH^- \rightarrow C_2H_5OH + Br^-$,

$$v = k[C_2H_5Br][OH^-].$$

Order of reaction

Partial order is the exponent of a particular concentration in a rate law.
If $v = k[\mathrm{A}]^n[\mathrm{B}]^m$, we say that the reaction is of the n'th order with respect to [A], and of the m'th order with respect to [B].

- Due to the law of mass action, for elementary reactions, the partial order coincides with the stoichiometric coefficient of a substance.

The order of a reaction is the sum of the partial orders, so the reaction in the above example is an $(n + m)$'th order reaction.

Additivity of rates

- In complex reactions, some substances will appear in more than one elementary reaction.
- The rate of change of the concentration of a substance is the sum of the rates of change due to each reaction in which that substance appears.
- The reverse of an elementary reaction is a separate elementary reaction.
- Example: In the S_N1 mechanism

$$\mathrm{C(C_6H_5)_3F} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{C^+(C_6H_5)_3} + \mathrm{F^-}$$

$$\mathrm{C^+(C_6H_5)_3} + \mathrm{OH^-} \xrightarrow{k_2} \mathrm{C(C_6H_5)_3OH}$$

$$\begin{aligned}\frac{d[\mathrm{C^+(C_6H_5)_3}]}{dt} &= k_1[\mathrm{C(C_6H_5)_3F}] - k_{-1}[\mathrm{C^+(C_6H_5)_3}][\mathrm{F^-}] \\ &\quad - k_2[\mathrm{C^+(C_6H_5)_3}][\mathrm{OH^-}]\end{aligned}$$

Additivity of rates

- Example: reversible dimerization

$$2\mathrm{A} \underset{k_d}{\overset{k_a}{\rightleftharpoons}} \mathrm{B}$$

Equivalent to

$$\begin{aligned} 2\mathrm{A} &\xrightarrow{k_a} \mathrm{B} & v_a &= k_a[\mathrm{A}]^2 \\ \mathrm{B} &\xrightarrow{k_d} 2\mathrm{A} & v_d &= k_d[\mathrm{B}] \end{aligned}$$

Rate equations:

$$\begin{aligned} \frac{d[\mathrm{A}]}{dt} &= -2v_a + 2v_b = -2k_a[\mathrm{A}]^2 + 2k_d[\mathrm{B}] \\ \frac{d[\mathrm{B}]}{dt} &= v_a - v_b \qquad = k_a[\mathrm{A}]^2 - k_d[\mathrm{B}] \end{aligned}$$

Law of microscopic reversibility

- Every elementary reaction is reversible.
- Required for consistency with equilibrium thermodynamics.
- Living organisms live far from equilibrium.
  $\implies$ Some reverse reactions are negligibly slow under physiological conditions.

Implications for modeling

- In a model, we would only include reactions that are significant under physiological conditions (e.g. ignore some reverse reactions).
- The full mechanism of a biochemical network can include many dozens of reactions.
- We don't usually need a fully detailed model in the sense that it lists every elementary reaction.
- Next lecture: some standard simplification methods