C7790 Introduction to Molecular Modelling
TSM Modelling Molecular Structures

Lesson 19
Kinetics

PS/2020 Distant Form of Teaching: Rev2

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Context

macroworld **microworld**

states

(thermodynamic properties, G, T,…)

phenomenological thermodynamics

equilibrium (equilibrium constant)

kinetics (rate constant)

free energy
(Gibbs/Helmholtz)

partition function

statistical thermodynamics

microstates

(mechanical properties, E)

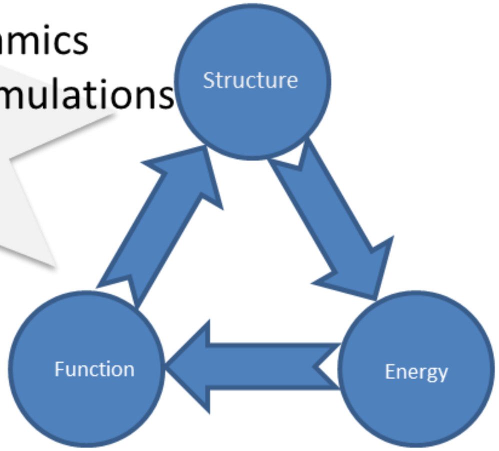
microstate ≠ microworld

Description levels (model chemistry):

- quantum mechanics
  - semiempirical methods
  - ab initio methods
  - post-HF methods
  - DFT methods
- molecular mechanics
- coarse-grained mechanics

Simulations:

- molecular dynamics
- Monte Carlo simulations
- docking
- …



Revision: Entropy and spontaneity

$$dS \geq 0$$

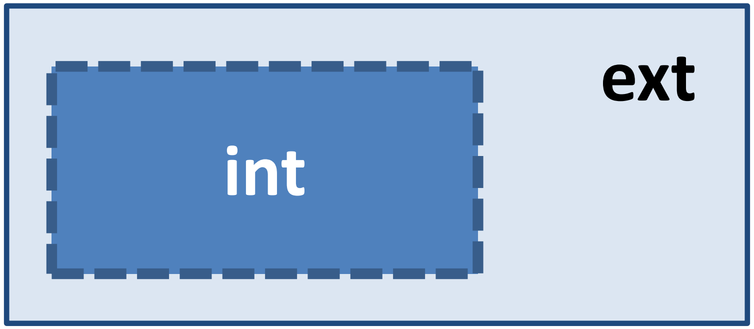
For isolated system, the direction of the time flow is identical with the increase of entropy.

irreversible process (spontaneous)

In isolated system, entropy increases until equilibrium is reached. Then, entropy reaches a maximum, constant value.

Spontaneous process:

$$\boxed{\Delta S_{ext} + \Delta S_{\text{int}} \geq 0}$$



$$\cancel{\Delta S_{\text{int}}}$$

Knowledge of the entropy change of the internal system (int, system of interest) is not sufficient to assess whether the change will take place spontaneously. It is necessary to assess the change of entropy of **system, including its surroundings**.

Revision: Free energy and process spontaneity

for conversion at constant temperature and pressure

$$\Delta G = \Delta H - T\Delta S < 0$$

spontaneous process

$$\Delta G = \Delta H - T\Delta S = 0$$

system is at equilibrium

$$\Delta G = \Delta H - T\Delta S > 0$$

non-spontaneous process

entropy of surroundings

entropy of the system

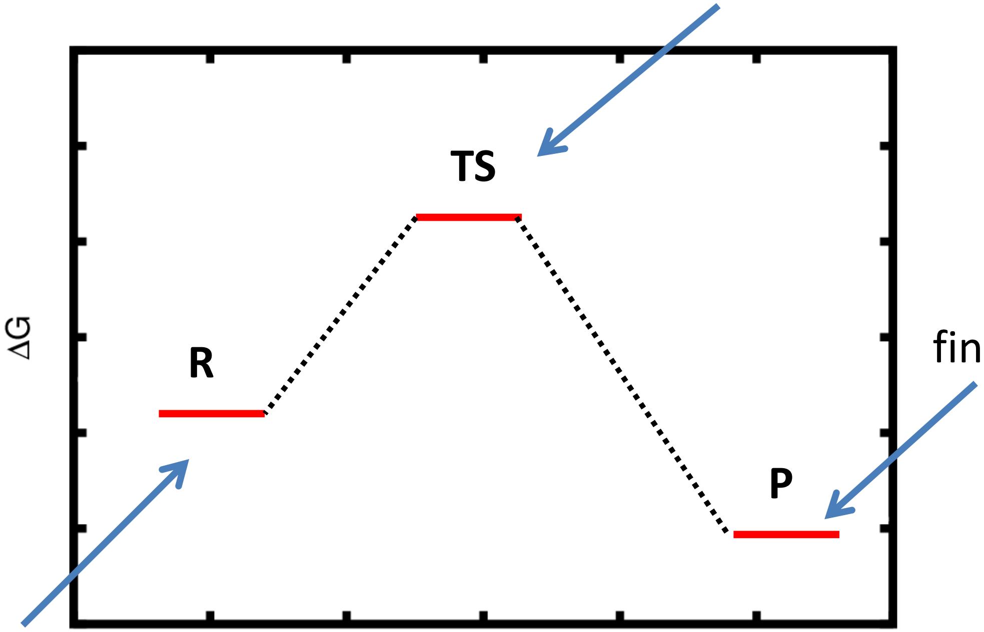
The change of Gibbs energy indicates whether the process can occur spontaneously.
However, it does not determine how long the actual transformation will take place.

Thermodynamics of chemical process

$$aA + bB \rightleftharpoons cC + dD$$

a, b, c, d - stoichiometric coefficients

activated complex (transition state)



change of Gibbs (free) energy

final state (products)

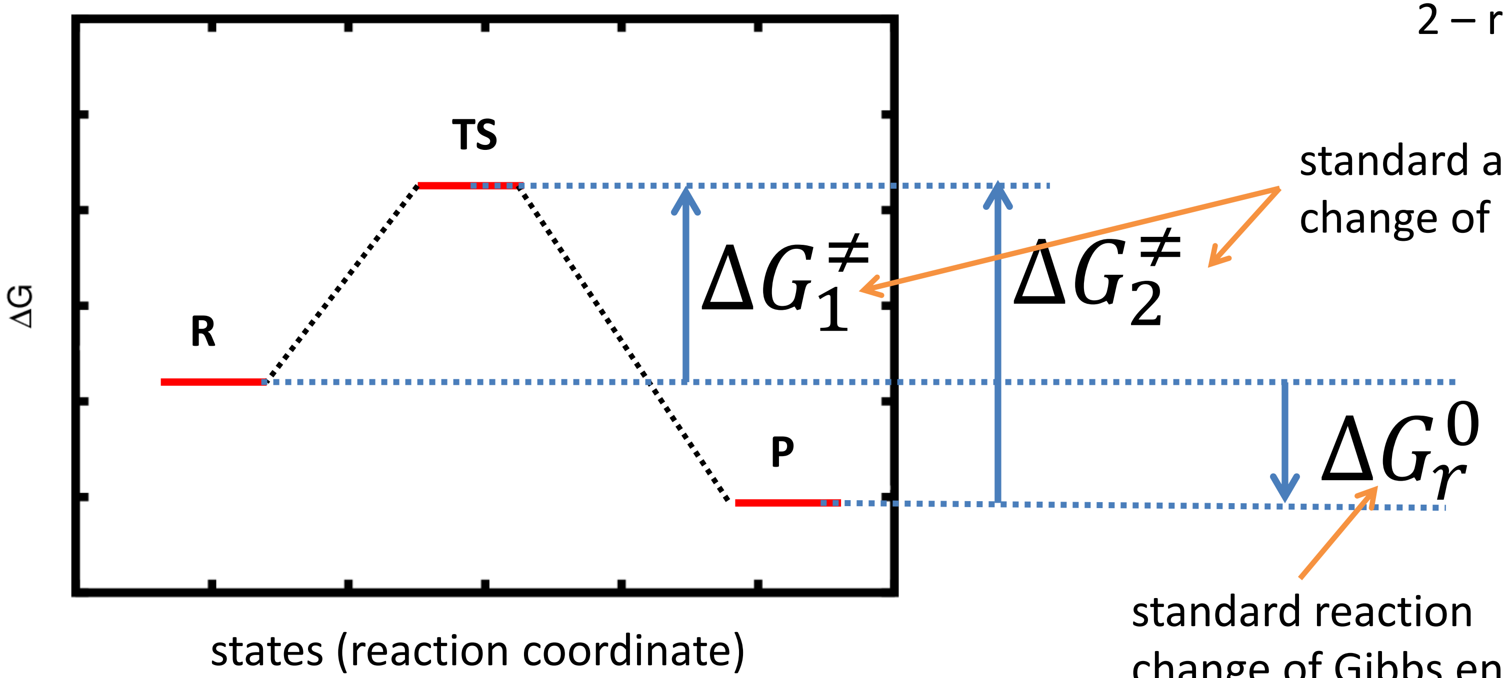
initial state (reactants)

states (reaction coordinate)

Thermodynamics of chemical process

$$aA + bB \underset{2}{\overset{1}{\rightleftarrows}} cC + dD$$

1 – forward reaction
2 – reverse reaction



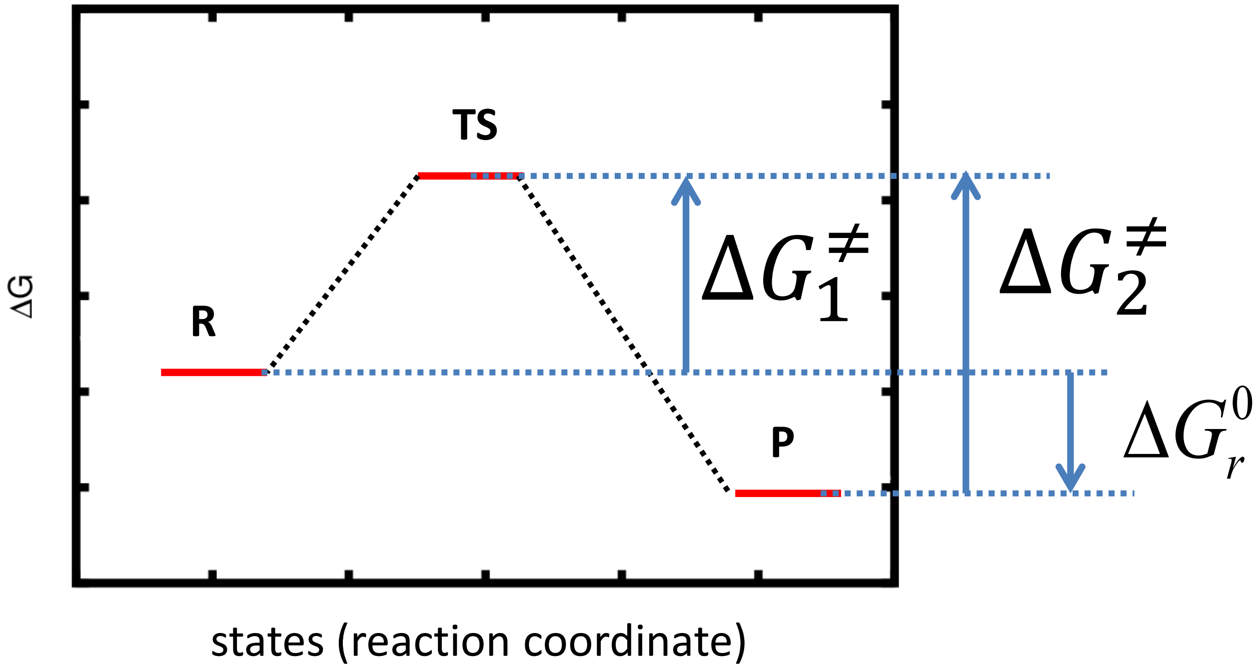
standard activation change of Gibbs energy

standard reaction change of Gibbs energy

$\Delta G_r^0, \Delta G_1^{\neq}, \Delta G_2^{\neq}$ do not tell nothing about spontaneity of the reaction!!!!

Thermodynamics of chemical process

$$aA + bB \underset{2}{\overset{1}{\rightleftarrows}} cC + dD$$



Thermodynamic cycle

$$\Delta G_1^{\neq} - \Delta G_2^{\neq} - \Delta G_r^0 = 0 \quad \rightarrow \quad \Delta G_r^0 = \Delta G_1^{\neq} - \Delta G_2^{\neq}$$

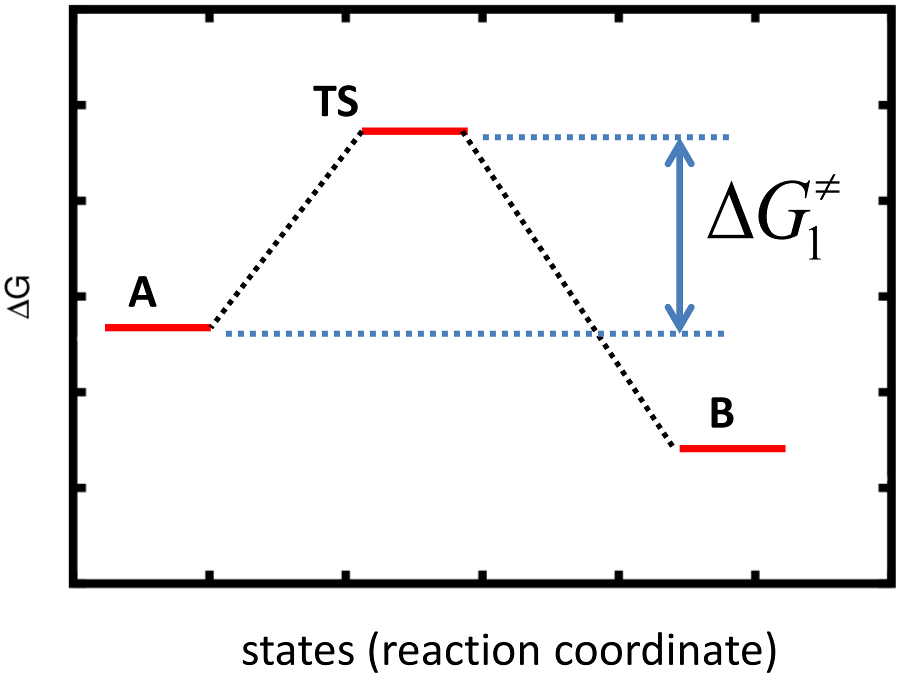
Kinetics

- **Evolution of chemical system in time (until equilibrium)**

i.e., what you should already know ….

Kinetics - summary

$$A \xrightarrow{k_1} B$$



rate of reaction,
change of substance concentration over time

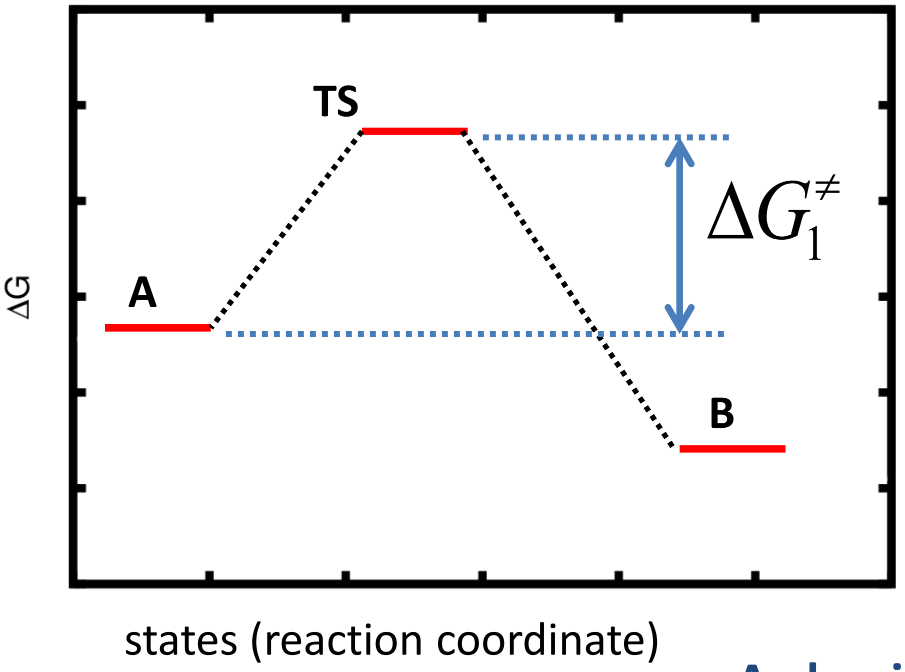
rate constant

$$\boxed{-\frac{d[A]}{dt}} = k_1[A]$$

actual concentration
of the substance

Kinetics - summary

$$A \xrightarrow{k_1} B$$



rate of reaction,
change of substance concentration over time

rate constant

$$-\frac{d[A]}{dt} = k_1[A]$$

actual concentration
of the substance

activation energy

$$k = Ae^{-\frac{E_a}{RT}}$$

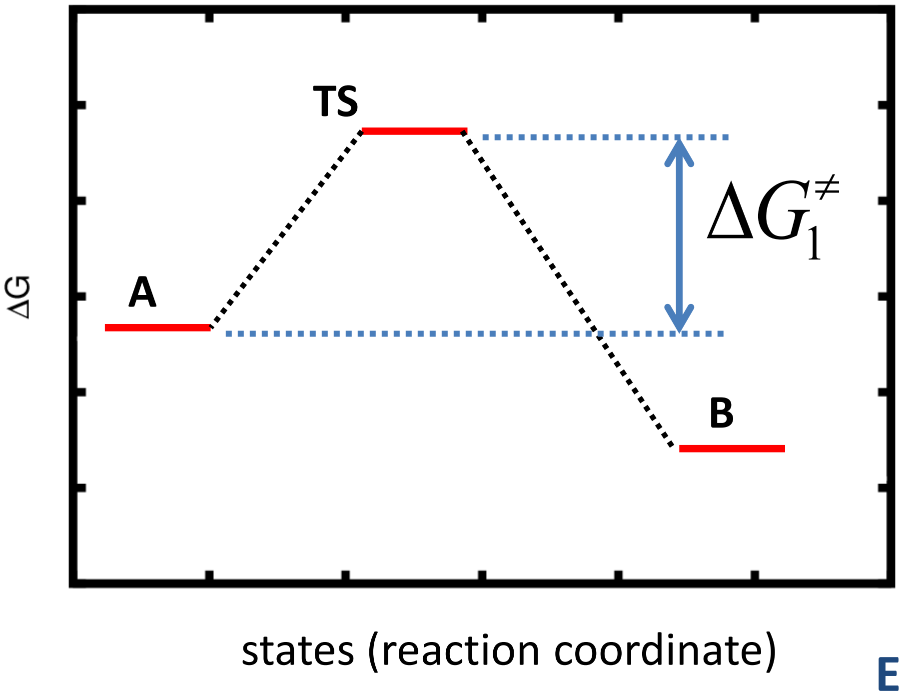
pre-exponential
factor

Arrhenius equation (empirical)

R - universal gas constant, T - absolute temperature, h - Planck's constant, k_B - Boltzmann constant

Kinetics - summary

$$A \xrightarrow{k1} B$$



rate of reaction,
change of substance concentration over time

rate constant

$$-\frac{d[A]}{dt} = k_1[A]$$

actual concentration
of the substance

$$k = \kappa \frac{k_B T}{h} e^{-\frac{\Delta G^{\neq}}{RT}}$$

Eyring equation (theoretical model)

standard activation Gibbs energy

R - universal gas constant, T - absolute temperature, h - Planck's constant, k_B - Boltzmann constant

Chemical transformation

$$aA + bB \longrightarrow cC + dD$$

Substances C and D are formed by reaction of A and B.

Principle questions:

- **How fast is the reaction?**
- How is it possible to influence the rate of reaction?

Reaction rate

Irreversible reaction:

$$aA + bB \xrightarrow{k} cC + dD$$

Sign convention for ν_i

final state	- positive value
initial state	- negative value

Rate of reaction (empirical relationship):

$$v = \frac{1}{a}\frac{d[A]}{dt} = \frac{1}{b}\frac{d[B]}{dt} = k[A]^{\alpha}[B]^{\beta}$$

partial order of reactio

change in concentration over time

rate constant

actual concentration

partial and total orders can be real numbers

total order of reaction $n = \alpha + \beta$

Arrhenius equation

Arrhenius equation defines **empirical relationship** between the rate constant and temperature:

activation energy

$$k = Ae^{-\frac{E_a}{RT}}$$

pre-exponential factor

The pre-exponential factor and activation energy are constants characteristic for given reaction. However, the relationship is valid only in a narrow temperature range.

Exercises:

- How does the rate constant change with increasing temperature?
- How is the activation energy determined?

Reversible reaction

Reversible reaction:

$$aA + bB \underset{k_2}{\overset{k_1}{\rightleftarrows}} cC + dD$$

forward reaction

$$v_1 = \frac{1}{a}\frac{d[A]}{dt} = \frac{1}{b}\frac{d[B]}{dt} = k_1[A]^{\alpha}[B]^{\beta}$$

$$v_2 = \frac{1}{c}\frac{d[C]}{dt} = \frac{1}{d}\frac{d[D]}{dt} = k_2[C]^{\gamma}[D]^{\delta}$$

reverse reaction

At equilibrium:

$$v_1 = v_2$$

Reversible elementary reaction

Reversible reaction:

$$aA + bB \underset{k_2}{\overset{k_1}{\rightleftarrows}} cC + dD$$

At equilibrium:

$$v_1 = k_1[A]^a[B]^b = v_2 = k_2[C]^c[D]^d$$

$$\frac{k_1}{k_2} = \frac{[C]^c[D]^d}{[A]^a[B]^b} = K$$

it is valid only in a limited extent because concentrations are not activities

$$\Delta G_r^0 = \Delta G_1^{\neq} - \Delta G_2^{\neq}$$

always valid, G - is a state function

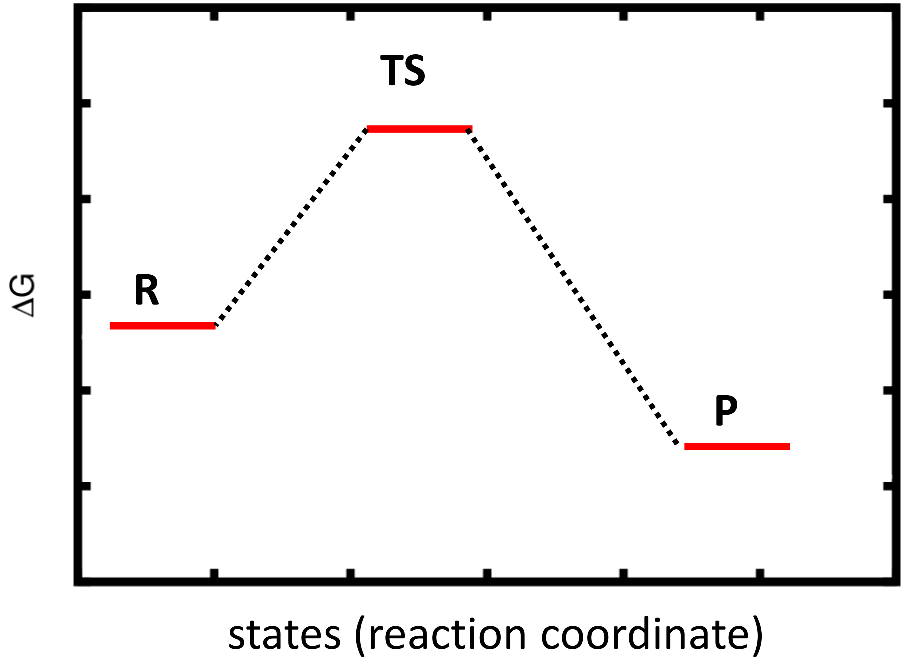
Exercises:

- Using the equations for the equilibrium constant and rate constant (Eyring equation) prove the equivalence between the provided relations.
- Under what conditions does equivalence apply?
- What does the comparison show?

Elementary reaction

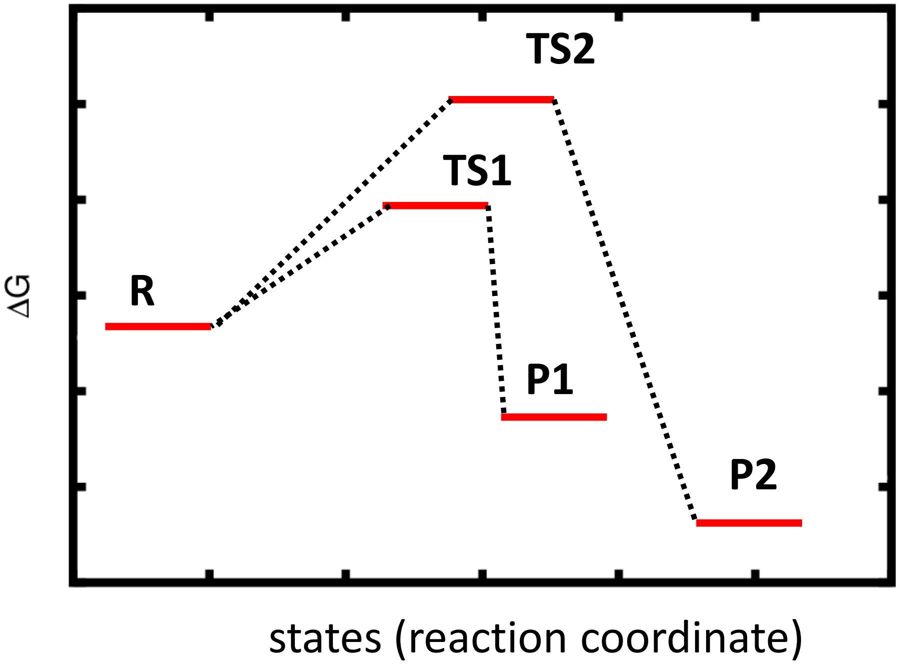
Elementary reaction is the transformation of reactants and products **separated by just one transition state**.

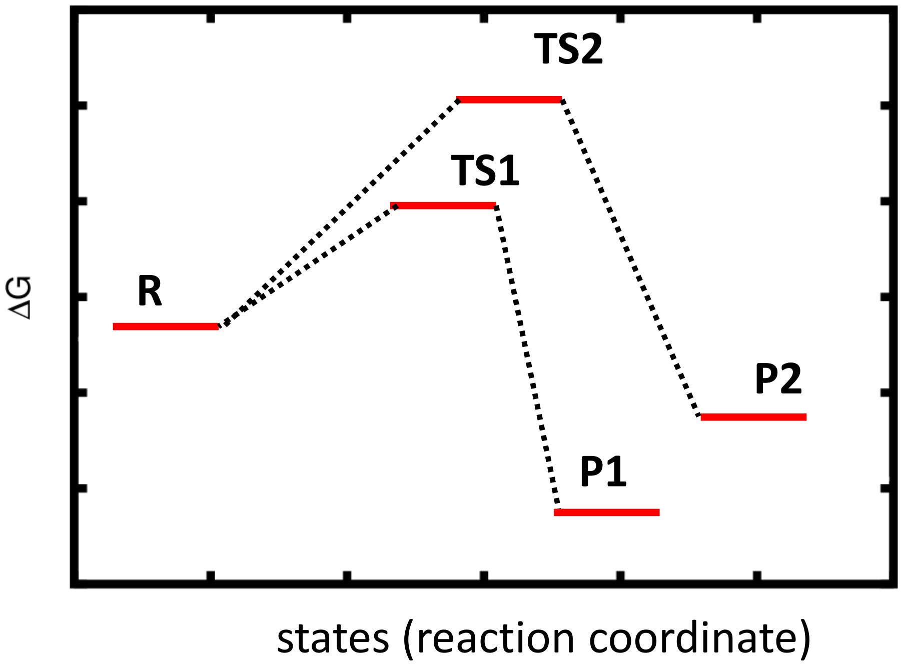
- partial orders of the reaction are stoichiometric coefficients
- overall order of the reaction determines molecularity of the process
- molecularity of elementary reaction is typically 1 (monomolecular) or 2 (bimolecular)



For consideration

- What is characteristic of an irreversible process?
- What is a kinetically controlled process?
- What is a thermodynamically controlled process?



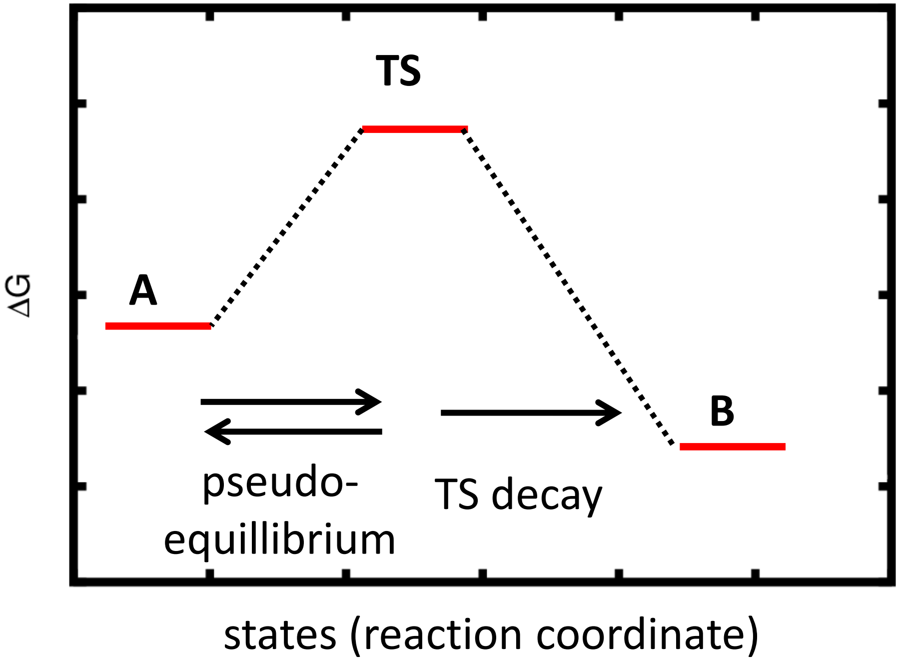


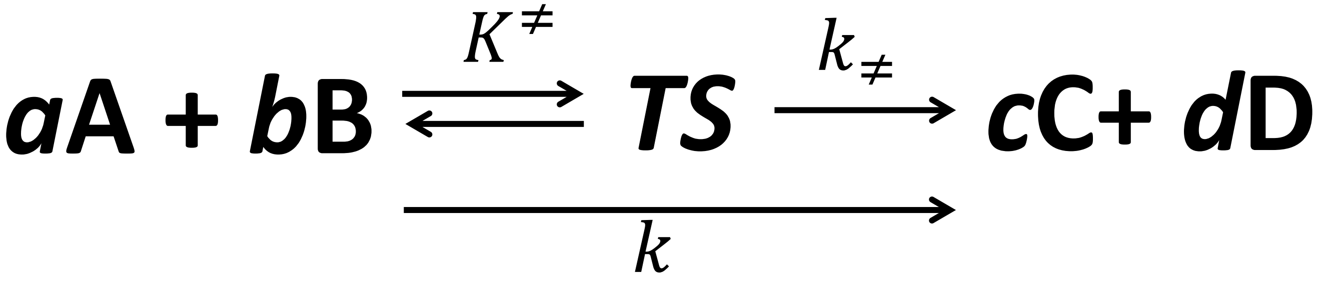
Theory of activated complex

The **theory of the activated complex** (also **transition state theory** - TST) describes the kinetics of the elementary reaction:

Assumptions:

a) activated complex is in pseudo-equilibrium with the initial state
b) activated complex decomposes into products and reactants
c) apparatus of statistical thermodynamics is used for derivation





$$aA + bB \underset{}{\overset{K^{\neq}}{\rightleftarrows}} TS \xrightarrow{k_{\neq}} cC + dD$$

$$aA + bB \xrightarrow[k]{} cC + dD$$

Theory of activated complex

$$\begin{tikzcd} aA + bB \arrow[r, shift left, "K^{\neq}"] \arrow[rr, bend right, "k"'] & TS \arrow[l, shift left] \arrow[r, "k_{\neq}"] & cC + dD \end{tikzcd}$$

ad a)

$$K^{\neq} = \frac{[TS]}{[A]^a[B]^b} \longrightarrow [TS] = K^{\neq}[A]^a[B]^b$$

ad b)

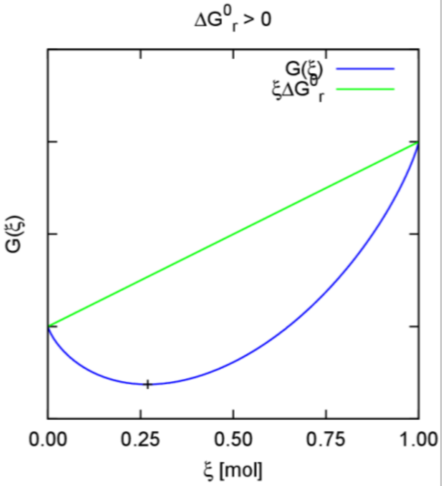
$$v = \frac{1}{a}\frac{d[A]}{dt} = \frac{1}{b}\frac{d[B]}{dt} = k_{\neq}[TS]$$

The resulting relationship

$$v = \frac{1}{a}\frac{d[A]}{dt} = \frac{1}{b}\frac{d[B]}{dt} = k_{\neq}K^{\neq}[A]^a[B]^b = k\,[A]^a[B]^b$$

$$\boxed{k = k_{\neq}K^{\neq}}$$

Theory of activated complex



$$aA + bB \underset{}{\overset{K^{\neq}}{\rightleftarrows}} TS$$

- Activation Gibbs energy is always a positive number, yet TS is present in the reaction mixture, see equilibrium for $\Delta G^0_r > 0$.
- Activation Gibbs energy corresponds to the change in which the reactants are quantitatively converted to the transition state. This is a hypothetical process that does not actually occur.

$$\Delta G^{\neq} = -RT\ln K^{\neq}$$

$$\downarrow$$

$$\boxed{K^{\neq} = e^{-\frac{\Delta G^{\neq}}{RT}}}$$

Theory of activated complex, cont.

$$\boldsymbol{TS} \xrightarrow{k_{\neq}} \boldsymbol{cC + dD}$$

original approach (via translational partition function)

$$k_{\neq} = \frac{1}{\tau}$$

average TS lifetime

$$\tau = \frac{\delta}{\bar{u}}$$

width of activated state (not well defined)

average velocity along reaction path

modern approach (via vibrational partition function)

$$k_{\neq} = \upsilon$$

rate constant is proportional to the frequency of vibration at which the TS decays into products or reactants (imaginary number = not observable)

Both approches lead to the same result (not well-defined properties fortunately cancel out).

$$\boxed{k_{\neq} = \frac{k_B T}{h}}$$

it depends only on temperature but not on molecular structure of TS

Eyring equation

$$\begin{tikzcd}
aA + bB \arrow[r, shift left, "K^{\neq}"] \arrow[rr, bend right, "k"'] & TS \arrow[l, shift left] \arrow[r, "k_{\neq}"] & cC + dD
\end{tikzcd}$$

$$k = k_{\neq} K^{\neq}$$

Eyring equation

$$k = \kappa \overline{\frac{k_B T}{h}}\, \overline{e^{-\frac{\Delta G^{\neq}}{RT}}}$$

transmission coefficient, correction term

R - universal gas constant, T - absolute temperature, h - Planck's constant, k_B - Boltzmann constant

Summary

- ➢ Description of the equilibrium and kinetics of chemical processes is important in several applications (Which?).
- ➢ **Equilibrium and kinetics can be quantified** using one thermodynamic quantity, namely **changes in the free energy**, which can be determined either experimentally or calculated using computational chemistry methods.

the activation free energy can be obtained by modelling

Eyring equation

$$k = \kappa \frac{k_B T}{h} e^{-\frac{\Delta G^{\neq}}{RT}}$$

transmission coefficient, correction term

TST is based on several oversimplification.

Thus, TST can fail in several cases: (they can be sometimes corrected by κ):

  - ➢ fate of products is not considered in TST (backward/inverse reaction is not considered)
  - ➢ tunneling (light atoms and low barriers), typically proton transfers
  - ➢ electronic state change (change from one to another potential energy surface)
  - ➢ others …

Recommended readings

- Helrich, C. S. *Modern Thermodynamics with Statistical Mechanics*; Springer: Berlin, 2009.
- Dill, K. A.; Bromberg, S. *Molecular Driving Forces: Statistical Thermodynamics in Biology, Chemistry, Physics, and Nanoscience*, 2nd ed.; Garland Science: London ; New York, 2011.

Homework

Homework exercise I

1. Determine how many times the reaction below slows down if the activation Gibbs energy increases by 0.25; 0.5; 1.0; 2.5; 5.0 and 10 kcal/mol. Consider standard conditions. Discuss the results.

$$\mathbf{A} \longrightarrow \mathbf{B}$$

use a spreadsheet to solve the exercise