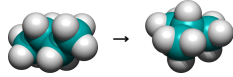


Elementary reactions

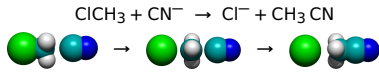
1/23
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stoichiometry = mechanism ($\text{Cl}^\bullet + \text{H}_2 \rightarrow \text{HCl} + \text{H}^\bullet$)

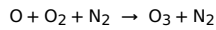
- monomolecular reactions (decay: $\text{N}_2\text{O}_4 \rightarrow 2\text{NO}_2$; radioactive decay; some isomerisations)



- bimolecular reactions (collision; most common)



- trimolecular reactions



(N_2 carries out the surplus energy)

Chain reactions

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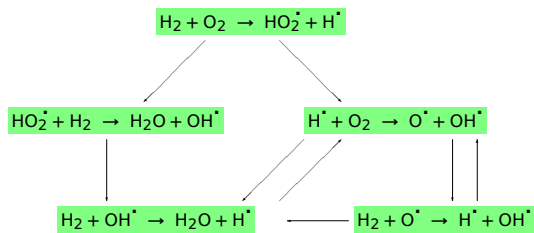
- initiation (typically free radicals are produced)
 - heat
 - chemical (peroxides)
 - light (UV)
- propagation (cyclic reaction with radical recovery)
 - chain transfer (no branching)
 - chain branching
- termination
 - recombination (of radicals)
 - reaction (low-reactive radical—inhibition)
 - deactivation at walls

Reaction mechanisms

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A (general) reaction is a sequence of elementary reactions = **reaction mechanism**.

Example: $2\text{H}_2 + \text{O}_2 \rightarrow 2\text{H}_2\text{O}$



radical A^\bullet

activated molecule A^* (energy-rich, local energy minimum)

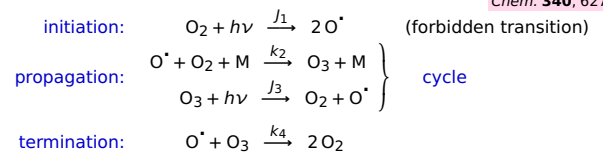
activated complex (transition state) AB^\ddagger , $\text{AB}^\#$ (saddle point)

Chain reactions – examples

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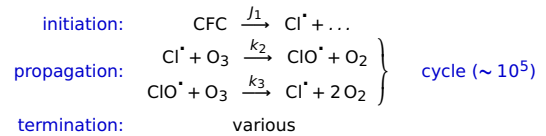
Simplified scheme of ozone cycle in stratosphere

by Zellner R.: *J. Anal. Chem.* **340**, 627 (1991)



$$J_1 \text{ is very small} \Rightarrow J_1 k_4 \ll J_3 k_2 [\text{M}] \Rightarrow J_1 [\text{O}_2] \ll J_3 [\text{O}_3] \Rightarrow [\text{O}_3] = [\text{O}_2] \sqrt{\frac{J_1 k_2 [\text{M}]}{J_3 k_4}}$$

Simplified scheme of ozone destruction:



Reaction mechanisms

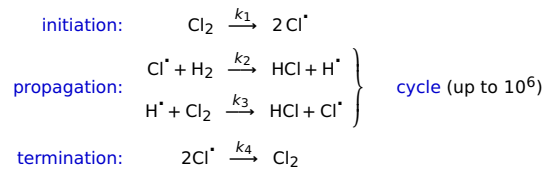
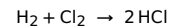
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We need to get rid of unstable (unknown) intermediates.

- rate-determining step
 - fastest (parallel reactions)
 - slowest (consecutive reactions)
- Bodenstein principle of (quasi)stationary state
 - intermediates fast reach (almost) constant concentrations
 - e.g.: $\text{A} \rightleftharpoons \text{A}^* \rightarrow \text{B} \quad \frac{d\text{c}_{\text{A}^*}}{d\tau} \approx 0$
- pre-equilibrium
 - reversible reaction part of chain
 - e.g.: $\dots \xrightarrow{\text{slow}} \text{A} + \text{B} \xrightleftharpoons[\text{fast}]{\text{fast}} \text{C} + \text{D} \xrightarrow{\text{slow}} \dots \quad \frac{\text{c}_{\text{C}}\text{c}_{\text{D}}}{\text{c}_{\text{A}}\text{c}_{\text{B}}} \approx K$
 - can be derived from the above principle (for $\gamma = 1$)

Example (not in detail)

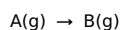
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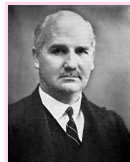
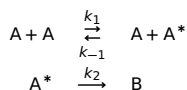
$$\frac{d\text{c}_{\text{HCl}}}{d\tau} = k_2 \text{c}_{\text{Cl}^\bullet} \text{c}_{\text{H}_2} + k_3 \text{c}_{\text{H}^\bullet} \text{c}_{\text{Cl}_2} \stackrel{\text{steady state}}{=} 2k_2 \sqrt{\frac{k_1}{k_4}} \text{c}_{\text{Cl}_2}^{1/2} \text{c}_{\text{H}_2}$$

Lindemann(-Hinshelwood) mechanism

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col02



Inelastic collisions in the gas phase activate molecules:



credit: (Lindemann) Wikipedia

$\text{c}_{\text{A}^*} \ll \text{c}_{\text{A}} \Rightarrow$ stationary state $\frac{d\text{c}_{\text{A}^*}}{d\tau} = 0 \Rightarrow$

$$-\frac{d\text{c}_{\text{A}}}{d\tau} = \frac{d\text{c}_{\text{B}}}{d\tau} = k_2 \frac{k_1 \text{c}_{\text{A}}^2}{k_2 + k_{-1} \text{c}_{\text{A}}}$$

$$-d\text{c}_{\text{A}}/d\tau = d\text{c}_{\text{B}}/d\tau$$

- $k_{-1} \text{c}_{\text{A}} \gg k_2$ (ambient pressures): $\frac{d\text{c}_{\text{B}}}{d\tau} = \frac{k_2 k_1}{k_{-1}} \text{c}_{\text{A}}$ 1st order
- $k_{-1} \text{c}_{\text{A}} \ll k_2$ (low pressures): $\frac{d\text{c}_{\text{B}}}{d\tau} = k_1 \text{c}_{\text{A}}^2$ 2nd order

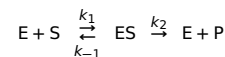
E.g.: cyclopropane \rightarrow propene, $\text{N}_2\text{O}_5 \rightarrow \text{NO}_2 + \text{NO}_3^\bullet$,
dimethyldiazene (azomethane) $\text{CH}_3\text{-N=N-CH}_3 \rightarrow \text{C}_2\text{H}_6 + \text{N}_2$

Enzyme catalysis: Michaelis-Menten kinetics

[xoctave; xcat; /octave/MichaelisMentenova.m Michaelis Menten]

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Mechanism of Michaelis and Menten (**E**nzyme, **S**ubstrate, **P**roduct):



stationary state (because $\text{c}_{\text{E}}, \text{c}_{\text{ES}} \ll \text{c}_{\text{S}}$):

$$\frac{d\text{c}_{\text{ES}}}{d\tau} = k_1 \text{c}_{\text{E}} \text{c}_{\text{S}} - (k_{-1} + k_2) \text{c}_{\text{ES}} = 0$$

balance: $\text{c}_{\text{E}} + \text{c}_{\text{ES}} = \text{c}_{\text{E0}}$

Eliminating c_{E} ($\Rightarrow \text{c}_{\text{ES}}$) from $\frac{d\text{c}_{\text{P}}}{d\tau}$:

$$\text{also from: } \frac{d\text{c}_{\text{P}}}{d\tau} = -\frac{d\text{c}_{\text{S}}}{d\tau} = k_1 \text{c}_{\text{E}} \text{c}_{\text{S}} - k_{-1} \text{c}_{\text{ES}}$$

$$\frac{d\text{c}_{\text{P}}}{d\tau} = k_2 \text{c}_{\text{ES}} = k_2 \frac{\text{c}_{\text{E0}}}{K_{\text{M}}/\text{c}_{\text{S}} + 1} = v_{\text{max}} \frac{\text{c}_{\text{S}}}{K_{\text{M}} + \text{c}_{\text{S}}}$$

where $K_{\text{M}} = \frac{k_2 + k_{-1}}{k_1} =$ **Michaelis constant** and $v_{\text{max}} = k_2 \text{c}_{\text{E0}}$

- $\text{c}_{\text{S}} \gg K_{\text{M}} \Rightarrow \frac{d\text{c}_{\text{P}}}{d\tau} = -v_{\text{max}}$ (zeroth order, most of E is saturated, ES)
- $\text{c}_{\text{S}} \ll K_{\text{M}} \Rightarrow \frac{d\text{c}_{\text{P}}}{d\tau} = -\frac{v_{\text{max}}}{K_{\text{M}}} \text{c}_{\text{S}}$ (first order, most of E is free, E)

Michaelis-Menten kinetics II

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Experimentally available: K_M and $v_{max} = k_2 c_{E0}$
(often not both c_{E0} and k_2 simultaneously)

$$\frac{dc_S}{d\tau} = -v_{max} \frac{1}{K_M/c_S + 1}$$

Integrated form

$$K_M \ln \frac{c_{S0}}{c_S} + c_{S0} - c_S = v_{max} \tau$$

cannot solve for $c_S(\tau)$ (using elem. functions) \Rightarrow numerical solution



credits: pitt.edu, Wikipedia



4 x Zn
credit: wikipedia

Babel of units

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Enzyme activity unit (amount of substance / time)

- SI: mol s^{-1} (katal)
- more common: $\mu\text{mol}/\text{min}$ ("enzyme unit", U)

Specific activity (per kg of enzyme)

- SI: $\text{mol s}^{-1} \text{kg}^{-1}$
- $\mu\text{mol min}^{-1} \text{mg}^{-1}$

Turnover number (per mole),

- SI: $\text{mol s}^{-1} \text{mol}^{-1} = \text{s}^{-1}$
- often min^{-1} etc.

Molar mass: $\text{g mol}^{-1} = \text{Da}$ (dalton)

or $1 \text{ g mol}^{-1} / N_A = \frac{1}{12} m(^{12}\text{C}) = 1 \text{ u} = 1.660539 \times 10^{-27} \text{ kg} = 1 \text{ Da}$

Example: $1 \mu\text{g}$ of enzyme ($M = 40 \text{ kDa}$) in the excess of substrate provides the reaction rate of $6 \mu\text{mol}$ of substrate/min. What is the turnover number (in s^{-1})?

1-5 0007

Deprecated units:
 $1 \text{ M} = 1 \text{ mol dm}^{-3}$
 $1 \text{ m} = 1 \text{ mol kg}^{-3}$
 (1 mol dm⁻³)
 $1 \text{ Da} = 1 \text{ g mol}^{-1}$
 $1 \text{ bar} = 10^5 \text{ Pa}$
 $1 \text{ \AA} = 10^{-10} \text{ m}$
 $1 \text{ cal}_{\text{th}} = 4.184 \text{ J}$
 (thermochemical)
 $1 \text{ cal}_{\text{it}} = 4.1868 \text{ J}$
 (intl./IAPWS)
 $1 \text{ cal}_{\text{UNS}} = 4.182 \text{ J}$
 (food)

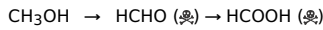
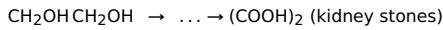
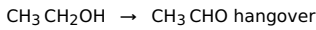
Metabolism of alcohols

10/23
col02

Alcohol dehydrogenase, various types

In liver and the lining of the stomach

Further oxidation to acids and $\text{H}_2\text{O} + \text{CO}_2$



Example. Calculate the time needed to metabolize $c_{S0} = 1 \text{ wt. } \%$ of ethanol to $c_S = 0.1 \%$

Data: $v_{max} = 0.12 \text{ g L}^{-1} \text{ hod}^{-1}$,

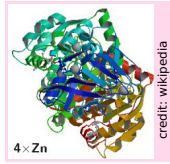
$$K_M = 0.06 \text{ g L}^{-1}$$

$$\rho_{\text{blood}} = 1.06 \text{ g cm}^{-3} \Rightarrow 1 \text{ wt. } \% = 1.06 \text{ g L}^{-1}$$

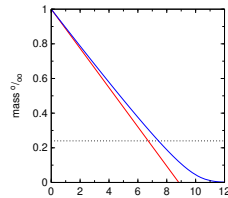
$$\text{0th order: } \tau = \frac{c_{S0} - c_S}{v_{max}} = \frac{(1 - 0.24) \times 1.06}{0.12} \text{ h} = 6.7 \text{ h}$$

$$\text{More accurate: } \tau = \frac{K_M \ln \frac{c_{S0}}{c_S} + c_{S0} - c_S}{v_{max}} = 7.4 \text{ h}$$

human:



4 x Zn
credit: wikipedia



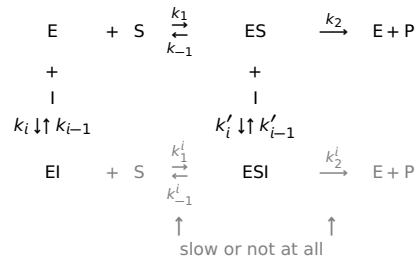
Other data: $K_M = 0.02$ to 0.05 g L^{-1} , absorption of ethanol in the body needed,...

Inhibition

14/23
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- reversible
- irreversible

reversible inhibition: the inhibitor is bound non-covalently (H-bonds, etc.), decreases the turnover



irreversible inhibition: "catalyst poisoning", usually covalently bound \Rightarrow inactive complex EI*

Michaelis-Menten kinetics III

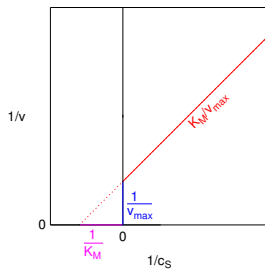
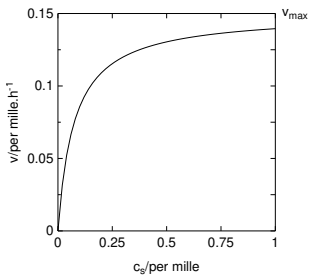
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Rate:

$$v = -\frac{dc_S}{d\tau} = v_{max} \frac{1}{K_M/c_S + 1}$$

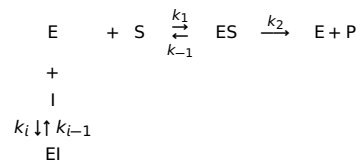
Linear in $(1/c_S, 1/v)$
(Lineweaver & Burk):

$$\frac{1}{v} = \frac{K_M}{v_{max}} \frac{1}{c_S} + \frac{1}{v_{max}}$$



Competitive reversible inhibition

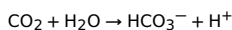
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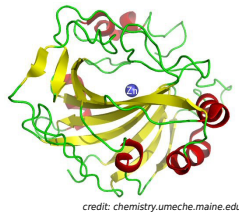
The inhibitor binds to the same site as the substrate ("competes" with the substrate)

Example—carbonic anhydrase

[plot/anhydrase.sh] 12/23
col02



$[\text{CO}_2]/\text{mmol dm}^{-3}$	$v/\text{mol dm}^{-3} \text{ s}^{-1}$
1.25	2.78×10^{-5}
2.5	5.00×10^{-5}
5.0	8.33×10^{-5}
20.0	16.7×10^{-5}



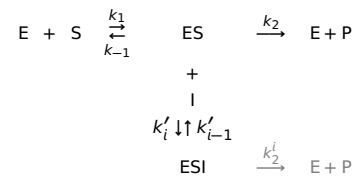
credit: chemistry.umeche.maine.edu

$$K_M = 0.01 \text{ mol dm}^{-3}, v_{max} = 25 \times 10^{-5} \text{ mol dm}^{-3} \text{ s}^{-1}$$

[according to DeVoe, Kistiakowski, JACS 83, 274 (1961)]

Uncompetitive reversible inhibition

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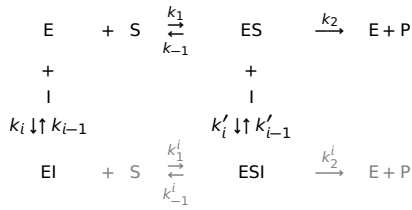
The inhibitor binds to the enzyme-substrate complex

Also anti-competitive

often partial (slows down the reaction)

Mixed (non-competitive) reversible inhibition

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col02



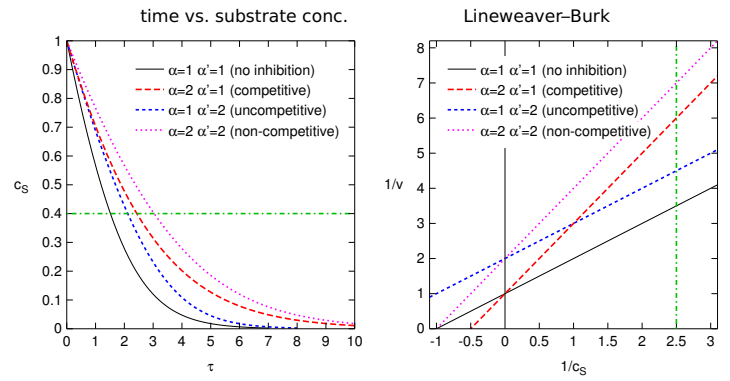
Mixed inhibition: the inhibitor bound both to E and ES

(Pure) non-competitive inhibition: inhibitor affects a different part of the enzyme,

$$k_i = k'_i, k_{i-1} = k'_{i-1}$$

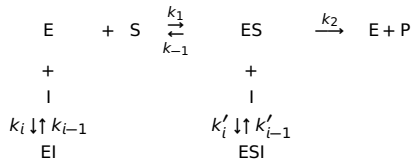
Reversible inhibition

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Reversible inhibition: some math

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col02



stationary state:

$$\frac{dc_{ES}}{d\tau} = k_1 c_E c_S - (k_{-1} + k_2) c_{ES} - k'_i c_I c_{ES} + k'_{i-1} c_{ESI} = 0$$

pre-equilibrium:

$$c_{EI} = \frac{k_i}{k_{i-1}} c_E c_I, \quad c_{ESI} = \frac{k'_i}{k'_{i-1}} c_{ES} c_I$$

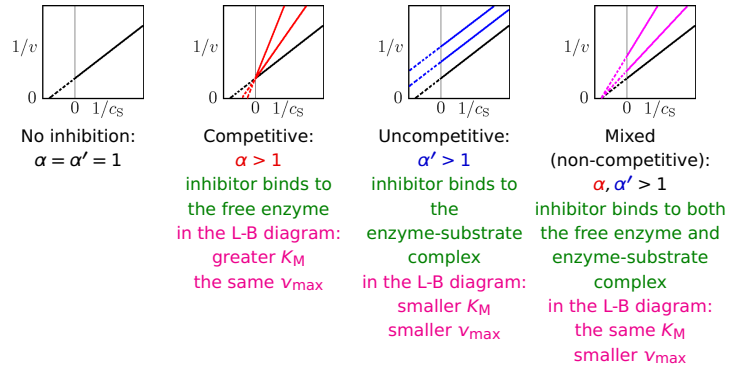
balance: $c_E + c_{ES} + c_{EI} + c_{ESI} = c_{E0}$

we assume $c_I \gg c_E, \Rightarrow c_I \approx c_{I0}$ is known (no balance of I needed)

Reversible inhibition - summary

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$$\frac{1}{v} = \frac{\alpha K_M}{V_{max}} \frac{1}{c_S} + \frac{\alpha'}{V_{max}}, \quad \alpha = 1 + \frac{k_i}{k_{i-1}} c_I, \quad \alpha' = 1 + \frac{k'_i}{k'_{i-1}} c_I$$



Reversible inhibition: some math

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balance + pre-equilibrium \Rightarrow

$$\begin{aligned}
 c_{E0} &= c_E + c_{EI} + c_{ES} + c_{ESI} \\
 &= \left(1 + \frac{c_{EI}}{c_E}\right) c_E + \left(1 + \frac{c_{ESI}}{c_{ES}}\right) c_{ES} \\
 &= \left(1 + \frac{k_i}{k_{i-1}} c_I\right) c_E + \left(1 + \frac{k'_i}{k'_{i-1}} c_I\right) c_{ES} \\
 &\equiv \alpha c_E + \alpha' c_{ES}
 \end{aligned}$$

stationary state \Rightarrow

$$0 = k_1 c_E c_S - (k_{-1} + k_2) c_{ES}$$

by inserting (the same as without inhibition):

$$v = \frac{dc_P}{d\tau} = k_2 c_{ES} = k_2 \frac{c_{E0}}{\alpha \frac{k_{-1} + k_2}{k_1} \frac{1}{c_S} + \alpha'} = v_{max} \frac{1}{\alpha K_M / c_S + \alpha'}$$

Lineweaver-Burk:

$$\frac{1}{v} = \frac{\alpha K_M}{V_{max}} \frac{1}{c_S} + \frac{\alpha'}{V_{max}}$$

Photochemistry instant

23/23
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Photon energy = $h\nu$ = energy source for the reaction

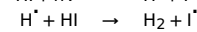
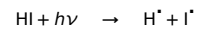
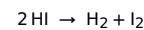
Planck constant: $h = 6.62607 \times 10^{-34} \text{ J s}$

Frequency ν , wave number $\tilde{\nu} = 1/\lambda$, wave length λ . It holds: $c = \lambda \nu$.

Quantum yield

$$\Phi = \frac{\text{\# of molecules transformed/decomposed/...}}{\text{\# of photons absorbed}}$$

Chain reactions: $\Phi > 1$. Example:



$$\Phi = 2$$

Example: How much HI decomposes by absorbing energy of 100J in the form of light of wave length 254 nm?

10mmol 0.27

Reversible inhibition: Lineweaver-Burk

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col02

$$\frac{1}{v} = \frac{\alpha K_M}{V_{max}} \frac{1}{c_S} + \frac{\alpha'}{V_{max}}, \quad \alpha = 1 + \frac{k_i}{k_{i-1}} c_I, \quad \alpha' = 1 + \frac{k'_i}{k'_{i-1}} c_I$$

