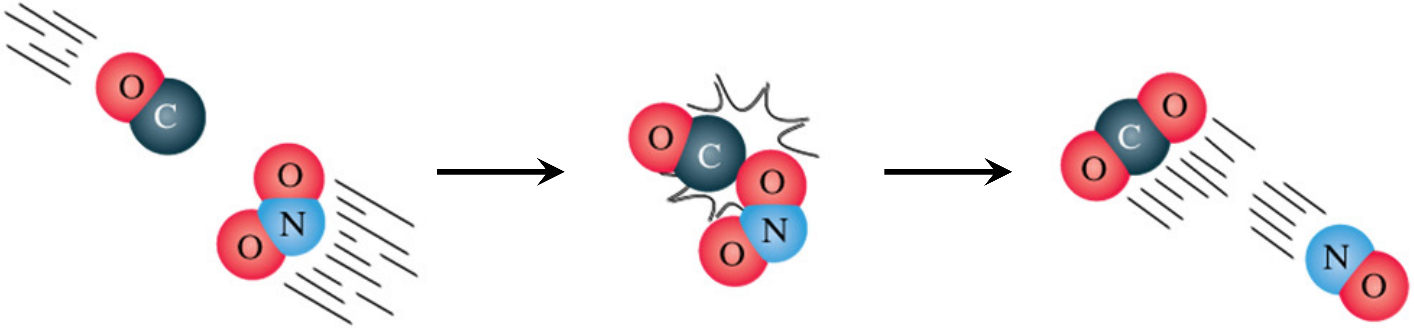
Chemistry and Introduction to Biochemistry
Chemical kinetics

$$2\ H_2\ (g) + O_2\ (g) \rightarrow 2\ H_2O\ (g)$$

The explosion of the Hindenburg Zeppelin on May 3, 1937

Chemical kinetics

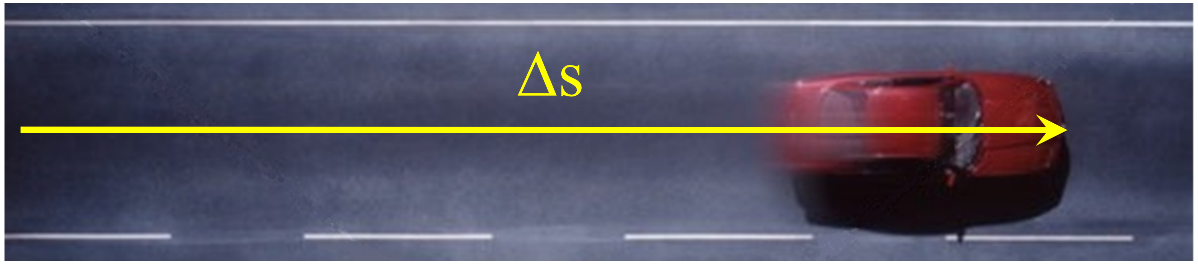
Unlike thermodynamics that deals with the relative stability between reagents and products in a chemical reaction, chemical kinetics deals with the study of the rate of a chemical reaction and its dependence on various factors.



In addition to describing the dependence of the reaction rate on experimental factors, kinetics also deals with examining the mechanism of the reaction, i.e. sequence of chemical or physical processes through which conversion between reagents and products takes place. In this way the study of the reaction rate aims at obtaining detailed information on the interaction between the molecules during the reaction.

Reaction rate

The concept of speed is encountered in many non-chemical contexts



Δt

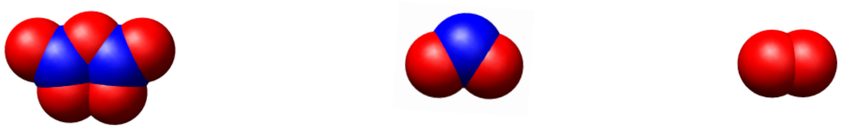
$$rate = \frac{path}{time\ elapsed} = \frac{\Delta s}{\Delta t}$$

The rate of a reaction is defined in a similar way: it corresponds to the variation of concentration of a chemical species in the unit of time

$$reaction\ rate = \frac{concentration\ change}{time\ interval}$$

Consider the decomposition reaction of N_2O_5 which takes place according to the following reaction:

$$2\ N_2O_5\,(g) \rightarrow 4\ NO_2\,(g) + O_2\,(g)$$



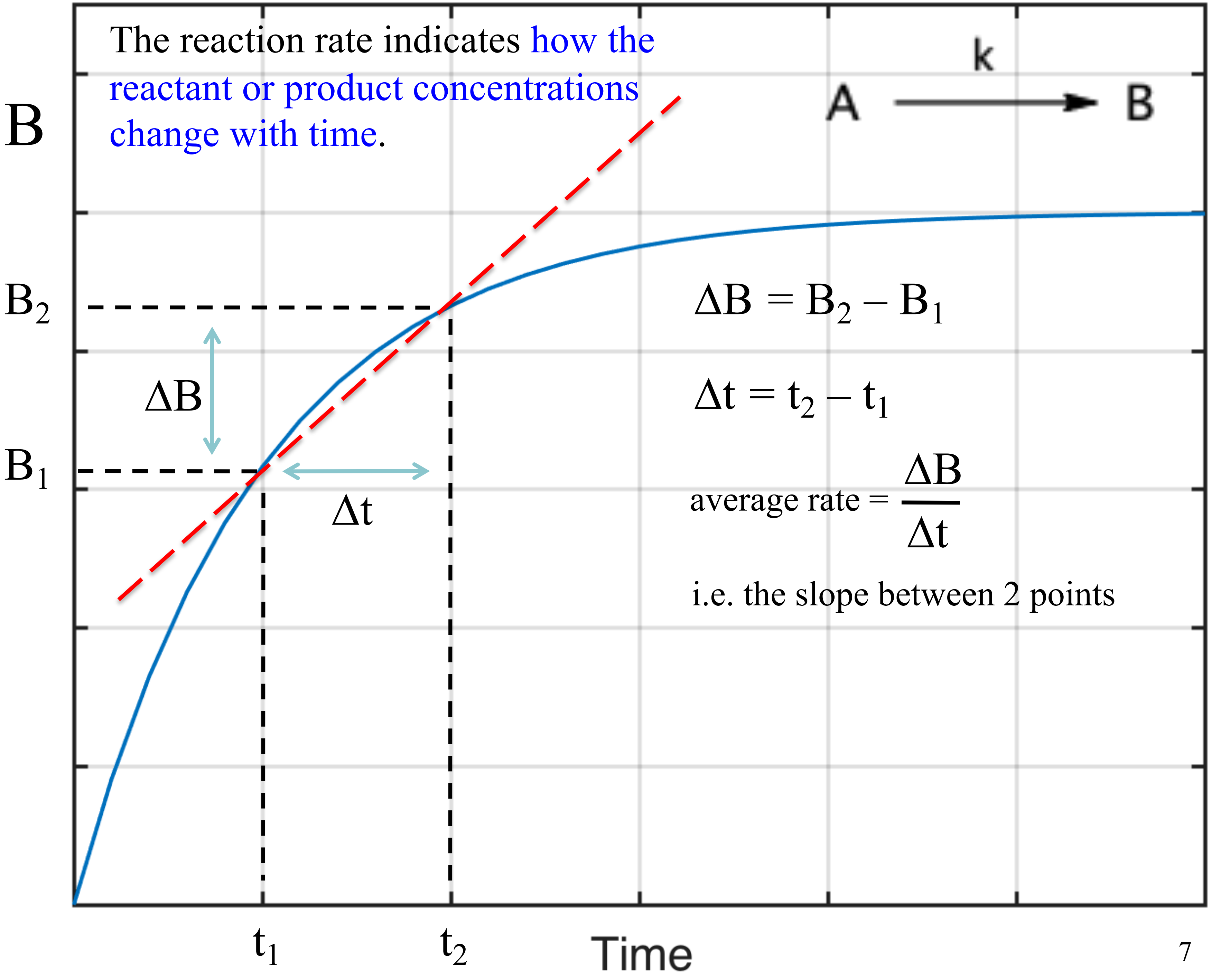
- the progress of the reaction can be followed in different ways: increase of the partial pressure of O_2 or NO_2 or the decrease of N_2O_5

- The amount of O_2 that has formed is related to the amount of N_2O_5 initially present: for each mole of O_2 formed, 2 moles of N_2O_5 have decomposed

- The reaction speed can be expressed, for any length of time, as the ratio between the concentration change of N_2O_5 and the elapsed time interval

$$reaction\ rate = \frac{[N_2O_5]\ change}{time\ interval} = -\frac{\Delta[N_2O_5]}{\Delta t}$$

The "-" sign is due to the fact that the $[N_2O_5]$ decreases over time.



The reaction rate indicates how the reactant or product concentrations change with time.

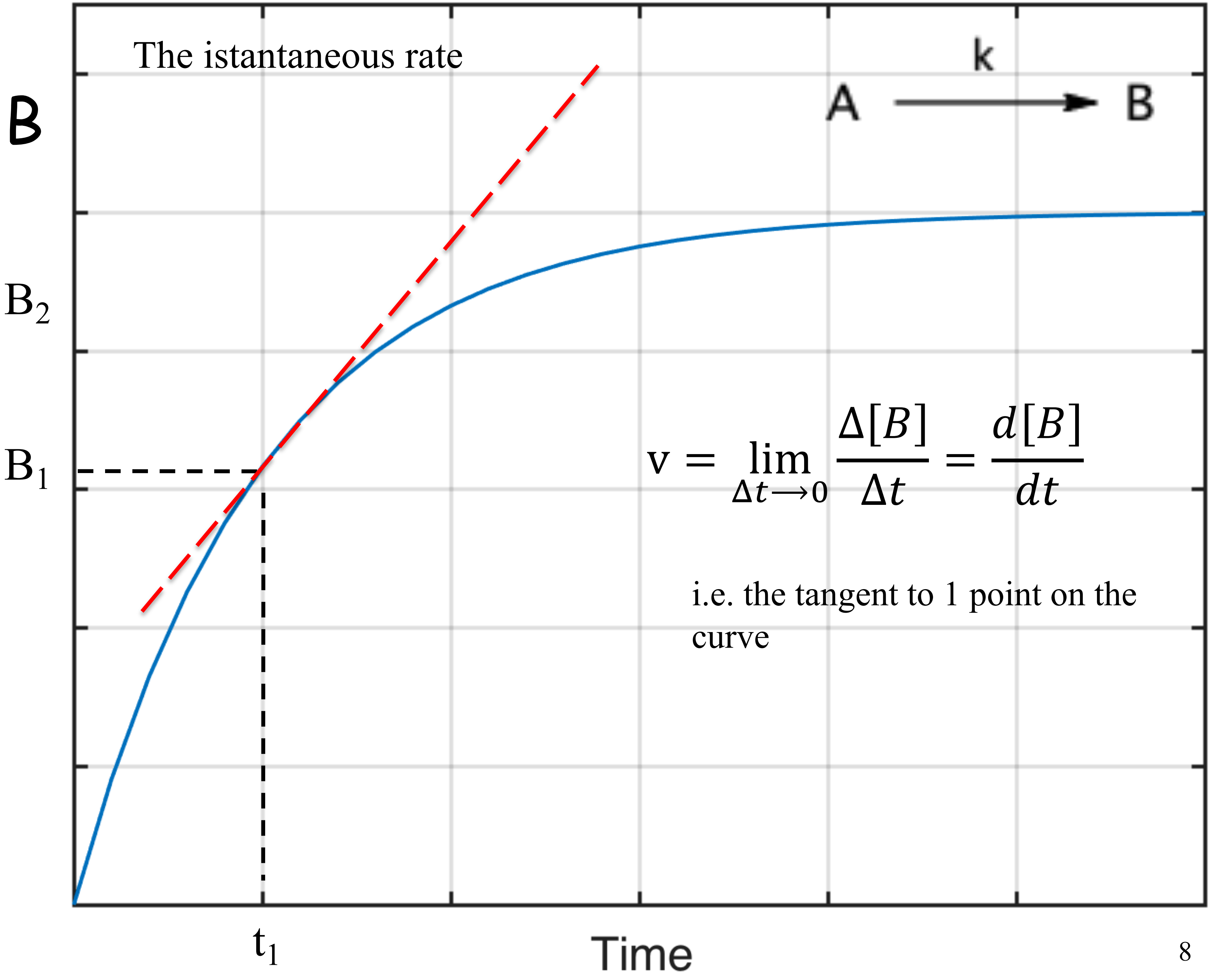
$$A \xrightarrow{k} B$$

$$\Delta B = B_2 - B_1$$

$$\Delta t = t_2 - t_1$$

$$\text{average rate} = \frac{\Delta B}{\Delta t}$$

i.e. the slope between 2 points



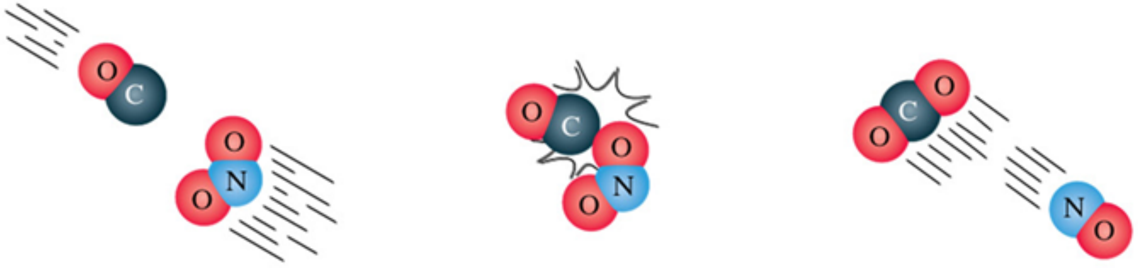
The istantaneous rate

$$v = \lim_{\Delta t \to 0} \frac{\Delta[B]}{\Delta t} = \frac{d[B]}{dt}$$

i.e. the tangent to 1 point on the curve

Reaction rates depend on several factors

- the nature of the reagents
- the concentration of reagents
- reaction temperature
- the presence of catalysts
- the area of the interface (heterogeneous reactions)



before the collision collision after the collision

Dependence of the reaction rate on concentration

$$a\,A + b\,B \xrightarrow{k} c\,C + d\,D$$

Experimentally it is found that the speed of a chemical reaction depends on the concentration of reagents. The equation which correlates the rate of a reaction with the concentrations of the reagents is known as the kinetic equation and has the form:

$$\mathrm{v} = -\frac{1}{a}\frac{d[A]}{dt} = -\frac{1}{b}\frac{d[B]}{dt} = \frac{1}{c}\frac{d[C]}{dt} = \frac{1}{d}\frac{d[D]}{dt} = -k \cdot [A]^p \cdot [B]^q$$

Dependence of the reaction rate on concentration

Experimentally it is found that the speed of a chemical reaction depends on the concentration of the reagents. The equation that correlates the rate of a reaction to the reactant concentrations is known as a kinetic equation or a rate law and has the form:

$$a\,A + b\,B \xrightarrow{k} c\,C + d\,D$$

$$\boxed{v = k \cdot [A]^p \cdot [B]^q}$$

i.e. the product of the concentrations of the reactants with appropriate exponents (p, q ..., generally different from the stoichiometric coefficients) multiplied by a constant (k). These coefficients are generally (but not always) integers and must be determined experimentally. The constant k is called a specific rate constant and depends only on the nature of the reagents and the temperature.

Order of reaction

For a given chemical reaction of which the kinetic equation is known, the order of reaction with respect to a certain component is the exponent of the concentration of that component in the kinetic equation

The total reaction order is, instead, defined as the sum of the exponents of all the reactants present in the kinetic equation.

For example, the generic reaction: a A + b B → c C + d D
which has a kinetic equation:

$$v = k \cdot [A]^p \cdot [B]^q$$

is of order p with respect to reagent A and of order q with respect to reagent B and of order p + q overall. Example, the reaction:

$2\ NO\ (g) + 2\ H_2\ (g) \rightarrow N_2\ (g) + 2\ H_2O\ (g)$
with rate law $v = -\ k\ [NO]^2[H_2]$

it is of the second order with respect to NO, first order with respect to H_2 and the third overall order. If a reagent does not appear in the kinetic equation for a given reaction, this is of zero order with respect to that reagent.

The specific rate constant

The specific rate constant k is the proportionality constant that relates rate and concentration at a given temperature. It is an important parameter since it allows to calculate the reaction rate at any concentration value.

The dimensions of the specific rate constant must be consistent with those of the other terms contained in the kinetic equation.

$$A \xrightarrow{k} B$$

$$v = k \cdot [A] \qquad \{k \equiv \text{time}^{-1}\}$$

$$A + B \xrightarrow{k} C + D$$

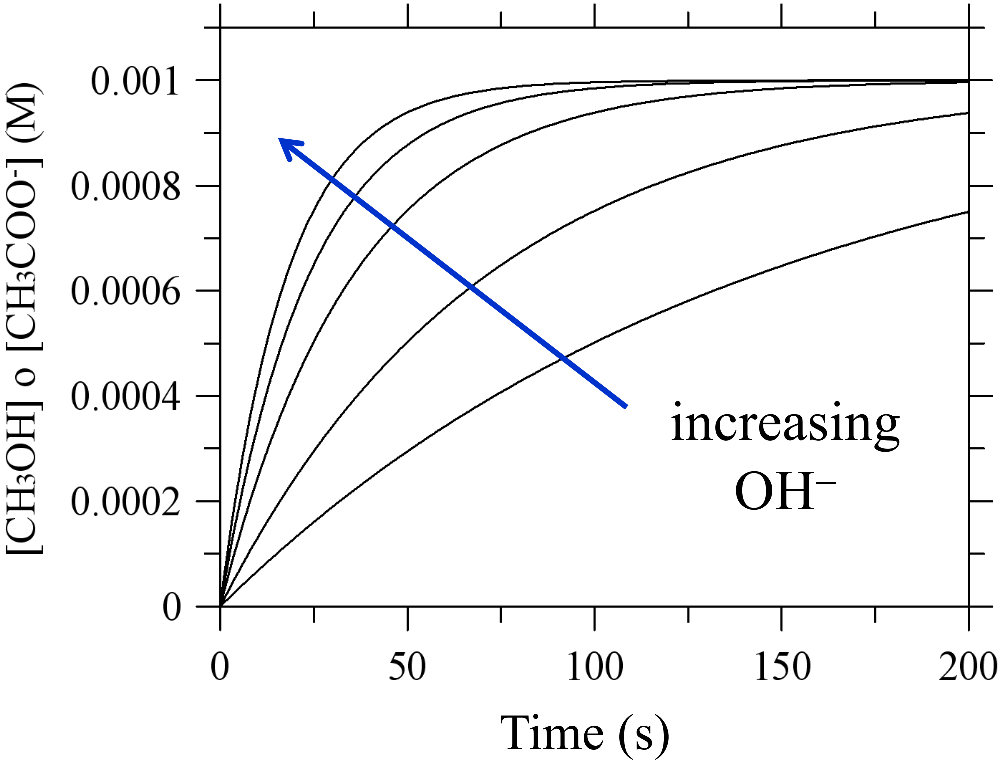
$$v = k \cdot [A] \cdot [B] \qquad \{k \equiv \text{concentration}^{-1} \cdot \text{time}^{-1}\}$$

Relationship between concentration and time: integrated kinetic laws

Sometimes it is useful and important to know how long a reaction must take place so that the concentration of a given reagent reaches a given value or to predict the value of the concentration of a reagent or product after a certain reaction time.

For this purpose we derive an equation that relates the concentrations and the time: the integrated kinetic equation.

$CH_3COOCH_3\ (aq) + OH^-\ (aq) \rightarrow CH_3COO^-\ (aq) + CH_3OH\ (aq)$



The integrated kinetic equation describes the time dependence of product formation or reagent disappearance

First-order reaction

$$A \xrightarrow{k} B$$

$$v = -\frac{d[A]}{dt} = k[A]$$ rate law

$$\frac{d[A]}{dt} = -k\,dt \rightarrow \int \frac{d[A]}{[A]} = -k \int dt$$ separation of variables

$$ln[A] = -k\,t + Q$$ time-integrated equation, where Q = costant

The integration constant Q can be calculated by imposing the condition that for t = 0, $[A] = [A]_0 \rightarrow \quad Q = \ln[A]_0$:

$$\ln[A] = -k\,t + \ln[A]_0 \quad \rightarrow \quad \ln[A] - \ln[A]_0 = -k\,t$$

$$ln\frac{[A]}{[A]_0} = -k\,t$$

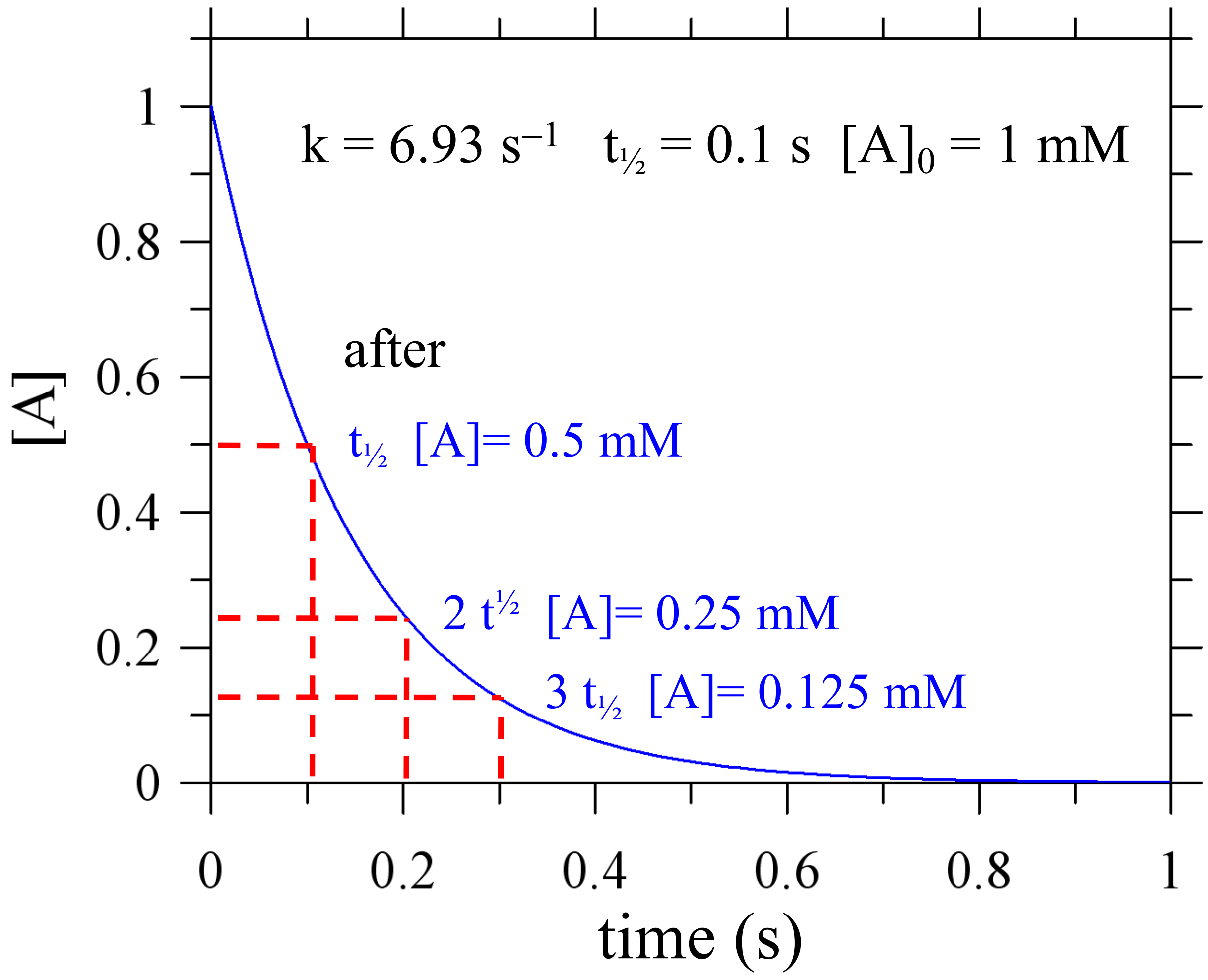
$$\boxed{[A] = [A]_0 e^{-k\,t}}$$

First-order reaction

$$A \xrightarrow{k} B$$

$$\boxed{[A] = [A]_0 e^{-k\,t}}$$

the time course is exponential



half-time $t_{1/2}$

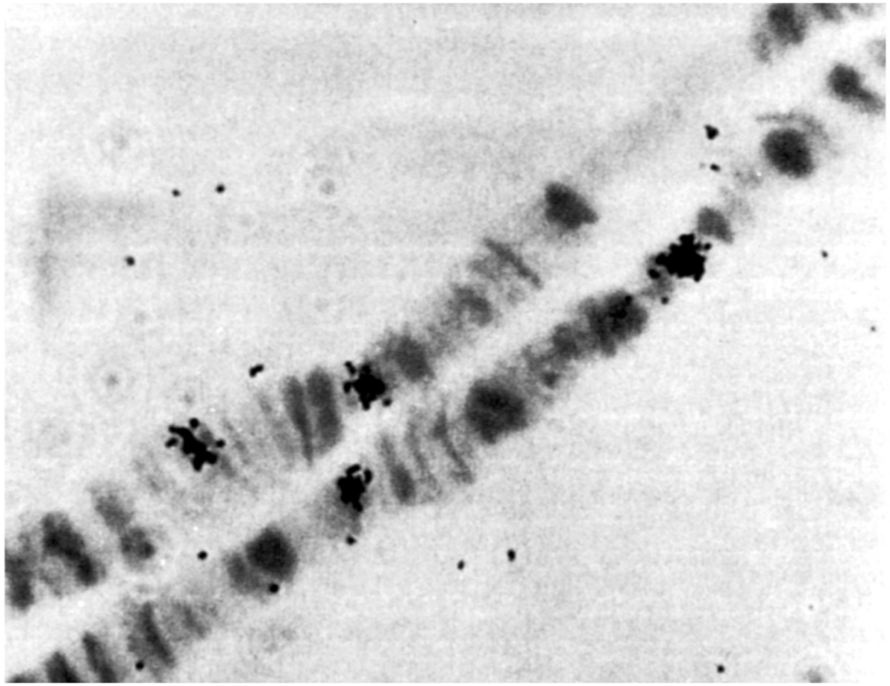
$$if \quad [A] = \frac{[A]_0}{2}$$

$$\boxed{t_{1/2} = \frac{\ln 2}{k}}$$

Radioisotopes in biology and medicine

- they are used as tracers or as sources of destructive energy (radiotherapy)
- they must have half-life of days or months
- they must not accumulate in the organism
- they must be transformed into stable isotopes

radionuclide	halftime ($t^{1/2}$)	radiation
^{3}H	12 years	β
^{14}C	5715 years	β
^{24}Na	15 ore	β
^{32}P	14 days	β
^{35}S	87 days	β
^{40}K	$1.25 \cdot 10^{9}$ years	β
^{45}Ca	163 days	β
^{125}I	59 days	γ
^{131}I	8 days	γ, β



Radiocarbon dating

Carbon has three isotopes: two stable (^{12}C and ^{13}C) and one radioactive (^{14}C). The latter is transformed by β decay (electrons) into nitrogen (^{14}N), with an average half-life (or half-life) of 5715 years.

$$\boxed{{}^{14}_{6}C \xrightarrow{k} {}^{14}_{7}N + {}^{0}_{-1}\beta}$$

$$k = \frac{\ln 2}{t_{1/2}} = \frac{0.693}{5715} = 1.2 \cdot 10^{-4} year^{-1}$$

The production of new ^{14}C occurs naturally in the upper layers of the troposphere and in the stratosphere, by the capture of thermal neutrons (cosmic rays) by nitrogen atoms.

production $$^{14}_{7}N + n \xrightarrow{k_f} {}^{14}_{6}C + {}^{1}_{1}H$$

decay $$^{14}_{6}C \xrightarrow{k_d} {}^{14}_{7}N + {}^{0}_{-1}\beta$$

The dynamic equilibrium that is established between production and radioactive decay keeps the concentration of ^{14}C in the atmosphere constant (where it is present mainly linked to oxygen in the form of CO_2).

$$\xrightarrow{production} {}^{14}_{6}C \xrightarrow{decay}$$

^{12}C	99%
^{13}C	1%
^{14}C	1 part in 10^{12}

All living organisms that are part of the C cycle continuously exchange C with the atmosphere through processes of respiration (animals) or photosynthesis (plant), or assimilate it by feeding on other living beings or organic substances. As a consequence, as long as an organism is alive, the ratio between its concentration of ^{14}C and that of the other two isotopes remains constant and equal to that found in the atmosphere.

After death, however, these processes terminate and the organism no longer exchanges C with the outside. As a result of the decay, therefore, the concentration of ^{14}C decreases in a regular way according to the formula:

$$ {}^{14}_{6}C \xrightarrow{k} {}^{14}_{7}N + {}^{0}_{-1}\beta $$

$$ \boxed{[{}^{14}_{6}C] = [{}^{14}_{6}C_0]e^{-k\,t}} $$

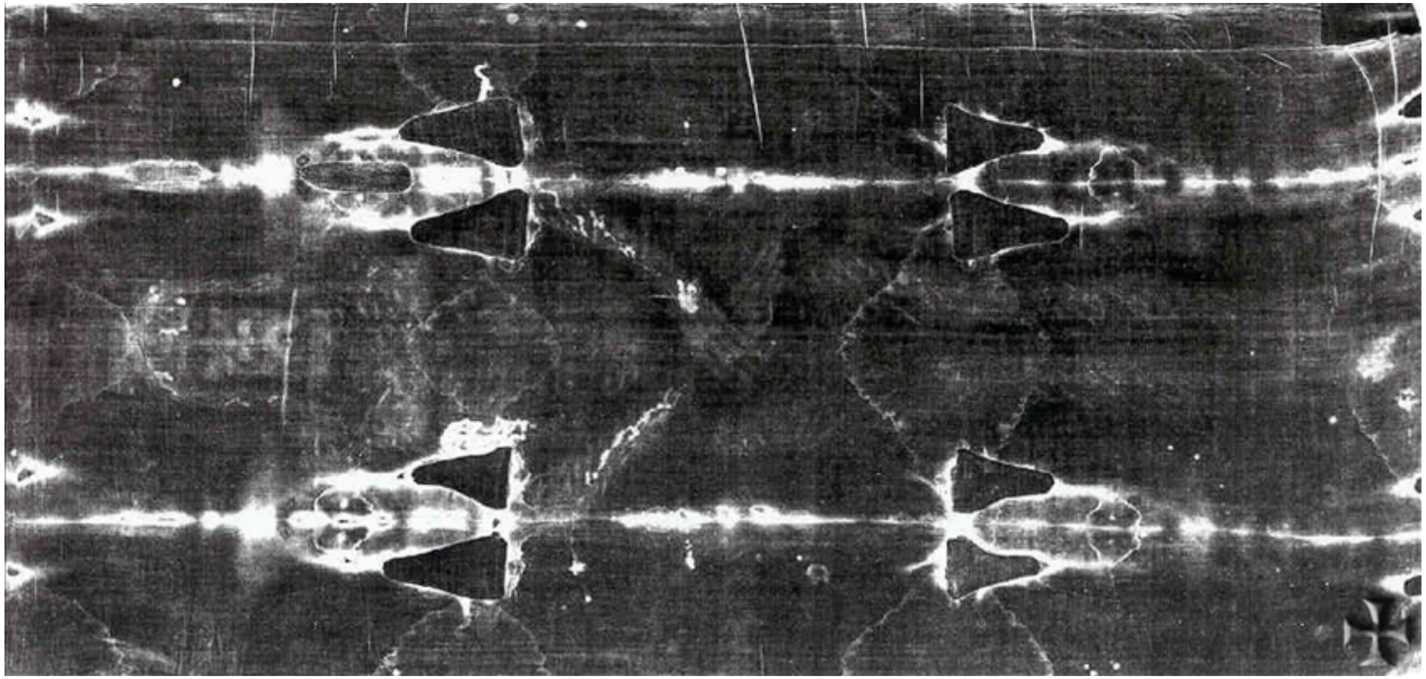
$$ t_{1/2} = \frac{\ln 2}{k} $$

$[^{14}\mathrm{C}]_0 = {}^{14}\mathrm{C}$ concentration at death time

The Shroud & $[^{14}C] = [^{14}C]_0\, e^{-kt}$

The ^{14}C radiometric examination of the on the Shroud in 1988 dated it between the years 1260 and 1390 (!?).

Half-life of ^{14}C = 5715 years



$$t_{1/2} = \frac{\ln 2}{k}$$

$$[^{14}C] = [^{14}C_0]e^{-k\,t} = [^{14}C_0]e^{-\frac{t_{death}}{t_{1/2}}\ln 2}$$

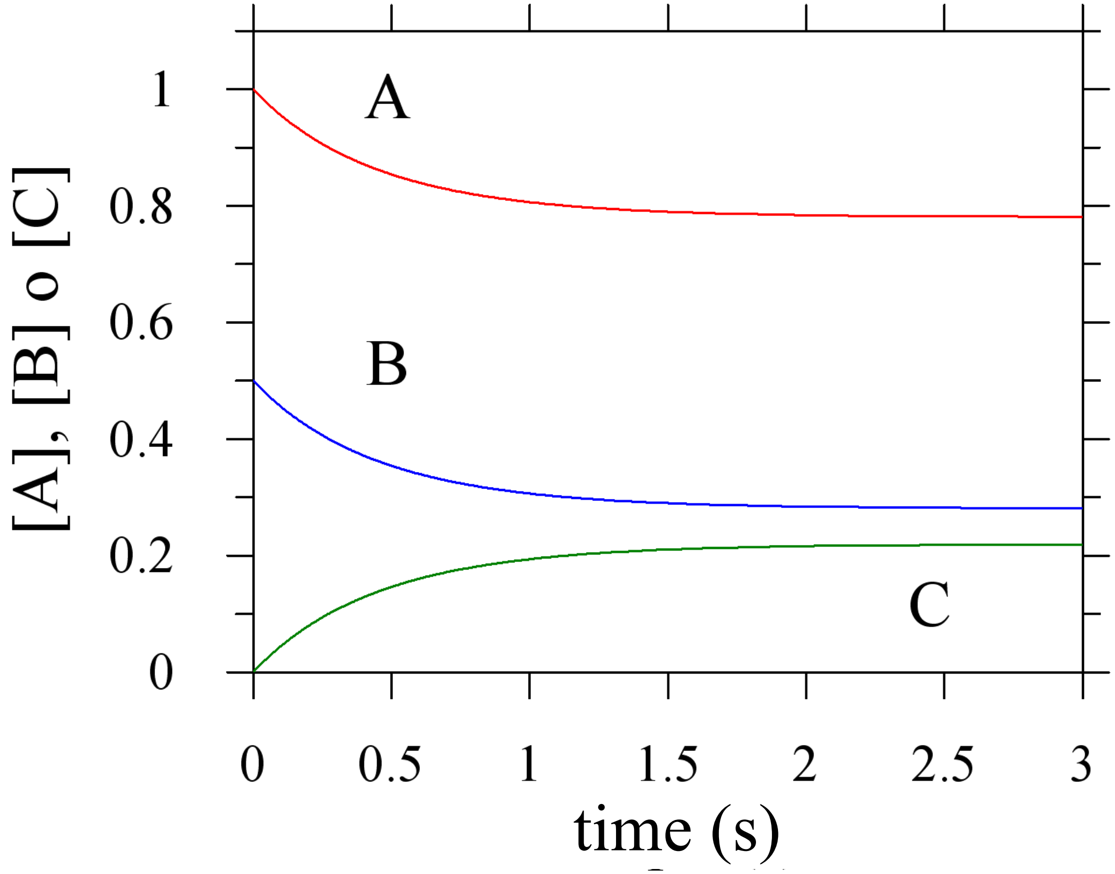
$$t_{death} = -\frac{t_{1/2}}{\ln 2}\, ln\frac{[^{14}C]}{[^{14}C_0]}$$

Reactions are usually reversible

$$A + B \underset{k_2}{\overset{k_1}{\rightleftharpoons}} C$$

Rate law:

$$v = \overbrace{k_1 \cdot [A] \cdot [B]}^{\text{forward rate } (v_D)} - \underbrace{k_2 \cdot [C]}_{\text{reverse rate } (v_R)}$$



At equilibrium $v_D = v_R$

and

$$K_{EQ} = \frac{[C]}{[A] \cdot [B]} = \frac{k_1}{k_2}$$

Reactions from a microscopic point of view

For any chemical reaction to take place the collision theory (M. Trautz & W. Lewis) establishes that 3 conditions must be met:

1. the reagent molecules must collide with each other

2. the reagent molecules must collide with enough energy to break the bonds involved in the reaction

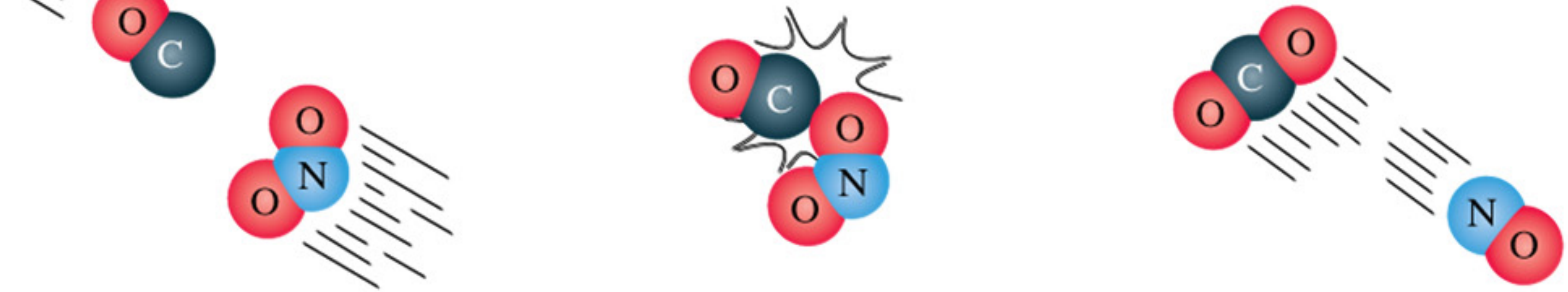
3. the molecules must collide according to an orientation that can allow the rearrangement of the atoms and the formation of the products

1. the reagent molecules must collide with each other

2. the reagent molecules must collide with enough energy to break the bonds involved in the reaction

3. the molecules must collide according to an orientation that can allow the rearrangement of the atoms and the formation of the products

$$CO\ (g) + NO_2\ (g) \rightarrow CO_2\ (g) + NO\ (g)$$



reagents

collisional complex

products

reagent approach

recognition

product separation

1. the reagent molecules must collide with each other
2. the reagent molecules must collide with enough energy to break the bonds involved in the reaction
3. the molecules must collide according to an orientation that can allow the rearrangement of the atoms and the formation of the products

A gas diffusion experiment

1. the reagent molecules must collide with each other
2. the reagent molecules must collide with enough energy to break the bonds involved in the reaction

3. the molecules must collide according to an orientation that can allow the rearrangement of the atoms and the formation of the products

productive collision

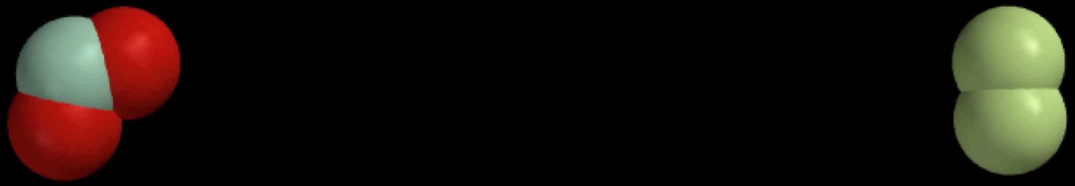
before the collision

collision

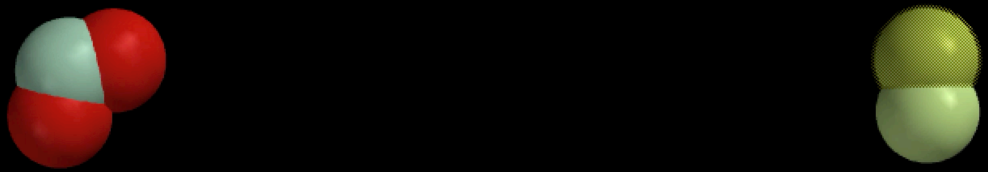
after the collision

unproductive collision

Improper orientation: non productive collision



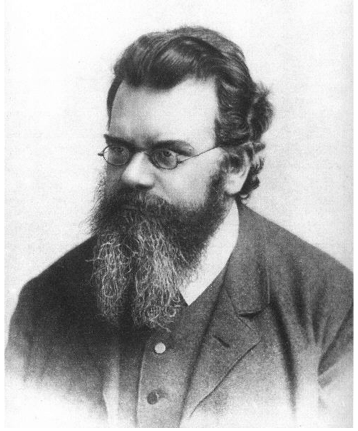
Proper orientation: productive collision



The kinetic theory of gases

The laws of gas provide a macroscopic description of the properties of gases (pressure, volume, density, etc.).
The molecular kinetic theory provides a description at the atomic or molecular level of gases, and is based on three postulates:

James Clerk Maxwell
(1831–1879)



Ludwig Eduard Boltzmann
(1844-1906)

- particle volume: a gas consists of a large set of particles. The volume of a single particle is negligible compared to the volume of the vessel, i.e. the particles have mass but no volume.

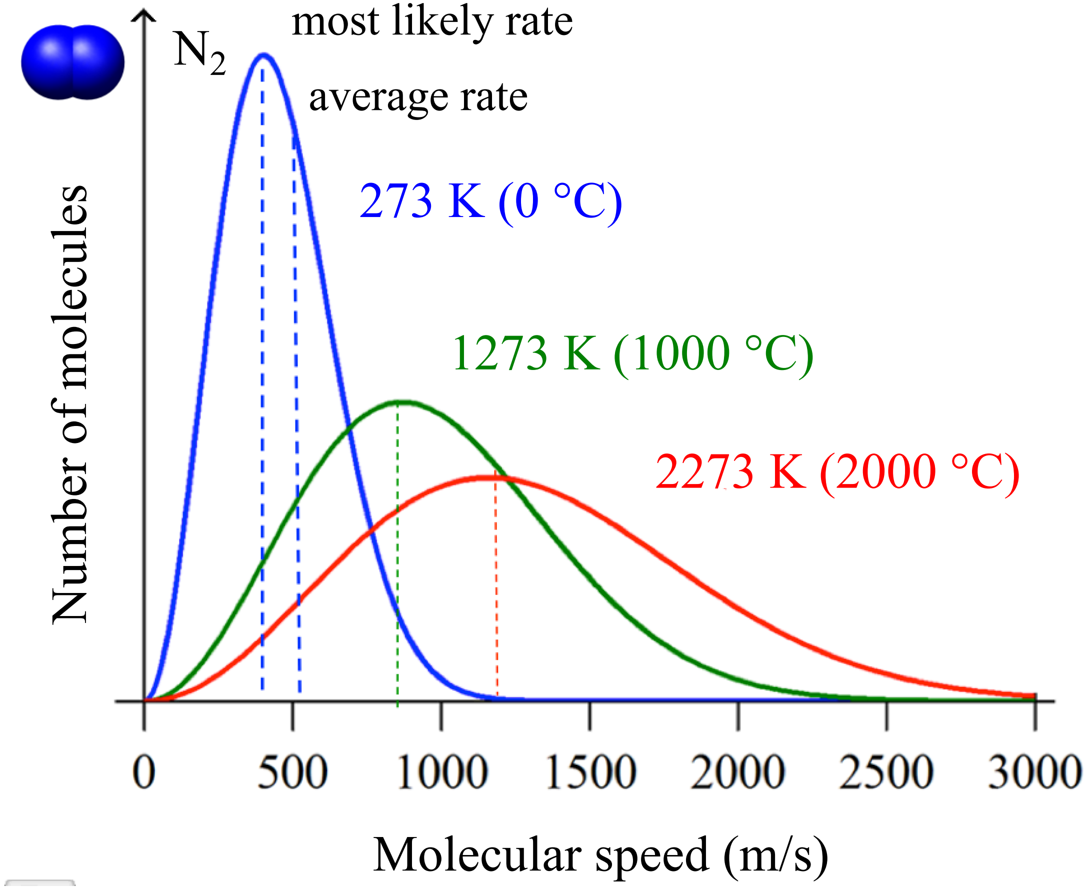
- Particle motion: the gaseous particles are subjected to a continuous random rectilinear motion, except when they strike against the vessel walls or against each other.

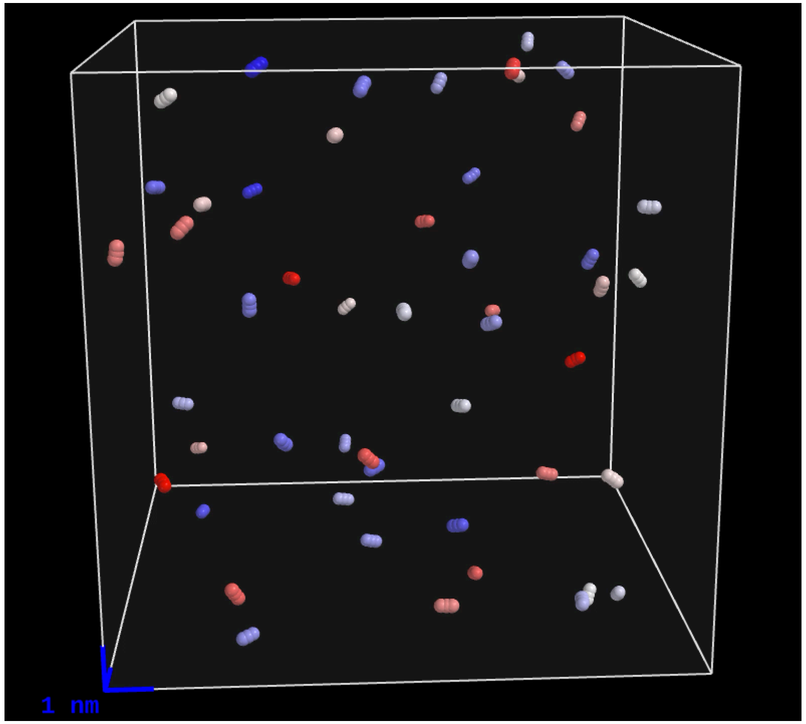
- Particle collisions: the collisions are elastic, ie the colliding molecules (rigid spheres) exchange energy but do not lose energy through friction processes. Thus their total kinetic energy Ek remains constant.

Particle motion: the gaseous particles are subjected to a continuous random rectilinear motion, except when they strike against the vessel walls or against each other.

The average kinetic energy of the particles is proportional to the temperature of the gas.

The Maxwell-Boltzmann distribution of molecular speeds $f(v)=4\pi\left(\frac{M}{2\pi RT}\right)^{\frac{3}{2}} v^2 e^{-\frac{Mv^2}{2RT}}$





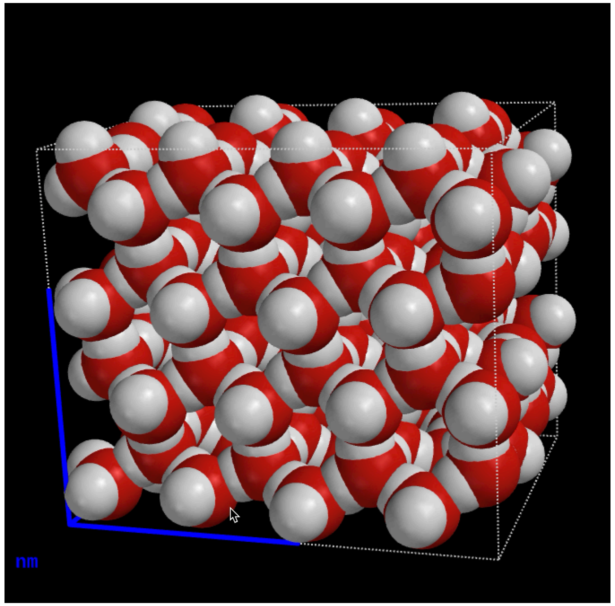
(1 m/s = 3.6 km/hr)

States of matter

The matter is made up of atoms. The physical state of matter depends on how the particles are arranged in space, the forces involved and the mobility of the particles

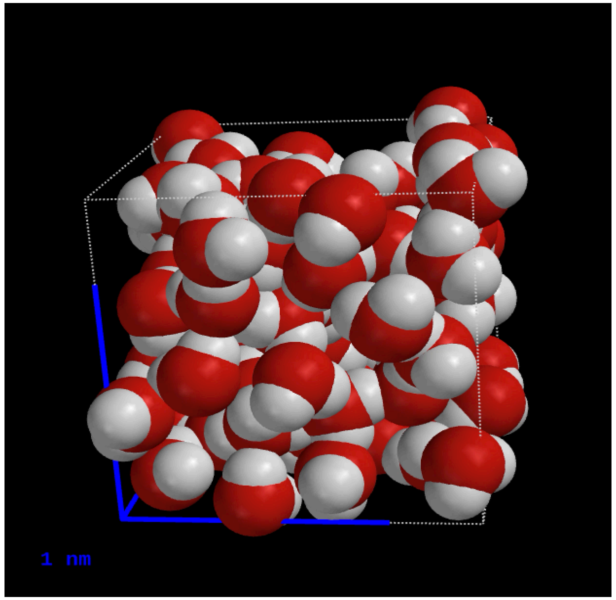
solid

- high cohesive forces
- strong packing
- regular spatial arrangement
- very low mobility



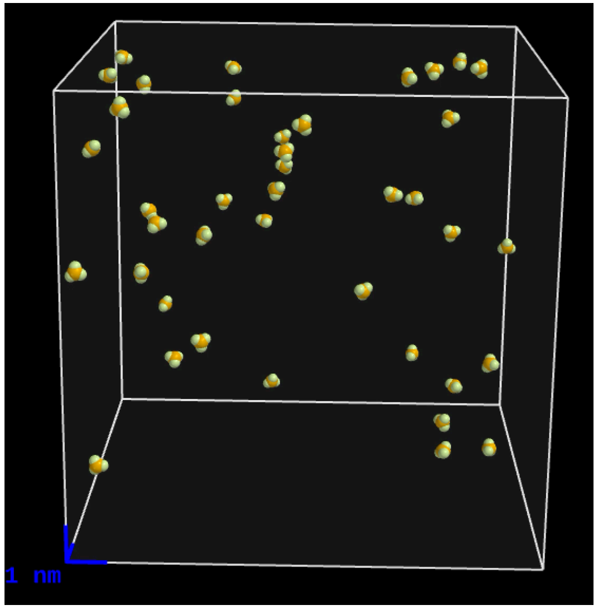
liquid

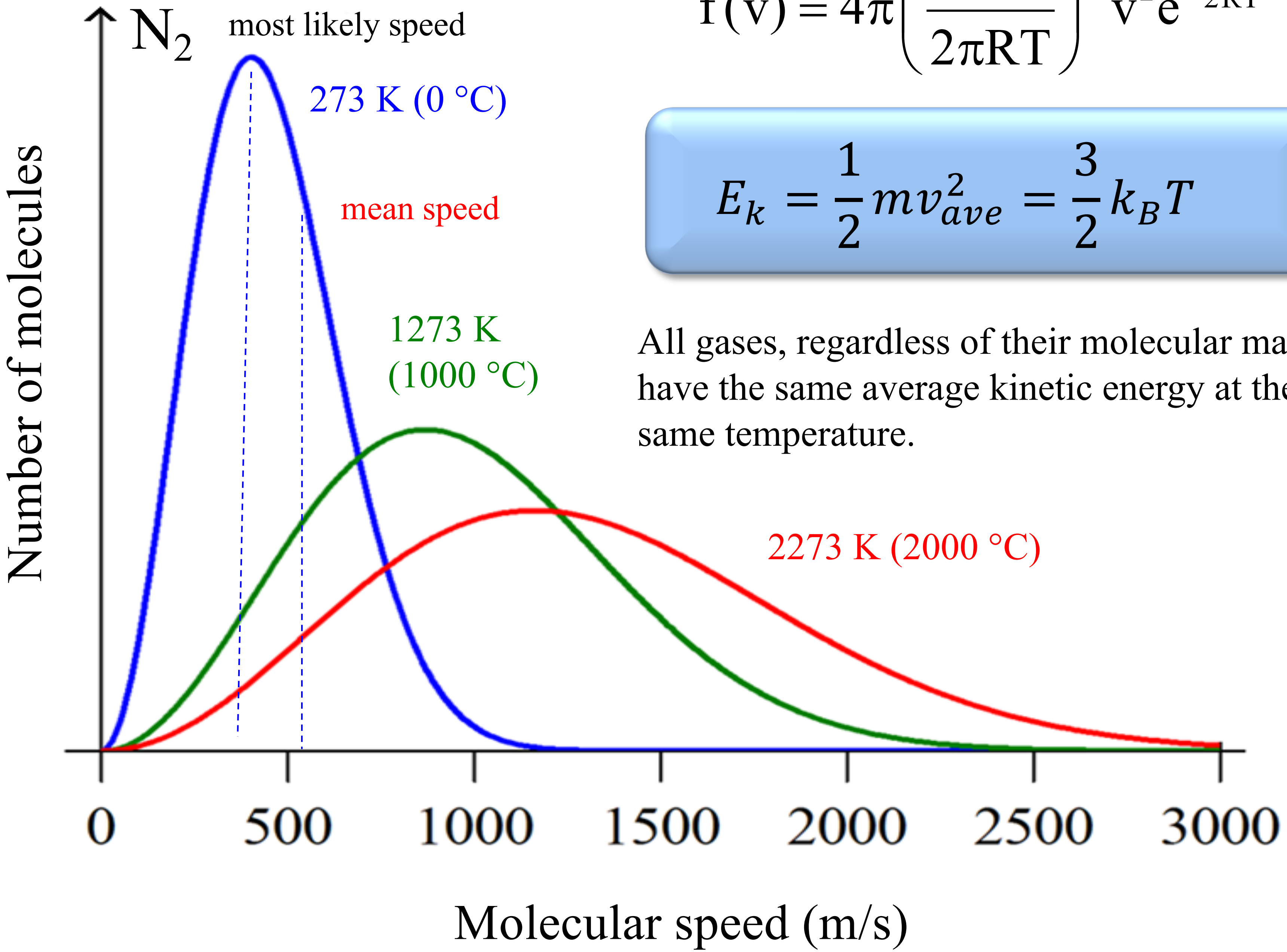
- weak cohesive forces
- strong packing
- irregular spatial arrangement
- high mobility



gas

- cohesive forces absent
- strongly separated
- random spatial arrangement
- very high mobility

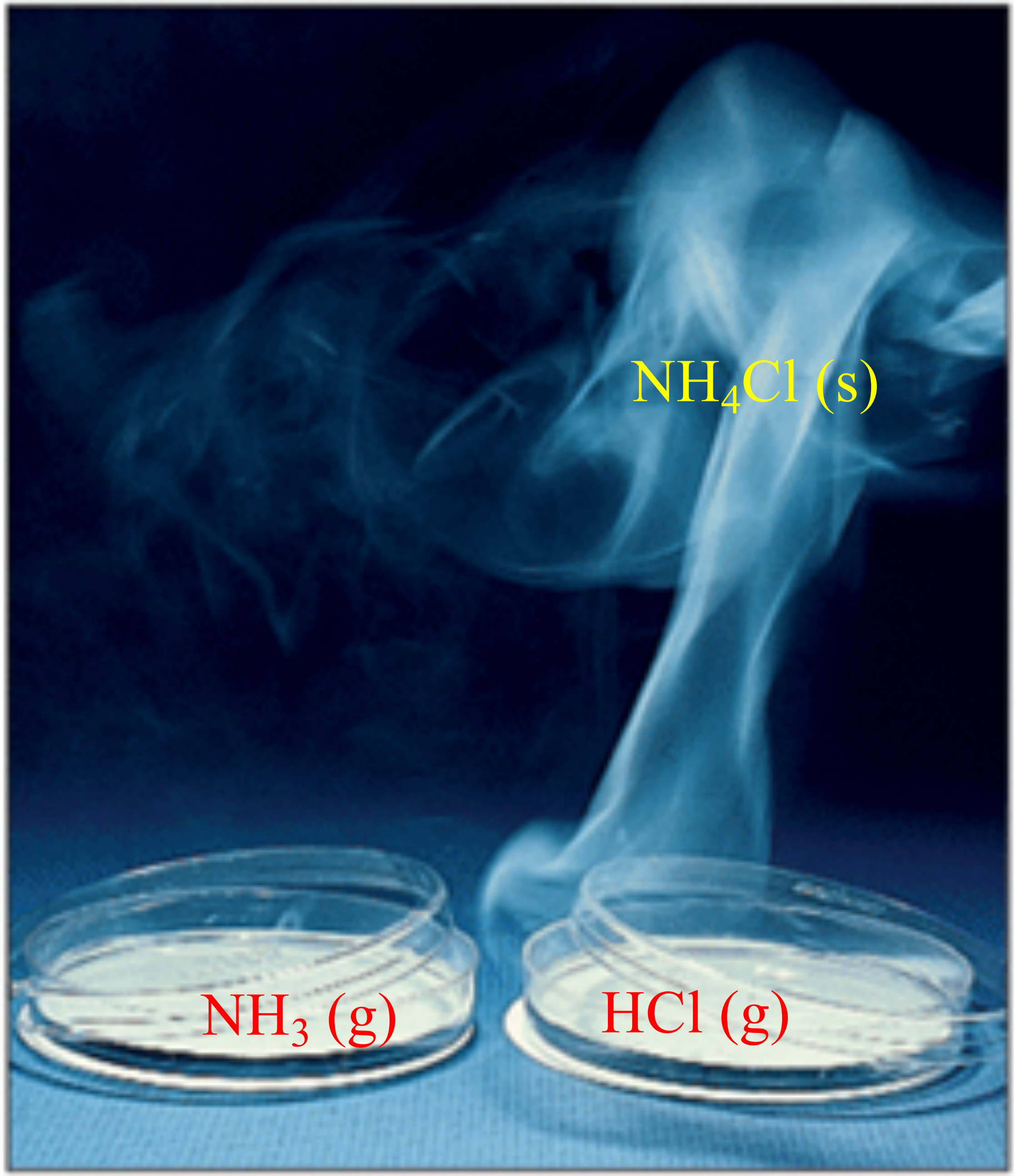


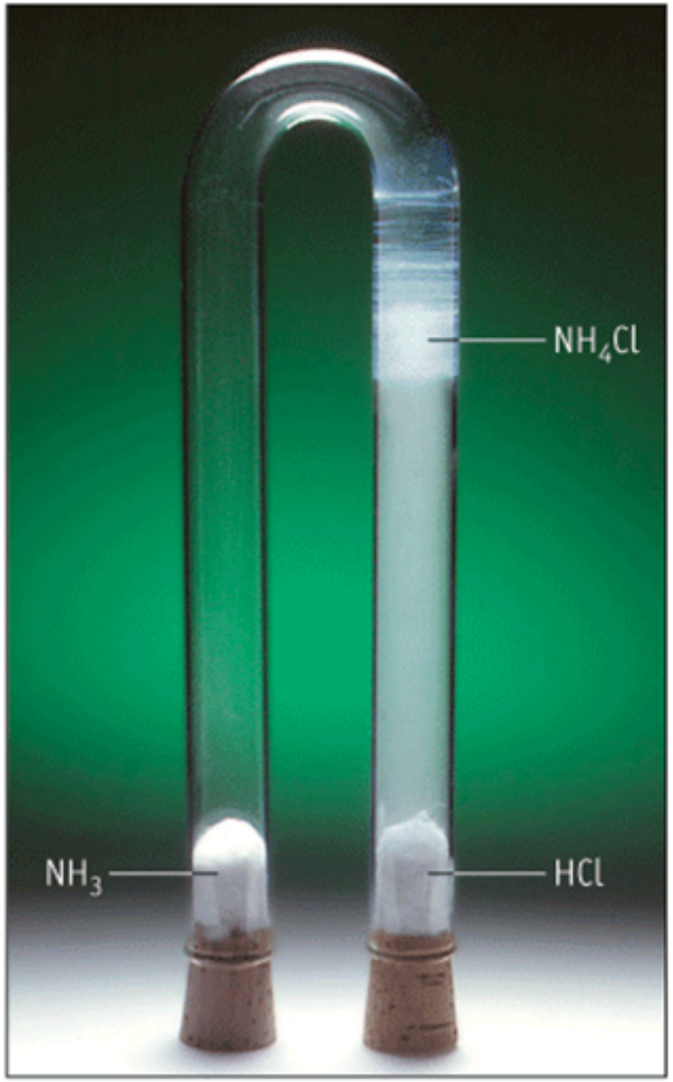


$$f(v) = 4\pi\left(\frac{M}{2\pi RT}\right)^{\frac{3}{2}} v^2 e^{-\frac{Mv^2}{2RT}}$$

$$E_k = \frac{1}{2}mv_{ave}^2 = \frac{3}{2}k_BT$$

All gases, regardless of their molecular mass, have the same average kinetic energy at the same temperature.

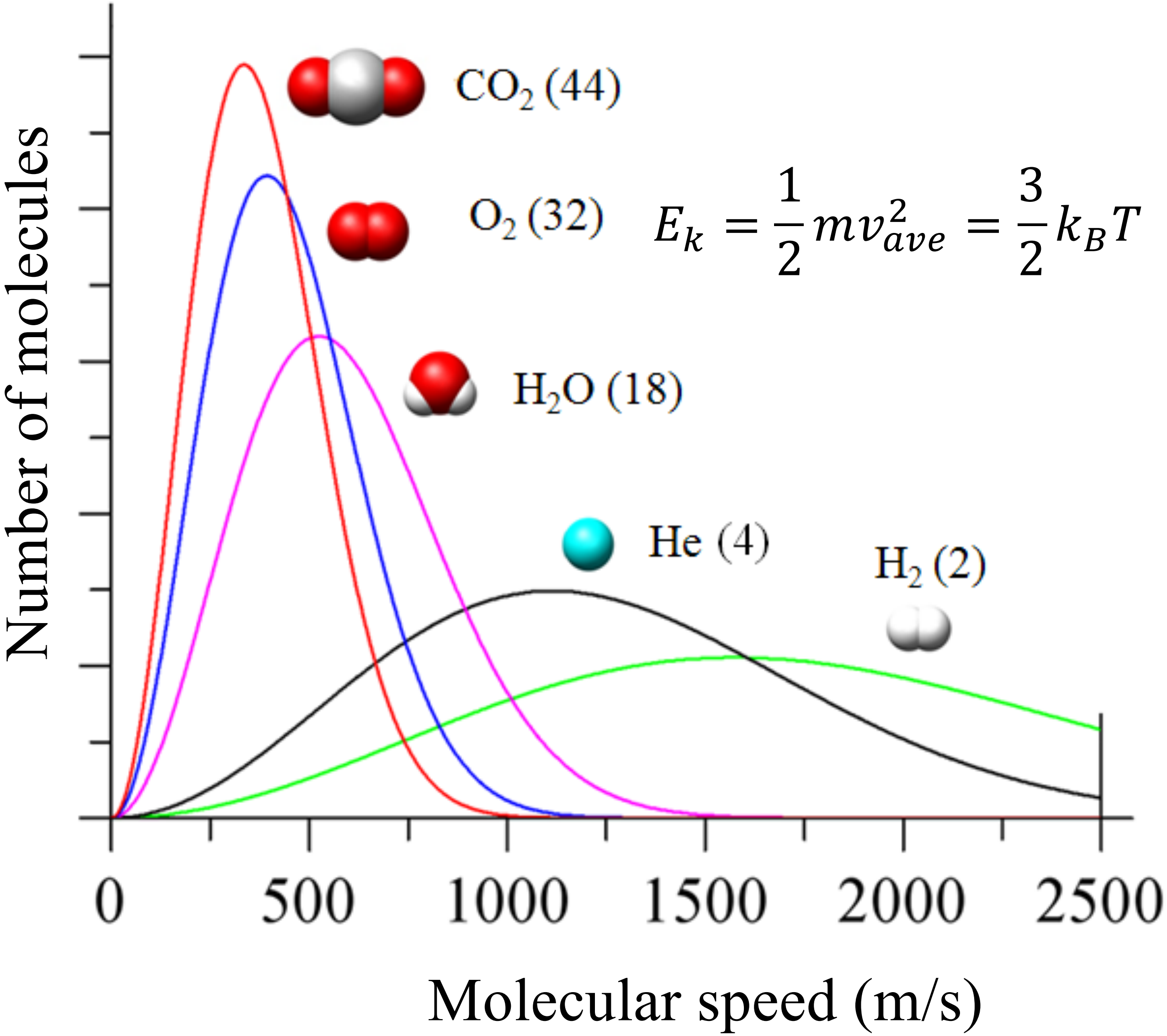




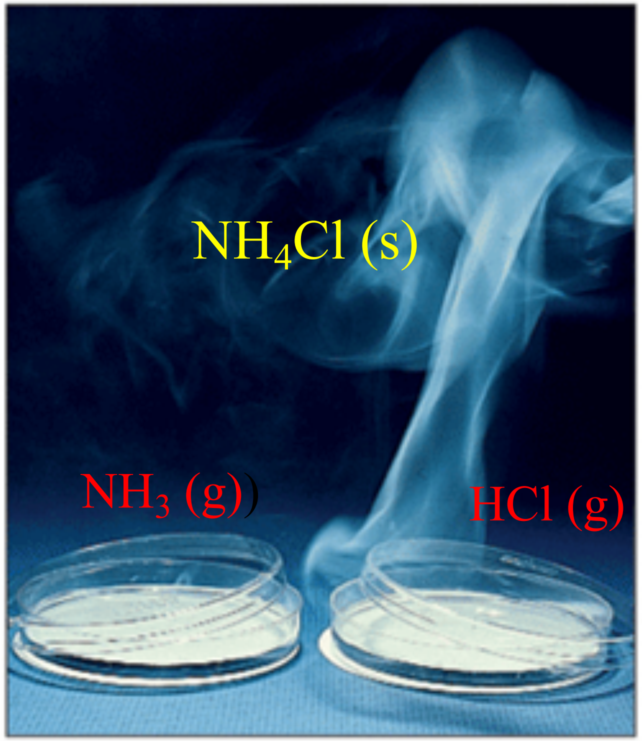
$$NH_3\ (g) + HCl\ (g) \rightarrow NH_4Cl\ (s)$$

The Maxwell-Boltzmann distribution of molecular speeds: effect of mass (at constant temperature)

Molecules with higher mass move at a lower speeds.



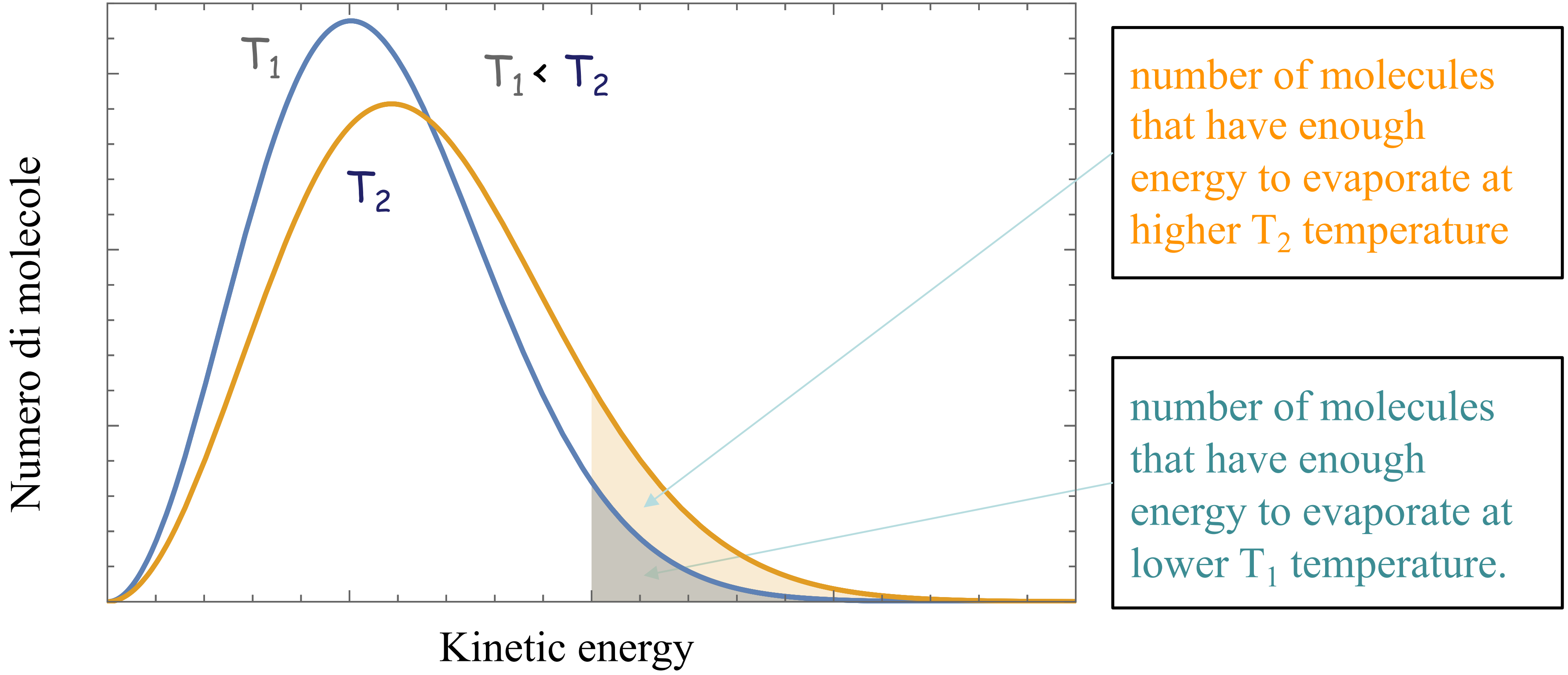
$$E_k = \frac{1}{2} m v_{ave}^2 = \frac{3}{2} k_B T$$



NH_3 (g) + HCl (g) → NH_4Cl (s)

Evaporation

It is the process in which a liquid substance turns into the gaseous state. The distribution of energies in liquids is similar to that of gases (Maxwell-Boltzmann distribution). As for gases, the average energy of the molecules in a liquid depends only on the temperature: the higher the temperature, the higher the average energy and the fraction of molecules with high kinetic energy.

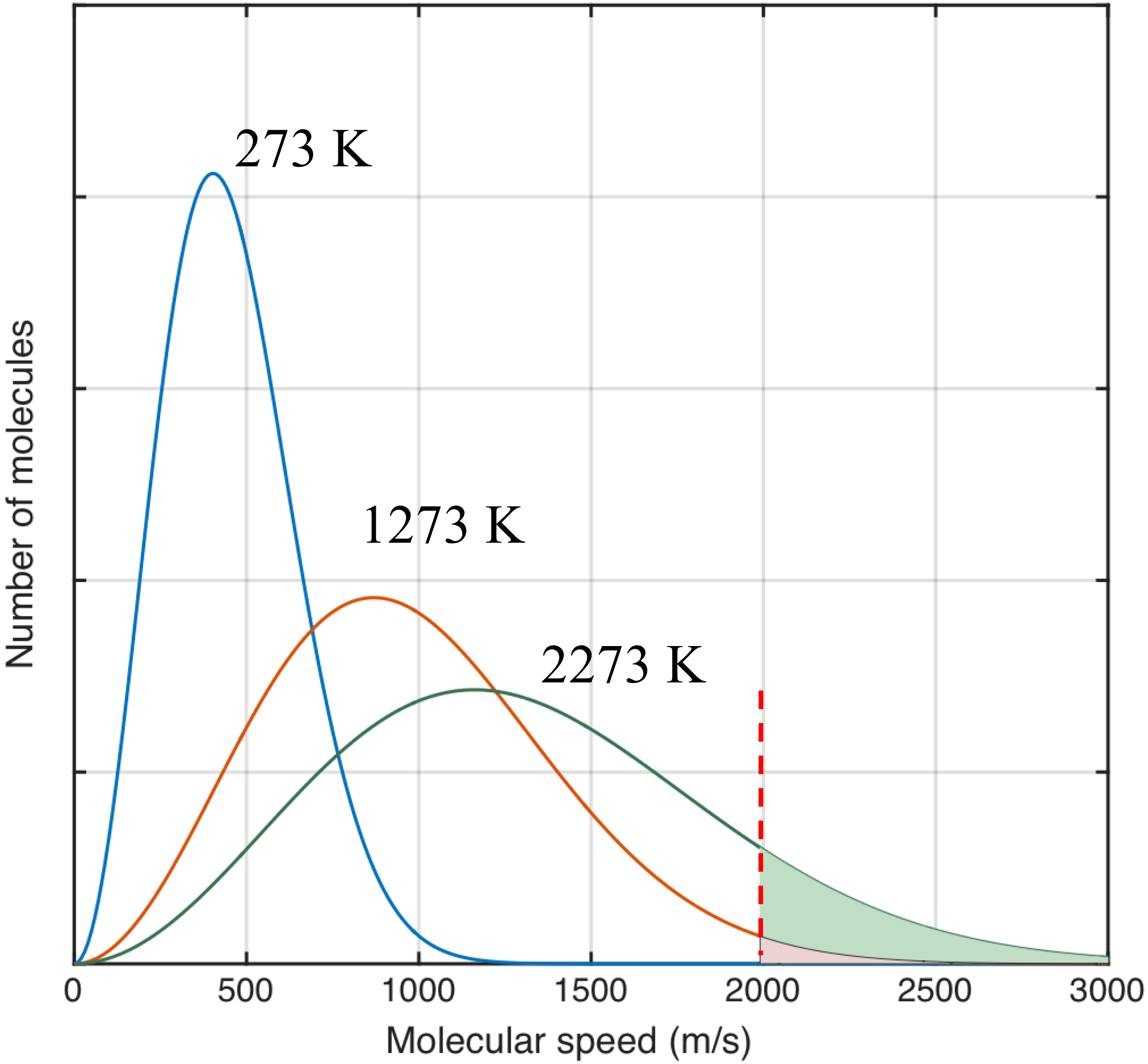


number of molecules that have enough energy to evaporate at higher T_2 temperature

number of molecules that have enough energy to evaporate at lower T_1 temperature.

H_2O $T_1 = 274$ K $T_2 = 373$ K

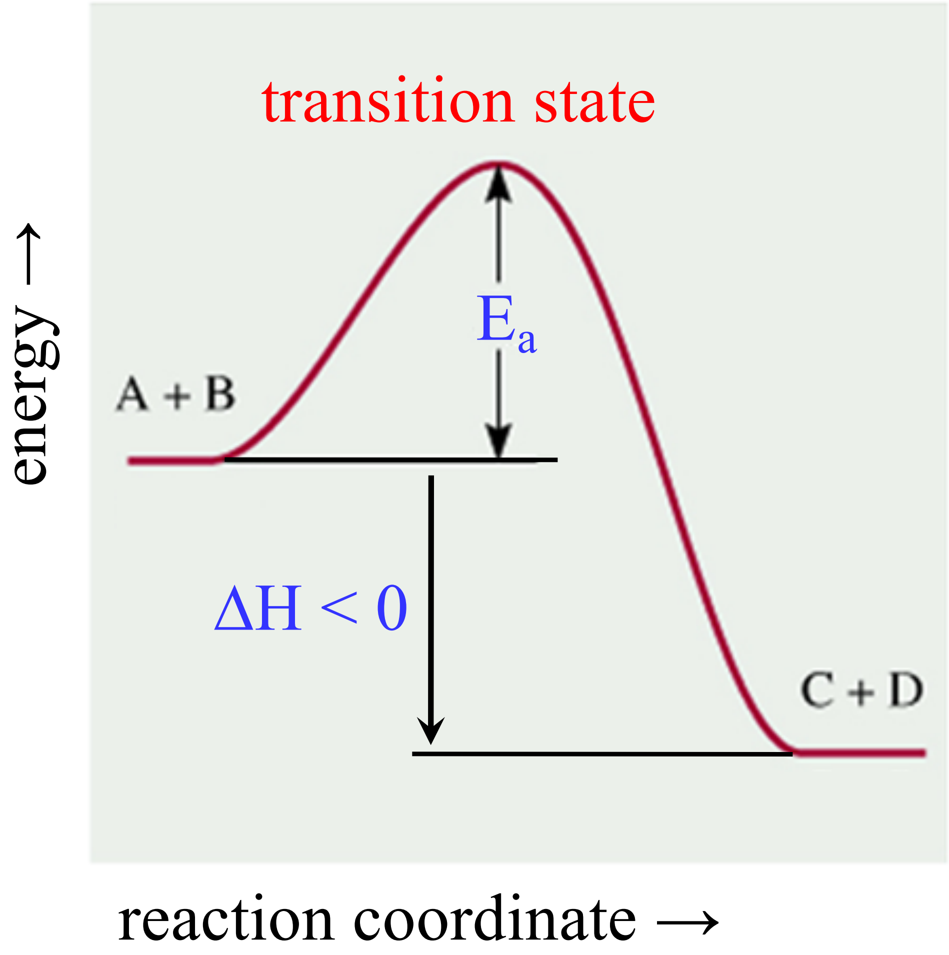
As the T (average E_k) increases the fraction of molecules with a given speed increases



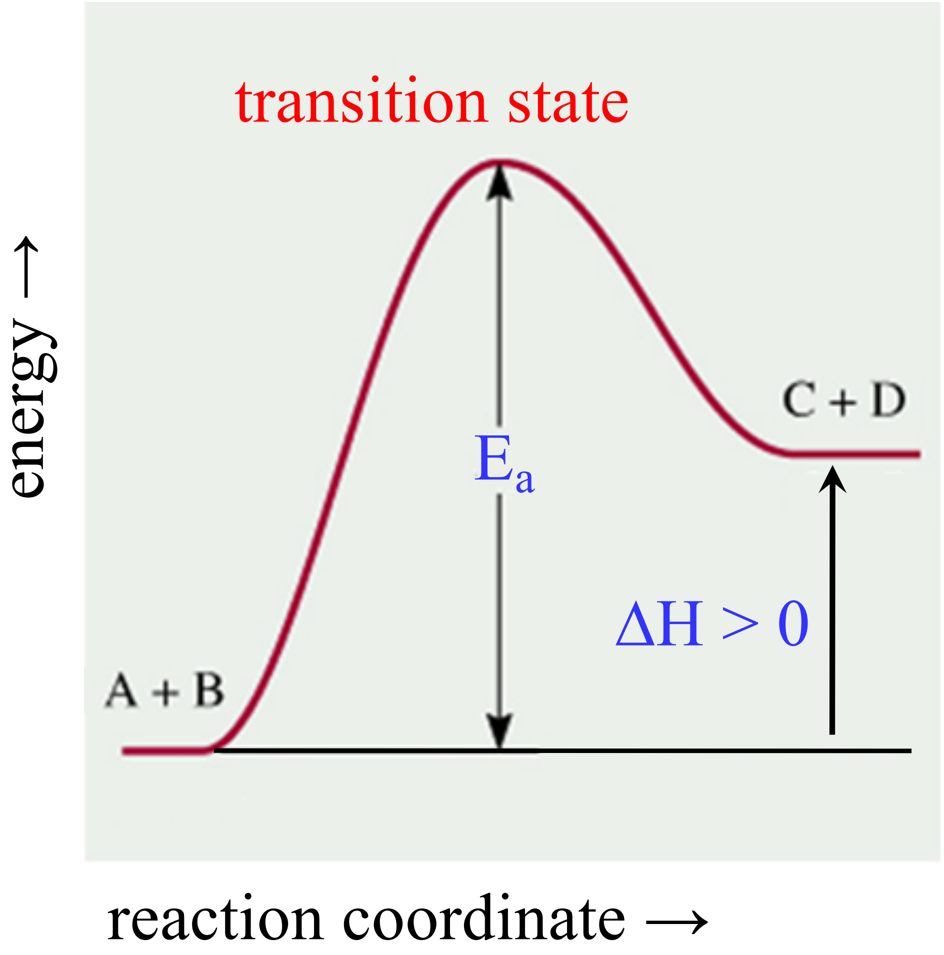
The minimum kinetic energy required for the reaction to occur is called activation energy E_a (the energy of the transition state)

$$A + B \leftrightarrows C + D$$

exothermic reaction



endothermic reaction



reaction coordinate = progress of the reaction

The Arrhenius equation

Correlates the temperature with the activation energy E_a (i.e. the minimum energy the molecules must possess for the reaction to proceed).

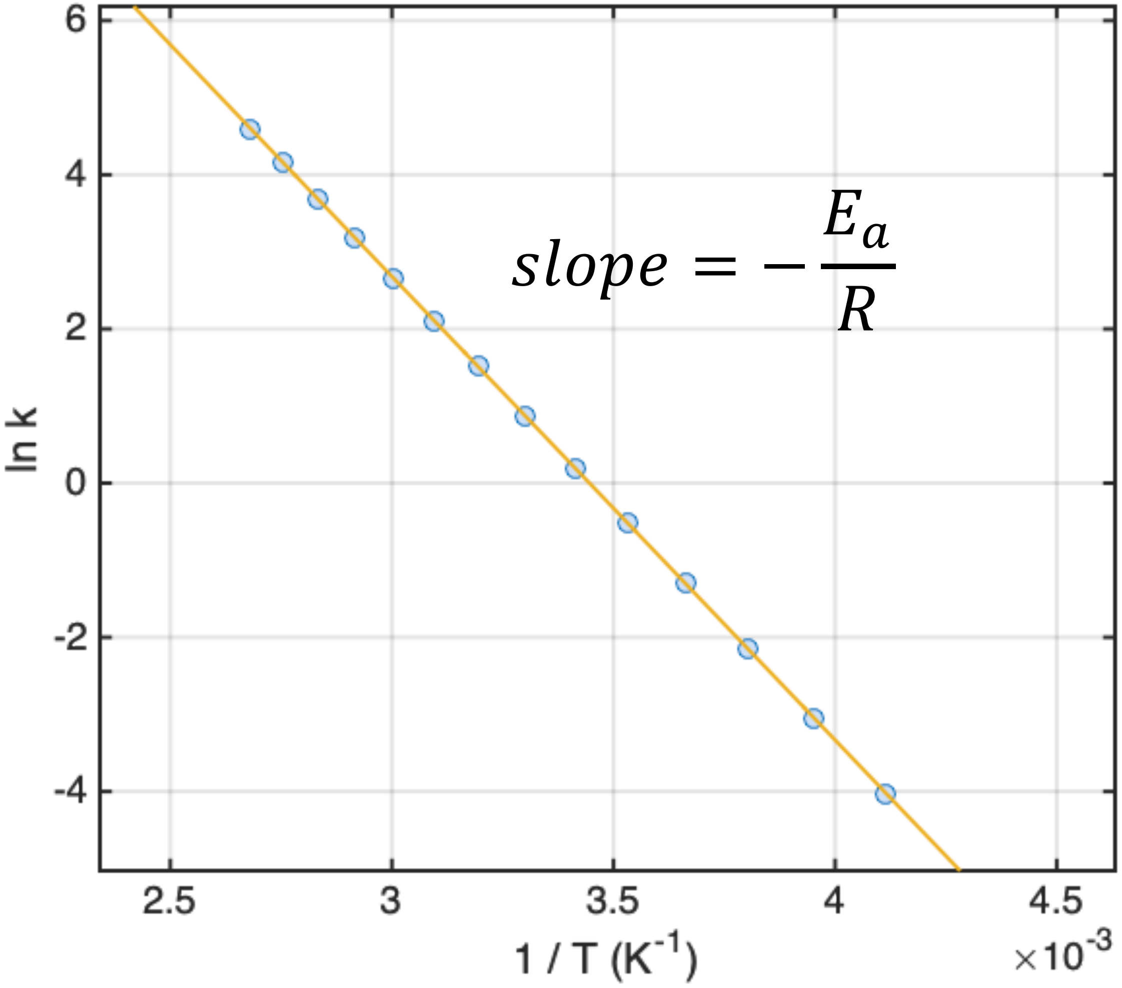
$$k = A \cdot e^{-\frac{E_a}{RT}}$$

$$\ln k = \ln A - \frac{E_a}{R} \cdot \frac{1}{T}$$

where:

k	specific rate constant
A	the frequency factor, which is correlated to the frequency of impacts and to the probability that they will occur with favorable orientation
E_a	activation energy
R	gas constant
T	absolute temperature

The Arrhenius equation E_a is always positive



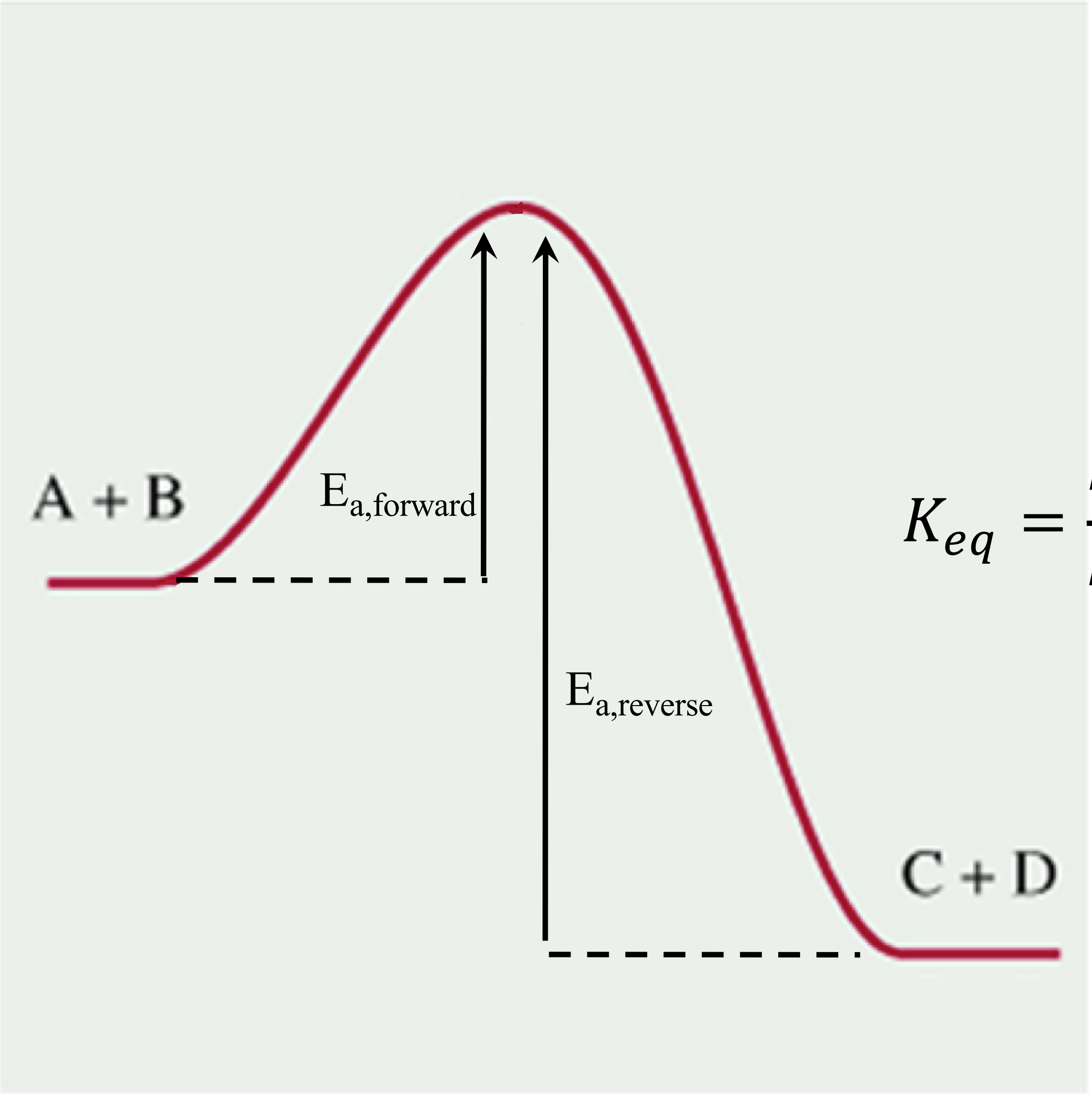
$$slope = -\frac{E_a}{R}$$

$$\ln k = \ln A - \frac{E_a}{R} \cdot \frac{1}{T}$$

$$A + B \underset{k_r}{\overset{k_f}{\rightleftharpoons}} C + D$$

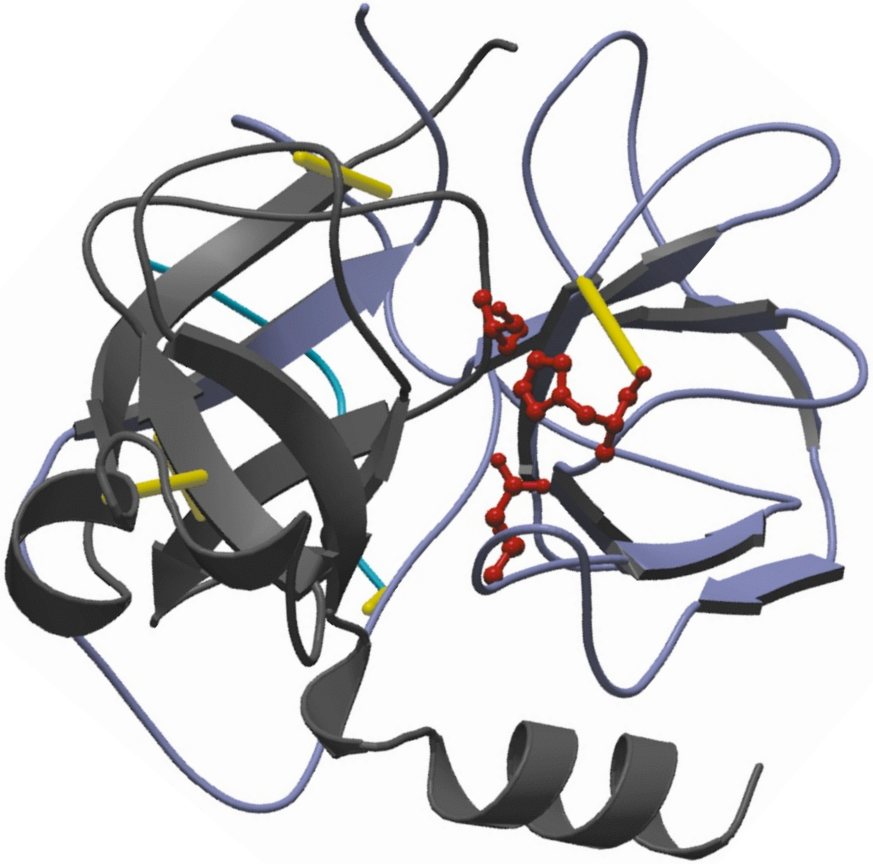
$$k_f = A \cdot e^{-\frac{E_{a,forward}}{RT}}$$

$$k_r = A \cdot e^{-\frac{E_{a\ reverse}}{RT}}$$

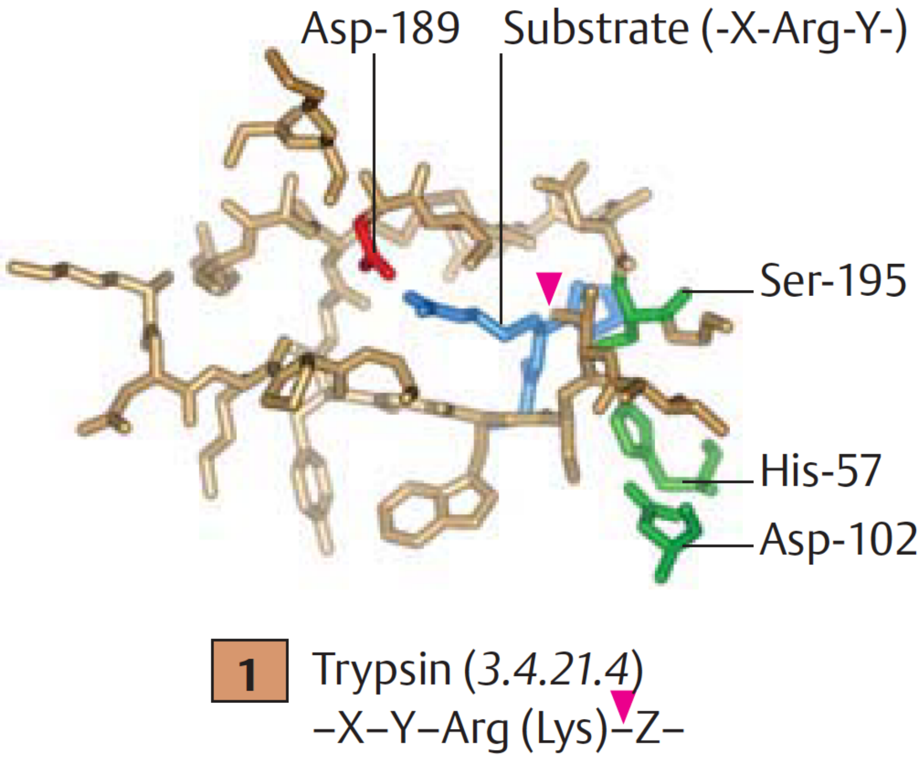


$$K_{eq} = \frac{k_f}{k_r} = e^{\frac{E_{a,reverse} - E_{a,forward}}{RT}}$$

Enzymes



trypsin



active site

The two reactions found in all enzymes

in the reaction $A \xrightarrow{k} B$ the kinetic law is:

$$v = -\frac{d[A]}{dt} = \frac{d[B]}{dt} = k \cdot [A]$$

and is first-order with respect to A.
Dimensions of k are time^{-1} (ex. s^{-1})

in the reaction $A + B \underset{k_2}{\overset{k_1}{\rightleftharpoons}} C$ the kinetic law is:

$$v = -\frac{d[A]}{dt} = -\frac{d[B]}{dt} = \frac{d[C]}{dt} = k \cdot [A] \cdot [B]$$

binding

and is first-order with respect to A & B, second-order overall.
Dimensions of k are $\text{concentration}^{-1} \cdot \text{time}^{-1}$ (es. $M^{-1}s^{-1}$)

Enzymes

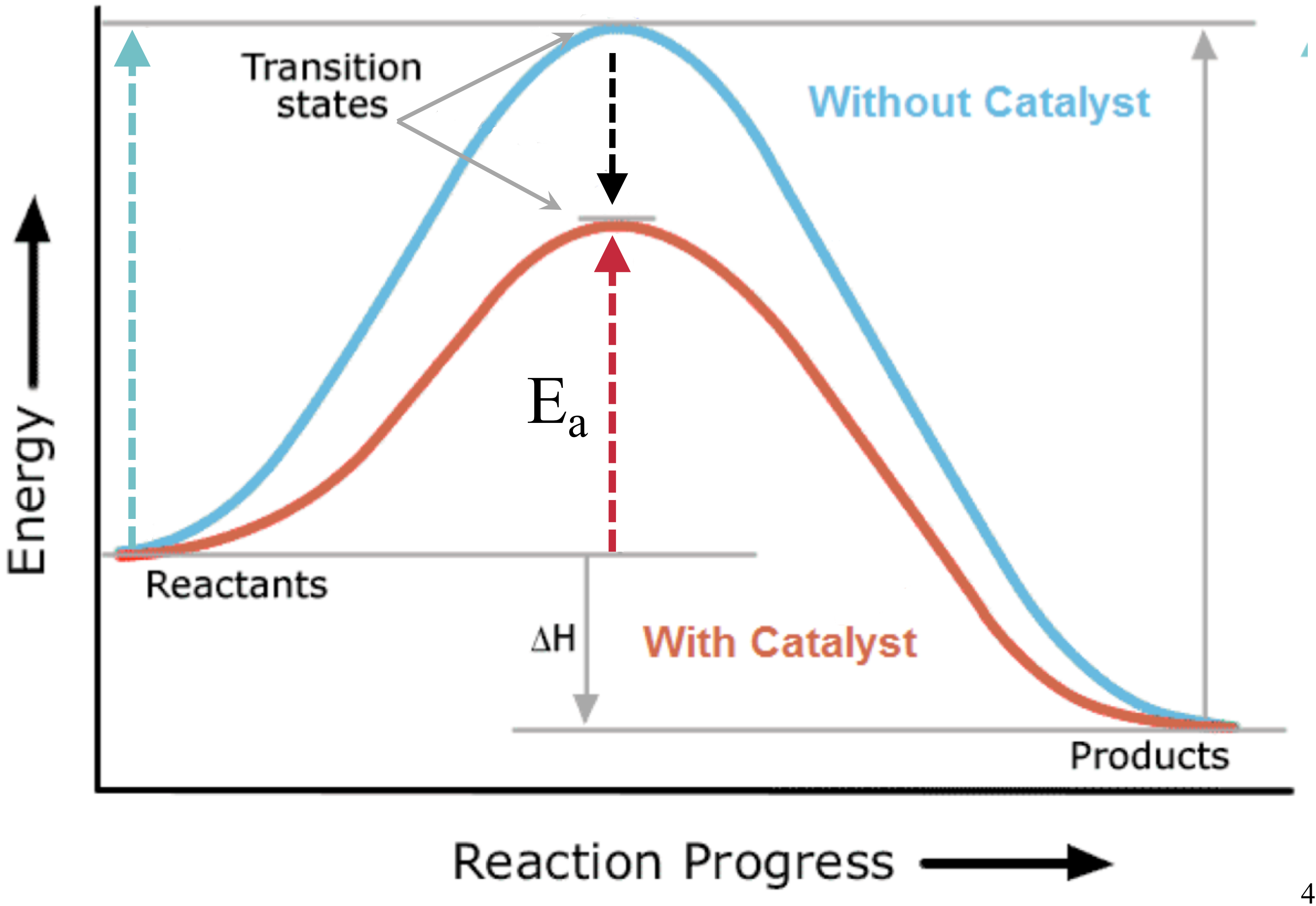
The word *enzyme* was used for the first time in 1878 by physiologist Wilhelm Kühne. He chose that word (ένζυμο in greek means “in yeast”) because it was believed that such entity could be found only in yeast cells.

An enzyme is a protein capable of catalyzing a chemical reaction.
The process of catalysis induced by an enzyme (as any other catalyst) consists of an acceleration of the speed of reaction and thus in a more rapid achievement of the state of thermodynamic equilibrium. **The activation energy is decreased**

An enzyme only accelerates the rate of chemical reactions, without intervening on processes that regulate its spontaneity.

Its role is to facilitate the reactions through the interaction between the substrate and its active site, forming a complex. The enzyme in fact is not consumed during the reaction.

The presence of a catalyst lowers the activation energy E_a



General properties of enzymes (and differences compared to non-biological catalysts)

Higher reaction rates: the velocities of the reactions catalyzed by enzymes are normally from 10^6 to 10^{14} higher than those of the corresponding non-catalyzed chemical transformations and at least several orders of magnitude higher than those of the corresponding reactions catalyzed by chemical means.

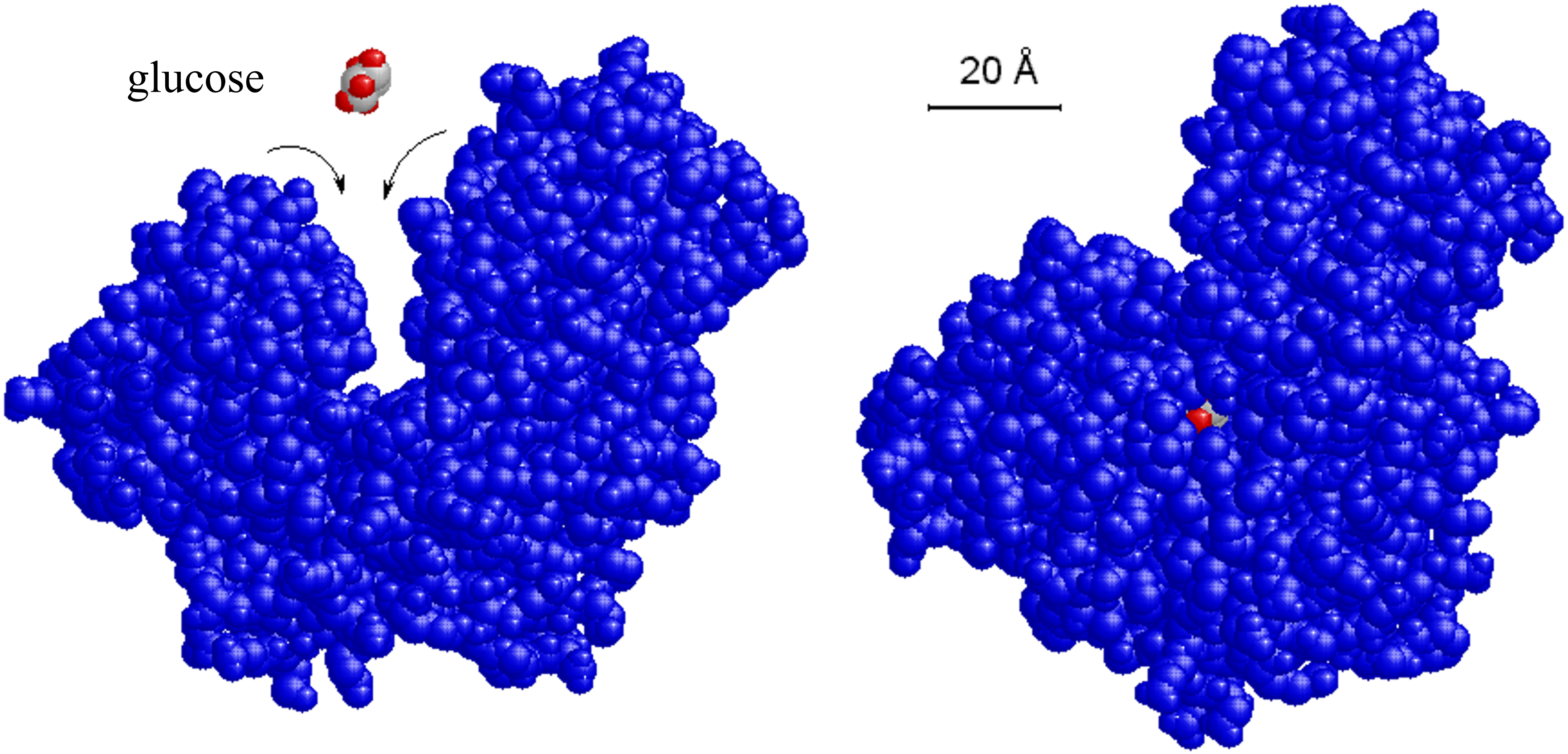
Milder reaction conditions: the reactions catalyzed by enzymes occur in relatively more moderate conditions: at ambient temperature and atmospheric pressure and pH close to neutrality. In contrast, chemical catalysis often requires high temperatures and pressures and extreme pH values.

Greater reaction specificity: the enzymes exhibit a degree specificity for substrates and products extraordinarily higher than chemical catalysts.

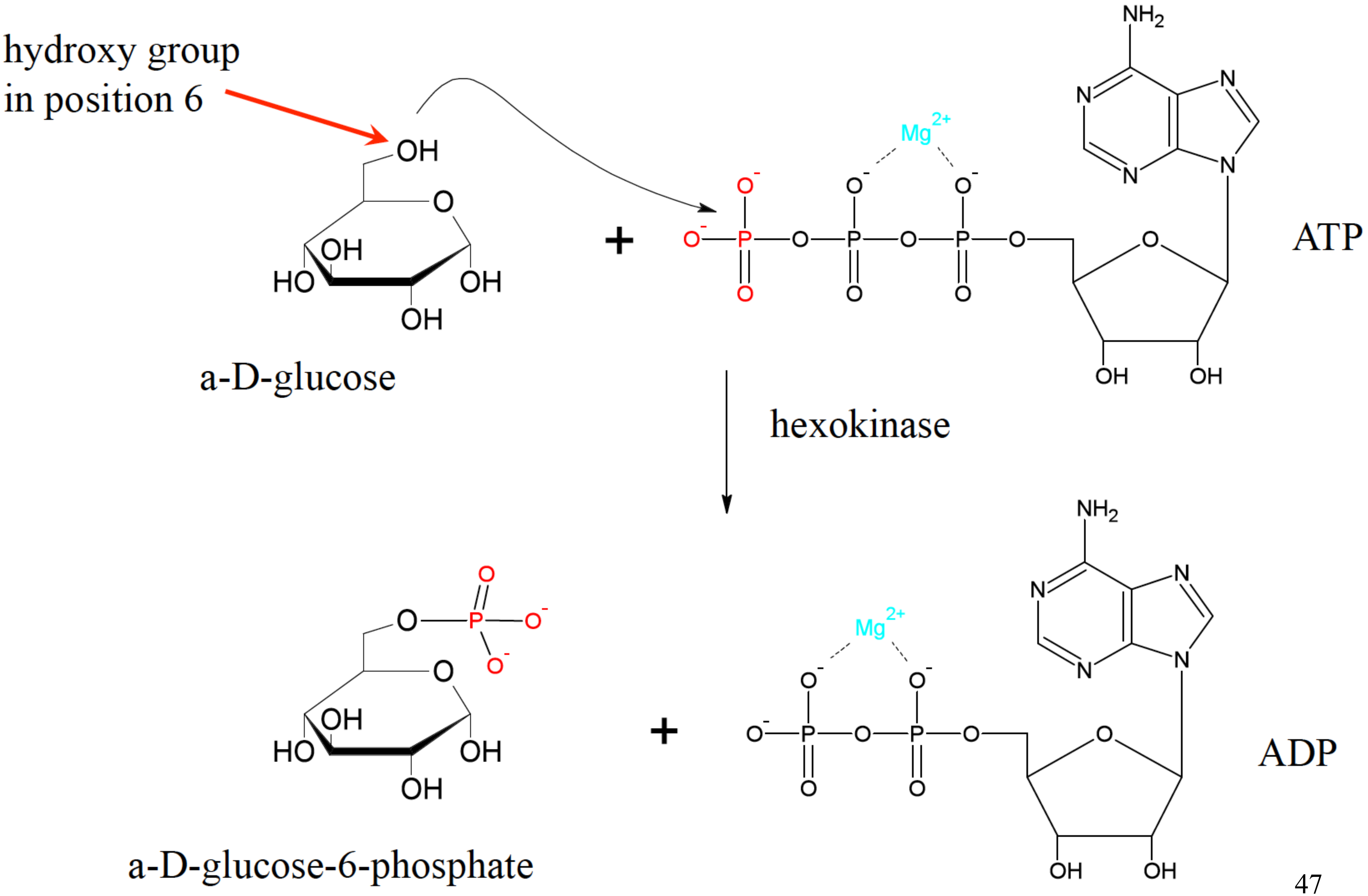
Regulation: the catalytic activities of several enzymes vary in response to varying concentrations of different effectors (activators & inhibitors). The regulatory mechanisms include: allosteric control, covalent modification of enzymes, as well as the variation of the concentration of the enzymes.

The hexokinase reaction

- substrate specificity
- induced fit



The hexokinase reaction



hydroxy group in position 6

a-D-glucose

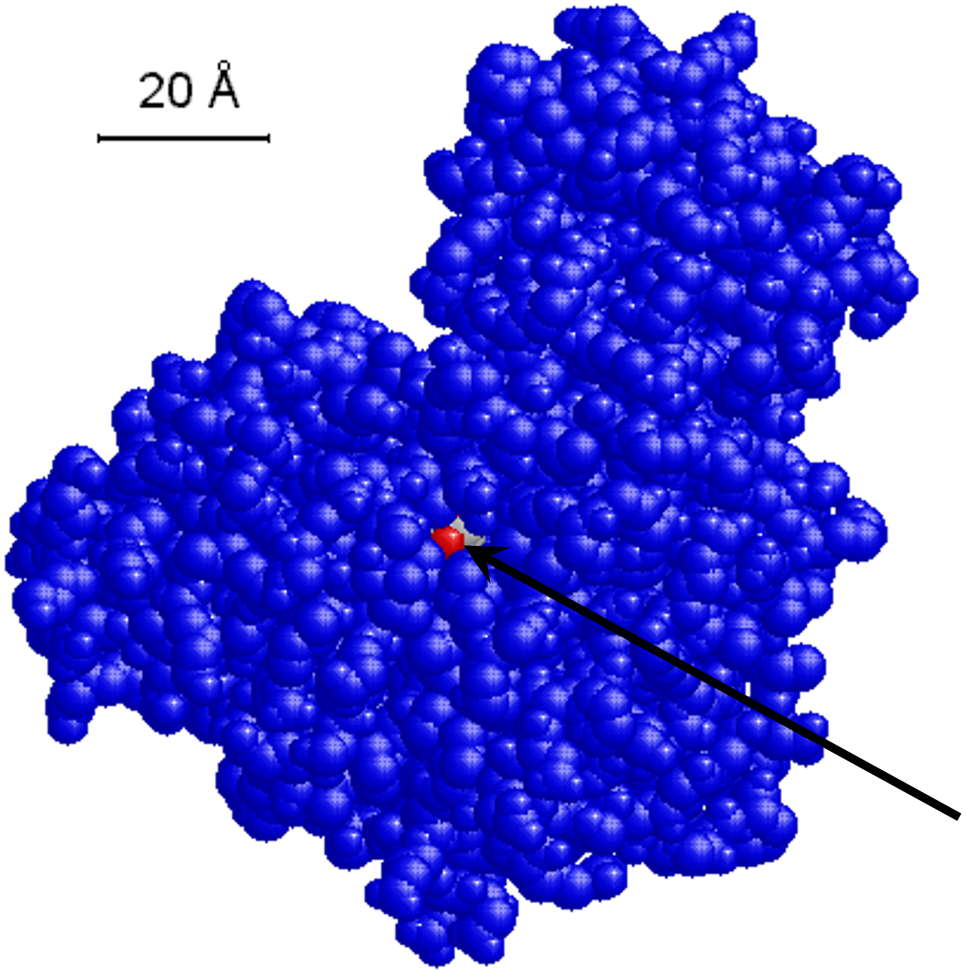
ATP

hexokinase

a-D-glucose-6-phosphate

ADP

The induced-fit accounts for the specificity of hexokinase



glucose
hydroxy group
in position 6

The Michaelis-Menten equation

Leonor Michaelis
(1875-1940)

Maud Menten
(1879-1960)

It describes the rate of an enzymatic reaction as a function of substrate concentration.

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} E + P$$

$$v_0 = \frac{V_{MAX}\,[S]}{K_M + [S]}$$

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} E + P$$

In the mechanism E and ES represent the free enzyme and the enzyme-substrate complex.
Each of the elementary reactions (here 2) is described by a specific rate constant :

k_1: rate constant for the formation of ES (a second-order rate constant with dimensions $M^{-1}s^{-1}$).

k_{-1}: rate constant for the dissociation of S from ES (a first-order rate constant with dimensions s^{-1}).

k_2: rate constant for the formation of P from ES (a first-order rate constant with dimensions s^{-1}).

Note: For simplicity it is assumed that the formation of product P is irreversible. This must be justified by experiment, and in general enzymes catalyze reversible reactions

.