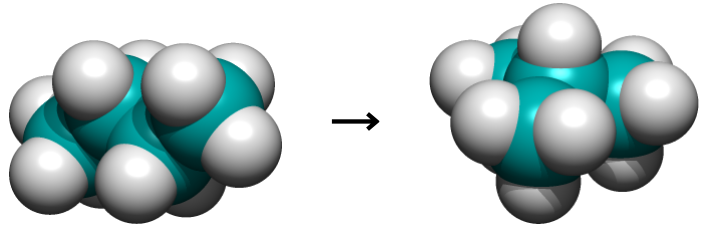
Elementary reactions

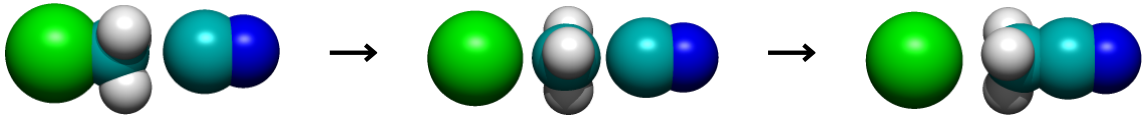
stoichiometry = mechanism ($Cl^{\bullet} + H_2 \rightarrow HCl + H^{\bullet}$)

- monomolecular reactions (decay: $N_2O_4 \rightarrow 2\,NO_2$; radioactive decay; some isomerisations)



- bimolecular reactions (collision; most common)

$$ClCH_3 + CN^- \rightarrow Cl^- + CH_3CN$$



- trimolecular reactions

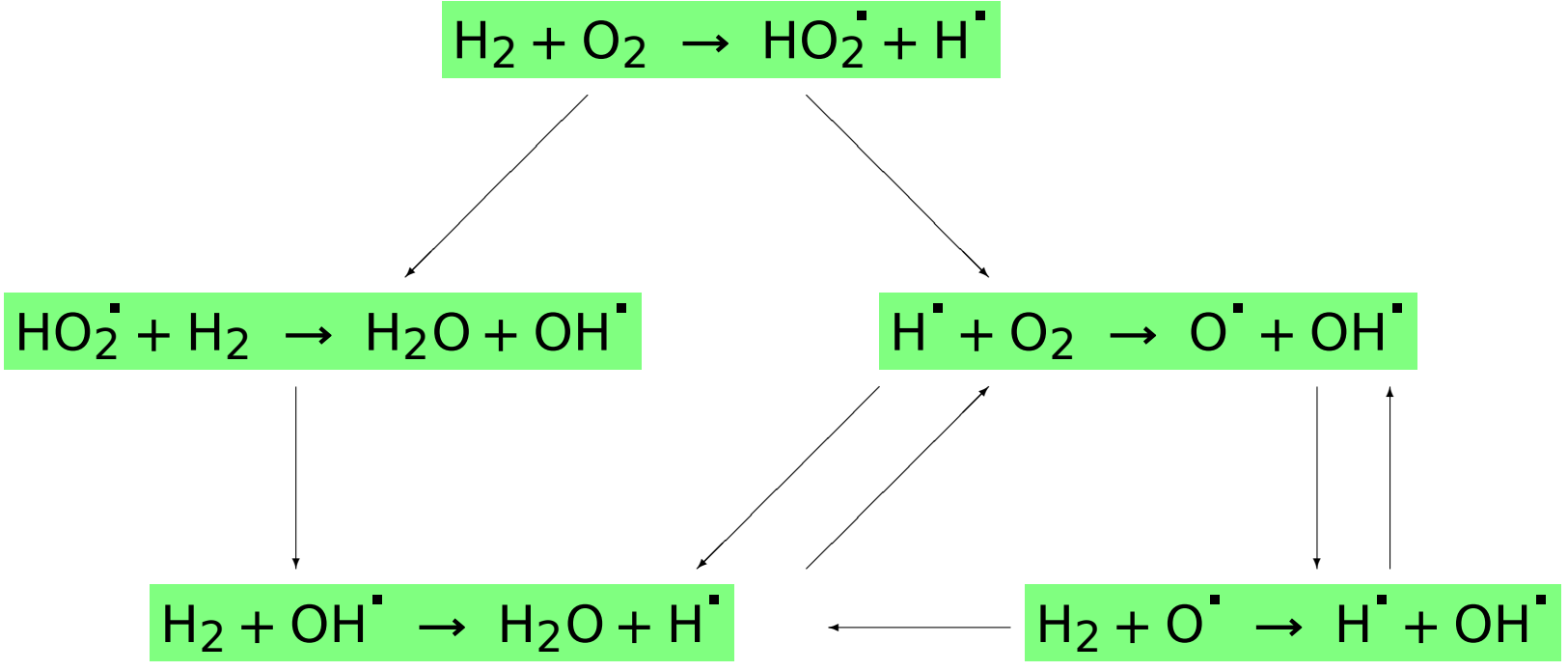
$$O + O_2 + N_2 \rightarrow O_3 + N_2$$

(N_2 carries out the surplus energy)

Reaction mechanisms

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

Example: $2\,H_2 + O_2 \rightarrow 2\,H_2O$



radical $A^{\bullet}$

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

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

Reaction mechanisms

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

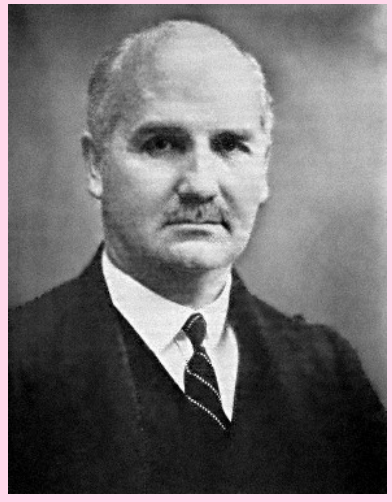
  e.g.: $\mathrm{A} \rightleftarrows \mathrm{A}^* \rightarrow \mathrm{B}$ $\quad \dfrac{\mathrm{d}c_{\mathrm{A}^*}}{\mathrm{d}\tau} \approx 0$

- pre-equilibrium
  reversible reaction part of chain

  e.g.: $\ldots \overset{\text{slow}}{\rightarrow} \mathrm{A} + \mathrm{B} \underset{\text{fast}}{\overset{\text{fast}}{\rightleftarrows}} \mathrm{C} + \mathrm{D} \overset{\text{slow}}{\rightarrow} \ldots$ $\quad \dfrac{c_{\mathrm{C}} c_{\mathrm{D}}}{c_{\mathrm{A}} c_{\mathrm{B}}} \approx K$

  can be derived from the above principle (for $\gamma = 1$)

Lindemann(-Hinshelwood) mechanism



credit: (Lindemann) Wikipedia

$$\mathrm{A(g)} \rightarrow \mathrm{B(g)}$$

Inelastic collisions in the gas phase activate molecules:

$$\mathrm{A} + \mathrm{A} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \mathrm{A} + \mathrm{A}^*$$

$$\mathrm{A}^* \xrightarrow{k_2} \mathrm{B}$$

$c_{A^*} \ll c_A \quad \Rightarrow \quad$ stationary state $\frac{\mathrm{d}c_{A^*}}{\mathrm{d}\tau} = 0 \quad \Rightarrow$

$-\mathrm{d}c_A/\mathrm{d}\tau = \mathrm{d}c_B/\mathrm{d}\tau$

$$-\frac{\mathrm{d}c_A}{\mathrm{d}\tau} = \frac{\mathrm{d}c_B}{\mathrm{d}\tau} = k_2 \frac{k_1 c_A^2}{k_2 + k_{-1} c_A}$$

- $k_{-1} c_A \gg k_2$ (ambient pressures): $\frac{\mathrm{d}c_B}{\mathrm{d}\tau} = \frac{k_2 k_1}{k_{-1}} c_A$ 1st order
- $k_{-1} c_A \ll k_2$ (low pressures): $\frac{\mathrm{d}c_B}{\mathrm{d}\tau} = k_1 c_A^2$ 2nd order

E.g.: cyclopropane → propene, $N_2O_5 \rightarrow NO_2 + NO_3^{\bullet}$,
dimethyldiazene (azomethane) $CH_3\text{-}N{=}N\text{-}CH_3 \rightarrow C_2H_6 + N_2$

Chain reactions

- 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

Chain reactions – examples

Simplified scheme of ozone cycle in stratosphere

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

initiation: $\mathrm{O_2} + h\nu \xrightarrow{J_1} 2\,\mathrm{O^{\bullet}}$ (forbidden transition)

propagation: $\left.\begin{aligned} \mathrm{O^{\bullet}} + \mathrm{O_2} + \mathrm{M} &\xrightarrow{k_2} \mathrm{O_3} + \mathrm{M} \\ \mathrm{O_3} + h\nu &\xrightarrow{J_3} \mathrm{O_2} + \mathrm{O^{\bullet}} \end{aligned}\right\}$ cycle

termination: $\mathrm{O^{\bullet}} + \mathrm{O_3} \xrightarrow{k_4} 2\,\mathrm{O_2}$

J_1 is very small $\Rightarrow J_1 k_4 \ll J_3 k_2[\mathrm{M}] \Rightarrow J_1[\mathrm{O_2}] \ll J_3[\mathrm{O_3}] \Rightarrow$ $[\mathrm{O_3}] = [\mathrm{O_2}]\sqrt{\dfrac{J_1 k_2[\mathrm{M}]}{J_3 k_4}}$

Simplified scheme of ozone destruction:

initiation: $\mathrm{CFC} \xrightarrow{J_1} \mathrm{Cl^{\bullet}} + \ldots$

propagation: $\left.\begin{aligned} \mathrm{Cl^{\bullet}} + \mathrm{O_3} &\xrightarrow{k_2} \mathrm{ClO^{\bullet}} + \mathrm{O_2} \\ \mathrm{ClO^{\bullet}} + \mathrm{O_3} &\xrightarrow{k_3} \mathrm{Cl^{\bullet}} + 2\,\mathrm{O_2} \end{aligned}\right\}$ cycle ($\sim 10^5$)

termination: various

Example (not in detail)

$$H_2 + Cl_2 \rightarrow 2\,HCl$$

initiation: $Cl_2 \xrightarrow{k_1} 2\,Cl^{\cdot}$

propagation: $Cl^{\cdot} + H_2 \xrightarrow{k_2} HCl + H^{\cdot}$, $H^{\cdot} + Cl_2 \xrightarrow{k_3} HCl + Cl^{\cdot}$ } cycle (up to 10^6)

termination: $2Cl^{\cdot} \xrightarrow{k_4} Cl_2$

$$\frac{dc_{HCl}}{d\tau} = k_2 c_{Cl^{\cdot}} c_{H_2} + k_3 c_{H^{\cdot}} c_{Cl_2} \overset{\text{steady state}}{=} 2k_2 \sqrt{\frac{k_1}{k_4}}\, c_{Cl_2}^{1/2} c_{H_2}$$

Enzyme catalysis: Michaelis–Menten kinetics

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

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

stationary state (because $c_\mathrm{E}, c_\mathrm{ES} \ll c_\mathrm{S}$):

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

balance: $c_\mathrm{E} + c_\mathrm{ES} = c_\mathrm{E0}$

Eliminating c_E ($\Rightarrow c_\mathrm{ES}$) from $\frac{\mathrm{d}c_\mathrm{P}}{\mathrm{d}\tau}$:

also from: $\frac{\mathrm{d}c_\mathrm{P}}{\mathrm{d}\tau} = -\frac{\mathrm{d}c_\mathrm{S}}{\mathrm{d}\tau} = k_1 c_\mathrm{E} c_\mathrm{S} - k_{-1} c_\mathrm{ES}$

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

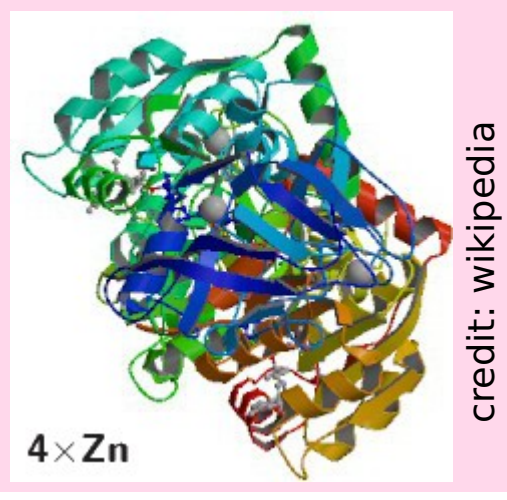
where $K_\mathrm{M} = \dfrac{k_2 + k_{-1}}{k_1}$ = Michaelis constant and $v_\mathrm{max} = k_2 c_\mathrm{E0}$

- $c_\mathrm{S} \gg K_\mathrm{M} \Rightarrow \dfrac{\mathrm{d}c_\mathrm{S}}{\mathrm{d}\tau} = -v_\mathrm{max}$ (zeroth order, most of E is saturated, ES)
- $c_\mathrm{S} \ll K_\mathrm{M} \Rightarrow \dfrac{\mathrm{d}c_\mathrm{S}}{\mathrm{d}\tau} = -\dfrac{v_\mathrm{max}}{K_\mathrm{M}} c_\mathrm{S}$ (first order, most of E is free, E)

Michaelis–Menten kinetics II

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

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



credit: wikipedia

Integrated form

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

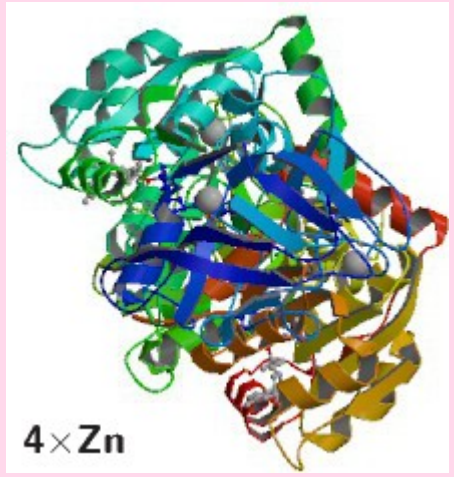
☹ cannot solve for $c_S(\tau)$ (using elem. functions) ⇒ numerical solution

credits: pitt.edu, Wikipedie

Metabolism of alcohols

Alcohol dehydrogenase, various types
In liver and the lining of the stomach
Further oxidation to acids and $H_2O + CO_2$

human:



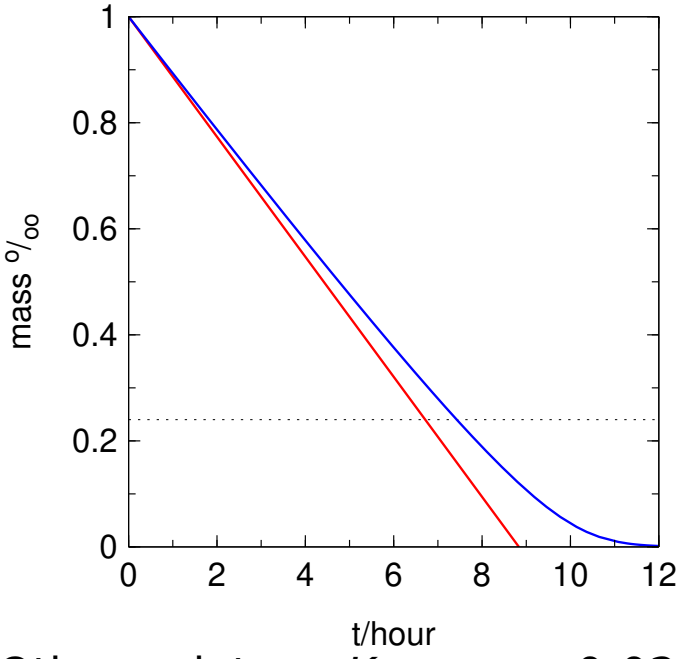
$$\begin{aligned} CH_3CH_2OH &\rightarrow CH_3CHO \text{ hangover} \\ CH_2OHCH_2OH &\rightarrow \ldots \rightarrow (COOH)_2 \text{ (kidney stones)} \\ CH_3OH &\rightarrow HCHO\ (☠) \rightarrow HCOOH\ (☠) \end{aligned}$$

Example. Calculate the time needed to metabolize $c_{S0} = 1$ wt. ‰ of ethanol to $c_S = 0.1$ ‰
Data: $v_{max} = 0.12\,\mathrm{g\,L^{-1}\,hod^{-1}}$,
$K_M = 0.06\,\mathrm{g\,L^{-1}}$.

$\rho_{blood} = 1.06\,\mathrm{g\,cm^{-3}} \Rightarrow 1$ wt. ‰ $= 1.06\,\mathrm{g\,L^{-1}}$

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

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



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

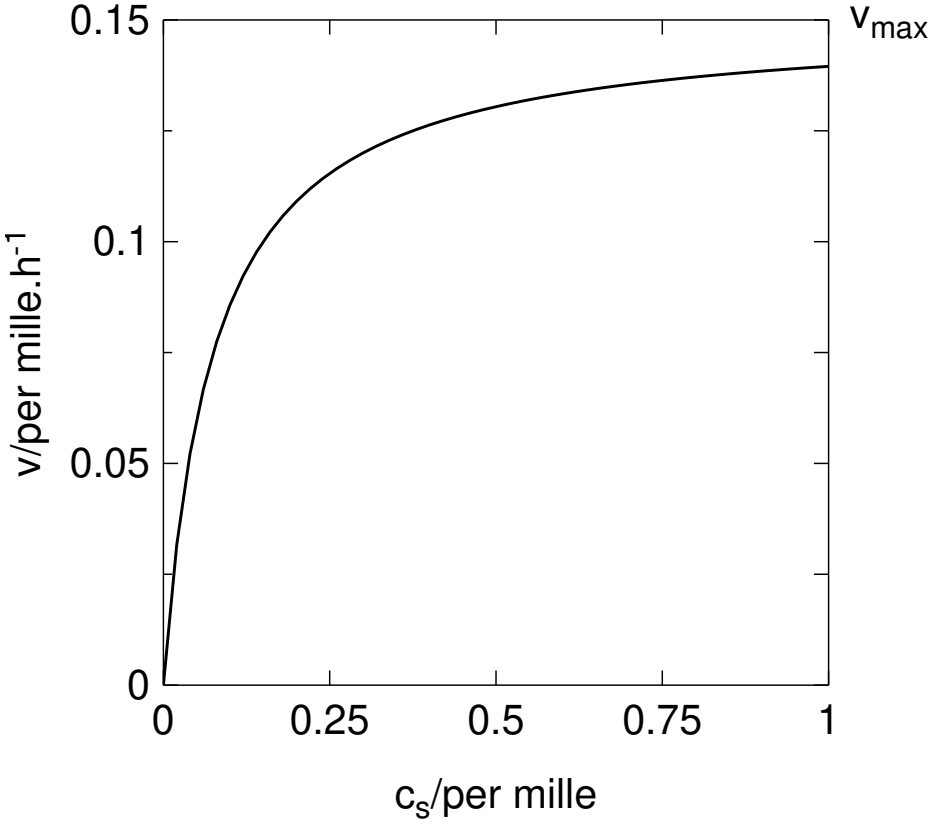
Michaelis–Menten kinetics III

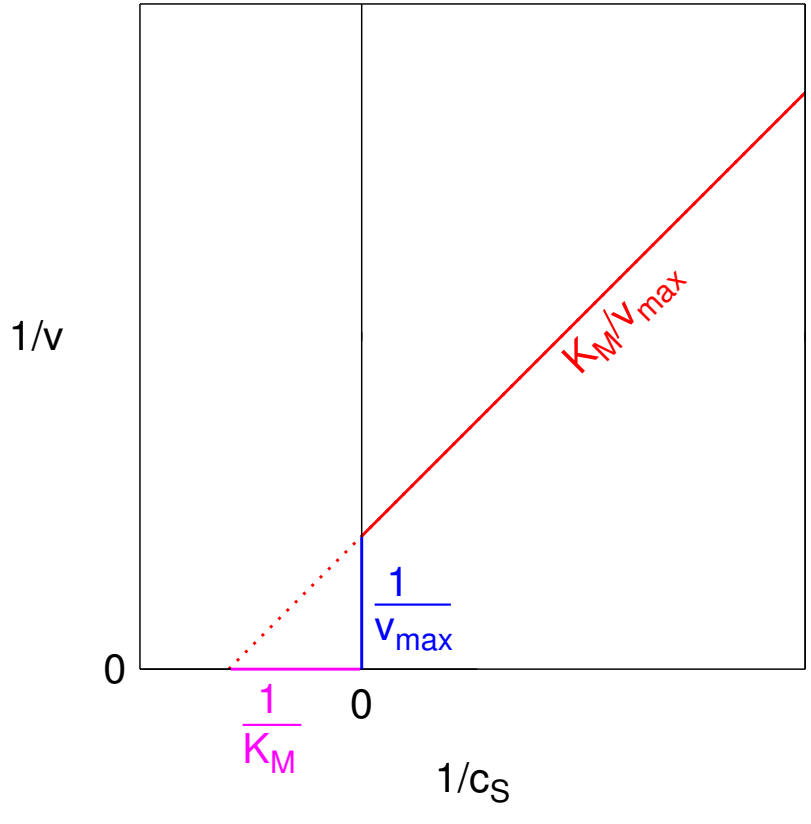
Rate:

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

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

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

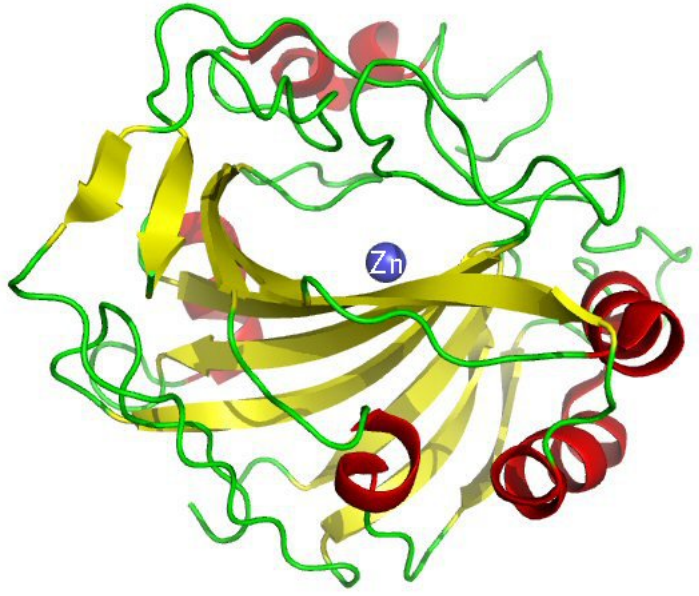




Example—carbonic anhydrase

$$CO_2 + H_2O \rightarrow HCO_3^- + H^+$$

$[CO_2]$/mmol dm^{-3}	v/mol dm^{-3} 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)]

Babel of units

Enzyme activity unit (amount of substance / time)

- SI: $\mathrm{mol\,s^{-1}}$ (katal)
- more common: μmol/min (“enzyme unit”, U)

Specific activity (per kg of enzyme)

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

Turnover number (per mole),

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

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

or $1\,\mathrm{g\,mol^{-1}}/N_\mathrm{A} = \frac{1}{12}m(^{12}\mathrm{C}) = 1\,\mathrm{u} = 1.660539\times10^{-27}\,\mathrm{kg} = 1\,\mathrm{Da}$

Deprecated units:

$1\,\mathrm{M} = 1\,\mathrm{mol\,dm^{-3}}$

$1\,\mathrm{m} = 1\,\mathrm{mol\,kg^{-3}}$ ($1\,\mathrm{mol\,dm^{-3}}$)

$1\,\mathrm{Da} = 1\,\mathrm{g\,mol^{-1}}$

$1\,\mathrm{bar} = 10^5\,\mathrm{Pa}$

$1\,\text{Å} = 10^{-10}\,\mathrm{m}$

$1\,\mathrm{cal_{th}} = 4.184\,\mathrm{J}$ (thermochemical)

$1\,\mathrm{cal_{it}} = 4.1868\,\mathrm{J}$ (intl./IAPWS)

$1\,\mathrm{cal_{IUNS}} = 4.182\,\mathrm{J}$ (food)

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

$4000\,\mathrm{s^{-1}}$

Inhibition

- reversible
- irreversible

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

$$
\begin{array}{ccccccc}
\mathrm{E} & + & \mathrm{S} & \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} & \mathrm{ES} & \xrightarrow{k_2} & \mathrm{E}+\mathrm{P} \\
+ & & & & + & & \\
\mathrm{I} & & & & \mathrm{I} & & \\
k_i \downarrow\uparrow k_{i-1} & & & & k_i' \downarrow\uparrow k_{i-1}' & & \\
\mathrm{EI} & + & \mathrm{S} & \underset{k_{-1}^i}{\overset{k_1^i}{\rightleftarrows}} & \mathrm{ESI} & \xrightarrow{k_2^i} & \mathrm{E}+\mathrm{P}
\end{array}
$$

slow or not at all

irreversible inhibition: “catalyst poisoning”, usually covalently bound ⇒ inactive complex EI*

Competitive reversible inhibition

$$\begin{array}{ccccccc} \mathrm{E} & + & \mathrm{S} & \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} & \mathrm{ES} & \xrightarrow{k_2} & \mathrm{E}+\mathrm{P} \\ + & & & & & & \\ \mathrm{I} & & & & & & \\ k_i \downarrow\uparrow k_{i-1} & & & & & & \\ \mathrm{EI} & & & & & & \end{array}$$

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

Uncompetitive reversible inhibition

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

$$+$$

$$\mathrm{I}$$

$$k_i' \downarrow\uparrow k_{i-1}'$$

$$\mathrm{ESI} \xrightarrow{k_2^i} \mathrm{E} + \mathrm{P}$$

The inhibitor binds to the enzyme-substrate complex

Also anti-competitive

often partial (slows down the reaction)

Mixed (non-competitive) reversible inhibition

$$
\begin{array}{ccccccc}
\mathrm{E} & + & \mathrm{S} & \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} & \mathrm{ES} & \xrightarrow{k_2} & \mathrm{E}+\mathrm{P} \\
+ & & & & + & & \\
\mathrm{I} & & & & \mathrm{I} & & \\
k_i \downarrow\uparrow k_{i-1} & & & & k'_i \downarrow\uparrow k'_{i-1} & & \\
\mathrm{EI} & + & \mathrm{S} & \underset{k^i_{-1}}{\overset{k^i_1}{\rightleftarrows}} & \mathrm{ESI} & \xrightarrow{k^i_2} & \mathrm{E}+\mathrm{P}
\end{array}
$$

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: some math

$$\begin{array}{ccccccc} \mathrm{E} & + & \mathrm{S} & \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} & \mathrm{ES} & \xrightarrow{k_2} & \mathrm{E}+\mathrm{P} \\ + & & & & + & & \\ \mathrm{I} & & & & \mathrm{I} & & \\ k_i \downarrow\uparrow k_{i-1} & & & & k'_i \downarrow\uparrow k'_{i-1} & & \\ \mathrm{EI} & & & & \mathrm{ESI} & & \end{array}$$

stationary state:

$$\frac{\mathrm{d}c_{\mathrm{ES}}}{\mathrm{d}\tau} = k_1 c_{\mathrm{E}} c_{\mathrm{S}} - (k_{-1} + k_2) c_{\mathrm{ES}} - k'_i c_{\mathrm{I}} c_{\mathrm{ES}} + k'_{i-1} c_{\mathrm{ESI}} = 0$$

pre-equilibrium:

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

balance: $c_{\mathrm{E}} + c_{\mathrm{ES}} + c_{\mathrm{EI}} + c_{\mathrm{ESI}} = c_{\mathrm{E0}}$

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

Reversible inhibition: some math

balance + pre-equilibrium ⇒

$$\begin{aligned} c_{\mathrm{E}0} &= c_{\mathrm{E}} + c_{\mathrm{EI}} + c_{\mathrm{ES}} + c_{\mathrm{ESI}} \\ &= \left(1 + \frac{c_{\mathrm{EI}}}{c_{\mathrm{E}}}\right) c_{\mathrm{E}} + \left(1 + \frac{c_{\mathrm{ESI}}}{c_{\mathrm{EI}}}\right) c_{\mathrm{ES}} \\ &= \left(1 + \frac{k_i}{k_{i-1}} c_{\mathrm{I}}\right) c_{\mathrm{E}} + \left(1 + \frac{k'_i}{k'_{i-1}} c_{\mathrm{I}}\right) c_{\mathrm{ES}} \\ &\equiv \alpha\, c_{\mathrm{E}} + \alpha' c_{\mathrm{ES}} \end{aligned}$$

stationary state ⇒

$$0 = k_1 c_{\mathrm{E}} c_{\mathrm{S}} - (k_{-1} + k_2) c_{\mathrm{ES}}$$

by inserting (the same as without inhibition):

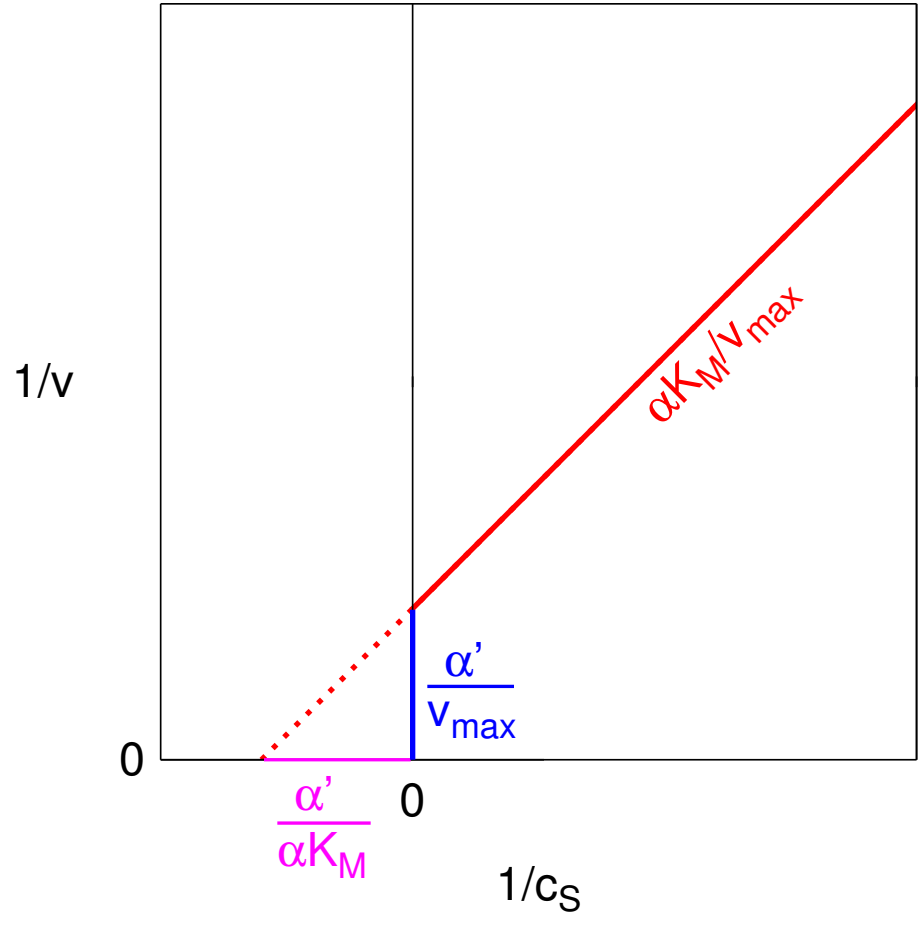
$$v = \frac{\mathrm{d}c_{\mathrm{P}}}{\mathrm{d}\tau} = k_2 c_{\mathrm{ES}} = k_2 \frac{c_{\mathrm{E}0}}{\alpha \frac{k_{-1}+k_2}{k_1} \frac{1}{c_{\mathrm{S}}} + \alpha'} = v_{\max} \frac{1}{\alpha K_{\mathrm{M}}/c_{\mathrm{S}} + \alpha'}$$

Lineweaver–Burk:

$$\frac{1}{v} = \frac{\alpha K_{\mathrm{M}}}{v_{\max}} \frac{1}{c_{\mathrm{S}}} + \frac{\alpha'}{v_{\max}}$$

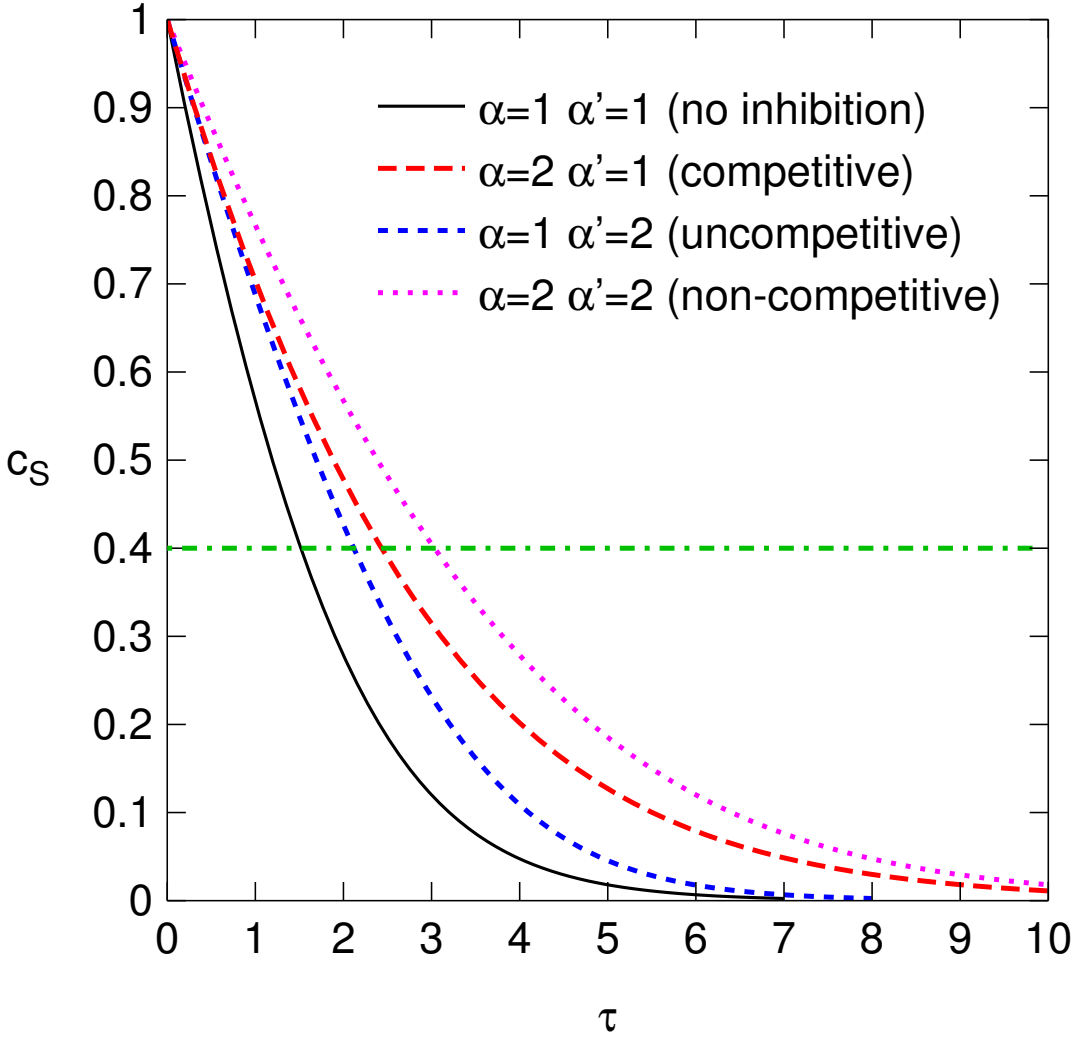
Reversible inhibition: Lineweaver–Burk

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

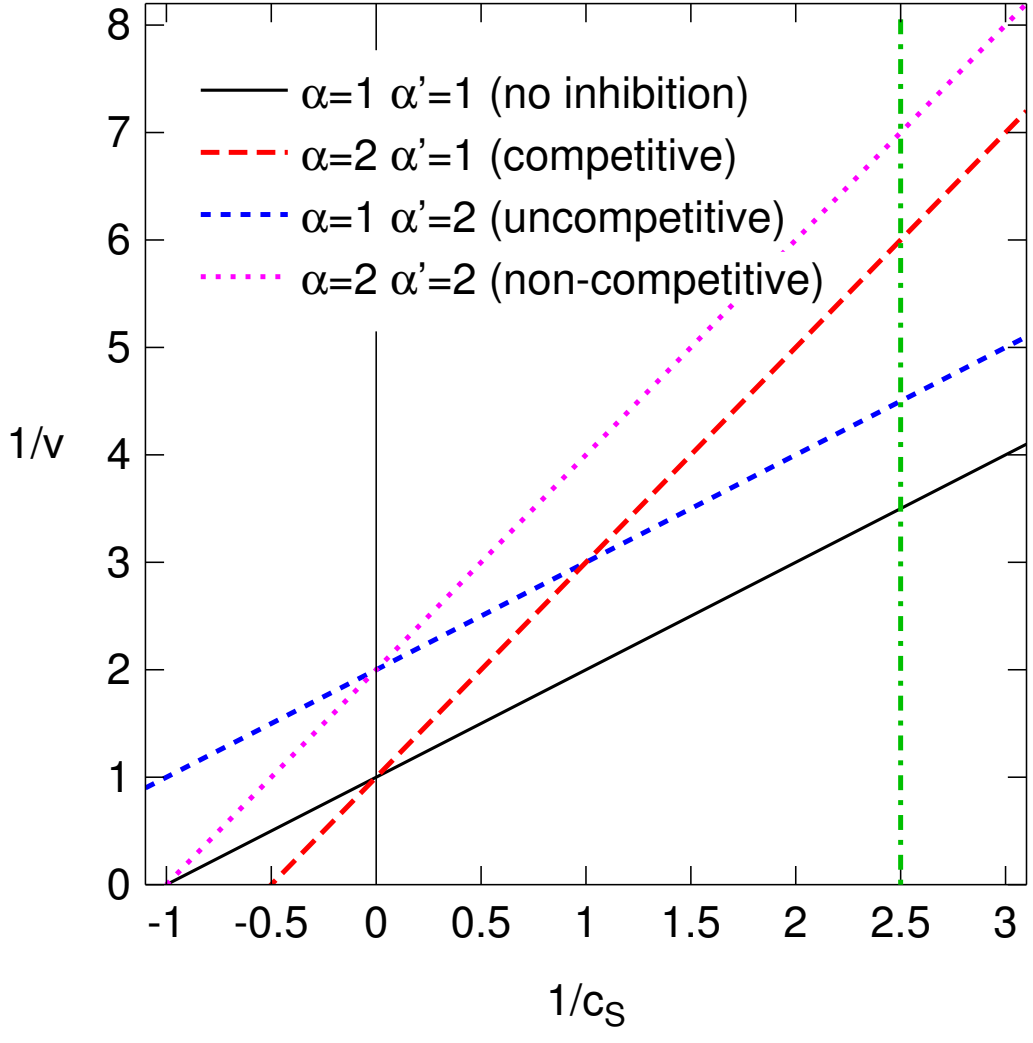


Reversible inhibition

time vs. substrate conc.

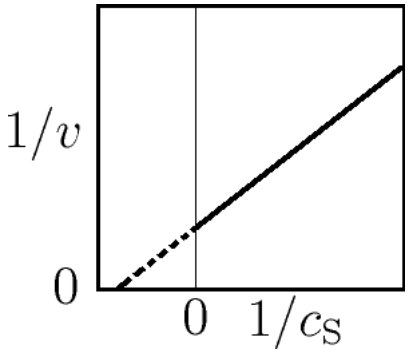


Lineweaver–Burk

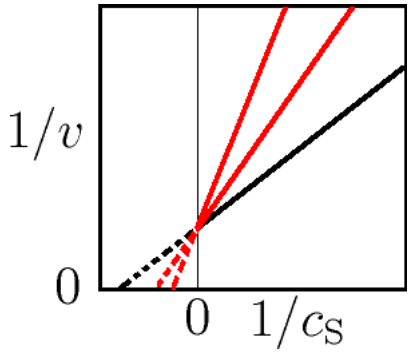


Reversible inhibition – summary

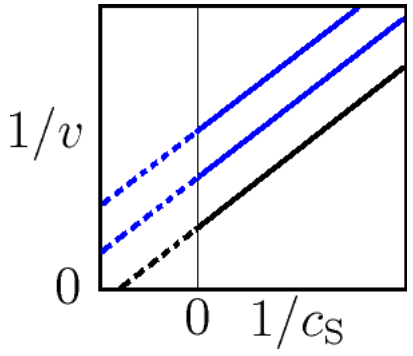
$$\frac{1}{v} = \frac{\alpha K_M}{v_{max}} \frac{1}{c_S} + \frac{\alpha'}{v_{max}}, \quad \alpha = 1 + \frac{k_i}{k_{i-1}} c_I, \quad \alpha' = 1 + \frac{k_i'}{k_{i-1}'} c_I$$



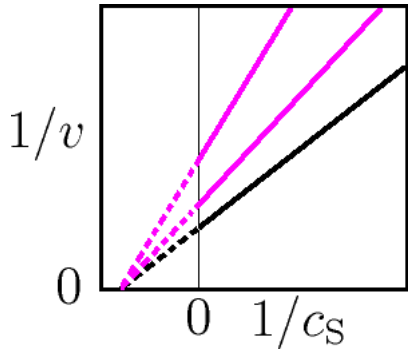
No inhibition:
$\alpha = \alpha' = 1$



Competitive:
$\alpha > 1$
inhibitor binds to the free enzyme
in the L-B diagram:
greater K_M
the same v_{max}



Uncompetitive:
$\alpha' > 1$
inhibitor binds to the enzyme-substrate complex
in the L-B diagram:
smaller K_M
smaller v_{max}



Mixed (non-competitive):
$\alpha, \alpha' > 1$
inhibitor binds to both the free enzyme and enzyme-substrate complex
in the L-B diagram:
the same K_M
smaller v_{max}

Photochemistry instant

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

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

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:

$$2\,\mathrm{HI} \rightarrow \mathrm{H_2} + \mathrm{I_2}$$

$$\begin{aligned} \mathrm{HI} + h\nu &\rightarrow \mathrm{H^{\bullet}} + \mathrm{I^{\bullet}} \\ \mathrm{H^{\bullet}} + \mathrm{HI} &\rightarrow \mathrm{H_2} + \mathrm{I^{\bullet}} \\ 2\,\mathrm{I^{\bullet}} &\rightarrow \mathrm{I_2} \end{aligned}$$

$$\Phi = 2$$

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

0.42 mmol