HOMEOSTASIS KINETICS Active ENZYME CATALYST REACTION Velocity

REACTION Velocity depends on Concentration and Activity

Kinetics is a branch of chemistry, which deals with the reaction velocities. Reaction velocity is defined as the change of concentration in time: $\vec{v} = \pm\frac{\Delta C}{\Delta t}$, where:

-ΔC is the change of concentration for direct reaction, $\Delta C=C_2-C_1<0$ negative as final smaller $C_2< C_1$ as initial, **+ΔC** change of concentration for reverse reaction is greater $C_2> C_1$ as initial and **Δt** is time interval from t_1 to t_2. "+" sign is used in the expressions velocity, if the reaction velocity is controlled by reaction product, because concentration of products grows.

but usually it is not possible to follow the change of concentration in indefinitely short time intervals.
Thus direct reaction forwards Initial compounds aA + bB <==> cC + dD reverse reaction backwards

used as *mass action Law* for Direct $\vec{v} = \vec{k}\cdot C_A^a \cdot C_B^b$ <=$\overset{\text{direct}}{\underset{\text{revers}}{\rightleftarrows}}$=> $\overleftarrow{v} = \overleftarrow{k}\cdot C_C^c \cdot C_D^d$ reverse reaction of reactants
So concentration change $\Delta C=C_2-C_1$ of initial compound, "-" sign is used to obtain a positive value of velocity.

FACTORS AFFECTING REACTION Velocity

Reaction velocity is depending on concentration **C** factors and on velocity constant $\vec{k}$ three affecting factors:

1) Velocity is proportional to reacting compounds concentration.

A reaction between two molecules cannot occur without their collision as the molecules can react with each other only if they meet each other.

The number of collisions of molecules is proportional to concentrations of all the reacting compounds; therefore the reaction velocity is proportional to concentrations of all reacting compounds, too.

(**A** and **B** - reacting compounds, **a** and **b** - coefficients) the reaction velocity is described by the following equation (called *law of mass action*): $\vec{v} = \vec{k}\cdot C_A^a \cdot C_B^b$, where

$\vec{k}$ is the *reaction velocity constant.* Constant $\vec{k}$ shows the reaction velocity $\vec{v} = \vec{k}\cdot 1\cdot 1$ at concentrations of all reacting compounds $C_A=C_B=1$, equal to **1**.

Reaction velocity constant is not dependent on the concentrations of reacting compounds and for a given reaction it remains constant at a given temperature.

2) Velocity $\vec{v}$ *is proportional to velocity constant* $\vec{k}$ *value as well as depends on:*

2.1) temperature **T***:*

Increase of temperature increases the value of reaction velocity constant from 2-4 times per 10 degree increase of temperature $T_2 = T_1+10> T_1$ (this point will in the further text). $\vec{k} = A\cdot e^{-\frac{Ea}{RT}}$

2.2) reaction velocity constant depends on activity of reacting compounds. If one compares two similar reactions $H_2 + Cl_2 \xrightarrow{k_1} 2HCl$ and $H_2 + Br_2 \xrightarrow{k_2} 2HBr$ chlorine is much active as bromine $\vec{k}_{Cl_2} > \vec{k}_{Br_2}$ at the same concentrations of hydrogen and halogen, one can see, that the first of the two reactions occurs faster (its velocity constant is greater), as **Cl** is more active, than **Br**.

2.3.1) reaction velocity constant is increased by presence of a catalyst. ↑
2.3.2) Inhibitors works opposite decrease the velocity constant.↓

3000 reactions velocity in human body **HOMEOSTASIS** regulate more as thousands ENZYMES-biocatalists.

2.1) TEMPERATURE INFLUENCE ON Velocity Constant OF REACTION

Raise of temperature is always followed by an increase of the reaction velocity. For the most of reactions increase of $\mathbf{t^0}$ by **10** degrees causes an increase of reaction velocity constant from **2** to **4** times.

Growth of the reaction velocity constant at an increase of temperature is characterized by the so - called *Vant Hoff's temperature coefficient*: $\gamma = \frac{\mathbf{k_{T+10}}}{\mathbf{k_T}}$ = 2 ÷ 4 times increase per **10**°, where

$\mathbf{k_T}$ and $\mathbf{k_{T+10}}$ are the reaction velocity constants at initial temperature **T** and at a temperature, higher by **10**°.

Vant Hoff's coefficient can be used for calculation of the reaction velocity constant at any given temperature, if the value of reaction velocity constant at another temperature is known: $\mathbf{k_{T_2} = k_{T_1} \cdot \gamma^{\frac{T_2 - T_1}{10}}}$

That exhibits Arrhenius velocity constant expression: $\vec{\mathbf{k}} = \mathbf{A} \cdot \mathbf{e}^{-\frac{Ea}{RT}}$, how the influence of temperature on reaction velocity is going to be explained. The first idea for explanation seems to be, that raise of temperature intensifies the thermal motion of molecules and therefore the collisions of molecules become more frequent.

Let us prove, if it is true. The number of collisions is proportional to square root of temperature (in **K**).

Let us see the ratio between the frequencies of collisions at **2** given temperatures - **308** K and **298** K:

$$\text{Increases Collisions} = \frac{\mathbf{n}_{308}}{\mathbf{n}_{298}} = \frac{\sqrt{308}}{\sqrt{298}} = \frac{17.54993}{17.26268} = \mathbf{1.0166} \text{ times per temperature increase } \mathbf{10}^\circ$$

As one can see, at a raise of temperature by **10** degrees the number of collisions increases only **1.0166** times. At the same time, when temperature is raised by **10** degrees, the reaction velocity grows **2-4** times. Thus,

*at a raise of temperature the reaction velocity grows **2 ÷ 4** times much faster,*
*than the number of collisions **1.0166** times.*

This means, that the effect of temperature on the reaction velocity cannot be explained just in terms of increase of the collision number $\mathbf{n_{T+10}}$ and T.

Another important experimental fact is, that if one compares the number of collisions to the reaction velocity, one can see, that:

in reaction velocity involved molecule count is much smaller, than total number of collisions, or, in other words, not every collision of molecules leads to reaction.

These two experimental facts of active collision formation leade to ***activation*** *theory*.

Inactive state Oxygen **Triplet** structure at Human body temperature 37° C (310 K) has three covalent bonds **•:O≡O:•**. Usually depicted double bond **:O=O:** , because fourth electron pair **••** is degenerated antybonding free radicals, which sum in **Triplet** oxygen gives double bond.

Heated up to over >80° C AIR **oxygen** at high temperatures turns to **activated** state **Singlet** **•::O-:-O::•** **oxygen** structure having one covalent bond. **Singlet** form of oxygen is **activated** form.

ACTIVATION ENERGY AND ACTIVATED COMPLEX

Activation energy $\mathbf{E_a}$ comes as second factor affecting velocity constant value after temperature **T** first. The main idea of **activation** theory is that not every collision of reagent molecules leads to chemical reaction. Reaction occurs only at a collision of *active molecules*, the energy reserve of which is equal to or exceeds a certain value, called ***activation*** *energy*. (able to react, when a collision occurs)

$\vec{k} = A \bullet e^{-\frac{Ea}{RT}}$ ***Activation** energy (E_a) is defined as the amount of energy, that has to be supplied to **1** mole of initial compounds to make all 100% active the molecules:*

1=EXP*(-E_a/**RT**)* so $\vec{k}$ =***A•1***, *where **A** is geometric factor.* Colliding molecules factor **A**=1•$\mathbf{N_o}$ is perfect multiply 1 with $\mathbf{N_o}$ of total molecules amount concentration. Geometry worse if <1 and absolutelly inactive if 0.

What is this **activation** energy $\mathbf{E_a}$ and what is it used for? To understand, why it is necessary to supply some amount of energy to molecules in order to make them able to react, one has to take into account, that before the new bonds in the molecules of reaction products are formed (this process will be followed by *liberation* of energy), the old bonds in the molecules of initial compounds have to be cracked or at least weakened, and this is the reason, why some amount of energy $\mathbf{E_a}$ has to be supplied to the molecules for **activation**.

It was found out, that the values of colliding molecule energies in fact are smaller, than the amount of energy $\mathbf{E_a}$, necessary for the complete cracking of bonds in the molecules of initial compounds. This means that the bonds in the molecules of initial compounds don't have to be cracked completely, but it is enough to supply some energy $\mathbf{E_a}$ to weaken them.

AIR **oxygen** at high temperature heated up to over >80º C turns to **activated** state **Singlet oxygen** **•::O-:-O::•** having one covalent bond is **activated** form of AIR oxygen by heating as temperature increase.

This last fact leads to an explanation in terms of the theory of *transition state **activated** complex*.

At constant human body temperature 310 K (37 º C) found heme containing ENZYMES are two types **Triplet** $\mathbf{O_2}$ in hemoglobin stored **inactive** and **Singlet** $\mathbf{O_2}$ **activated** without heating oxygen by ENZYMES. **Triplet** $\mathbf{O_2}$ with three covalent bonds **•:O≡:::≡O:•** found on heme iron $\mathbf{Fe^{2+}}$ bound by donor-acceptor bond in **myoglobin**, **hemoglobin** proteins for safe isolate storage and transport of $\mathbf{O_2}$ in human body blood circulation.

Activated oxygen **Singlet** molecule **•::O-:-O::•** having one covalent bond found on heme iron $\mathbf{Fe^{3+}}$ by donor acceptor bond in **peroxidases**, **dismutases**, **CATALASES** proteins for oxidation, peroxidation and for toxic peroxide **2H:-••:O-:-O:••-:H** conversion to biological goods oxygen $\mathbf{O_2}$, water $\mathbf{2H_2O}$, heat **Q**.

So when **activated** complex, is formed old bonds are not completely cracked leaving free radical electrons ↑• at atoms like ↑**•::O-:-O::•**↑ and the new covalent bonds as paired electrons **:**↑↓ can be formed.

For instance, if a reaction in the beginning an **activated** complex is formed, in which **A** is still partly bound to **B** but formation of a bond between **A** and **C** has already started: **AB + C** $\xrightarrow{Ea}$ **(C...A...B)** **→AC+B**

*transition state **activated** complex*

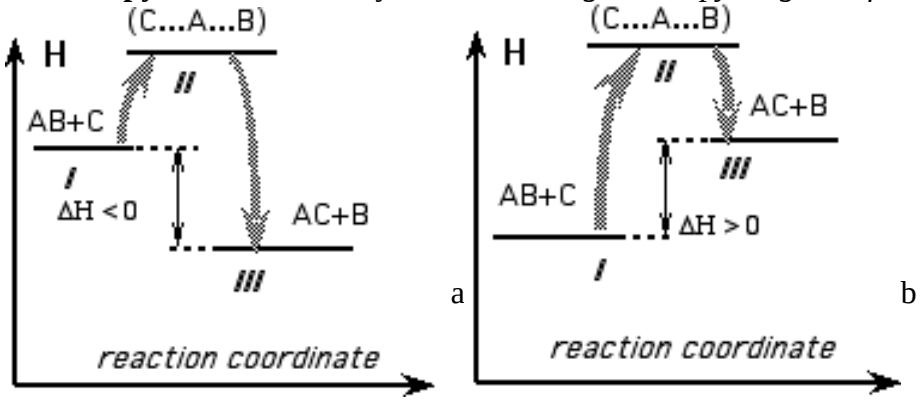
Activated complex is a short-living particle 10^{-13} femto seconds and formation of it requires extra energy $\mathbf{E_a}$. Thus, **activation** energy $\mathbf{E_a}$ is used to form the **activated** complex. **Activated** complex decays, forming the reaction products and in this process energy is liberated.

If one draws the so-called energetic diagram profile of reaction, see fig., one can see the connection between the **activation** energy and the reaction heat

For an exothermic reaction (**ΔH**<0) exposes enthalpy **H** of the system versus reaction coordinate (time). Before the reaction, when the molecules of initial compounds **AB** and **C** are present, their summary enthalpy is **1**.

H enthalpy heat content of system

Fig. Enthalpy diagrams for a-**exothermic**, b - **endothermic** reactions.



When the **activation** energy $\mathbf{E_a}$ is supplied, the **activated** complex **(C...A...B)** is formed and its enthalpy corresponds to level II - higher, than energy level of the initial compounds. Decay of the **activated** complex leads to formation of final products **AC** and **B**. Enthalpy level III of the products in an exothermic reaction is lower than the energy level I of initial compounds.

The amount of energy for products **AC** and **B**, that is liberated, when the **activated** complex **(C...A...B)** decays between levels II and III, consists of two parts - one part, equal to $\mathbf{E_a}$ is returned back and the remaining difference between levels I and III enthalpy heat content change **ΔH**<0 negative of reaction. as **exothermic**.

All-in-all one can say, that in the case of exothermic reaction, the **activation** energy has to be supplied only in the beginning - as soon as the first molecules have reacted, an amount of evolved energy, even greater than $\mathbf{E_a}$

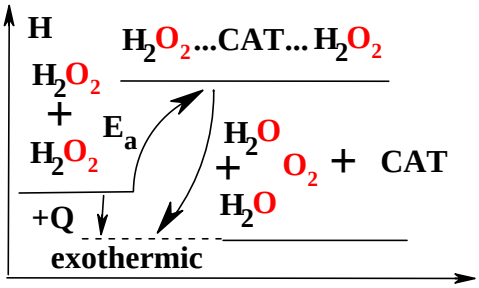
(that was initially supplied) is liberated and this energy can be now assigned to next molecules, they become active and the reaction continues itself without additional supply of energy.

Activation energy has to be supplied to first starting reacting initial compounds even if the reaction is spontaneous from thermodynamic point of view. AIR 20.95% oxygen $\mathbf{O_2}$ strong oxidising agent easy burn organic compounds in spontaneous reactions called combustion. Explains why organic compounds **inactive** as are all the time in contact with at low temperature <80º C in air or even ≈90º C in water thermal organisms. Living matter spontaneously combusted to $\mathbf{CO_2}$ and $\mathbf{H_2O}$. Oxygen **Triplet** structure $\mathbf{O_2}$ is inactivate and safe for life matter. Obviously safely (healthy) exist together with human organisms for long periods of time without combustion reaction. Why oxidation doesn't start with oxygen $\mathbf{O_2}$? Why pure oxygen $\mathbf{O_2}$ is danger for human organism as concentration in blood plasma becomes $[O_2]=30\ 10^{-5}$M and what means the oxidative stress of human organism? Why is danger deficiency of oxygen $\mathbf{O_2}$ in blood plasma below concentration $[O_2]<10^{-5}$M and what means hypoxia in human organism? What is the normal concentration level of oxygen $\mathbf{O_2}$ in arterial blood and in venous blood of human organism? (arterial $[\mathbf{O_{2aquaArterial}}] =6\ 10^{-5}$M; $[\mathbf{O_{2aquaVenous}}]=1{,}85\bullet10^{-5}$ M venous)

Endothermic reaction enthalpy **H** level **I** of the initial compounds is a lower, than the enthalpy **H** level **III** of products. In this case the amount of energy, liberated at the decay of the **activated** complex is smaller, than the **activation** energy $\mathbf{E_a}$, which was supplied to the molecules of initial compounds. The energy difference is taken from the surroundings and therefore the reaction is **endothermic**. **Endothermic** reaction, the reaction cannot continue just by itself produced energy.

For students self studies exercise: http://aris.gusc.lv/BioThermodynamics/CATALASE.pdf

ENZYME CATALASE driven radical reaction on active site heme iron $\mathbf{Fe^{3+}}$ converts two toxic radical peroxide molecules $\mathbf{2H{:}\text{-}\bullet\bullet{:}O\text{-}{:}\text{-}O{:}\bullet\bullet\text{-}{:}H}$ to biological goods oxygen $\mathbf{O_2}$, water $\mathbf{2H_2O}$, heat **Q** and leaving CATALASE unchanged.



$$\mathbf{2H_2O_2 + CAT \rightarrow H_2O_2 \ldots CAT \ldots H_2O_2 \rightarrow O_2 + 2H_2O + Q + CAT}$$

toxic compound — transition state active complex — oxygen water heat biological goods — CATALASE goods

$$\vec{k} = A \bullet e^{-\frac{Ea}{RT}}$$

1. **Catalase** (**CAT**) is involved to reaction active transition state complex formation $\mathbf{H_2O_2 \ldots CAT \ldots H_2O_2}$ and on finish released into products $\mathbf{O_2 + 2H_2O + Q}$ free unchanged **CAT**.
2. **Catalase** (**CAT**) decrease **activation** energy $\mathbf{E_a}$ from 79000 J/mol to 29 J/mol times 2724 less.
3. **Catalase** (**CAT**) improve geometric factor A=0.01 to A=0.13 times 13 better.
4. **Catalase** (**CAT**) increase reaction velocity constant from $\sqrt{\vec{k}} = 1.9\bullet10^{-8}\ M^{-1}s^{-1}$ to $^{CAT}\sqrt{\vec{k}} = 0.36\ M^{-1}s^{-1}$ times $30\bullet10^6$ thirty million more.

Square root of velocity constant as Enzyme governed complex reaction **1.** is gradual-consequtive (see p.7).

ACTIVATION ENERGY SUPPLY

Activation energy can be supplied to a reaction in several different ways:

1) *as thermal energy* - by heating of compounds, hyperthermic shock. AIR **oxygen** heated up to over >80º C at high temperature turns to **activated singlet** state $\uparrow\bullet{::}O\text{-}{:}\text{-}O{::}\bullet\uparrow$ having one covalent bond because one electron pair $:\uparrow\downarrow$ degenerated antybonding radicals of two free electrons $\uparrow\bullet$and $\bullet\uparrow$ are **activated** by temperature increase. Organic molecules too make electron pair degeneration as antybonding radicals $\uparrow\bullet$and $\bullet\uparrow$ by increase of temperature .

2) *as visible light or **UV** radiation energy also chain (radical) reaction.* **Activation** by light or ultraviolet radiation photons takes a place. Photochemical **activation** by light or **UV** radiation photons are absorbed by particular bonds in the molecules of initial compounds and it is possible to find such a wavelength to light photons that only one bond in the molecule is **activated** and, consequently, just the one suspected reaction occurs. Green plants use red and blue photons.

3) ***activation** energy supplied by ionizing radiation (initiate chain (radical) reactions)* - **γ**-rays, **X**-rays, **α**-particles, accelerated electrons $\mathbf{e^-}$, $\mathbf{\beta^-}$, $\mathbf{\beta^+}$ particles. Ionizing radiation has enough energy to activate any chemical bond. Initiate many radical side-chain reactions, because the energies of ionizing radiation are up to $\mathbf{10^6}$ times higher, than the ones of or visible light and many bonds are **activated** as electron pair degenerated antybonding free electron radicals $\uparrow\bullet$ un $\bullet\uparrow$ at the same time.

4) for some reactions, that don't require high **activation** energies, $\mathbf{E_a}$ can be supplied even by ultrasound.

Maxwell-Boltzmann's ENERGETIC DISTRIBUTION OF MOLECULES

1 mole of a compound at a given temperatures T_1, T_2, T_3 have average energies as heat content H_1 H_2 H_3. At given temperatures energetic distributions of molecules exists around average energy values, characteristic for actual temperatures T_1, T_2, T_3.

At the same time, the molecules, having greater and smaller energies, than **H** are present, too, but, the greater is the difference between the energy of a molecule and the average energy **H**, the smaller grows the summary number N_E of molecules, that have this energy value **E** greater or equal to E_a. In *equation: of* ***Maxwell-Boltzmann's*** :

$$N_E = N_o \bullet e^{\frac{-|E-H|}{RT}},$$

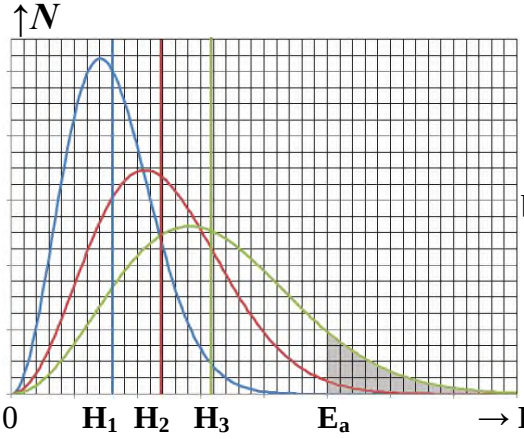
where N_E is the number of molecules, having energy greater or equal to E_a ; N_o is 1 mol Avogadro number of molecules $N_o = 6.023 \bullet 10^{23}$ molecules/mol; heat content **H** is standard enthalpy value of **1** mole compound.

From the last equation one can see, that, the greater is the difference between the demanded energy E_a and the average energy **H**, the smaller becomes the number of molecules, which can have the energy value $E \geq E_a$.

A graph of the energetic distribution of molecules at a given temperatures is shown in fig.., where the number of molecules, having a given energy value **E** is shown versus the demanded energy value.

If, for instance, an **activation** energy level E_a is necessary for a given reaction, all the molecules, having energies $E \geq E_a$, equal or greater than E_a will be active (able to react). The number of active molecules can be found as the shadow area in fig., which can be found as an integral area of the distribution curve in limits from $E = E_a$ till $E = \infty$.

Fig. Energetic distribution of molecules at a given temperatures T_1, T_2, T_3.



N_E - number of molecules, having energy value $E \geq E$.

If the energetic distributions at three given temperatures are compared (see fig.), one can see that for a higher temperature the average energy is shifted towards the greater energies and the distribution curve becomes broader. The number of active molecules at a higher temperature becomes higher, too (compare the marked areas for distribution curves at temperatures T_1, T_2, T_3 as $T_1 < T_2 < T_3$.

ARRENIUS'S EQUATION FOR REACTION VELOCITY CONSTANT

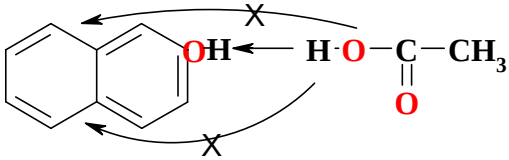
The connection between the reaction velocity constant and **activation** energy is expressed by Arrhenius's equation: $\vec{k} = A \bullet e^{-\frac{Ea}{RT}}$ where **A** pre-exponential factor (geometric factor), $e^{-E_a/RT}$ is *Boltzmann's factor*.

Boltzmann's factor shows relative fraction number N_E/N_o active colliding molecules having energy $E \geq E_a$ and expressed relative fraction $N_E/N_o < 1$ less as one shows the part of maximum number **1**.

As **activation** energy E_a for a given reaction is smaller $E_a/RT \rightarrow 0$, the greater is the number of active molecules and the greater becomes the reaction velocity constant.

At the same time, the greater is temperature, the greater is the value of Boltzmann's factor and the greater becomes the reaction velocity constant.

If *Boltzmann's factor* becomes equal to **1** as exponent $e^0 = 1$ has to be taken into zero power. Zero make value $E_a = 0$ or high temperature. If no **activation** energy is required, the reaction should occur at every collision for initial compounds molecules. Velocity constant ***k*** becomes equal to geometric factor **A** so-called *steric factor*.

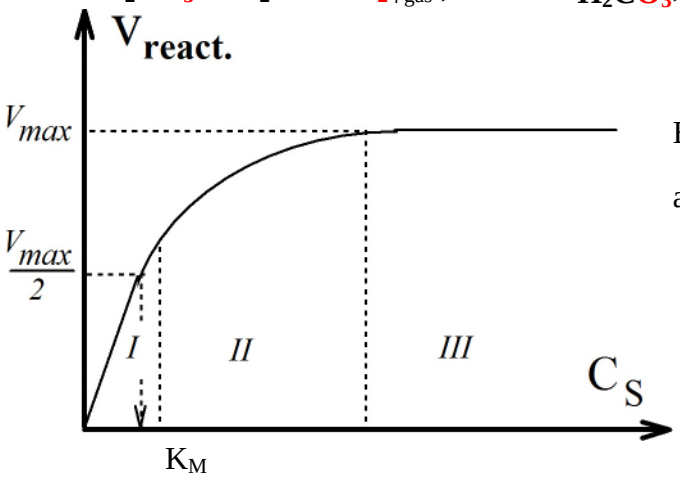


Correct collision geometry for more complicated molecules show zero geometric, pre exponential factor **A=0**. A collision can be insuccessive; if the collision angle is non-effective β-naphtole reacts with acetic acid. In this reaction a collision will be successive (reaction will occur) only in the case, if the collision angle is such, that **OH** group of the acid hits **OH** group of α-naphtole. All other angles of collision (crossed-out directions of collision in the scheme of reaction) are non-effective. If bigger and more complicated are the reacting molecules, than smaller becomes the pre-exponential factor **A**.

REACTION ORDER First-order reactions

Many human body reactions, in which one molecule of initial compound is transformed to products. Metabolic decomposition and isomerization reactions are first-order reactions. First-order reactions describe active mass Law**: A => Products,** Velocity depends on concentration as first-order powered reaction $\vec{v} = \vec{k} \cdot C_A^1$

$H_2CO_3 \rightarrow H_2O + CO_2\uparrow_{gas}$.; $\vec{v} = \vec{k} \cdot C_{H_2CO_3}$; decomposition of carbonic acid to water and $CO_2\uparrow_{gas}$



Zero-order reactions.

ENZYME governed reactions: $\vec{v}_{react.} = \frac{v_{max} C_S}{K_m + C_S}$

at low substrate concentrations C_S are first order reaction $\vec{v} = v_{max}/K_M \cdot C_S$, because reaction **activation** energy $E_a=0$ minimization increase velocity constant million times, but at concentrations $C_S=4 \cdot K_M$ becomes independent on concentration as constant $\vec{v} = v_{max}$, so $\vec{v} = \vec{k} \cdot C_S^0$ zero order $1 = C_S^0$ reaction $\vec{v} = \vec{k}$ is constant

Second-order reactions

All life organisms synthesis reactions are **Second order** reactions: **polymerization**, **polycondensation** of polypeptides, nucleic acids DNA,RNA, polysaccharides.

Second-order reactions always involve two molecules and they can correspond to schemes:

$2A \rightarrow$ Prod, $v = k C_A^2$, n=2 or $A + B \rightarrow$ Prod, $v = k C_A C_B$, n=1+1=2 . For example, reactions $Gly_{aqua} + Gly_{aqua} \xrightarrow{Ribosome} Gly\text{-}Gly_{aqua} + H_2O$.....dipeptide polycondensation in Ribosomes is second-order reactions.

Third-order reactions

Third-order reactions involve a simultaneous collision of three molecules and, therefore, real third-order reactions are observed very seldom - the probability of a simultaneous collision of three molecules is very low.

By the most, the reactions, that formally have third order, practically occur in two second-order stages.

Third-order reactions can correspond to active mass law: $2A + B \rightarrow$ Prod, $\vec{v} = \vec{k} \cdot C_A^2 \cdot C_B$, $n = 2+1 = 3$

One of the few reactions, which really occur as a third-order reaction, is: $2NO + H_2 \rightarrow N_2O + H_2O$

$\vec{v} = \vec{k} \cdot [NO]^2 \cdot [H_2]$; For this reaction it is experimentally proved, that the reaction velocity is really proportional to the concentration of **NO** in second power and to the concentration of H_2 in first power, which means, that really a simultaneous collision of three molecules has to occur.

> *Reactions, having greater order than third, are practically impossible - probability of a simultaneous collision of **4** and more molecules is so little, that such reactions should proceed in years.*

In fact, many reactions, those have a formal order, greater than third, such as, for instance,

$$FeS_2 + 11O_2 \rightarrow 2Fe_2O_3 + 8SO_2\uparrow,$$

which has formally eleventh order (FeS_2 as a solid is not included into reaction velocity equation), may occur in a few seconds. This can be explained only in the way, that these reactions occur in many second-order stages and the equations of reaction, similar to the previous one, are just the summary equations of complicated step-by-step processes.

COMPLEX and ENZYME governed REACTIONS in human organism

Complex reactions are all 3000 in human body maintaining **HOMEOSTASIS** governed by ENZYMES.

Human body complex reactions are foure 4 of five 5 exept 2. parallel non Enzymatic reactions:

1. gradual-sequential reactions,
3. joint-tandem reactions,
4. competitive-regulatory reactions and
5. radical Enzymatic reaction.

Enzymatic reactions — 5 complex reactions — Non Enzymatic reactions the HAZARD for organism LIFE

Page 7th : http://aris.gusc.lv/BioThermodynamics/Kinetics.pdf

1. GRADUAL-CONSECUTIVE
organized as sequence of **ENZYMES** in
Glycolysis, Krebs cycle, Replication,
Polymerisation (Polycondensation)

1. Chaotic

Page 7th : http://aris.gusc.lv/BioThermodynamics/74LidzsvarsDabaEngl.pdf

ENZYMES are **SPECIFIC** and **SELECTIVE**
single product **Impossible=>**

2. PARALLEL products formation
multiple products

3. JOINT-TANDEM SYNTHESIS
Ribosomes polypeptides,
Photosynthesis glucose and oxygen

Thermodynamics forbiddens
$\Delta G=\Delta H-\Delta S\cdot T>0$ is positive no reaction possible

4. COMPETITIVE regulation as **inhibition** and **allostery**
sensitive to concentration O_{2aqua}, HCO_3^-, H^+
His63,58 as for hemoglobin, His64 for myoglobin
as regulated back response prevent over production
pH=7.36, arterial $[O_{2aqua}]=6\cdot10^{-5}$ M, venouse $[O_{2aqua}]=1.8\cdot10^{-5}$ M.

4. Chaotic

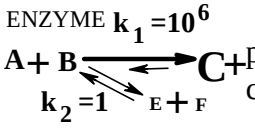
5. ENZYMATIC RADICAL REACTIONS
in isolated active site single product
prevent radical-chain initiation

non-ENZYMATIC radical-chain reaction
multiple chain products formation

1. PARALLEL Products avoid **ENZYMES** governed **REACTIONS**

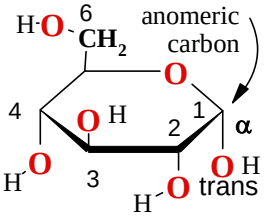
In vitro organic compounds of human organism have been converted to many different reaction products, but in vivo ENZYMES perform just one product formation. Enzyme favors just one reaction with million times higher velocity as well per 10^6 produced bio molecules are possible just one 1 parallel side product or ever less formed. As ENZYME governed reaction drive reactions in needed direction for **HOMEOSTASIS** PATHWAY.

Parallel reactions in human body prevent ENZYMES. So single product forming as one biologic product of one initial compound.



A and **B** may react, forming two different kinds of products. The two possible kinds of products are formed in different amounts, because ENZYME governed reaction velocity constant k_1 is million times greater as parallel unfavorable reaction constant value k_2.

ENZYMES drive the favorite reaction with the efficiency 100% and with the velocity constant 1000000 times greater as other parallel reactions. Human organism biochemical reactions are governed by ENZYMES, which selectively faster forming perfect single product needed for life and never have made side products.



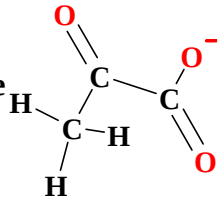
2.GRADUAL (CONSECUTIVE) ENZYME supported EQUILIBRIA SEQUENCE

Glycolysis is most popular gradual equilibria sequence in human organism **HOMEOSTASIS** PATHWAYS.

Glc $\underset{1}{\overset{\text{Glc transporter}}{\rightleftharpoons}}$ **Glc** $\underset{2}{\overset{\text{Hexokinase}}{\rightleftharpoons}}$ **Glc6P** $\underset{3}{\overset{\text{Isomerase}}{\rightleftharpoons}}$ **Fruc6P** $\underset{4}{\overset{\text{Kinase1}}{\rightleftharpoons}}$ **Fruc6P1P** $\underset{5}{\overset{\text{Aldolase}}{\rightleftharpoons}}$ **GlycAld**

Glycolysis PAYHWAY start with entrance **glucose** (**Glc**) from blood plasma into cytosol:

GlycAld $\underset{6}{\overset{\text{DHkinase}}{\rightleftharpoons}}$ **13BPG** $\underset{7}{\overset{\text{Kinase}}{\rightleftharpoons}}$ **3PG** $\underset{8}{\overset{\text{Mutase}}{\rightleftharpoons}}$ **2PG** $\underset{9}{\overset{\text{PyruvateKinase}}{\rightleftharpoons}}$ **2 pyruvate**



In fact is a gradual reaction consisting of nine consecutive equilibria. Each next conversion followed after prior one. On end of Glycolysis **pyruvate** is final product before entrance into mitochondria for Krebs cycle. Oxygen O_2 asimilation in organism and CO_2 respiration out.

I) $O_{2AIR}+H_2O \overset{\text{aquaporin}}{\rightleftharpoons} H_2O+O_{2aqua}$; **deoxy**$(H^+\text{His63,58})_4Hb_T + 4O_{2aqua} \leftarrow [O_2]=6\cdot10^{-5}\text{ M}\rightarrow$ **oxyHb**$_R(O_2)_4+4H^+$,

II) $Q_{aqua} + CO_{2aqua} + 2H_2O \overset{CA}{\longleftrightarrow} H_3O^+ + HCO_3^- \overset{\text{membrane}}{\rightleftharpoons} H_2O + H_2CO_3 + Q(gas) \rightleftharpoons H_2O + CO_2\uparrow_{gas} + H_2O$.

3. ENZYMATIC JOINT TANDEM EQUILIBRIA drive forbidden REACTIONS

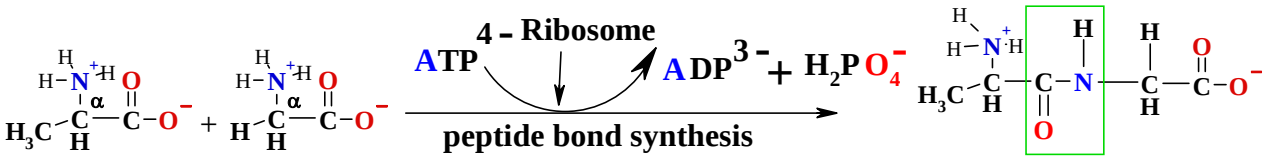
http://aris.gusc.lv/BioThermodynamics/BioChemicalPprocesE.pdf

Green plants **Photosynthesis** reaction is thermodynamically forbidden as endoergic ΔG_r= +2970,441 $^{kJ}/_{mol}$: $6CO_2 + 6\,H_2O + Q$ —x no → $C_6H_{12}O_6 + 6\,O_2$ and as endothermic reaction $\Delta H_{reac}>0$ ΔH_{reac}= +2805,27 $^{kJ}/_{mol}$. Tandem reactions are very common in biochemistry. Here the most common case is, that the equilibrium of building-up free energy rich compounds like protein, **glucose** $C_6H_{12}O_6$, **oxygen** $6\,O_2$ in which entropy lowered and *Gibbs energy* is growing-accumulate. As the reaction alone is thermodynamically forbidden, the **red** and **blue** light photon absorption in Joint - Tandem reaction lowers *Gibbs's energy* in products $C_6H_{12}O_6 + 6O_2$ wich becomes compensate for the overall process thermodynamically possible. Global **P**hotosynthesis oxygen equilibrium concentration is 20.95%=[$O_2\uparrow_{gaiss}$]. To decrease concentration, for example, 2%=[$O_2\uparrow_{gaiss}$] **Plant Enzymes P**hotosynthesis quick restore Global concentration in air 20,95%. Global **P**hotosynthesis equilibrium further shift supplying the heat **Q** and CO_2 . Therefore Global warming promote increase of **Q** and CO_2 and so furthere **P**hotosynthesis, but in Ace Age **P**hotosynthesis stop down:

$$6CO_2 + 6\,H_2O + Q \xrightarrow[\text{light: red, blue}]{E=h\nu\ \text{PRC}\ \text{photo synthesis}} C_6H_{12}O_6 + 6\,O_2 \quad (\text{combustion})$$

The ENZYME complex Ribosomes are for Peptide Bond synthesis: ala + gly→ala-gly+ H_2O with free energy ΔG_{reac}=**+17.2** $^{kJ}/_{mol}$ transfer shift **ATP** hydrolyze exoergic free energy $\Delta G_{hydrolize}$= **-30.5** $^{kJ}/_{mol}$ which part is used free energy store ΔG_{reac} =**+17.2** $^{kJ}/_{mol}$ in one mole of peptide bond.

Ala [A] Alanine + Gly [G] Glycine $\xrightarrow[\text{peptide bond synthesis}]{\text{4 - Ribosome; ATP; ADP}^{3-} + H_2PO_4^-}$ Ala-Gly AlaninoGlycine AG

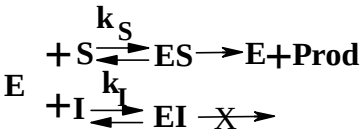


4. COMPETITIVE regulated ENZYME EQUILIBRIA allostery and inhibition

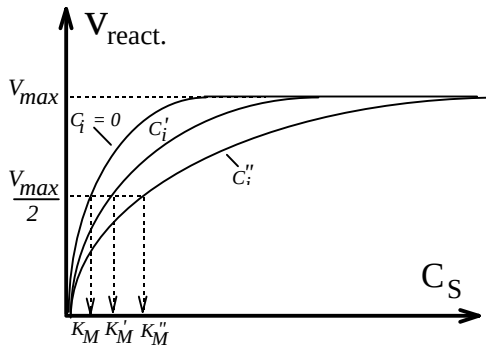
with O_{2aqua}, HCO_3^-, H^+ concentrations sensitive His63,58 hemoglobin and His64 myoglobin through back response regulated shift of equilibrium according Le Chatelier's Principle (Theorem) stabilising pH=7.36, arterial concentration [O_{2aqua}]=$6\cdot10^{-5}$ M and venous concentration [O_{2aqua}]=$1.8\cdot10^{-5}$ M.

In competitive equilibria two different initial compounds substrate **S** *and inhibitor* **I** *compete on one ENZYME regulate decrease the product* amount **[Product]** *and the velocity through distinguish equilibria* K_{eq},, $\mathbf{K_I}$ according Le Chatelier's principle-theorem in expressions, *increasing* $\mathbf{K_M}$ in velocity $\mathbf{v_{react}}$:

$$K_{eq}=\frac{[\text{products}]}{[\text{initial\_compounds}]}=\frac{[E]\bullet[\text{Product}]}{[E]\bullet[S]}=\frac{[\text{Product}]}{[S]};\ \mathbf{K_I}=\frac{[EI]}{[E]\bullet[I]};\ \vec{\mathbf{v}}_{react}=\frac{v_{max}C_S}{K_M+C_S}.$$



ENZYME governed reactions are regulated by inhibitors **I** concentration which slow down velocity of **E+S** reaction. Inhibitor molecule **I** compete with substrate molecule **S** and shift substrate reaction to left according Le Chatelier theorem by decrease of ENZYME concentration $\mathbf{C_E}$ involved into competitive inhibition equilibrium. Physiologic ENZYME regulation is an equilibrium which shifting to right side promoted by inhibitor concentration $\mathbf{C_I}$ increase, for example, using medicine (aspirin, warfarin e.c.).



$$\vec{\mathbf{v}}_{react.} = \frac{\mathbf{v_{max}} \mathbf{C_S}}{\mathbf{K_m} + \mathbf{C_S}}$$

The main conclusion about the competitive inhibition is. Competitive inhibition causes an increase of the Michaelis's constant K_M, value but doesn't affect the maximal velocity of reaction v_{max}..

Note, that Michaelis's constant $\mathbf{K_M}$ has the meaning of a substrate concentration $\mathbf{C_S}$ at which the reaction velocity reaches **1/2** of maximal $\mathbf{v_{react} = v_{max} / 2}$.

5. ENZYMATIC restricted RADICAL REACTION EQUILIBRIA and non ENZYMATIC radical-chain multiple reactions products formation

ENZYMATIC reactions avoid open radical – chain reactions n one manner. Human organism ENZYMES realized radical reactions occur in proteins closed active site pocket on prosthetic group heme iron Fe^{3+}. Cell ENZYMES driven radical reactions as **oxidation**, **peroxidation** form the stabilr products and Catalase toxic peroxide **2H:-••:O-:-O:••-:H** converted to biological goods oxygen $\mathbf{O_2}$, water $\mathbf{2H_2O}$, heat **Q** .

Activated oxygen **Singlet** molecule **•::O-:-O::•** having one covalent bond found on ENZYME heme pockets iron Fe^{3+} by donor acceptor bond (in **peroxidases**, **dismutases**, **CATALASES**). ENZYMES active site pockets are isolated by hydrophobic pocket from surrounded water medium $\mathbf{H_2O}$ + $\mathbf{O_2}$ with oxygen concentration (from $[O_2]=1{,}85 \cdot 10^{-5}$ M in venozām blood up to $[\mathbf{O_2}]=6 \cdot 10^{-5}$ M in arterial blood). Increased oxygen concentration is termed hyperoxia and medical symptom is called oxidative stress. Oxidative stress risk is proportional to oxygen or peroxide concentration. Five times higher oxygen concentration **singlet** risk increases five times. Peroxide accumulation risk decreases $30 \bullet 10^6$ thirty million times with enzyme CATALASE. $\vec{\mathbf{v}} \sim [\mathbf{O_2}]$ or $\vec{\mathbf{v}} \sim [\mathbf{H_2O_2}]$

Non ENZYMATIC radical-chain reactions hazards as multiple damages generation.

Non-ENZYMATIC radical-chain reaction produce many different products, that forbidden in life strategy, which damages life molecular structures and ENZYMATIC complexes natural processes Oxidative stress and technology hazards was the reason for Apollo cosmos project closing in 73rd of 20 century.

That not acceptable in ENZYME governed radical reactions, where necessary form one specific product.

Radical formation from $\mathbf{H_2}$ and $\mathbf{Br_2}$ begins by light radiation ***initiation*.**

Initiation is first stage of radical formation as activated particles with low activation energy $\mathbf{E_a}$=>0 kJ/mol. The radical here is photochemical: $\mathbf{Br_2}$ molecules absorb light photons, forming from bromine molecule $\mathbf{Br_2}$ uncoupled bromine atom radicals **Br•** + **Br•** with unpaired electron **•: Br-:-Br** $\xrightarrow{\sim h\nu}$ **Br• + Br•**

Propagation is second stage of radical-chain reaction. Where active particles **Br•** radicals are short-living active particles, that react in the ***propagation***: **Br•+ H-:-H → H• + H-:-Br** .

In this reaction a stable molecule of product **HBr** is formed and a new radical active particle - **H•** atom is formed. **H•** reacts further and continue the radical-chain ***propagation***: **H• + Br-:-Br → Br• + H-:-Br** .

Here again a product (**HBr**) molecule is formed and an **Br•** atom is created again, **Br•** radical atom can react with next $\mathbf{H_2}$ molecule and so the radical-chain reaction could ***propagate*** forever.

Termination is third stage radical- chain reaction. Radical-chain ***termination*** occurs, if two active particles meet to form non-radical molecule and no radical-chain ***propagation*** is possible after this. In case of $\mathbf{H_2}$ and $\mathbf{Br_2}$ reaction one can imagine **3** different reactions, in which radical-active particles die:

Br• + H• → HBr; Br• + Br• → Br_2; H• + H• → H_2

Reaction velocity in the case of a radical-chain reaction is determined by the velocity of radical-chain ***initiation*** and radical-chain ***termination*:**

a) if *initiation* and *termination* occurs at the same velocity, chain will *propagate* with constant velocity (because the number of active radical particles is constant then),

b) if the velocity of *initiation* is greater, than the one of *termination*, the number of active radical particles is growing and the velocity of radical-chain *propagation* (of product formation) is growing, too,

c) if the velocity of *termination* is higher, than the velocity of *initiation*, the number of the active radical particles is decreasing and the velocity of *propagation* product formation is decreasing, interrupt reaction.