From order to disorder

From the Chemistry Exam to the Final Exam in Biochemistry

Dr. Lengyel Anna

Units

multiple	prefix	symbol	sub-multiple	prefix	symbol
10^{1}	deca	da	10^{-1}	deci	d
10^{2}	hecto	h	10^{-2}	centi	c
10^{3}	kilo	k	10^{-3}	milli	m
10^{6}	mega	M	10^{-6}	micro	μ
10^{9}	giga	G	10^{-9}	nano	n
10^{12}	tera	T	10^{-12}	pico	p
10^{15}	peta	P	10^{-15}	femto	f
10^{18}	exa	E	10^{-18}	atto	a

Gas laws

Give the relationship between the state marker parameters (pressure (p), temperature (T), volume (V), molar amount (n).

State marker parameters: depend only on the current equilibrium state of the system, but not on the path by which the system arrived at its present state.

Process functions are e.g. mechanical work and heat, they describe quantitatively the transition between equilibrium states of a thermodynamic system.

Boyle's law: Relationship between the pressure and volume of the ideal gas at constant temperature.

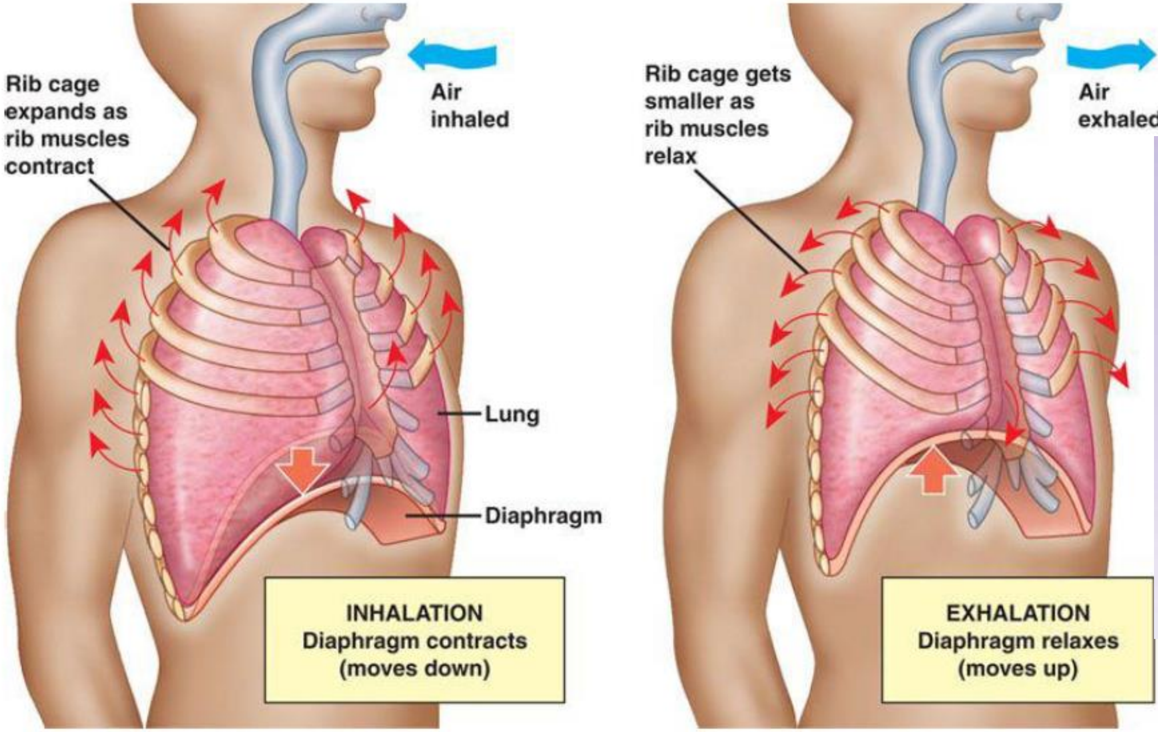
$$p \cdot V = k$$

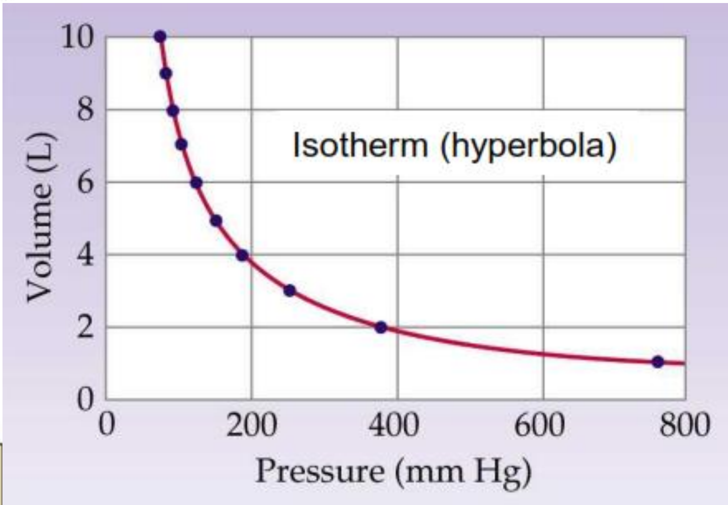
T and n are constant (*isotherm*)

for two different states of the gas:

$$p_1 \cdot V_1 = p_2 \cdot V_2$$

Boyle’s law





During an inhalation, the lungs expand, the pressure in the lungs decreases, and air flows towards the lower pressure in the lungs. During an exhalation, lung volume decreases, pressure within the lungs increases, and air flows from the higher pressure in the lungs to the outside.

Question

For a perfect gas, according to Boyle's law (where p = Absolute pressure, V = Volume, and T = Absolute temperature)

1. V/T = constant, if p is kept constant
2. p V = constant, if T is kept constant
3. T/p = constant, if V is kept constant
4. p/T = constant, if V is kept constant

Question

When two bodies are in thermal equilibrium with a third body, they are also in thermal equilibrium with each other. This statement is called

1. Second law of thermodynamics
2. First law of thermodynamics
3. Kelvin Planck's law
4. Zeroth law of thermodynamics

Question

First law of thermodynamics provides

a. a statement that energy balance occurs when a system undergoes the change of state or the process
b. a statement about whether the change of state or the process is at all feasible or not
c. both a. and b.
d. none of the above

Question

Which of the following statements best describes the Second Law of Thermodynamics?

a) The internal energy of the universe is constant.
b) Energy can be neither created nor destroyed.
c) When an isolated system undergoes a spontaneous change, the entropy of the system will increase.
d) At absolute zero, the entropy of a perfect crystal is considered to be zero.

Thermodynamics

The zeroth law of thermodynamics: If two systems are each in thermal equilibrium with a third, they are also in thermal equilibrium with each other (thermometer, thermostat).

The first law of thermodynamics: energy can not be created or destroyed, just transformed in other types of energy (law of conservation of energy)

In a closed system the internal energy (E) remains constant till work (W) or heat (Q) change it: $\Delta E = Q + W$ **Q: reaction heat**

- Without expansion work: $\Delta E = Q_V$ (Q_V: reaction heat by constant volume)
- With expansion work: $\Delta E = Q_p - p\Delta V$ (Q_p :reaction heat by constant pressure)

$$Q_p = \underbrace{\Delta E + p\Delta V}_{\Delta H}$$

$\Delta H = \Delta E + p\Delta V$ ΔH = Enthalpy change (reaction heat at a constant pressure)

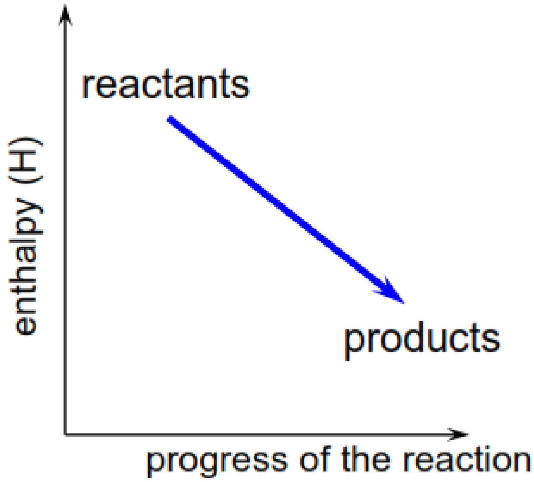
Hess' law: the enthalphy change of a chemical reaction depends only on the starting and the final states of the system, and it is independent of reaction pathway. (law of conservation of energy for chemical reactions)

Enthalpy chage (reaction heat) of a chemical reaction:

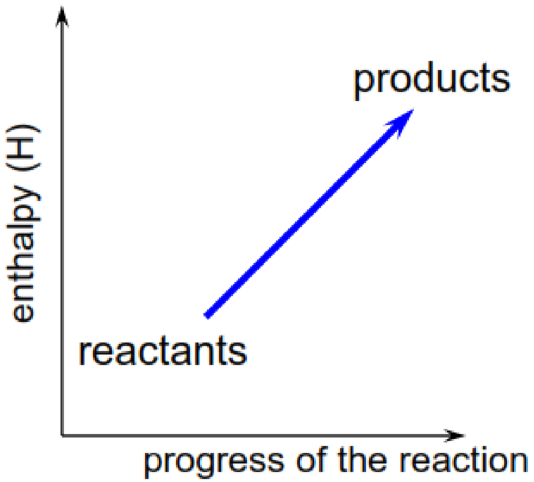
$$\Delta H = \Sigma H_{\text{products}} - \Sigma H_{\text{reactants}}$$

Reaction heat at a constant pressure (ΔH)

exothermic reaction
$\Delta H < 0$



endothermic reaction
$\Delta H > 0$



Enthalpy (H) is the measure of the energy of a thermodynamic system

The second law of thermodynamics: In spontaneous processes entropy increases (direction of reactions).

Entropy change: $\Delta S = S_{\text{final state}} - S_{\text{initial state}}$

The 2nd law: $\Delta S_{\text{total}} > 0$ $(\Delta S_{\text{system}} + \Delta S_{\text{surrounding}} > 0)$

Entropy (S): the measure of disorder (J/ K) $S = k \ln W$

k: Boltzmann's constant ($1.381 \cdot 10^{-23}$ J/K)
W: number of microstates, which give a certain macrostate

Spontaneous processes: take place without external force

Non-spontaneous processes: do not take place, requires external energy

The third law of thermodynamics:

the entropy of a perfect crystal at 0 K temperature is 0 J/K.

Effect of temperature on entropy change during chemical reactions:

$$\Delta S = \frac{\Delta Q}{T} \qquad \text{at a constant pressure: } \Delta S = \frac{\Delta H}{T}$$

ΔQ: reaction heat

Spontaneous chemical reactions occurs in that direction which decreases enthalpy and increases entropy.

enthalpy = free energy + energy 'stored' in disorder

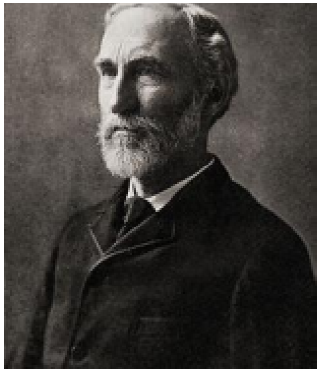
$$H = G + TS$$

Free energy (G): the work capacity of the system

Free energy change in chemical reactions:

$$\Delta G = G_{\text{final state}} - G_{\text{initial state}}$$

$$\boxed{\Delta G = \Delta H - T\Delta S \qquad \text{Gibbs equation}}$$



Josiah Willard Gibbs
(1839-1903)

If **$\Delta G < 0$** the process takes place spontaneously, exergonic

If **$\Delta G > 0$** the process doesn't take place, endergonic

If **$\Delta G = 0$** no net transformation, equilibrium

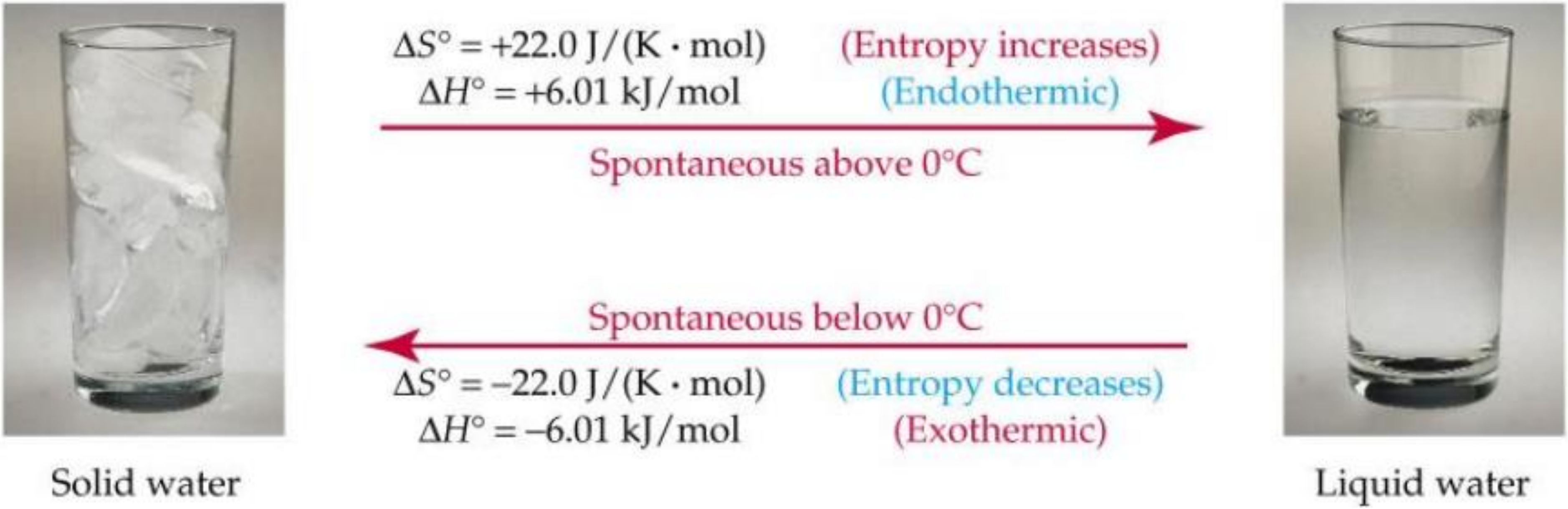
In the equilibrium: $\Delta G = 0$

$$0 = \Delta G^\circ + RT \ln K$$

$$\Delta G^\circ = - RT \ln K$$

For standard state reactants and products:

standard free energy change: $\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$



$\Delta S^\circ = +22.0\ \mathrm{J/(K \cdot mol)}$ (Entropy increases)

$\Delta H^\circ = +6.01\ \mathrm{kJ/mol}$ (Endothermic)

Spontaneous above 0°C

Spontaneous below 0°C

$\Delta S^\circ = -22.0\ \mathrm{J/(K \cdot mol)}$ (Entropy decreases)

$\Delta H^\circ = -6.01\ \mathrm{kJ/mol}$ (Exothermic)

Solid water

Liquid water

Free energy and chemical equilibrium – the extent of the reaction

Characterization of the composition of the reaction mixture: reaction quotient (Q) or mass-action ratio

$$a\,A + b\,B = c\,C + d\,D \qquad Q = \frac{[C]^c[D]^d}{[A]^a[B]^b}$$

at any moment of the reaction

(here [X] doesn't mean equilibrium conc.!)

The direction of the reaction always depends on the actual composition!

(Le Châtelier-Braun principle)

$$\Delta G = \Delta G^\circ + RT \ln Q$$

Question

The energy of an isolated system

a. is always decreasing
b. is always constant
c. is always increasing
d. none of the above

glucose + $P_i \rightarrow$ glucose-6-phosphate + H_2O $\Delta G°' = 13.8$ kJ/mol

ATP + $H_2O \rightarrow$ ADP + P_i $\Delta G°' = -30.5$ kJ/mol

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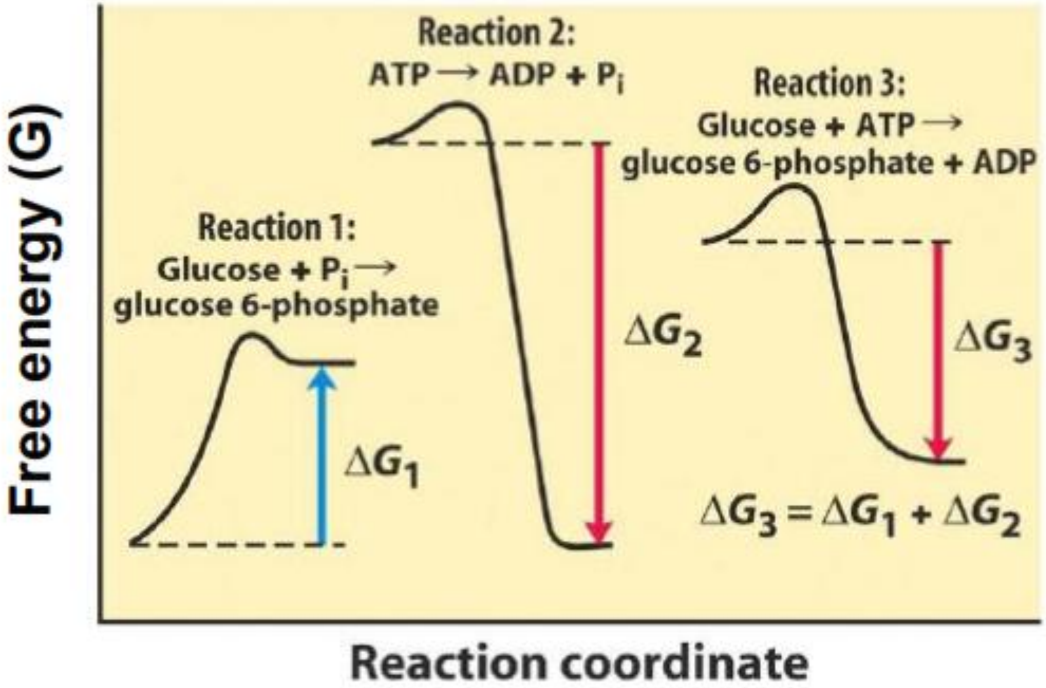
ATP + glucose → ADP + glucose-6-phosphate $\Delta G°' = 13.8 - 30.5 = -16.7$ kJ/mol



$\Delta G = \Delta G° + RT \ln Q$

Anaerobe and aerobe metabolysis: fill-up of the 'ATP-stock'

Energy production of anaerobic cells: fermentation

glucose → 2 lactate $\Delta G°' = -218$ kJ/mol

Fill-up of the 'ATP-stock':

glucose + 2 P_i + 2 ADP → 2 lactate + 2ATP + 2 H_2O $\Delta G°' = -158$ kJ/mol

Energy production of aerobic cells:

glucose → 6 CO_2 + 6 H_2O $\Delta G°' = -2880$ kJ/mol

During the aerobe oxidation of 1 glucose molecule 32 ATP form!

$32 \cdot 30$ kJ = 960 kJ energy is stored

glucose + 6 O_2 + 32 P_i + 32 ADP → 6 CO_2 + 2 H_2O + 32 ATP

$\Delta G'° = -1920$ kJ/mol

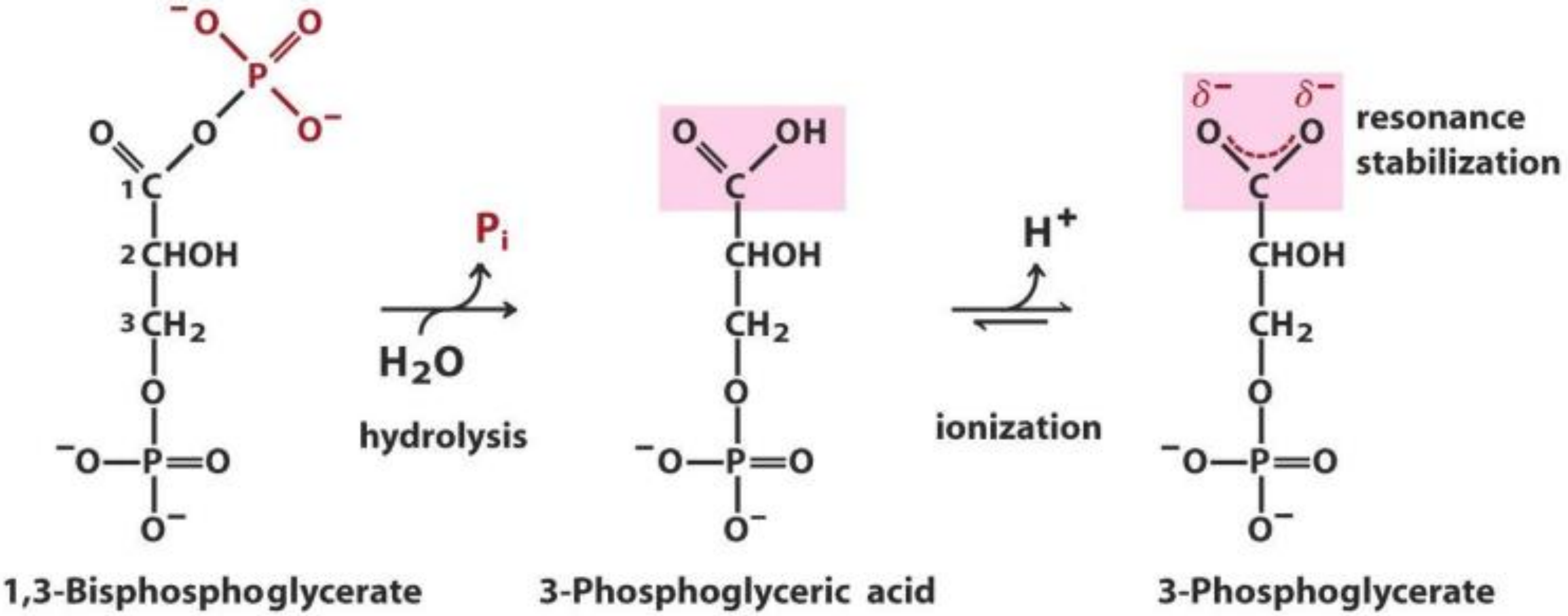
Question

Which of the following statements will always apply when a reversible chemical reaction has attained equilibrium?

a) All reactants will convert to products
b) The reaction proceeds alternately in the forward and reverse directions
c) The Gibbs free energy of the system reaches a minimum
d) The forward reaction will dominate over the reverse reaction

Question

Calculate the free energy of the phosphoglycerate kinase reaction under standard circumstances! Which partial reaction is exergonic, and which is endergonic?



$$\text{1,3-Bisphosphoglycerate}^{4-} + H_2O \longrightarrow \text{3-phosphoglycerate}^{3-} + P_i^{2-} + H^+$$

$$\Delta G'^{\circ} = -49.3 \text{ kJ/mol}$$

ATP *(aq)* + H_2O *(l)* → ADP *(aq)* + P_i^- *(aq)* + H^+ *(aq)*   ΔG'= -30 kJ/mol

Living systems are never in thermodynamical equilibrium

The direction of the reactions is determined by the actual intracellular concentrations of the metabolites involved

„Thermodynamically favoured” does not necessarily mean „quick”

Reaction rate is independent of ΔG.

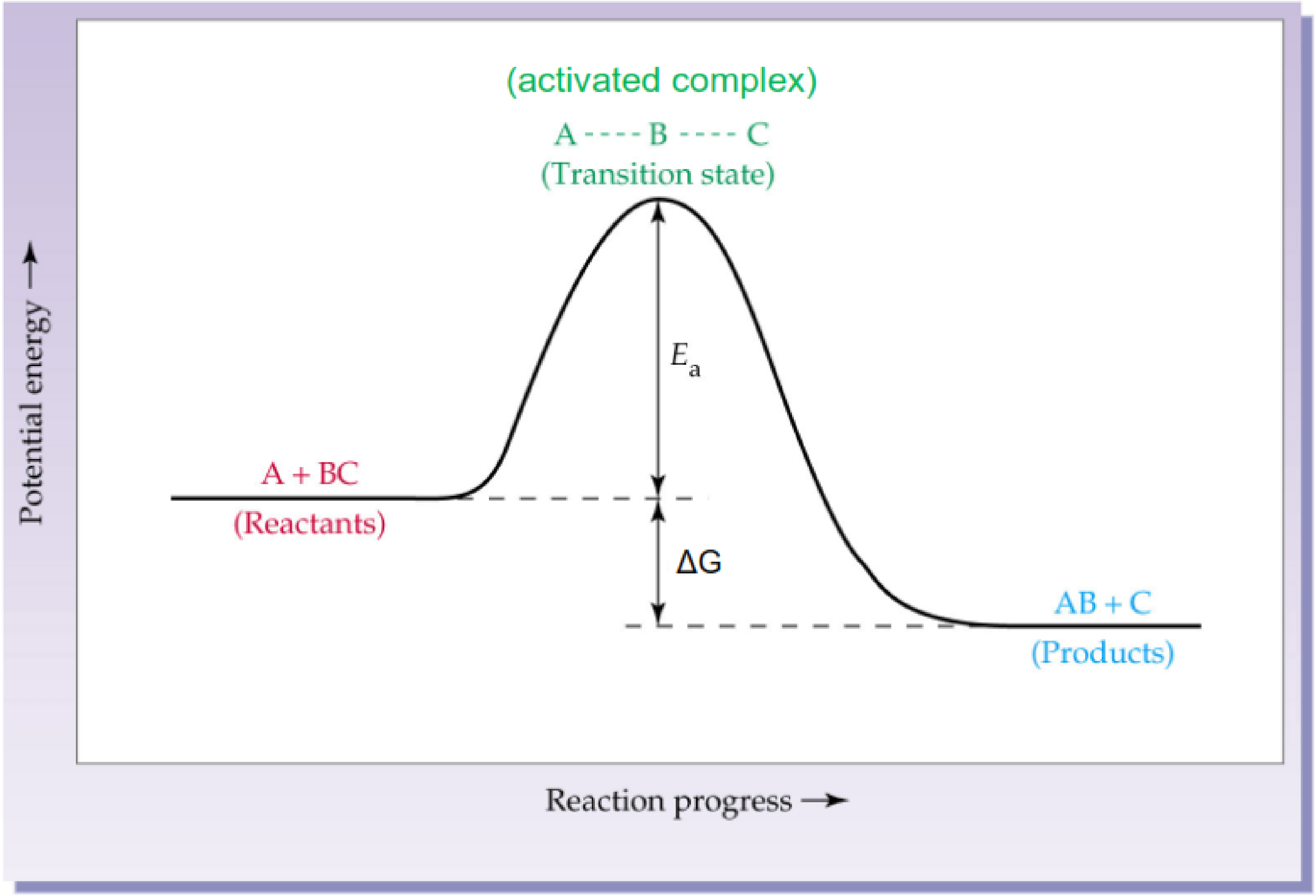
Catalysts (e.g. enzymes) do **not** influence the „position” of chemical equilibrium, they only accelerate the reactions leading to it.

Every elementary reaction is reversible – in theory

In biochemistry a reaction is called „irreversible” when:

under cellular conditions (temperature, concentrations) one of the reactions appears to be *undetectably slow*.

Reaction kinetics



E_a: activation energy: the energy, which is needed to form the activated complex

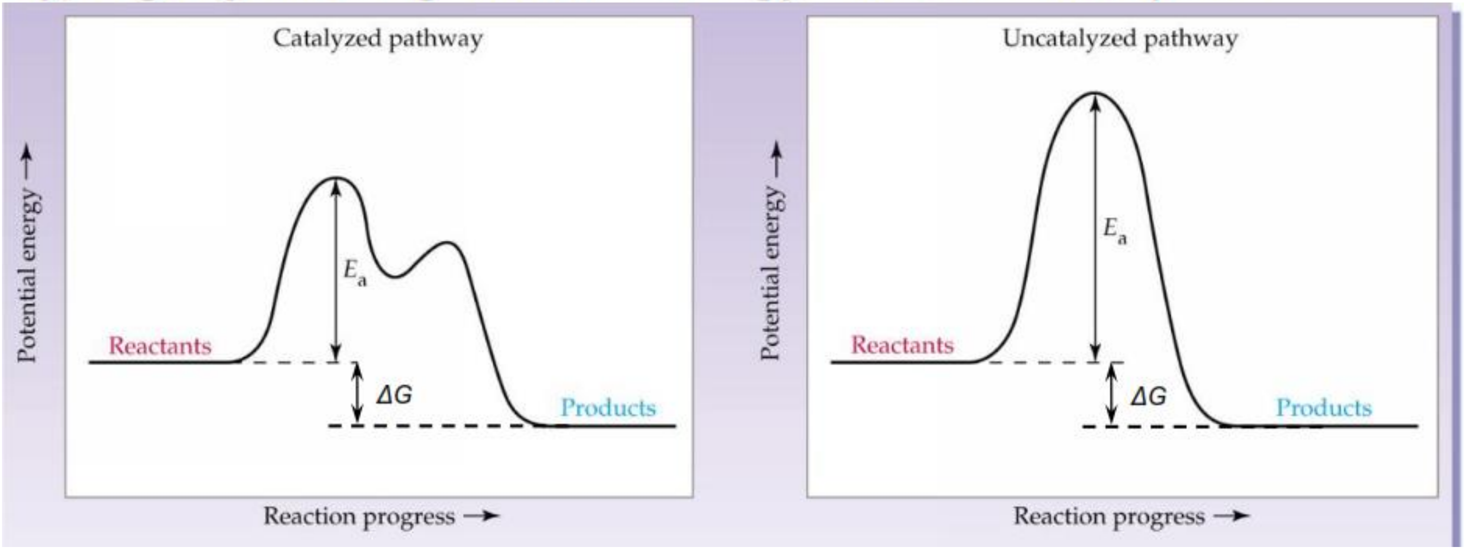
ΔG: reaction free energy

Catalysis

Catalyst: a substance which increases the rate of the reaction without being consumed by the reaction.

In the absence of catalyst the reaction is much slower.

The catalyst decreases the activation energy by opening an other reaction pathway, e.g. by forming a lower energy activated complex.



In biological systems the enzymes catalyse the transformations of molecules.

homogenous catalyst: is in the same phase as the reactants

heterogeneous catalyst: exist in different phase as the reactants.

Inhibitor: decreases the rate of a reaction without being consumed by the reaction.

The rate of a reaction

It’s a measure of how fast the changes are taking place in a reaction per unit time:

- increase in the concentration of the product(s) or
- decrease in the concentration of the reactant(s).

It depends on:

- the chemical quality of the reactants
- the concentration of the reactants
- the temperature
- the physical state of the reactants

Rate law:

Equation which describes the rate of the reaction as a function of the concentration of the reactants.

Rate limiting step: the slowest step in a reaction mechanism

Stoichiometric equation:

$$\underbrace{a\,\mathrm{A} + b\,\mathrm{B}}_{\text{reactants}} \rightarrow \underbrace{c\,\mathrm{C} + d\,\mathrm{D}}_{\text{products}}$$

capital letters (A, B, C, D): compounds or elements

small letters (a, b, c, d): stoichiometric coefficients

Rate law:

$$\boxed{\mathbf{v = k\,[A]^{x}\,[B]^{y}}}$$

v: rate of the reaction

k: rate constant

square brackets ([A], [B]): concentrations (mol/dm^3)

x, y: exponents, reaction order

Reaction order: the sum of the exponents in the rate law

$v = k\,[A]^x\,[B]^y \qquad x + y = \text{reaction order}$

e.g. if x = 1 the rate depends linearly on the concentartion of A

if x = 2 the rate is the quadratic function of the concentartion of A, etc.

The exponents must be determined by experiment, they cannot be deduced from the stoichiometry of the reaction!

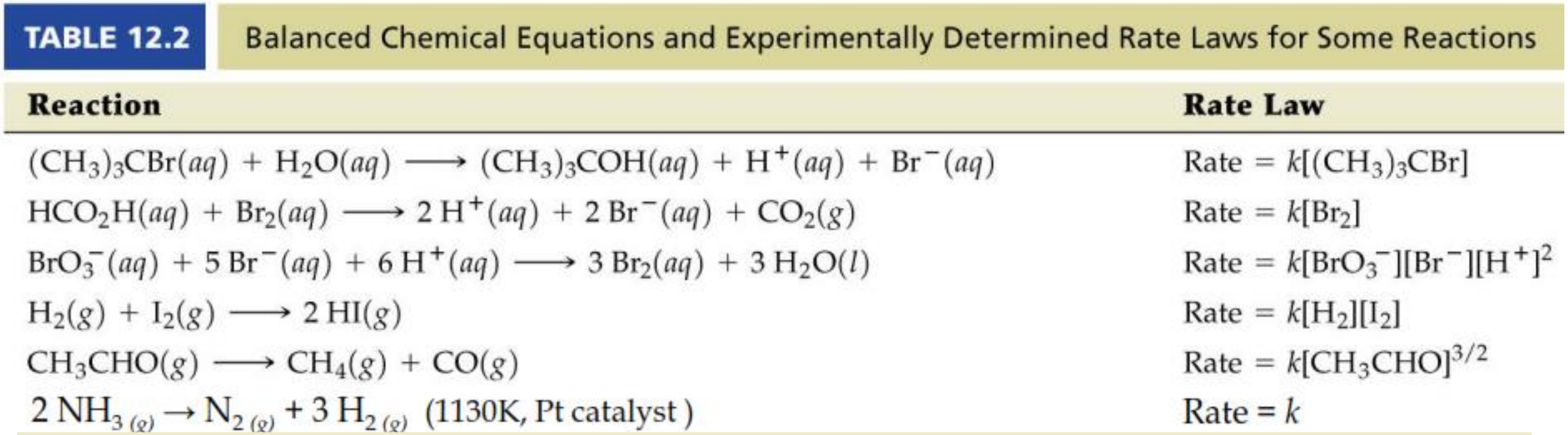
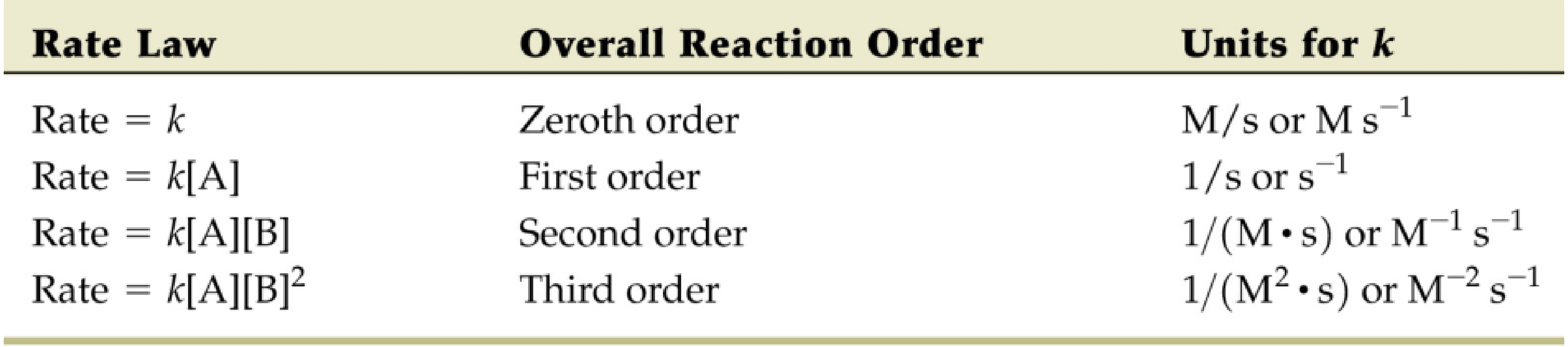


TABLE 12.2 Balanced Chemical Equations and Experimentally Determined Rate Laws for Some Reactions

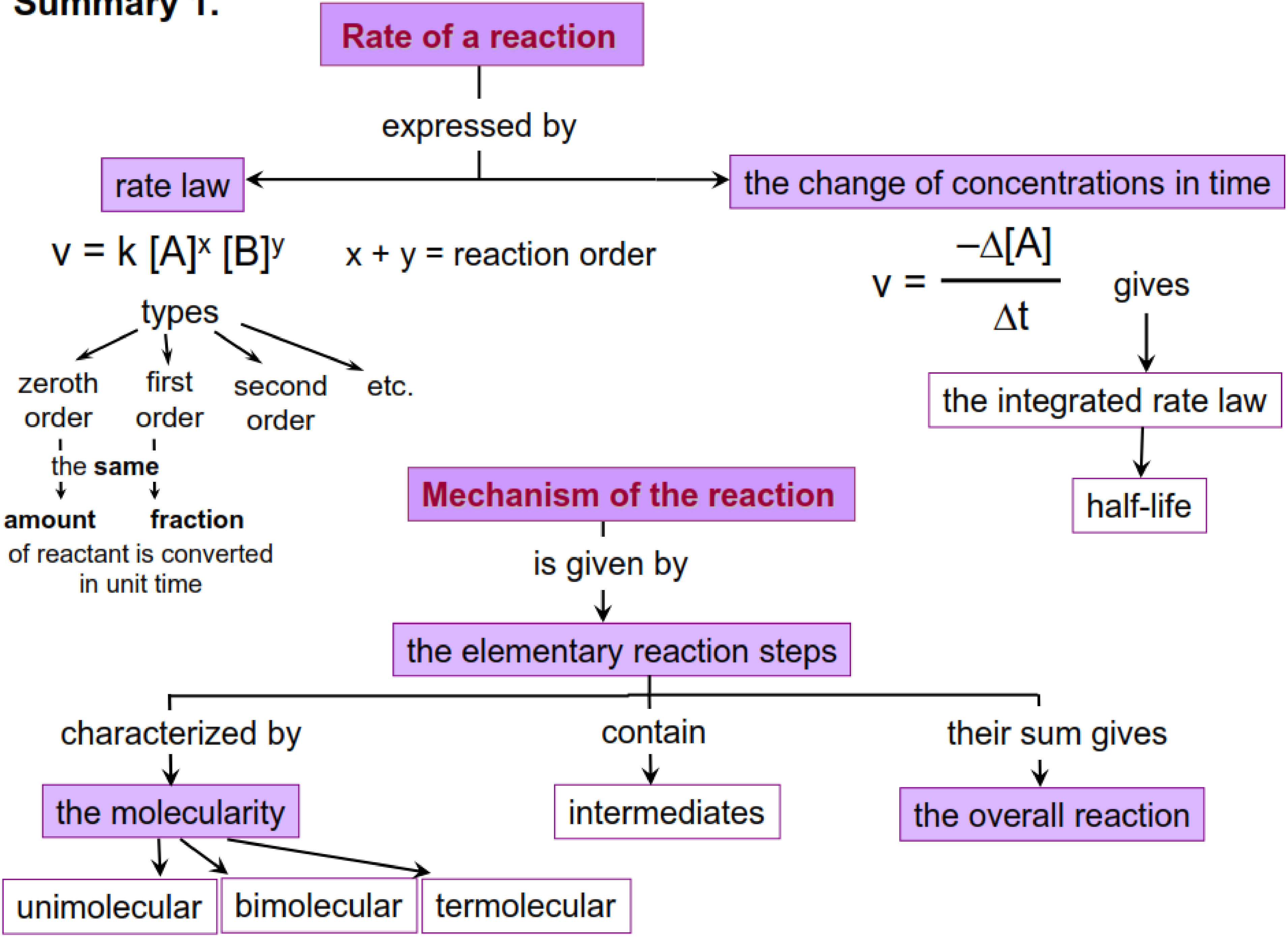
Reaction	Rate Law
$(CH_3)_3CBr(aq) + H_2O(aq) \longrightarrow (CH_3)_3COH(aq) + H^+(aq) + Br^-(aq)$	$\text{Rate} = k[(CH_3)_3CBr]$
$HCO_2H(aq) + Br_2(aq) \longrightarrow 2\,H^+(aq) + 2\,Br^-(aq) + CO_2(g)$	$\text{Rate} = k[Br_2]$
$BrO_3^-(aq) + 5\,Br^-(aq) + 6\,H^+(aq) \longrightarrow 3\,Br_2(aq) + 3\,H_2O(l)$	$\text{Rate} = k[BrO_3^-][Br^-][H^+]^2$
$H_2(g) + I_2(g) \longrightarrow 2\,HI(g)$	$\text{Rate} = k[H_2][I_2]$
$CH_3CHO(g) \longrightarrow CH_4(g) + CO(g)$	$\text{Rate} = k[CH_3CHO]^{3/2}$
$2\,NH_{3\,(g)} \rightarrow N_{2\,(g)} + 3\,H_{2\,(g)}$ (1130K, Pt catalyst)	$\text{Rate} = k$



Rate Law	Overall Reaction Order	Units for *k*
$\text{Rate} = k$	Zeroth order	M/s or $M\,s^{-1}$
$\text{Rate} = k[A]$	First order	1/s or s^{-1}
$\text{Rate} = k[A][B]$	Second order	$1/(M \cdot s)$ or $M^{-1}\,s^{-1}$
$\text{Rate} = k[A][B]^2$	Third order	$1/(M^2 \cdot s)$ or $M^{-2}\,s^{-1}$

The rate always has unit of M/s, but the units of the rate constant (k) depend on the overall reaction order:

Summary 1.



Rate of a reaction

expressed by

rate law

the change of concentrations in time

$v = k\,[A]^x\,[B]^y$ $x + y =$ reaction order

types

zeroth order

first order

second order

etc.

the **same**

amount **fraction**

of reactant is converted in unit time

$$v = \frac{-\Delta[A]}{\Delta t}$$

gives

the integrated rate law

half-life

Mechanism of the reaction

is given by

the elementary reaction steps

characterized by

contain

their sum gives

the molecularity

intermediates

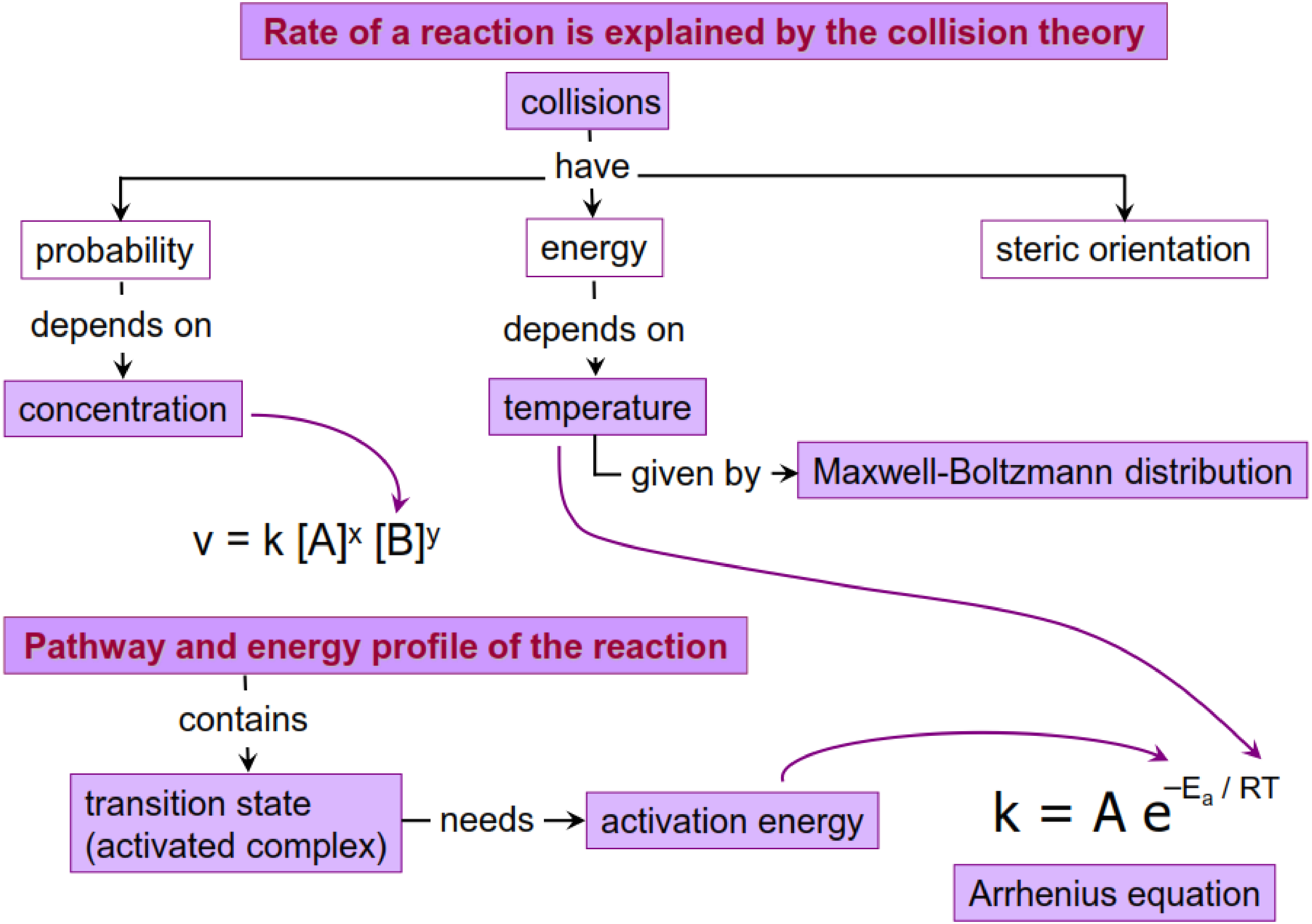
the overall reaction

unimolecular

bimolecular

termolecular

Summary 2.



Rate of a reaction is explained by the collision theory

collisions

have

probability

energy

steric orientation

probability depends on concentration

energy depends on temperature

temperature given by → Maxwell-Boltzmann distribution

$$v = k [A]^x [B]^y$$

Pathway and energy profile of the reaction

contains

transition state (activated complex)

needs → activation energy

$$k = A e^{-E_a / RT}$$

Arrhenius equation

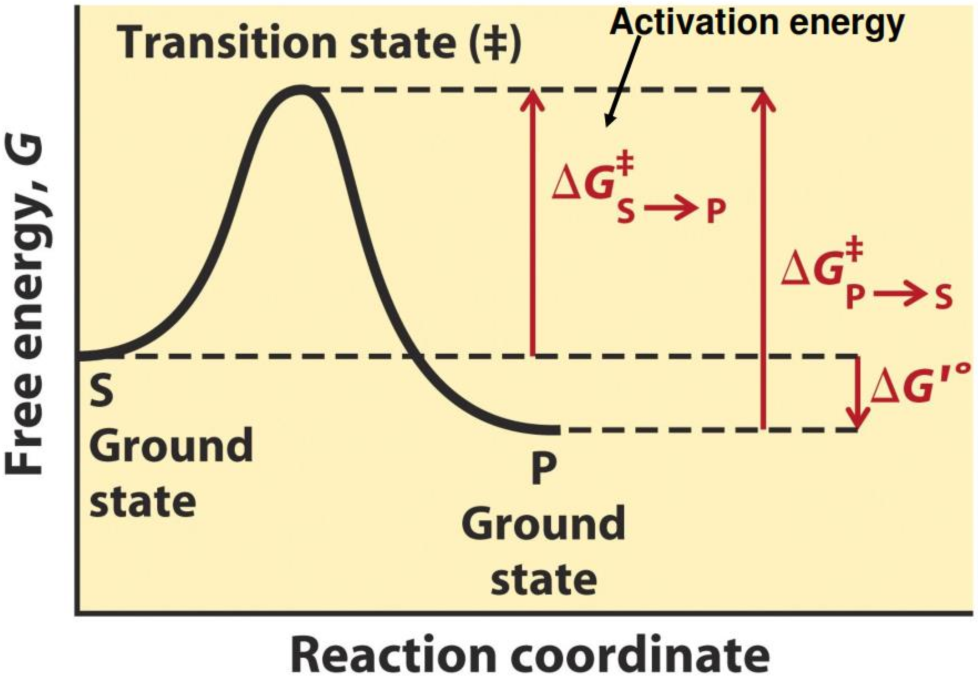
Question

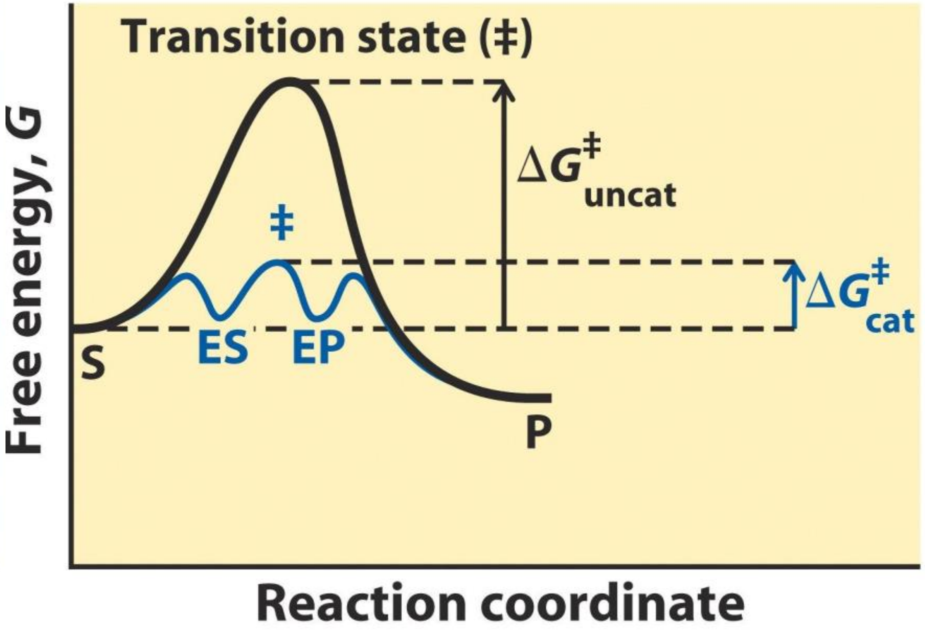
Which of the following is true of enzymes?

I. They increase the rate of reaction by stabilizing the transition state
II. They raise activation energy to shift the equilibrium to favor the products
III. They lower activation energy by altering the products of a reaction

A. I only
B. II+III
C. I+III
D. III only

Enzymes





$$E + S \rightleftharpoons ES \rightleftharpoons EP \longrightarrow E + P$$

Classification of enzymes

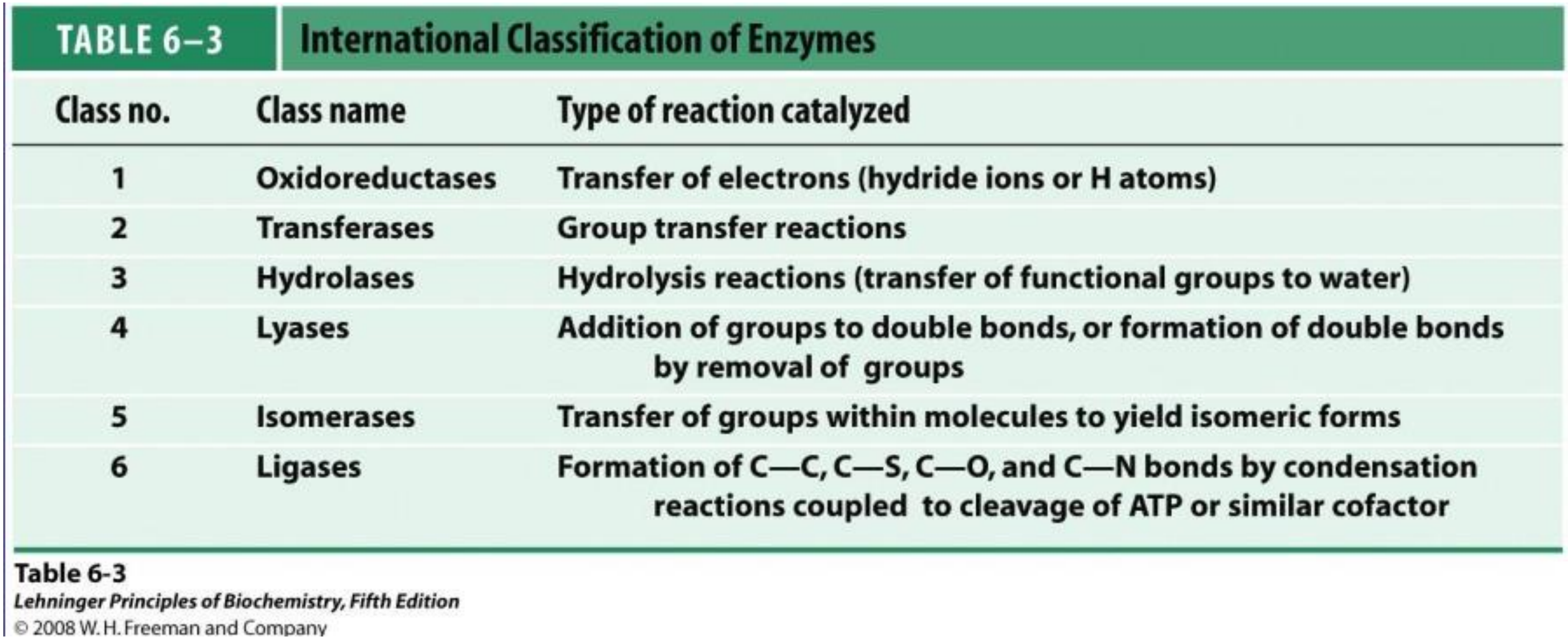


TABLE 6–3 **International Classification of Enzymes**

Class no.	Class name	Type of reaction catalyzed
1	Oxidoreductases	Transfer of electrons (hydride ions or H atoms)
2	Transferases	Group transfer reactions
3	Hydrolases	Hydrolysis reactions (transfer of functional groups to water)
4	Lyases	Addition of groups to double bonds, or formation of double bonds by removal of groups
5	Isomerases	Transfer of groups within molecules to yield isomeric forms
6	Ligases	Formation of C—C, C—S, C—O, and C—N bonds by condensation reactions coupled to cleavage of ATP or similar cofactor

Table 6-3
Lehninger Principles of Biochemistry, Fifth Edition

Cofactors

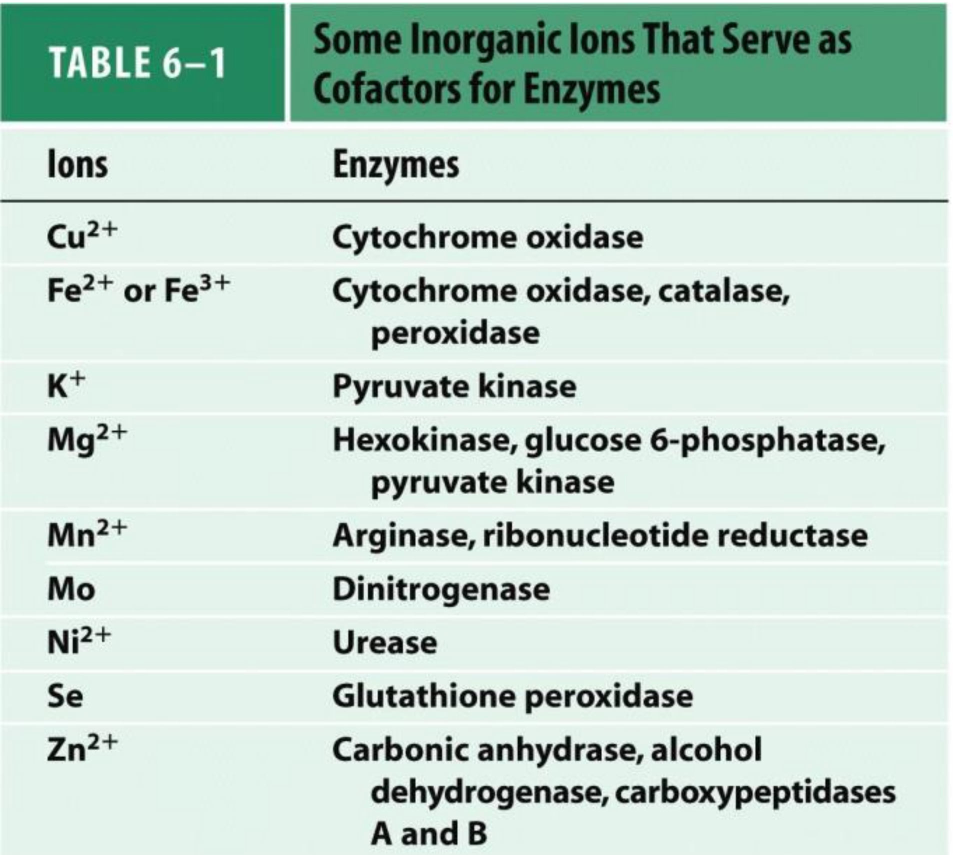
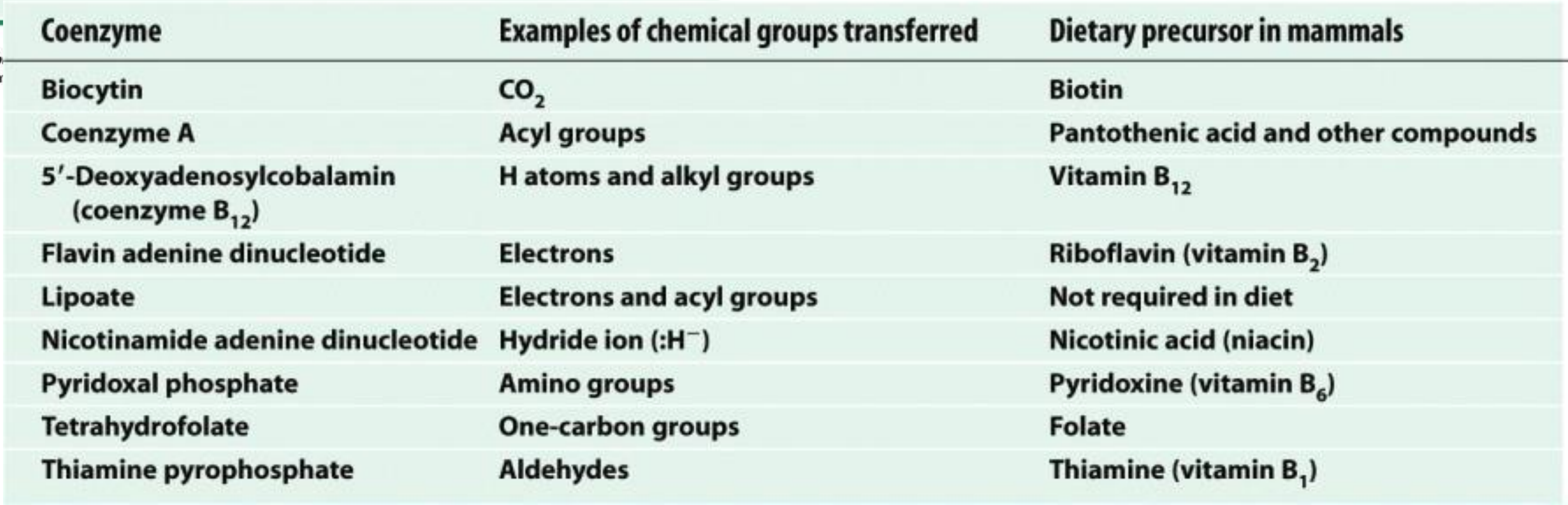


TABLE 6–1 Some Inorganic Ions That Serve as Cofactors for Enzymes

Ions	Enzymes
Cu^{2+}	Cytochrome oxidase
Fe^{2+} or Fe^{3+}	Cytochrome oxidase, catalase, peroxidase
K^{+}	Pyruvate kinase
Mg^{2+}	Hexokinase, glucose 6-phosphatase, pyruvate kinase
Mn^{2+}	Arginase, ribonucleotide reductase
Mo	Dinitrogenase
Ni^{2+}	Urease
Se	Glutathione peroxidase
Zn^{2+}	Carbonic anhydrase, alcohol dehydrogenase, carboxypeptidases A and B

Table 6-1
Lehninger Princip



Coenzyme	Examples of chemical groups transferred	Dietary precursor in mammals
Biocytin	CO_2	Biotin
Coenzyme A	Acyl groups	Pantothenic acid and other compounds
5′-Deoxyadenosylcobalamin (coenzyme B_{12})	H atoms and alkyl groups	Vitamin B_{12}
Flavin adenine dinucleotide	Electrons	Riboflavin (vitamin B_2)
Lipoate	Electrons and acyl groups	Not required in diet
Nicotinamide adenine dinucleotide	Hydride ion ($:H^-$)	Nicotinic acid (niacin)
Pyridoxal phosphate	Amino groups	Pyridoxine (vitamin B_6)
Tetrahydrofolate	One-carbon groups	Folate
Thiamine pyrophosphate	Aldehydes	Thiamine (vitamin B_1)

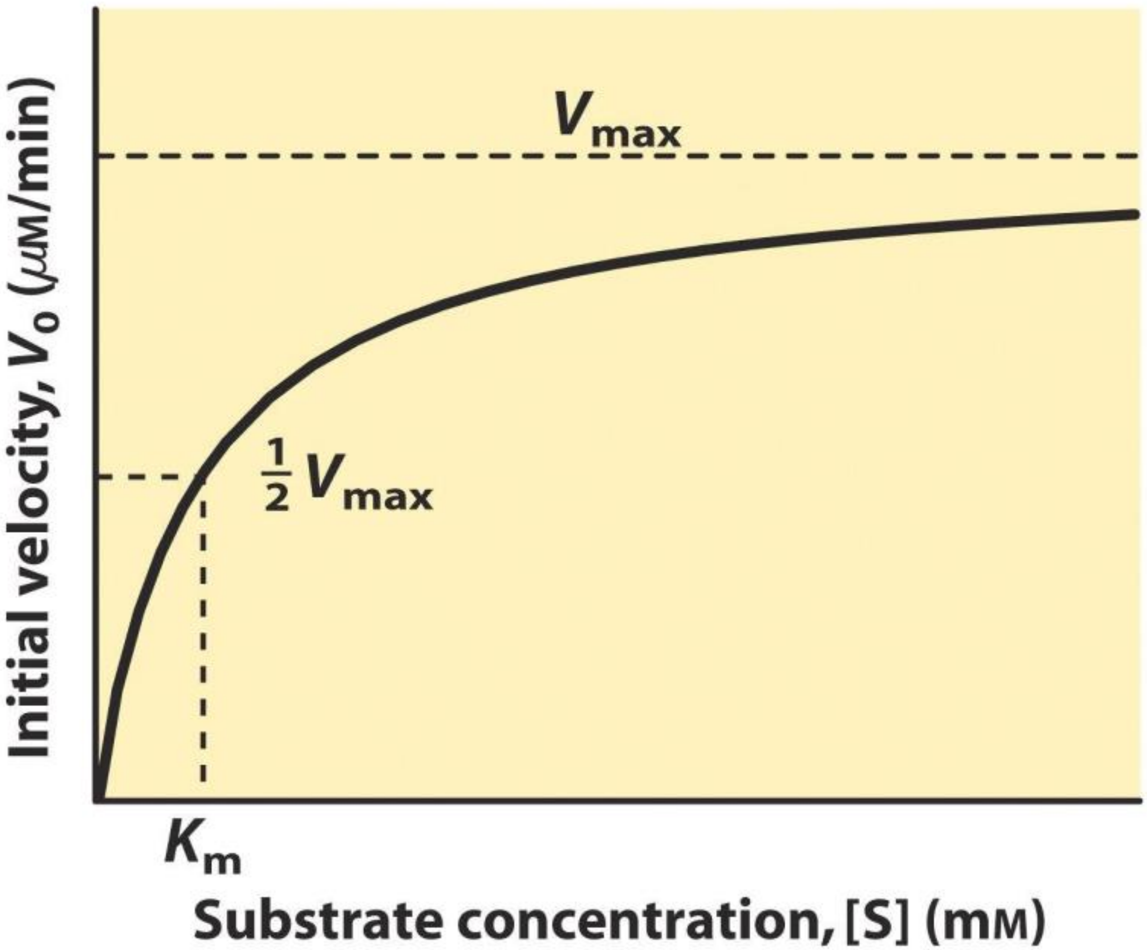
Isoenzymes (isozymes)

Isozymes catalyze the same reaction,

but may differ in:

- sequence, structure, subunit composition
- encoding gene or even chromosome
- necessary cofactors
- substrate affinity (K_M)
- localization (among organs or organelles).

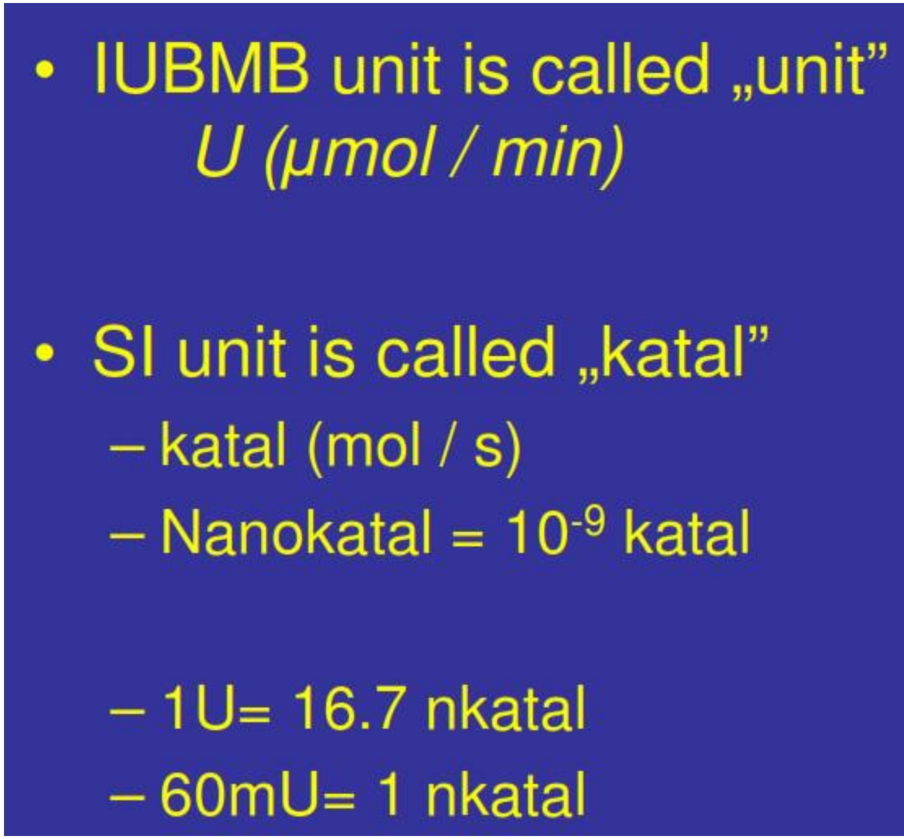
Affinity



K_M is numerically equivalent to the substrate concentration at which the reaction rate is half of the maximal ($v = ½·v_{max}$), which is thus at half saturation. K_M measures also the affinity of the enzyme towards the substrate.

Definition: The activity of a catalyst (a.k.a. catalytic activity) is a measure of how fast a catalyst converts starting materials into products.

Enzyme activity is a measure of the quantity of active enzyme present: moles of substrate converted per unit time.
The SI unit is the katal, the enzyme amount capable to convert 1mol substrate in a second, but this is an excessively large unit. A more practical and commonly used value is enzyme unit (U), 1 µmol in 1 minute.
Pure enzymes have well-defined specific activities on this scale between 5 and 500 U/mg.



- IUBMB unit is called „unit"
  U (µmol / min)
- SI unit is called „katal"
  - katal (mol / s)
  - Nanokatal = 10^{-9} katal
  - 1U= 16.7 nkatal
  - 60mU= 1 nkatal

Enzyme inhibitions

Reversible:

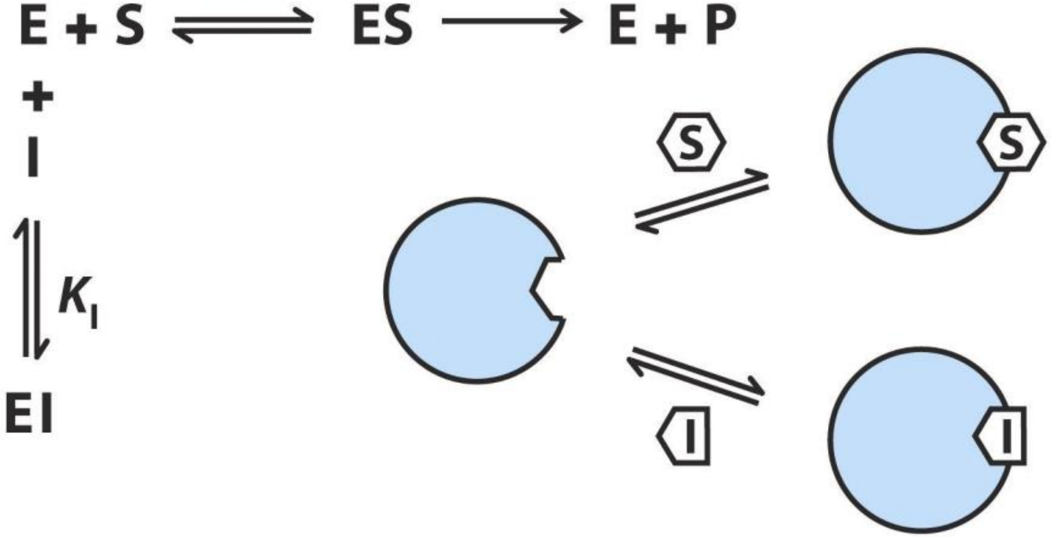
- Michaelis-Menten type:

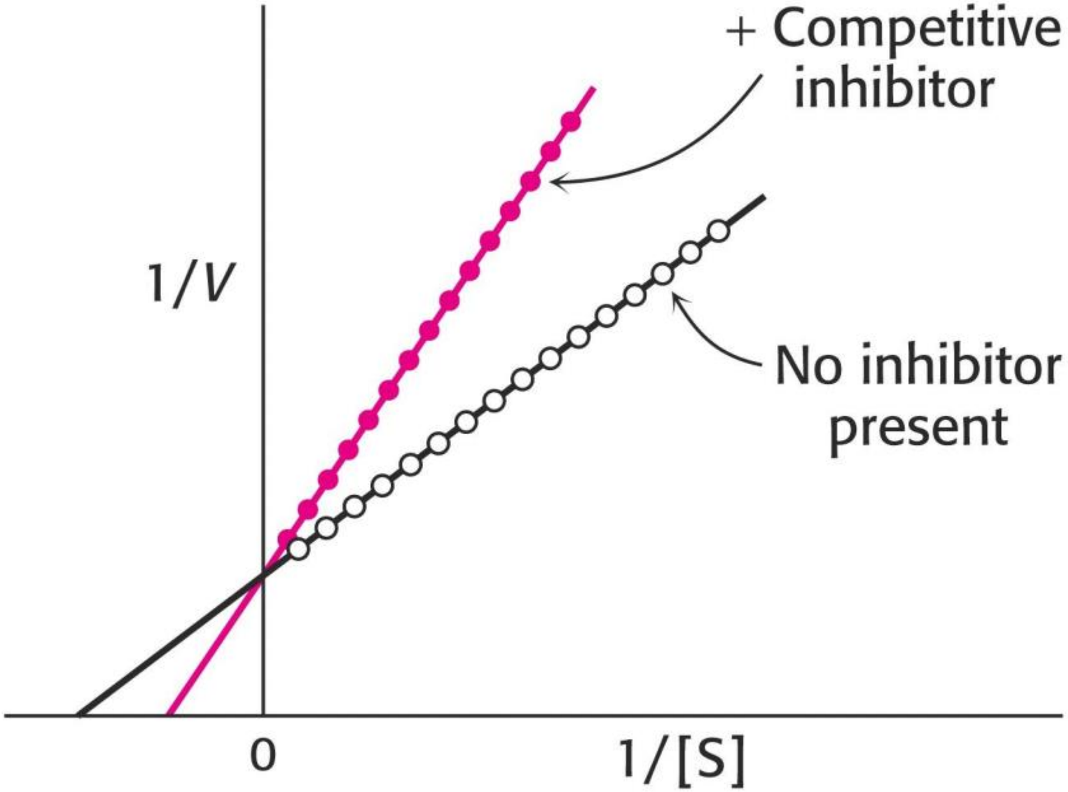
competitive inhibition
uncompetitive inhibition
mixed inhibition (incl. noncompetitive inhibition)

- Allosteric regulation
- Covalent modification
- Binding protein association

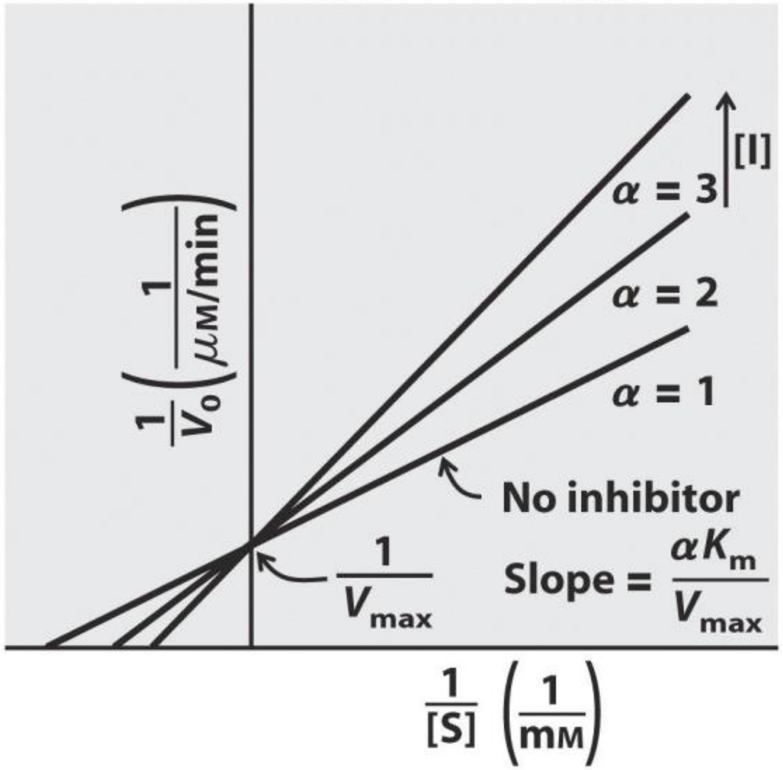
Irreversible: inactivation of the enzyme

Competitive inhibition

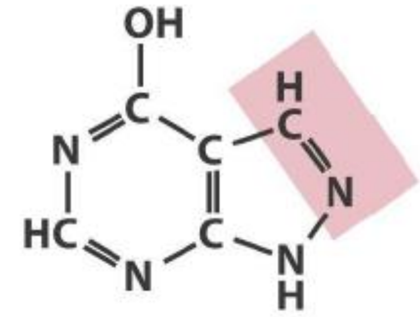




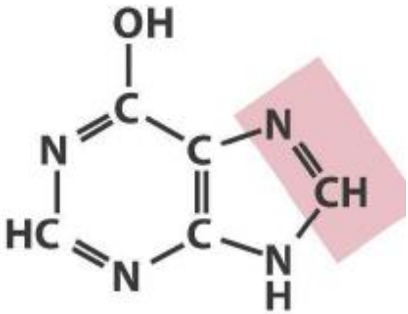
$$\frac{1}{V_0} = \left(\frac{\alpha K_m}{V_{max}}\right)\frac{1}{[S]} + \frac{1}{V_{max}}$$



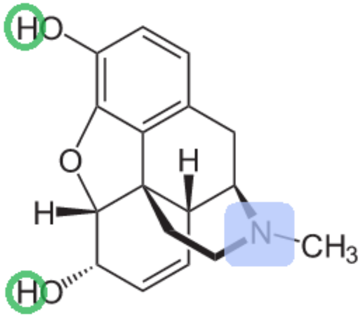
Pharmaceuticals



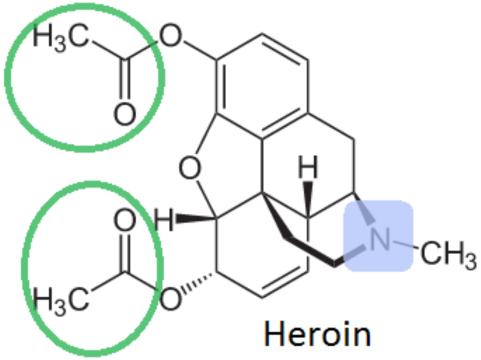
Allopurinol



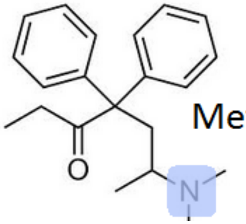
Hypoxanthine (enol form)



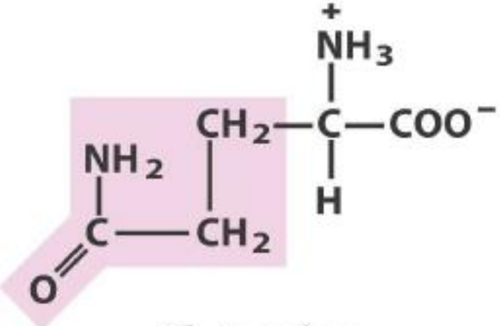
Morphine



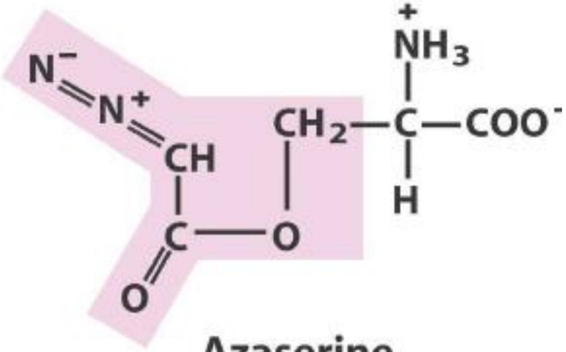
Heroin



Methadone

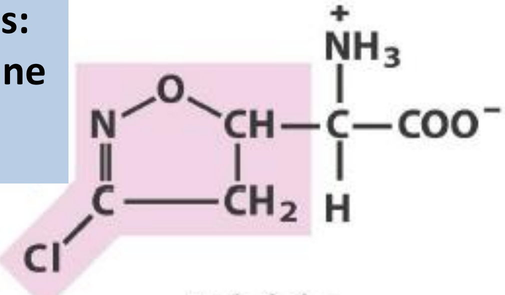


Glutamine

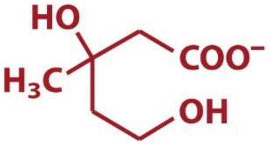


Azaserine

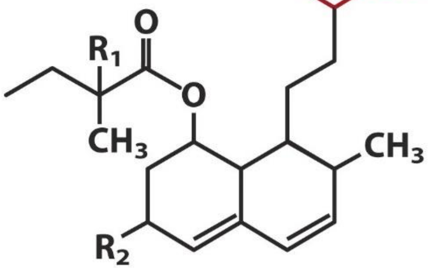
Glutamine analogues: inhibitors of glutamine amidotransferase



Acivicin

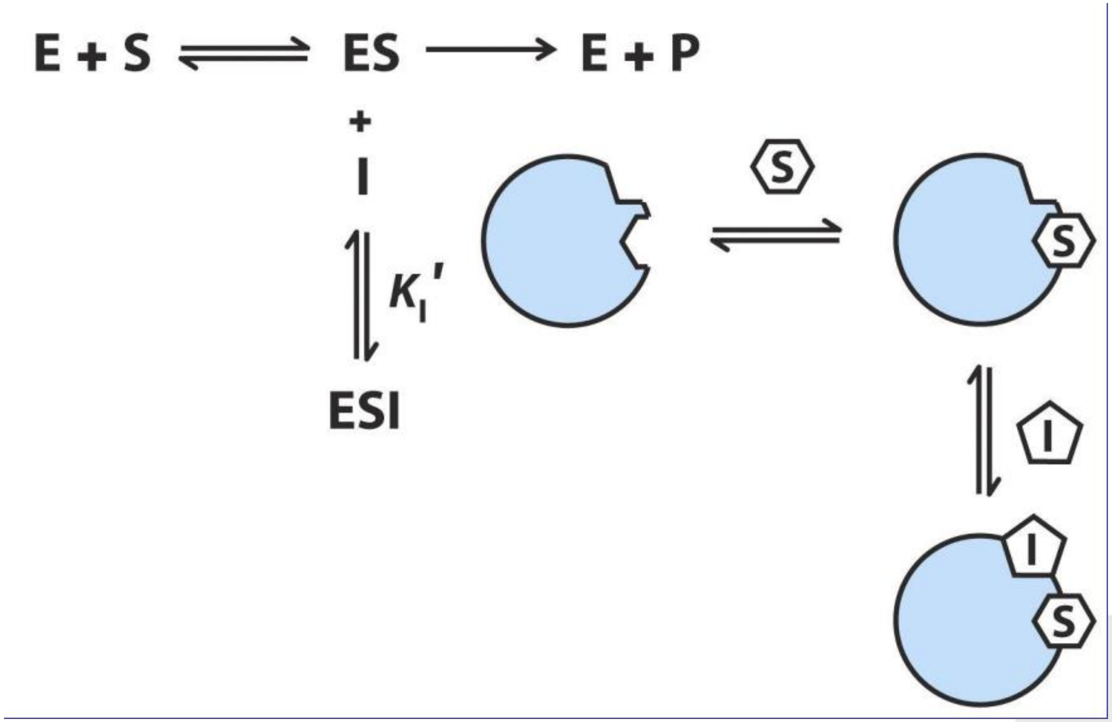


Mevalonate



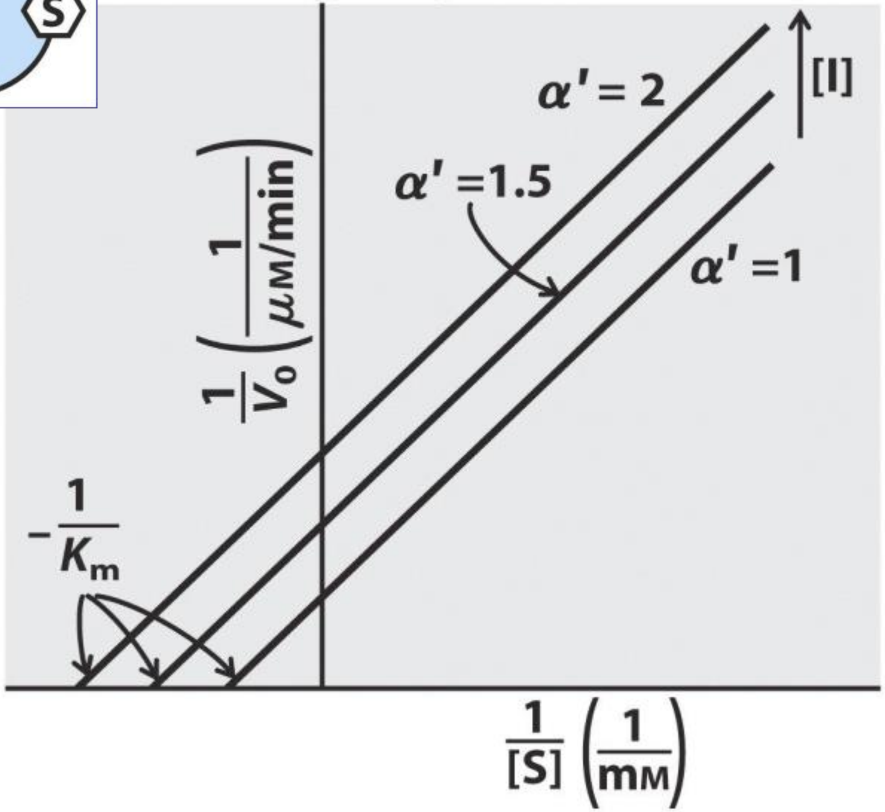
$R_1 = H$	$R_2 = H$	**Compactin**
$R_1 = CH_3$	$R_2 = CH_3$	**Simvastatin (Zocor)**
$R_1 = H$	$R_2 = OH$	**Pravastatin (Pravachol)**
$R_1 = H$	$R_2 = CH_3$	**Lovastatin (Mevacor)**

Uncompetitive inhibition



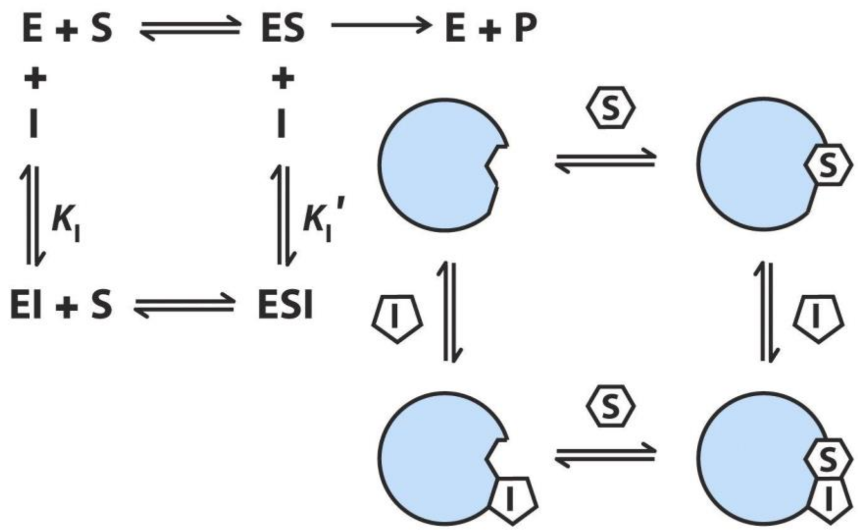
$$\begin{tikzcd} E + S \arrow[r, shift left] & ES \arrow[l, shift left] \arrow[r] & E + P \\ & + \, I \arrow[d, shift left, "K_I'"] & \\ & ESI \arrow[u, shift left] & \end{tikzcd}$$

$$\frac{1}{V_0} = \left(\frac{K_m}{V_{max}}\right)\frac{1}{[S]} + \frac{\alpha'}{V_{max}}$$

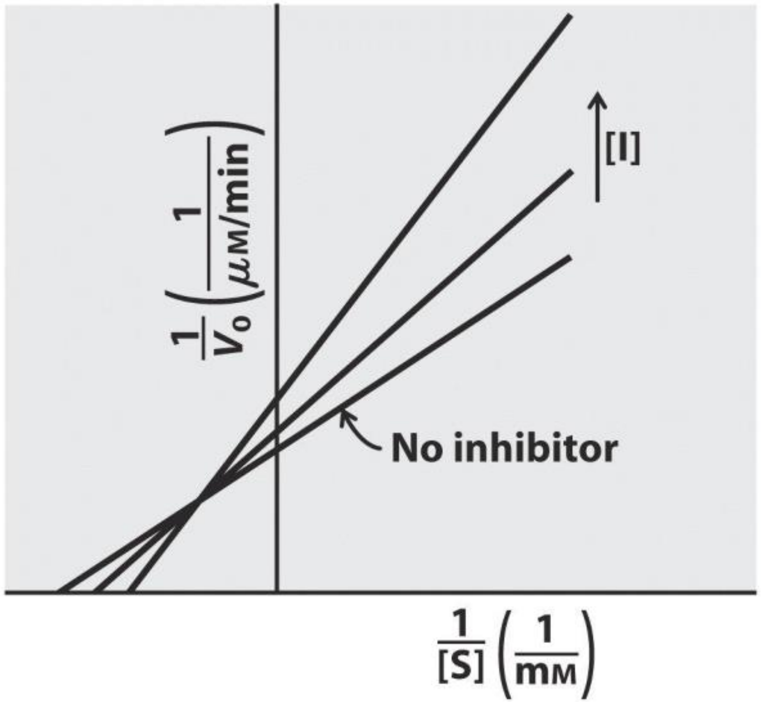


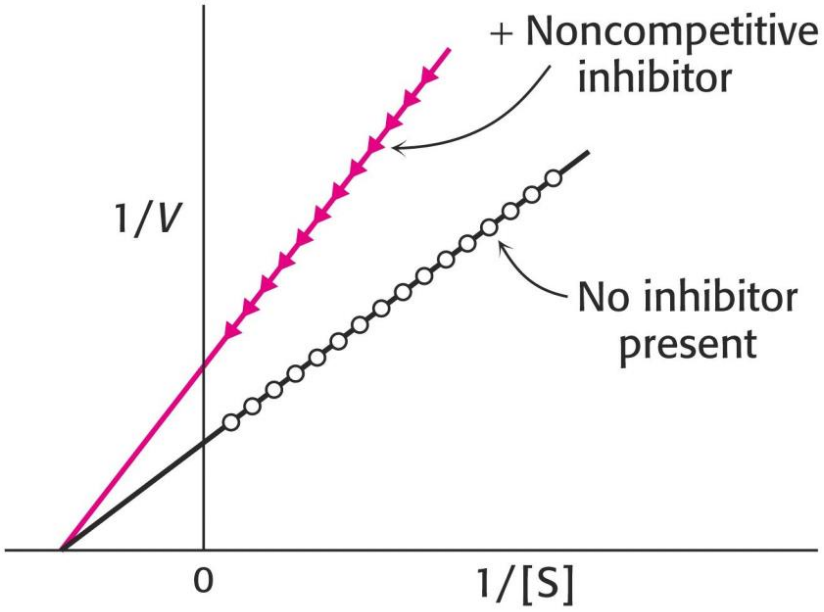
Mixed type inhibition Noncompetitive inhibition

(c) Mixed inhibition



$$\frac{1}{V_0} = \left(\frac{\alpha K_m}{V_{max}}\right)\frac{1}{[S]} + \frac{\alpha'}{V_{max}}$$





Question

Potassium cyanide is a poison which combines with cytochrome a_3 to prevent binding of oxygen to the enzyme without altering the K_M of the reaction with respect to reduced cytochrome c. Which type of inhibition does this represent?

a. Competitive inhibition
b. Uncompetitive inhibition
c. Noncompetitive inhibition
d. Irreversible inhibition

Summary

- Competitive inhibitors increase the K_M-value, but the v_{max} remains unchanged. (Active center)
- Uncompetitive inhibitors (rare) bind specifically the enzyme-substrate complex. They decrease v_{max} and the apparent K_{M}-value.
- Mixed type inhibitors increase the K_{M}-value and decrease v_{max}.
- As a special case of the mixed type, the noncompetitive inhibitors decrease only the v_{max} but the K_{M}-value remains unchanged. In the case of single-substrate enzymes, this type does not occur.

Allosteric inhibition (or activation)

- Homotropic – the substrate and the modulator are the same
- Heterotropic – they are different

Covalent modifications

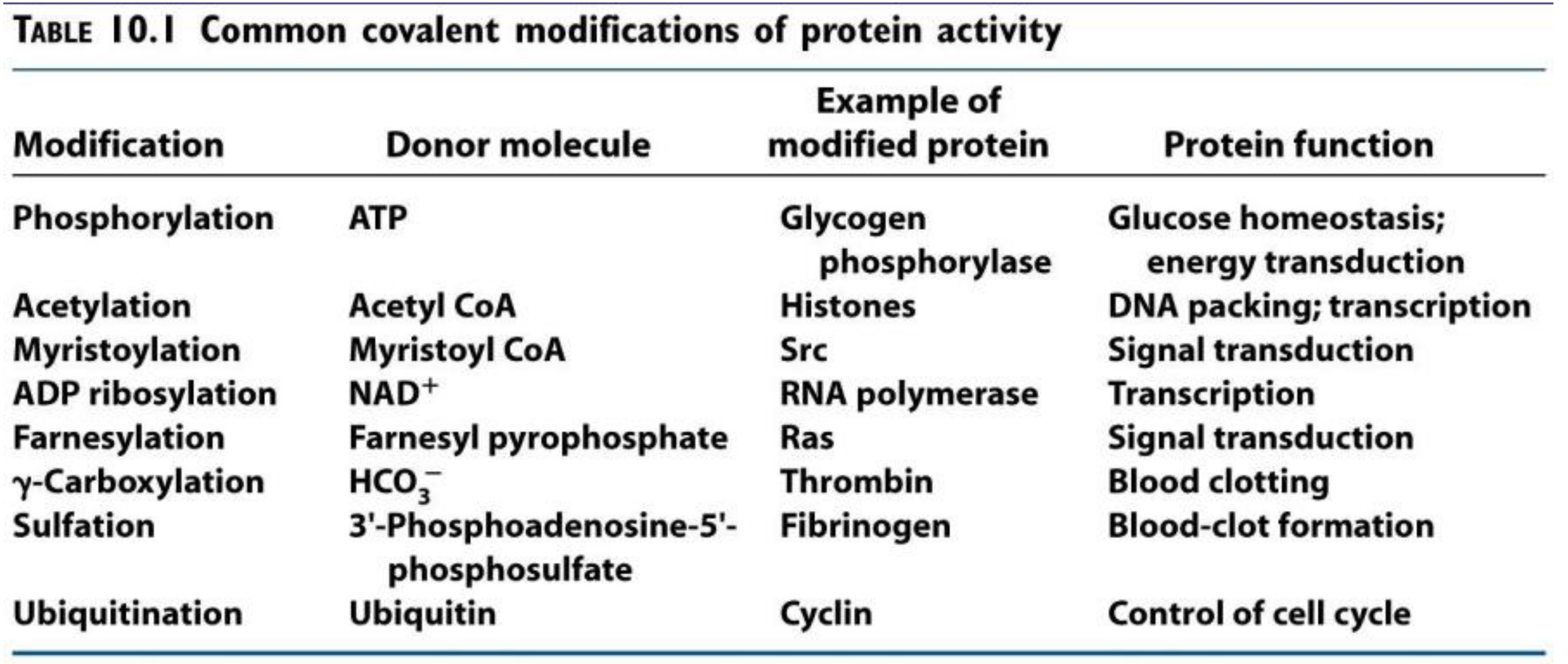


TABLE 10.1 Common covalent modifications of protein activity

Modification	Donor molecule	Example of modified protein	Protein function
Phosphorylation	ATP	Glycogen phosphorylase	Glucose homeostasis; energy transduction
Acetylation	Acetyl CoA	Histones	DNA packing; transcription
Myristoylation	Myristoyl CoA	Src	Signal transduction
ADP ribosylation	NAD^+	RNA polymerase	Transcription
Farnesylation	Farnesyl pyrophosphate	Ras	Signal transduction
γ-Carboxylation	HCO_3^-	Thrombin	Blood clotting
Sulfation	3'-Phosphoadenosine-5'-phosphosulfate	Fibrinogen	Blood-clot formation
Ubiquitination	Ubiquitin	Cyclin	Control of cell cycle

Binding protein association (Sequestrational regulation)

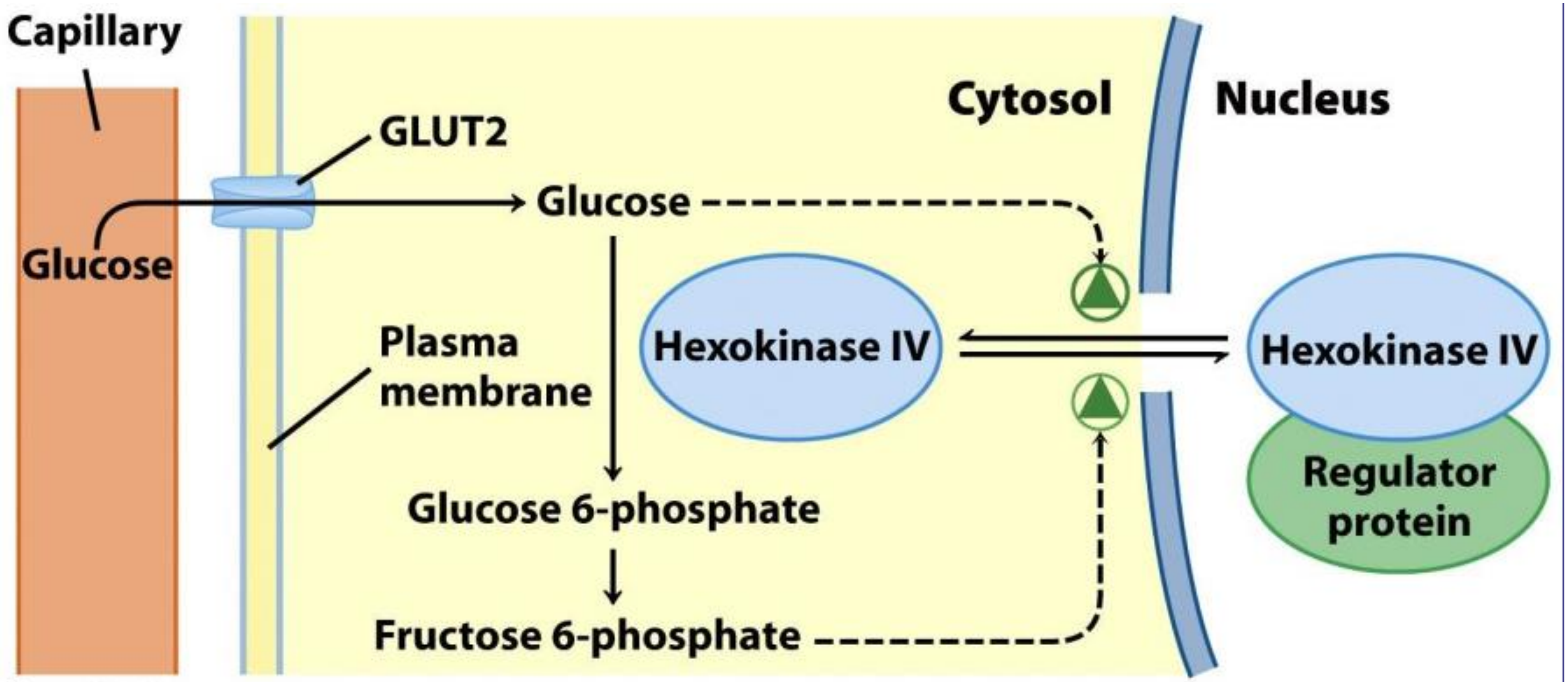


Figure 15-13
Lehninger Principles of Biochemistry, Fifth Edition

Question

In the first step of glycolysis, hexokinase produces glucose-6-phosphate. G-6-P itself can also bind to hexokinase at the active site, blocking access to ATP. This is an example of:

a) allosteric inhibition
b) feedback inhibition
c) noncompetitive inhibition
d) uncompetitive inhibition