2023 **Aris Kaksis Riga Stradin's University**: aris.kaksis@rsu.lv

High rate protolysis attractors with molecules functional Activity promote homeostasis progress

Reaction progress velocity proportional to Concentration and **velocity** constant (**Activity**)

Kinetics reaction velocity is 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 $C_2 < C_1$ as initial, **+ΔC** change of concentration for reverse reaction is $C_2 > C_1$ 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.

Thus direct reaction forwards Initial compounds aA + bB <==> cC + dD reverse reaction backwards used as *mass action Law* for Direct $\vec{v} = \vec{k} \cdot C_A^a \cdot C_B^b$ $\underset{\text{revers}}{\overset{\text{direct}}{<=\!=>}}$ $\vec{v} = \vec{k} \cdot C_C^c \cdot C_D^d$ 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 $\overleftarrow{k}$ three affecting factors:

1) Velocity is proportional to reacting compounds concentration.

Two molecules reacts in their collision as they meet each other.

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

(**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**: $\vec{k} = A \cdot e^{-\frac{Ea}{RT}}$

Increase of temperature per 10 degree $T_2 = T_1 + 10 > T_1$ increases the value of constant 2-4 times.

2.2) reaction velocity constant depends on activity of reacting compounds. If one compares two similar reactions $H_2 + Cl_2 = \vec{k}_{Cl_2}$ => **2 HCl** and $H_2 + Br_2 = \vec{k}_{Br_2}$ => **2 HBr** chlorine is much active as bromine $\vec{k}_{Cl_2} > \vec{k}_{Br_2}$ at the same concentrations of hydrogen and halogen, 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 blocking the catalysts.↓

The perfect order irreversible **HOMEOSTASIS** create high rate protolysis self-organization attractors.. pH=7.36, enzyme Carbonic Anhydrase reactivity, water concentration $[H_2O]$=55.3 $^{mol}/_{Liter}$, air oxygen 20.95 %, osmolar concentration 0.305 M, ionic strength 0.25 M, temperature 310.15 K degree etc. [1]

1. David R. Lide. CRC Handbook of Chemistry and Physics .90th ed. Taylor and Francis Group LLC; 2010 .

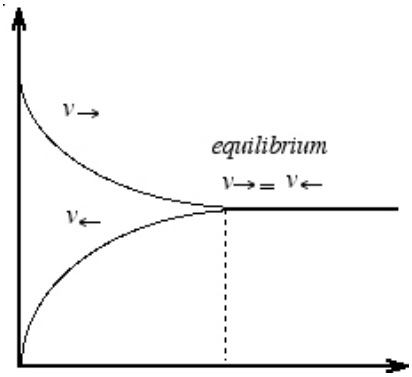
8. Alberty RA. Biochemical Thermodynamic's : Applications of Mathematics. John Wiley & Sons, Inc. 1-463, (2006)

ACTIVE mass velocity for Le Chatelier's principle reaching of Prigogine attractor

Direct reaction forwards => aA + bB <=> cC + dD <=reverse reaction.

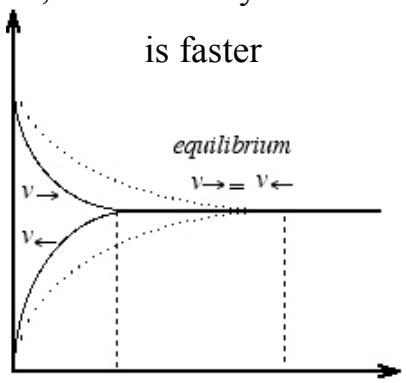
Mass action Law for Direct $\vec{v} = \vec{k} \bullet C_A^a \bullet C_B^b$ <=$\xleftrightarrow[\text{revers}]{\text{direct}}$=> $\overleftarrow{v} = \overleftarrow{k} \bullet C_C^c \bullet C_D^d$ for Reverse reaction .

v, Ms^{-1} velocity)



0 $t_{Attractor}$ t, sec;

v, Ms^{-1} velocity is faster



0 $t_{Attractor}$ t, sec

Velocity of reaction for Direct reaction decreases and for Reverse reaction increases.

Thousands of Biochemical reactions have been studied as water equilibria processes. Reaction is irreversible if reverse constant is zero $\overleftarrow{k} = 0$ or close to zero and attractor reaching time $t_{Attractor}$ is slow or trends to infinit long time $t_{Attractor} => \infty$.

If reverse velocity constant is positive $\overleftarrow{k} > 0$, than attractor ($t_{Attractor}$) constant velocity $\vec{v} = \overleftarrow{v}$ reaching limit just direct reaction velocity constant $\vec{k}$.

Attractor free energy change minimum at equilibrium state reaching time $t_{Attractor}$ depends on Direct reaction velocity. For example, Hydrogen peroxide conversion to life resources O_{2aqua}+H_2O+Q is slow $k_{\rightarrow}=1.191 \bullet 10^{-8}$ Ms^{-1}. CATALASE peroxide consume thirty million times $30 \bullet 10^6$ faster. Irreversible CATALASE reactivity for peroxide consuming is Prigogine attractor, that indispensible for Life driving to product 100% efficiency with erasing H_2O_{2aqua} molecules and conversion to life resources O_{2aqua}+H_2O+Q:

Carbonic dioxide 0,03% of air do not act with water : $CO_2{\uparrow}_{gas}+\Delta G_{aqua} \Leftrightarrow Q+CO_{2aqua}$; just solute in water with solubility $[CO_{2aqua}]=K_{eqH2O}*[CO_2{\uparrow}_{air}]= 1,882*0,0004=0,00075125$ M. Enzyme carbonic anhydrase **CA** drive irreversible water solute carbonic dioxide reaction with two water molecules: $CO_{2aqua}+2H_2O+Q = \underline{CA} \rightarrow H_3O^+ + HCO_3^-$, so increase ratio behalf aqua $[CO_{2aqua}+HCO_3^-]/[CO_2{\uparrow}_{air}]=30,6$ times. Limestone, dolomite, chalk and marble rocks formation amount drive **CA** reaction. OH^- reaction is slow and weak concentration $C_{OH^-}=10^{-6,64}$ M.

4th , 45rd page.

Irreversible homeostasis enzymes reactivity progress are Ilya Prigogine declared attractors for organism complex reaction five types, which inactive compounds convert to following favored irreversible proceses, that works as Brownian molecular engines and drive organism to evolution, homeostasis, survival.

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*: $\gamma = \frac{k_{T+10}}{k_T} = 2 \div 4$ 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: $k_{T2} = k_{T1} \bullet \gamma^{\frac{T_2 - T_1}{10}}$

That exhibits Arrhenius velocity constant expression: $\vec{k} = A \bullet e^{-\frac{Ea}{RT}}$, 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:

$$\text{Increases Collisions} = \frac{n_{308}}{n_{298}} = \frac{\sqrt{308}}{\sqrt{298}} = \frac{17.54993}{17.26268} = \mathbf{1.0166} \text{ times per temperature increase } \mathbf{10°}$$

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 lead to ***activation*** *theory*.

In AIR up to temperature 80º C **inactive** state Oxygen **Triplet** structure has three covalent bonds **•:O≡O:•**. Usually depicted double bond **:O=O:** , because third electron pair **••** is degenerated antibonding free radicals, which compensate in sum the **Triplet** oxygen and gives double bond.

Heated up to over >80º 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 $\vec{k} = A \bullet 1$*, where **A** is geometric factor.* Colliding molecules factor $A=1 \bullet N_o$ is perfect multiply 1 with N_o of total molecules amount concentration. Geometry worse if <1 and absolutelly inactive if 0.

Activation energy **E**$_a$ is necessary to supply amount of energy to molecules that makes them able to react before the new bonds in the 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 **E**$_a$ has to be supplied to the molecules for **activation**.

Ihe values of colliding molecule energies are smaller, than the amount of energy **E**$_a$, necessary for the complete cracking of bonds in 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 **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** O_2 in hemoglobin stored **inactive** and **Singlet** O_2 **activated** without heating oxygen by ENZYMES. **Triplet** O_2 with three covalent bonds **•:O≡:::≡O:•** found on heme iron Fe^{2+} bound by donor-acceptor bond in **myoglobin**, **hemoglobin** proteins for safe isolate storage and transport of O_2 in human body blood circulation.

Activated oxygen **Singlet** molecule **•::O-:-O::•** having one covalent bond found on heme iron Fe^{3+} by donor acceptor bond in **oxidases**, **dismutases**, Reaction for **2H-O-O-H** peroxide conversion to biological goods oxygen O_2, water $2H_2O$, heat **Q** as attractor=reactivity of **CATALASE** is increased 30 million times ($30*10^6$).

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*

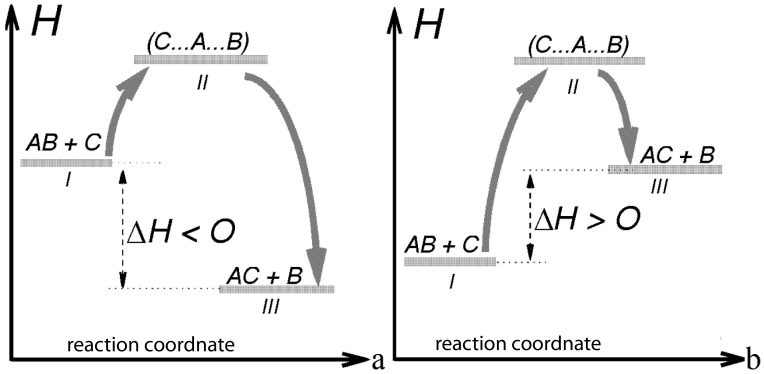
Activated complex is a short-living particle 10^{-13} femto seconds and formation of it requires extra energy **E**$_a$. Thus, **activation** energy **E**$_a$ is used to form the **activated** complex. **Activated** complex decays, forming the reaction products and in this process energy is liberated.

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 **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 **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 **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.

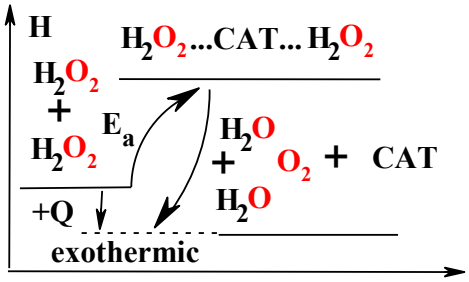
Activation energy has to be supplied to first starting reacting initial compounds even if the reaction is favored, spontaneous with free energy change minimum ΔG_{min}. AIR 20.95% oxygen O_2 strong oxidising agent easy burn organic compounds in spontaneous reactions called combustion. Oxygen **Triplet** structure 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. 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 for thermal organisms. Organic matter spontaneously combusted to CO_2 and H_2O at high temperature with active singlet oxygen. Why oxidation doesn't start with oxygen O_2? Why pure oxygen 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 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 O_2 in arterial blood and in venous blood of human organism?

(arterial $[O_{2aquaArterial}] = 6\ 10^{-5}$M; $[O_{2aquaVenous}] = 1{,}85 \bullet 10^{-5}$ 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 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

CATALASE irreversible radical reaction in collirion with iron Fe^{3+} on active site heme converts each radical peroxide radical molecule **H:-••:O-:-O:••-:H** to life resources oxygen O_2, water $2H_2O$, heat **Q** and in products CATALASE leaving unchanged.



$$2H_2O_2 + CAT \rightarrow H_2O_2 \ldots CAT \ldots H_2O_2 \rightarrow O_2 + 2H_2O + Q + CAT$$

reactive compound — transition state active complex — oxygen life — water — heat — resources — CATALASE

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

1. **Catalase** (**CAT**) is involved to reaction active transition state complex formation $H_2O_2 \ldots CAT \ldots H_2O_2$ and on finish released into products $O_2 + 2H_2O + Q$ free unchanged **CAT**.
2. **Catalase** (**CAT**) decrease **activation** energy 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 $\sqrt{\vec{k}} = 1.9 \bullet 10^{-8}\ M^{-1}s^{-1}$ to $^{CAT}\sqrt{\vec{k}} = 0.36\ M^{-1}s^{-1}$ times $30 \bullet 10^6$ thirty million more.

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

A C T I V A T I O N E N E R G Y S U P P L Y

Activation energy can be supplied to a reaction in certain 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 ↑•::O-:-O::•↑ having one covalent bond because one electron pair :↑↓ degenerated anti bonding two free electrons ↑•and •↑ radicals are **activated** by temperature increase. Organic molecules too make electron pair degeneration as anti bonding radicals 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 e^-, β^-, β^+ 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 10^6 times higher, than the ones of or visible light and many bonds are **activated** as electron pair degenerated antybonding free electron radicals ↑• un •↑ at the same time.

4) for some reactions, that don't require high **activation** energies, 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*** : 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.

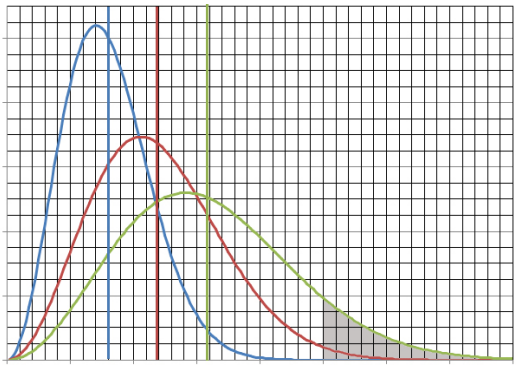
$$N_E = N_o \bullet e^{\frac{-|E-H|}{RT}},$$

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

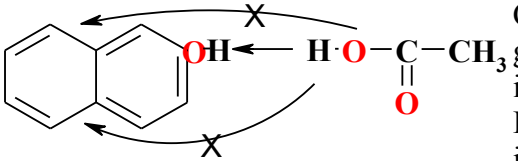
The connection between the reaction velocity constant and **activation** energy is expressed by Arrhenius's equation: $\vec{k} = A \bullet e^{-\frac{Ea}{RT}}$ where **A** pre-exponential factor (geometric factor), $e^{-E_a/RT}$ is *Boltzmann's factor*.

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*.

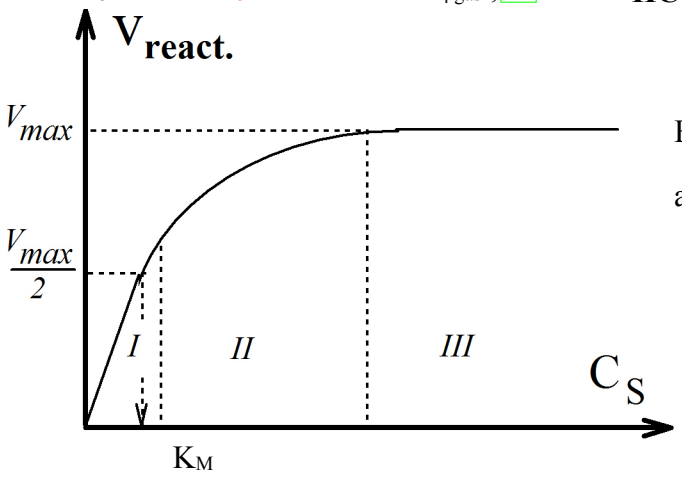


Correct collision geometry for more complicated molecules show zero geometric, pre exponential factor **A=0**. A collision can be insuccessive; if the collision angle is non-effective β-naphtole reacts with acetic acid. In this reaction a collision will be successive (reaction will occur) only in the 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

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

$H_3O^+ + HCO_3^- \rightarrow 2H_2O + CO_2\uparrow_{gas}$; $\vec{v} = \vec{k} \cdot C_{HCO_3^-}$; decomposition of bicarbonate 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 $\vec{v} = {}^{vmax}/K_M \cdot C_S$, because reaction **activation** energy $E_a = 0$ minimization increase velocity constant million times, but at high 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

All life organisms synthesis reactions are **First order** as polymer is bound to enzyme and substrate is singular reactant A: **polymerization**, **polycondensation** of polypeptides, nucleic acids DNA,RNA, polysaccharides.

Second-order reactions

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, water reaction ionisation-neutralisation **$H_2O + H_2O + Q + \Delta G <=> H_3O^+ + OH^-$** is second order reaction direct and reverse.

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.*

Many reactions have a formal order like : $FeS_2 + 11O_2 \rightarrow 2Fe_2O_3 + 8SO_2\uparrow$,
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.

Biochemical reaction converts substrata A → to singular Product

in first order velocity $\vec{v}=\vec{k}\bullet C^{1}_{A1}$ or in zero order (power) with constant rate $\vec{v}=\vec{k}\bullet C^{o}_{A2}=\vec{k}$.

Low reactant concentration C_{A1} is smaller about excess concentration C_{A2} , because $C_{A1} < C_{A2}$. Enzyme E as catalyst converts reactant-substrata A to singular Product releasing unchanged initial form :

E + A → Products+ E . If substrate is in high excess, than velocity will be independent on substrate A concentration. Reaction is zero order with constant velocity $\vec{v}=\vec{k}\bullet C^{o}=$ constant.

On surface of catalyst occur nor first order reaction, nor zero order reaction, if reactant concentration C_{A1} is smaller about excess concentration C_{A2} for compound A : $C_{A1} < C_{A2}$.

Enzyme loins in catalyst infinite times colliding with reactant A yielding singular Product.

First order reaction velocity constant. First power reaction A → Products. Reaction velocity expression $\mathbf{v} = \vec{k}\bullet\mathbf{C_A}$ or definition of velocity, that is $\vec{v}=-\frac{dC_A}{dt}$. Both equations left sides are the same value-velocity **v**.

Right side of equations are equal too: $\vec{k}\bullet\mathbf{C_A}=-\frac{dC_A}{dt}$. Rearrange concentrations left side, but time on right saide: $\frac{dC_A}{C_A}=-\vec{k}\,\mathbf{dt}$. Both sides have to integrate on time interval from t = 0 to final moment t, when reactant concentration at start from C^0_A to final concentration C_A. Integration interval left side is from C^0_A to C_A, and right side from 0 to t is the final moment of experiment.

$$\frac{dx}{x}=\mathrm{d}(\ln x)\ ;\ \frac{dC_A}{C_A}=\mathrm{d}(\ln C_A)\ ;\ \mathrm{d}(\ln C_A)=-\vec{k}\,\mathbf{dt}\ ;\ \int_{C_A^o}^{C_A}\mathrm{d}(\ln C_A)=\int_0^t -\vec{k}\,\mathbf{dt}$$

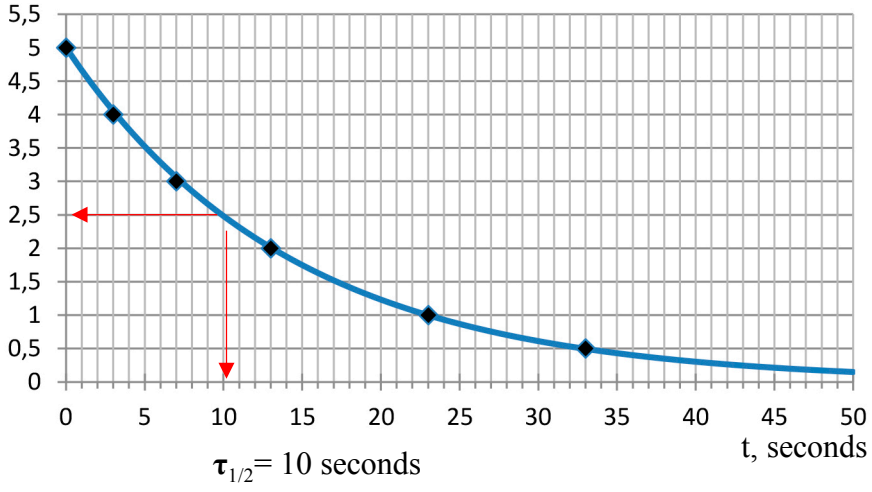
Integration result is: $\ln C_A-\ln C^0_A=-\vec{k}\,(t-0)$ jeb $\vec{k}\bullet t=\ln C^0_A-\ln C_A=\ln\frac{C_A^{\,o}}{C_A}$ un $\vec{k}=\frac{1}{t}\ln\frac{C_A^{\,o}}{C_A}$.

First order reaction half period. Half life time $\boldsymbol{\tau_{1/2}}$ is the time, in which reactant concentration decreases per half. During one half life time t = $\boldsymbol{\tau_{1/2}}$, reactant concentration ratio becomes 2 = $C^0_A/\ C_A$ and concentration ratio yield logarithm of two $\ln\frac{C_A^{\,o}}{C_A}=\ln 2=0.693$.

Reaction velocity constant is $\vec{k}=\frac{\ln 2}{\tau_{1/2}}$ or half life time is $\boldsymbol{\tau_{1/2}}=\frac{\ln 2}{\vec{k}}$.

Equation calculate first order reaction velocity constant from experiment in picture. If known initial reactant concentration C^0_A and after time t determination of rest concentration C_A, calculate the constant of velocity $\vec{k}$.

Concentration



Picture. Reactant concentration decrease on first order reaction.

Using in reaction velocity constant expression $\boldsymbol{\tau_{1/2}}$=10 sec. and ln2 obtain the velocity constant $\vec{k}$ for reaction. $\tau_{1/2}$ half life time, half decay time, half decomposition time, half elimination time, in which substrate amount decreases per half.

Constant $\vec{k}=\frac{\ln 2}{\tau_{1/2}}=\frac{0{,}693}{10\_\mathbf{s}}=0.0693\ \mathrm{s^{-1}}$;

Energy change **minimum** and **reactivity drive reaction complexes irreversibly** in **homeostasis**

Organism biochemical environment forming fast equilibria drive life processes with molecules functional activity attractors: generate concentration gradients, air 20.95% [O_2] , water concentration [H_2O]=55.3457 M, osmolar concentration 0,305 M, ionic strength 0,25 M, pH=7,36 hydroxonium [$\mathbf{H_3O^+}$]=$10^{-7,36}$ M, temperature 310,15 K.

Five types complex ordered reactions versus chaos and pollution of non Enzymatic reactions:

5 complex Enzyme reactions

Enzyme governed complexe reactions drive the LIFE in 5 ways

Versus non Enzymatic reactions

chaos and contamination

7th page : Velocity KINETICS of REACTION dependence on Attractors create molecules functional Activity

1. GRADUAL-CONSECUTIVE organized favored reaction sequence of **ENZYME** complexes for Glycolysis, Krebs cycle; Polycondensation: Replication, Polymerisation, Proteins Translation Synthesis

1. Chaotic

2. ENZYMES specificity 100% efficiency of product **singularity**

2. PARALLEL reaction preseeding in chemistry as side products

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

3. Thermodynamic forbidden, impossible reaction
unfavored has positive free energy change
$\Delta G=\Delta H-\Delta S\cdot T>0$

1 st 5 th page:
Thermodynamic attractor with functionally active O_{2aqua}, CO_{2aqua}

4. COMPETITIVE regulation as **inhibition** and **allostery**
sensitive to concentration O_{2aqua}, HCO_3^-, H^+ (**Le Chatelier** principle)
His63,58 as for hemoglobin, His64 as for myoglobin as regulated back response
prevent (hypo amount) deficiency and (hyper amount) overproduction

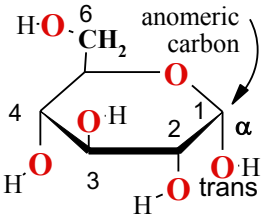
4. Chaotic

so stabilises Physiologic pH=7.36, arterial [O_{2aqua}]=$6\cdot10^{-5}$ M and venous [O_{2aqua}]=$0{,}426\cdot10^{-5}$ M.

Photosynthesis global stabilises oxygene concentration [O_{2AIR}]= 20,95% in Earth Atmosphere.

5. Enzyme radical driven reactivity the process for maintanance of homeostasis producing resources

5. Contamination destructive chemistry with the chaotic radical chain reactions in multiple parallel products



1. GRADUAL (CONSECUTIVE) favored **REACTION SEQUENCES**

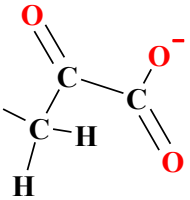
Glycolysis is most popular gradual favored equilibria sequence in human organism

Hess law application in **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. Oxygen O_2 assimilation **I)** and oxidation products H^+, HCO_3^- exhalation **II)**.

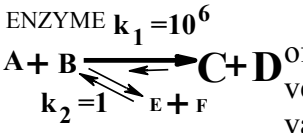
I) $O_{2gas}+H_2O<=>H_2O+O_{2aqua}$; $4O_{2aqua}+(H^+His63,58)_4Hb_T$..salt bridge$(HCO_3^-)_4<=>Hb_R(O_2)_4+4H^++4HCO_3^-$

Deoxy hemoglobin Hb_T (Tense) and **oxy** hemoglobin Hb_R (Relax)

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

2. Enzymes specificity 100% of product singularity; Chaos and pollutions by PARALLEL 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. Hess law application to **HOMEOSTASIS** PATHWAY is singularity of reactivity as Prigogine attractor.

ENZYME reaction singularity of reactivity is Prigogine attractor.
Life processes do not have parallel reactions..



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 reactions are governed by ENZYMES, which selectively faster forming perfect single product for life and never have made side products.

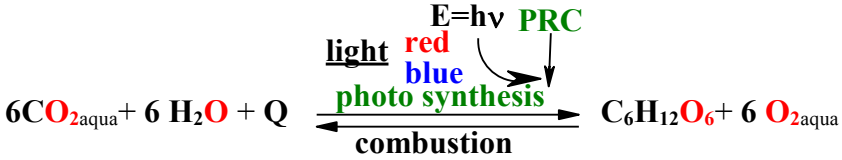
3. JOINT TANDEM EQUILIBRIA drive unfavored, forbidden synthesis **REACTIONS**

Hess law application.

Green plants **Photosynthesis** reaction is thermodynamically forbidden as endoergic $\Delta G_r = 2921{,}5$ $^{kJ}/_{mol}$: $6CO_{2aqua}+6H_2O+Q$—x of→$C_6H_{12}O_6+6O_{2aqua}$ and as endothermic reaction $\Delta H_{reac}>0$ $\Delta H_{reac}= 2812{,}6$ $^{kJ}/_{mol}$ precede sunny, warm climatic circumstances as in summer.

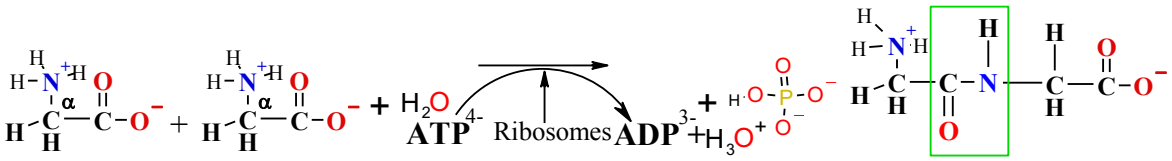
Joint, tanden reactions solve by Hess law application where in unfavored reaction forms free energy rich compounds like protein, **glucose** $C_6H_{12}O_6$, **oxygen** 6 O_2 in which entropy lowered and is growing-accumulate *Gibbs energy*. The reaction alone is thermodynamically forbidden, but the **red** and **blue** light photon absorption *Gibbs's energy* accumulate in products wich becomes compensate for the overall process as thermodynamically favored according Hess law.

. Thermodynamic forbidden, unfavored reaction in **plant** photo synthetic center by joint, tandem ENZYME driven **red** and **blue** light photon absorption for free energy accumulation in products:



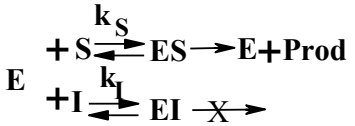
The ENZYME complex Ribosomes are for Peptide Bond synthesis: gly + gly→gly-gly+ H_2O at Lehninger biochemical conditions pH=7,36 un [H_2O]=55,3 M: with free energy $\Delta G_{eq}= 9{,}2$;$\Delta G_{Hess}=57{,}3$ $^{kJ}/_{mol}$ transfer shift ATP^{4-} hydrolyze exoergic free energy $\Delta G_{LehningerEq}=-30{,}5$ $^{kJ}/_{mol}$ which part is used free energy store $\Delta G_{eq}= 9{,}2$ $^{kJ}/_{mol}$ in one mole of peptide bond.

Glycine Gly [G] Glycine Gly [G] GlycinoGlycine Gly-Gly GG



4. COMPETITIVE regulator, allosterator and inhibitor **REACTIONS**

His63,58 hemoglobin and His64 myoglobin with O_{2aqua}, HCO_3^-, H^+ concentrations sensitive reversible equilibria according Le Chatelier's principle prevent overproduction, deficiency and stabilising pH=7.36, arterial concentration [O_{2aqua}]=$6\cdot10^{-5}$ M and venous concentration [O_{2aqua}]=$1.8\cdot10^{-5}$ M.

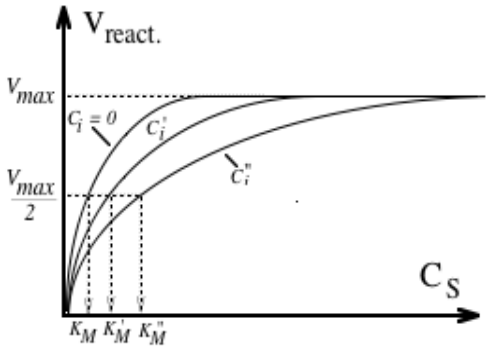


ENZYME governed reactions are regulated by inhibitors **I** concentration which shift to left **E+S** reaction. Inhibitor molecule **I** compete with substrate molecule **S** and shift substrate reaction to left according Le Chatelier theorem by decrease of ENZYME concentration C_E involved into competitive inhibition equilibrium.

In competitive equilibria two different initial compounds substrate **S** *and inhibitor, allosterator* **I** *compete on one ENZYME regulate decrease the product* **[Product]** efficiency in K_{eq}, K_I *equilibria via* [**E**] concentration according Le Chatelier's principle *increasing* $\mathbf{K_M}$ in velocity $\mathbf{v_{react}}$ expression,:

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

Physiologic ENZYME regulation is an equilibrium which shifting to right side promoted by inhibitor concentration C_I increase, for example, using medicine (aspirin, warfarin e.c.).



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

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 K_M has the meaning of a substrate concentration C_S at which the reaction velocity reaches $^1/_2$ of maximal

$$v_{react}=v_{max}/2 \quad .$$

5. Reaction complexes use peroxide radical enzymatic as molecular engines for homeostasis support

Exoergic dismutation catalase reaction converts peroxide H_2O_2 to life resourses: $O_{2aqua}+H_2O+Q$. Essential unsaturated fatty acid elongation C20:4 and ethyl group $-CH_2-CH_2-$ convertion to cis double bond $^{H}>C=C<^{H}$ in peroxisomes occurs exoergic, favored enzymatic convertion with negative free energy change like:

ΔG_{eq}=-48,127 $^{kJ}/_{mol}$. CATALASE as indispensable **Life** engine erase peroxide H_2O_2 to zero. Catalase in complex reaction sequence favors stabile unsaturated fatty acid product efficiency ● 100% because erasing peroxide H_2O_2: $K_{eq}=10^{8,43}=\frac{[fumarate^{2-}]\cdot[HSCoA^{2-}]\cdot[H_2O]\cdot[H_2O_2]}{[Succinate^{2-}]\cdot[O_2]\cdot[H_3O^+]}\xrightarrow{CATALASE}$, as peroxide consumed to zero $[H_2O_2]^2=0$ $^{mol}/_{liter}$ and process velocity limits only dehydrogenase enzyme.

Irreversible Catalase reactivity is Prigogine attractor indispensable Brownian molecular engine which drive Life for evolution, survival and homeostasis.

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** oxygen •::O-:-O::• risk increases five times. $\vec{v}\sim[O_2]$.

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 space project closing in 72rd of 20 century.

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

Radical formation from H_2 and Br_2 begins by light radiation ***initiation.***

Initiation is first stage of radical formation as activated particles with low activation energy E_a=>0 kJ/mol. The radical here is photochemical: Br_2 molecules absorb light photons, forming from bromine molecule 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 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 H_2 and 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.