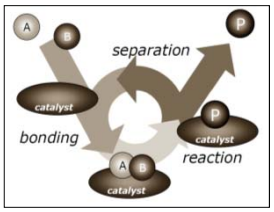
Atkins de Paula P Chem, 9th Edition,
Chapter 23,Catalysis, pp.876-908.



SF Chemical Kinetics.

Lecture 4-5

Catalysis:

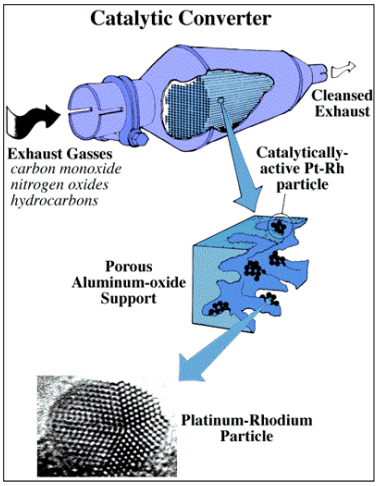
Heterogeneous Catalysis & Biocatalysis.

Lecture preview.

- In this lecture we focus attention on the catalysis of chemical reactions.
- We consider:
  - Heterogeneous catalysis on solid surfaces
  - Enzymatic bio-catalysis . Michaelis-Menten single enzyme/substrate kinetics.
- Common concept: Adduct formation / Binding Interaction between catalyst and reactant.

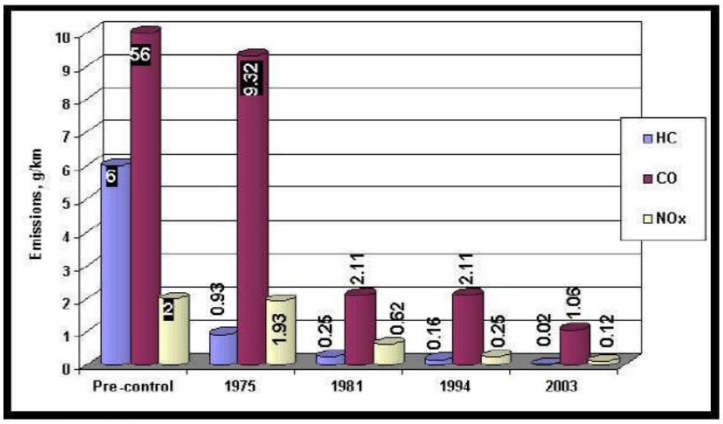
Catalysis.

- Catalysis involves the enhancement of the rate of a reaction by a substance, which is not consumed in the reaction. It turns out that the vast majority of all industrial chemical reactions involve surfaces as the catalysts. The kind of processes involved range from hydrogenation of hydrocarbons to detoxification of exhaust gases. The catalytic converter in an automobile is a classic example.
- The image presented across illustrates the general principles: a particular metal surface (in this case, a Pt-Rh alloy) is known to catalyze the desired reaction. In order to maximize the surface area of the metal per weight, small particles are used. You can almost count the atoms in the particle shown, which was from a real catalyst and was studied by Scanning Electron Microscopy. The particle shown has 500-600 atoms, based on a rough estimate from the number of atoms at its circumference. Oxide substrates are also a general characteristic of such catalysts.



EXHAUST EMISSION STANDARDS

GASOLINE PASSENGER CARS US / FEDERAL



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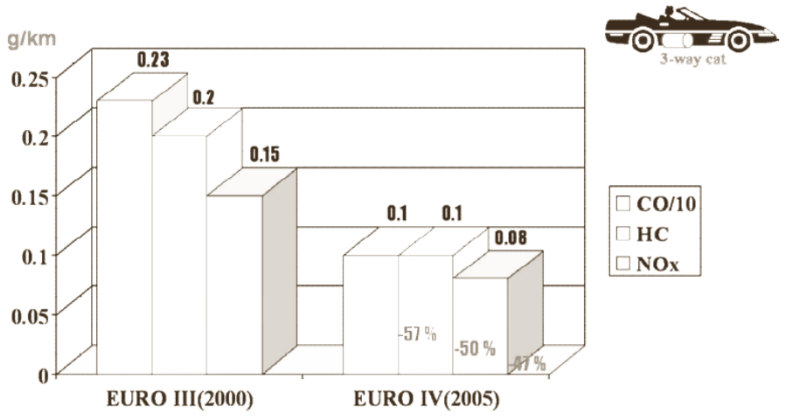
http://www.pt.hut.fi/teke/opetus/uusitutkinto/ymparistokatalyysi/luentokalvot/hUT2006%20Introduction.pdf

EUROPE EMISSION STANDARDS FOR PASSENGER CARS, PETROL



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CATALYST'S FUNCTION

THREE-WAY CATALYST

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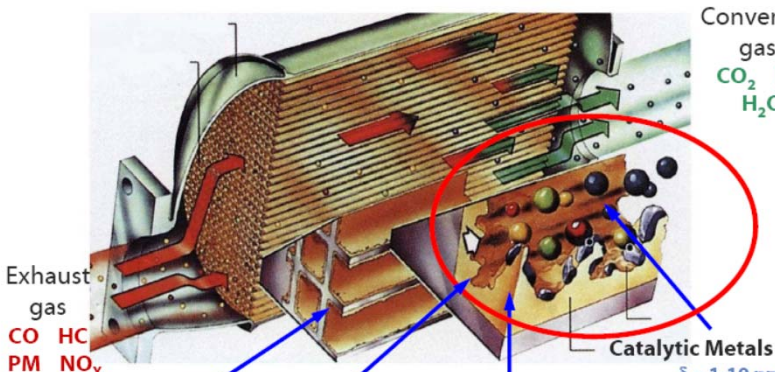
Exhaust Gas Catalyst



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AUTOMOBILE EXHAUST GAS CATALYSIS

The overall catalytic reactions:

$CO + ½\ O_2 \Rightarrow CO_2$ (1)

hydrocarbons + $O_2 \Rightarrow H_2O + CO_2$ (2)

$NO + CO \Rightarrow ½\ N_2 + CO_2$ (3)

hydrocarbons + $NO \Rightarrow N_2 + H_2O + CO_2$ (4)

as well as

$CO + H_2O \Rightarrow CO_2 + H_2$ (5)

hydrocarbons + $H_2O \Rightarrow CO + CO_2 + H_2$ (6)

and possibly Some side reactions to produce:
NH_3, N_2O, H_2S and SO_3

The desired products are N_2, CO_2 and H_2O

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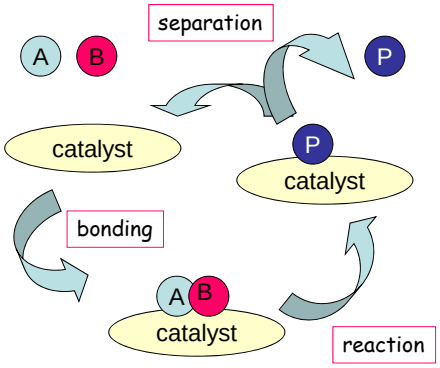
Catalysis: general comments.

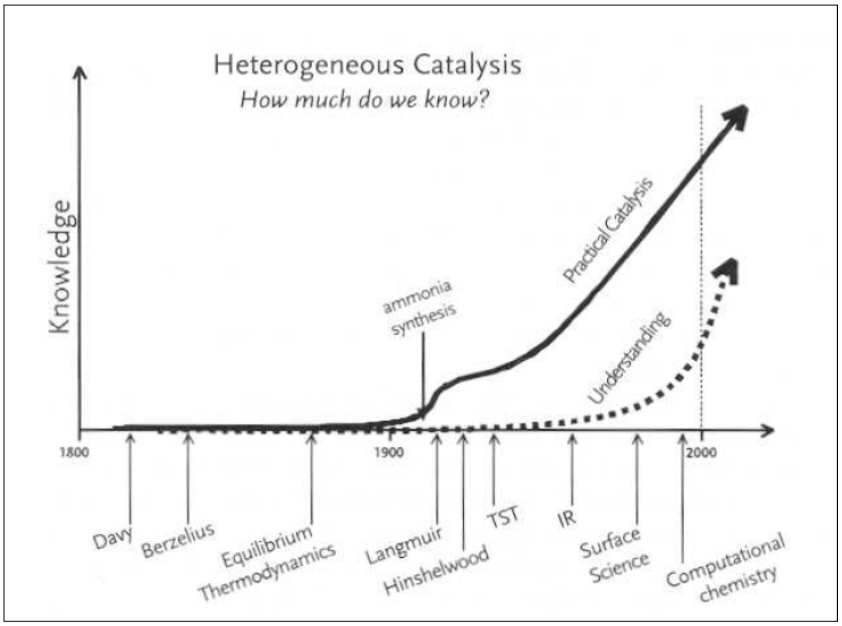
- Catalysts come in a variety of forms varying from atoms and molecules to large structures such as enzymes and zeolites.
- The catalyst offers an alternative low energy pathway for the reaction, which is perhaps more complex, but energetically more favourable.
- The activation energy for the catalytic reaction is significantly smaller than that of the uncatalyzed reaction. Hence the rate of the catalyzed reaction is much larger.
- Sabatier Principle:
  - The successful combination of catalyst and reaction is that in which the interaction between catalyst and reacting species is not too weak but also not too strong.

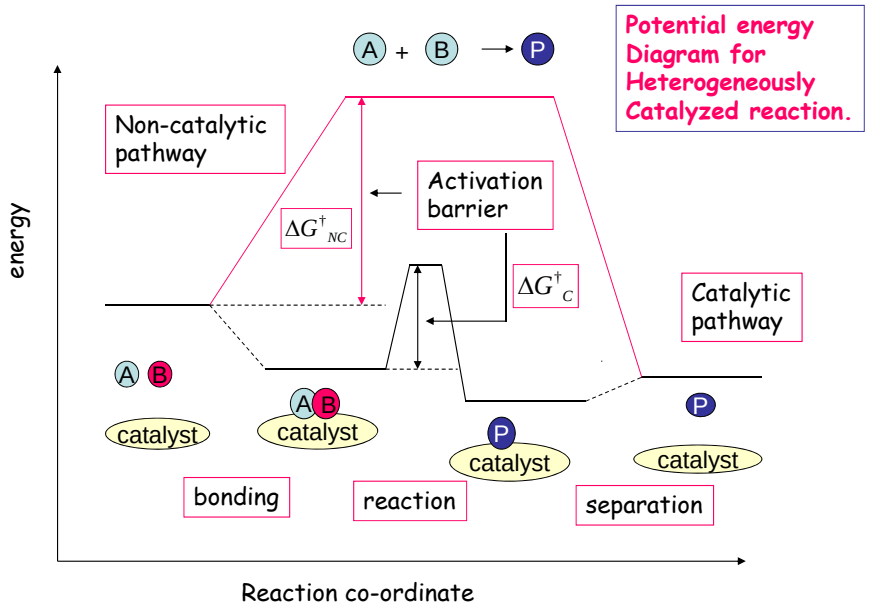
- The overall change in free energy ΔG^0 for the catalytic reaction equals that of the uncatalyzed reaction. Hence the catalyst does not effect the equilibrium constant (recall that $\Delta G^0 = -RT \ln K$) for the reaction A +B → P. Thus if a reaction is thermodynamically unfavourable, a catalyst cannot change the situation. A catalyst changes the kinetics but not the thermodynamics of a reaction.
- The catalyst accelerates both the forward and the reverse reaction to the same extent. If a catalyst accelerates formation of product P from reactants A and B, it will do the same for the decomposition of P into A and B.

Catalysis.

- A catalyst accelerates the rate of a reaction without itself being consumed in the process.
- The catalyst achieves its function by forming bonds with the reacting molecules and allowing these to react to form a product, which detaches from the catalyst, and leaves it unaltered such that it is available for the next reaction.
- Hence the elementary steps involved in a catalytic process involve:
  - Chemical bonding
  - Chemical reaction
  - Separation
- Catalysis is subdivided into 3 sub-areas:
  - Homogeneous catalysis
  - Biocatalysis
  - Heterogeneous catalysis.



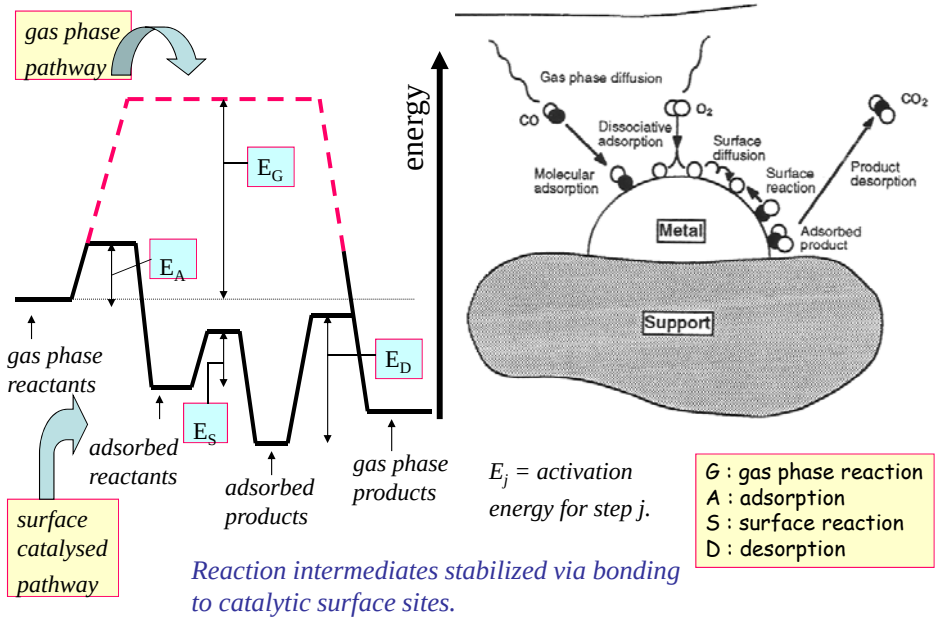

Heterogeneous Catalysis
How much do we know?
Knowledge
ammonia synthesis
Practical Catalysis
Understanding
1800
1900
2000
Davy
Berzelius
Equilibrium Thermodynamics
Langmuir
Hinshelwood
TST
IR
Surface Science
Computational chemistry


A + B → P
Potential energy Diagram for Heterogeneously Catalyzed reaction.
Non-catalytic pathway
Activation barrier
$\Delta G^{\dagger}_{NC}$
$\Delta G^{\dagger}_{C}$
Catalytic pathway
energy
A B
catalyst
A B
catalyst
P
catalyst
P
catalyst
bonding
reaction
separation
Reaction co-ordinate

Surface reactions.

- Diffusion of reactants to the active surface.
- Adsorption of one or more reactants onto the surface.
- Surface reaction .
- Desorption of products from the surface.
- Diffusion of products away from the surface.

Catalysis at solid surfaces



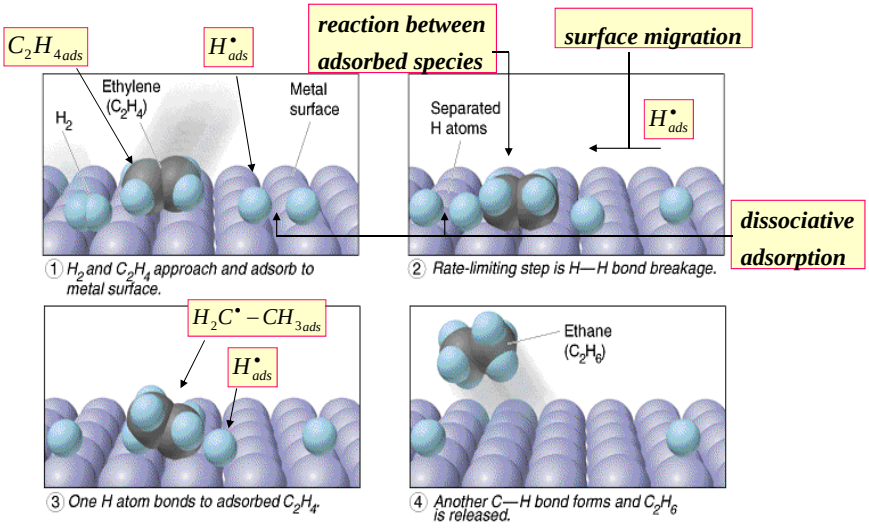
E_j = activation energy for step j.

G : gas phase reaction
A : adsorption
S : surface reaction
D : desorption

Reaction intermediates stabilized via bonding to catalytic surface sites.

The Metal-Catalyzed Hydrogenation of Ethylene

$$H_2C{=}CH_2\,(g) + H_2(g) \longrightarrow H_3C{-}CH_3\,(g)$$



Processes Based on Catalysis

Table 16.7 Some Modern Processes Based on Catalysis

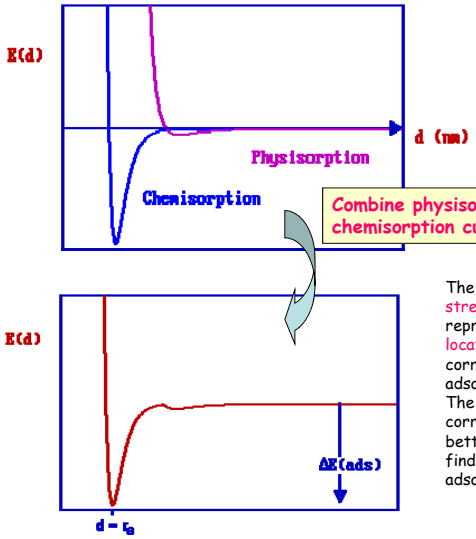
Reactants	Catalyst	Product	Use
Homogeneous			
Propylene, oxidizer	Mo(VI) complexes	Propylene oxide	Polyurethane foams; polyesters
Methanol, CO	$[Rh(CO)_2I_2]^-$	Acetic acid	Poly (vinyl acetate) coatings; poly(vinyl alcohol)
Butadiene, HCN	Ni/P compounds	Adiponitrile	Nylons (fibers, plastics)
α-Olefins, CO, H_2	Rh/P compounds	Aldehydes	Plasticizers, lubricants
Heterogeneous			
Ethylene, O_2	Silver, cesium chloride on alumina	Ethylene oxide	Polyesters, ethylene glycol, lubricants
Propylene, NH_3, O_2	Bismuth molybdates	Acrylonitrile	Plastics, fibers, resins
Ethylene	Organochromium and titanium halides on silica	High-density polyethylene	Molded products

Reaction	Catalyst
Catalytic cracking of crude oil	Zeolites
Hydrotreating of crude oil	Co–Mo, Ni–Mo, Ni–W (sulfidic form)
Reforming of naphtha (to gasoline)	Pt, Pt–Re, Pt–Ir
Alkylation	H_2SO_4, HF, solid acids
Polymerization of ethylene, propylene, a.o.	Cr, $TiCl_x/MgCl_2$
Ethylene epoxidation to ethylene oxide	Ag
Vinyl chloride (ethylene + Cl_2)	Cu (as chloride)
Steam reforming of methane to CO + H_2	Ni
Water-gas shift reaction	Fe (oxide), Cu–ZnO
Methanation	Ni
Ammonia synthesis	Fe
Ammonia oxidation to NO and HNO_3	Pt–Rh
Acrylonitrile from propylene and ammonia	Bi–Mo, Fe–Sb (oxides)
Hydrogenation of vegetable oils	Ni
Sulfuric acid	V (oxide)
Oxidation of CO & hydrocarbons (car exhaust)	Pt, Pd
Reduction of NOx (in exhaust)	Rh, vanadium oxide

How do molecules bond to surfaces?

- *Two principal modes of adsorption of molecules to surfaces.*
  - *Physical Adsorption* : the only bonding is by weak Van der Waals - type forces. There is no significant redistribution of electron density in either the molecule or at the substrate surface.
  - *Chemisorption* : a chemical bond, involving substantial rearrangement of electron density, is formed between the adsorbate and substrate. The nature of this bond may lie anywhere between the extremes of virtually complete ionic or complete covalent character.

Potential energy versus distance curves for physisorption and chemisorption.



The weak physical adsorption forces and associated long-range attraction will be present to varying degrees in all adsorbate / substrate systems. However, in cases where chemical bond formation between the adsorbate and substrate can also occur, the PE curve is dominated by a much deeper chemisorption minimum at shorter values of d .

The depth of the chemisorption well is a measure of the strength of binding to the surface - in fact it is a direct representation of the energy of adsorption, whilst the location of the global minimum on the horizontal axis corresponds to the equilibrium bond distance (r_e) for the adsorbed molecule on this surface.
The energy of adsorption is *negative*, and since it corresponds to the energy *change* upon adsorption it is better represented as $\Delta E(ads)$. However, you will also often find the depth of this well associated with the enthalpy of adsorption, $\Delta H(ads)$.

Terminology.

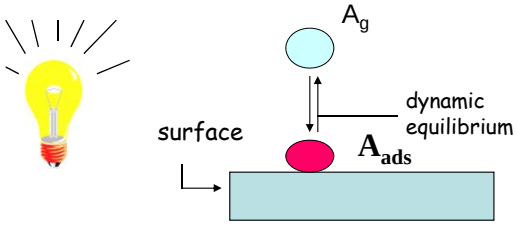
- *Substrate* - frequently used to describe the solid surface onto which adsorption can occur; the substrate is also occasionally (although not here) referred to as the adsorbent.
- *Adsorbate* - the general term for the atomic or molecular species which are adsorbed (or are capable of being adsorbed) onto the substrate.
- *Adsorption* - the process in which a molecule becomes adsorbed onto a surface of another phase (note - to be distinguished from absorption which is used when describing uptake into the bulk of a solid or liquid phase)
- *Coverage* - a measure of the extent of adsorption of a species onto a surface (unfortunately this is defined in more than one way !). Usually denoted by the lower case Greek "theta", q
- *Exposure* - a measure of the amount of gas which as surface has seen; more specifically, it is the product of the pressure and time of exposure (normal unit is the Langmuir, where 1 L = 10-6 Torr s).

Typical Characteristics of Adsorption Processes

	Chemisorption	**Physisorption**
Temperature Range (over which adsorption occurs)	Virtually unlimited (but a given molecule may effectively adsorb only over a small range)	Near or below the condensation point of the gas (e.g. Xe < 100 K, CO_2 < 200 K)
Adsorption Enthalpy	Wide range (related to the chemical bond strength) - typically 40 - 800 kJ mol^{-1}	Related to factors like molecular mass and polarity but typically 5-40 kJ mol^{-1} (i.e. ~ heat of liquefaction)
Crystallographic Specificity (variation between different surface planes of the same crystal)	Marked variation between crystal planes	Virtually independent of surface atomic geometry
Nature of Adsorption	Often dissociative May be irreversible	Non-dissociative Reversible
Saturation Uptake	Limited to one monolayer	Multilayer uptake possible
Kinetics of Adsorption	Very variable - often an activated process	Fast - since it is a non-activated process

Irving Langmuir (1881 - 1957)

Employed at General Electric (industrial research).
Examined oxygen adsorption on tungsten filaments of light bulbs.
1932: Nobel Prize in Chemistry.



1915. Langmuir adsorption Isotherm.

$$\theta = \frac{Kp}{1+Kp}$$

Adsorption at gas/solid interface.

Adsorption. Term used to describe the process whereby a molecule (the **adsorbate**) forms a bond to a solid surface (an **adsorbent**).

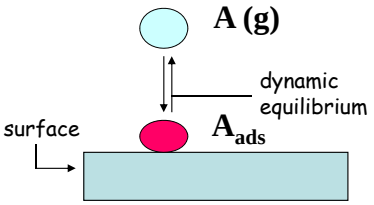
Fractional surface coverage θ

$$\theta = \frac{N_S}{N_\Sigma}$$

← *number of sites occupied by adsorbate*

← *total number of adsorption sites*

When $\theta = 1$, $N_S = N_\Sigma$ and an adsorbed monolayer is formed.
The fractional coverage θ depends on pressure of adsorbing gas phase species.
This $\theta = \theta(p)$ relationship is called an adsorption isotherm.



Langmuir Adsorption Isotherm.

Simple approach to quantitatively describe an adsorption process at the gas/solid interface.

$$N_\Sigma = N_S + N_V$$

← Number of Vacant sites

Assumptions :

- solid surface is homogeneous and contains a number of equivalent sites, each of which is occupied by a single adsorbate molecule
- a dynamic equilibrium exists between gas phase reactant and adsorbed species
- no interactions between adsorbed species
- adsorbed species localised, ΔH_{ads} is independent of coverage θ

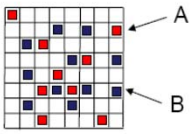
The mean-field approximation

Modeling reaction kinetics, often the mean-field (MF) approximation is assumed.

In MF, it is assumed that the reactants are randomized on the surface. This is valid if:

- The surface is uniform
- The adsorbate-adsorbate interaction is small

When the MF applies, the reaction kinetics can be formulated in using coverages.



N is total number of surface sites
N_A is number of sites occupied by A
N_B is number of sites occupied by B
N_* is number of unoccupied sites

$\theta_A = N_A / N$: coverage of A
$\theta_B = N_B / N$: coverage of B
$\theta_* = N_* / N$: "coverage" of empty sites

associative adsorption

$A(g) + S \underset{k_D}{\overset{k_A}{\rightleftharpoons}} A_{ads}$ — *adsorption rate constant* (k_A); *desorption rate constant* (k_D)

$A_2(g) + S \underset{k_D}{\overset{k_A}{\rightleftharpoons}} 2\,A_{ads}$

surface adsorption site

dissociative adsorption

$K = \frac{k_A}{k_D}$ — K measures affinity of a particular molecule for an adsorption site.

At equilibrium : $R_A = R_D$ → $k_A p(1-\theta) = k_D \theta$

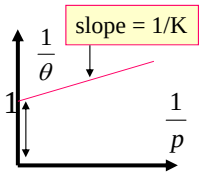
Rate of adsorption :

$R_A = k_A p N_V = k_A p(1-\theta) N_\Sigma$

pressure; *fractional coverage of vacant sites*

$\theta = \frac{Kp}{1+Kp}$ ← ***Langmuir adsorption isotherm : associative adsorption.***

$\frac{1}{\theta} = 1 + \frac{1}{Kp}$



Rate of desorption :

$R_D = k_D N_S = k_D \theta N_\Sigma$

fractional surface coverage

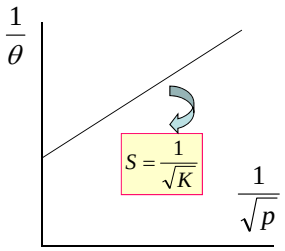
A similar analysis can be done for dissociative adsorption.

Adsorption rate: $R_A = k_A p N_\Sigma^2 (1-\theta)^2$

Desorption rate: $R_D = k_D N_\Sigma^2 \theta^2$

At equilibrium : $R_A = R_D$

$k_A p(1-\theta)^2 = k_D \theta^2$



Adsorption isotherm for dissociative adsorption.

$\frac{\theta^2}{(1-\theta)^2} = \frac{k_A}{k_D} p = Kp$

$\theta = \frac{\sqrt{Kp}}{1+\sqrt{Kp}}$

$\frac{1}{\theta} = 1 + \frac{1}{\sqrt{Kp}}$

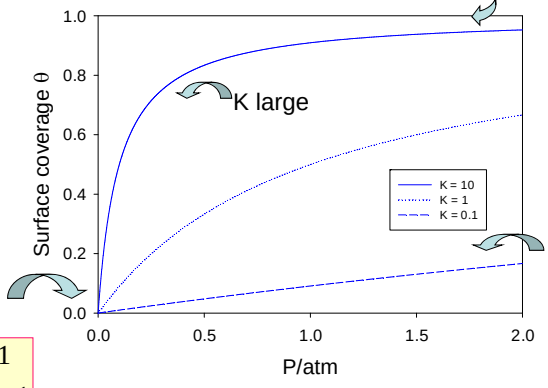
Langmuir Adsorption Isotherm.

high p limit : monolayer formed

$Kp >> 1$

$1 + Kp \cong Kp$

$\theta \to 1$



Low p limit : Henry Law

$Kp << 1$

$1 + Kp \cong 1$

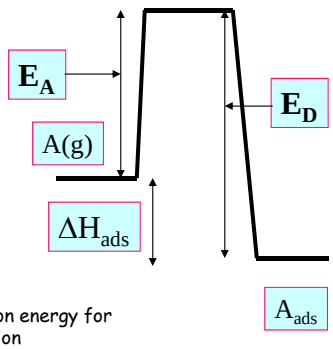
$\theta \cong Kp$

$$\theta = \frac{Kp}{1 + Kp}$$

Adsorption Energetics

Adsorption of a gas on a solid is an exothermic process : ΔH_{ads} is negative.

Both adsorption and desorption processes follow the Arrhenius equation.



adsorption pre-exponential factor

$$k_A = A_A \exp\left[-\frac{E_A}{RT}\right]$$ ← activation energy for adsorption

$$k_D = A_D \exp\left[-\frac{E_D}{RT}\right]$$ ← activation energy for desorption

temperature (K)

desorption pre-exponential factor

$$K = \frac{k_A}{k_D} = \frac{A_A}{A_D} \exp\left[-\frac{\Delta H_{ads}}{RT}\right]$$

$$\Delta H_{ads} = E_A - E_D$$

R = gas constant = 8.314 J mol^{-1} K^{-1}

How is ΔH_{ads} measured ?

$$\Delta G^0_{ads} = -RT\ln K = \Delta H^0_{ads} - T\Delta S^0_{ads}$$

entropy of adsorption

entalphy of adsorption

Gibbs energy of adsorption

$$\ln K = -\frac{\Delta H^0_{ads}}{RT} + \frac{\Delta S^0_{ads}}{R}$$

$$\left(\frac{\partial \ln K}{\partial T}\right)_\theta = \frac{\Delta H^0_{ads}}{RT^2}$$

constant surface coverage

Langmuir adsorption assumed

$$Kp = \frac{\theta}{1-\theta}$$

$$\ln K + \ln p = \ln\left\{\frac{\theta}{1-\theta}\right\}$$

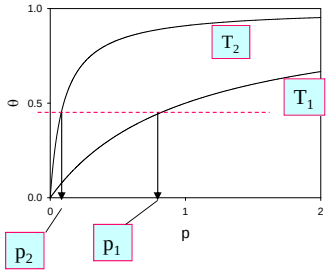
$$\left(\frac{\partial \ln K}{\partial T}\right)_\theta + \left(\frac{\partial \ln p}{\partial T}\right)_\theta = 0$$

$$\left(\frac{\partial \ln p}{\partial T}\right)_\theta = -\left(\frac{\partial \ln K}{\partial T}\right)_\theta$$

constant surface coverage

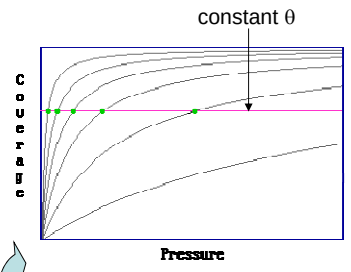
$$\left(\frac{\partial \ln p}{\partial T}\right)_\theta = -\frac{\Delta H^0_{ads}}{RT^2}$$

$$\left[\ln\left(\frac{p_1}{p_2}\right)\right]_\theta = \frac{\Delta H^0_{ads}}{R}\left\{\frac{1}{T_1} - \frac{1}{T_2}\right\}$$

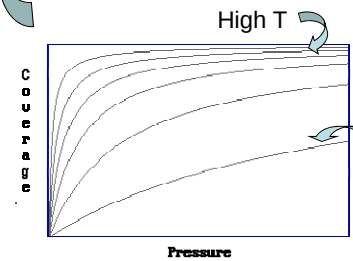


Determine adsorption Isotherm curves at Various temperatures.

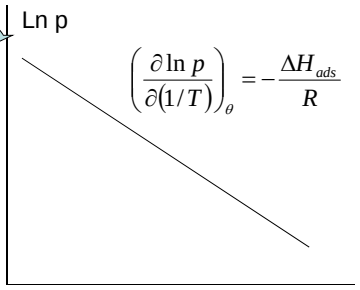
Measure values of p and T at a constant surface coverage. Using this idea, p_1, p_2, T_1 and T_2 can be measured so ΔH_{ads} can be determined.



Read off p,T data at constant coverage.



Determine adsorption isotherm at various temperatures.

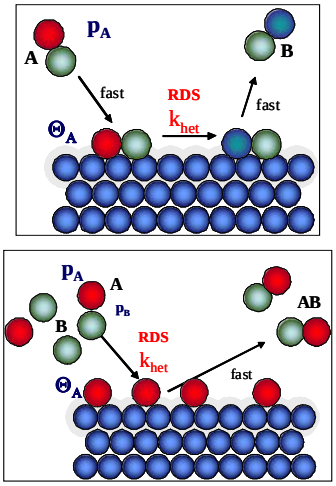


$$\left(\frac{\partial \ln p}{\partial (1/T)}\right)_\theta = -\frac{\Delta H_{ads}}{R}$$

Plot of ln p versus 1/T at constant surface coverage is linear.
Slope of plot enables one to evaluate ΔH_{ads}.
This can be repeated for various set values of the surface coverage, to enable ΔH_{ads} to be determined over the entire range of surface coverage θ .

Kinetics of surface reactions

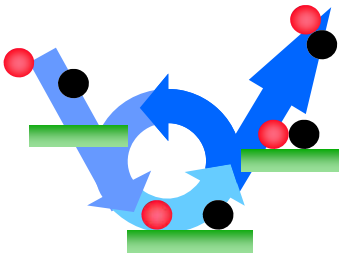
- We probe the reaction kinetics of surface processes assuming Langmuir adsorption isotherm.
- Two principal types of reaction mechanism are usually considered:
  - Langmuir- Hinshelwood
  - Eley- Rideal.
- In the *Langmuir-Hinshelwood* mechanism the reactants are all adsorbed on the surface and react at the surface.
- In the *Eley-Rideal* mechanism one has reaction between a reactant in the gas phase and a reactant adsorbed on the surface.



Langmuir - Hinshelwood Kinetics

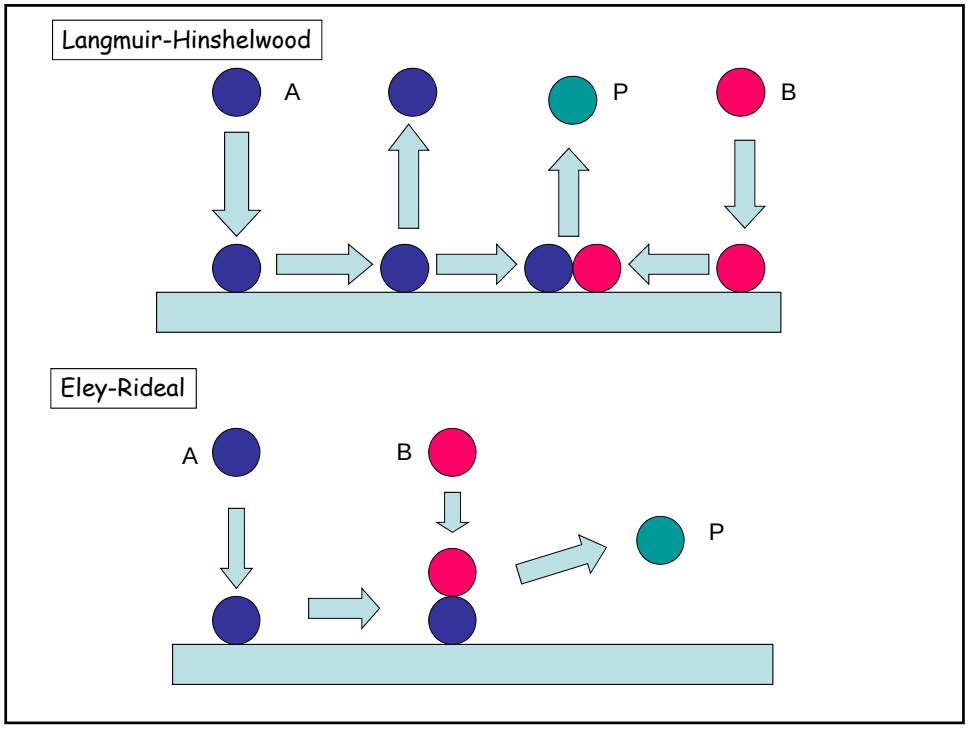
1915
Langmuir
Isotherm

1927
Kinetics of
Catalytic
Reactions



Cyril Norman Hinshelwood
1897 - 1967
Nobel Prize 1956

Irving Langmuir
1881 - 1957
Nobel Prize 1932



Kinetics of surface reactions.

Langmuir-Hinshelwood Mechanism

Unimolecular: single molecular species A adsorbs on surface, reacts and the product P does not adsorb.

$$A(g) \rightarrow A_{ads} \rightarrow P(g)$$

Reaction rate

$$R = k\theta_A$$

Surface coverage of adsorbed gas

$$\theta_A = \frac{K_A p_A}{1 + K_A p_A}$$

Surface coverage related to gas pressure p via Langmuir adsorption isotherm

$$R = \frac{kK_A p_A}{1 + K_A p_A}$$

Example: decomposition of NH_3 on W surfaces. Rate 1st order at low p, while as pressure increases it changes to zero order corresponding to saturation kinetics.

Limiting situations.

High pressures.

$Kp >> 1$

$R \cong k$

Rate independent of Gas pressure p Zero order kinetics.

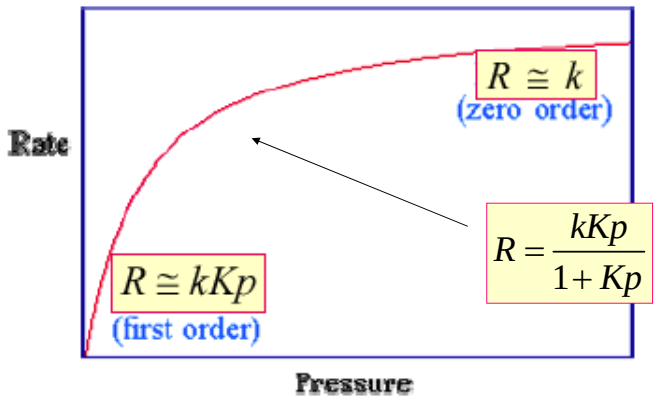
Adsorption rate very large when p is high. Decomposition step rds.

Low pressures.

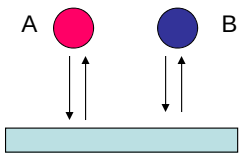
$Kp << 1$

$R \cong kKp$

Rate depends linearly on gas Pressure p First order kinetics. Adsorption process is rate determining when p is low. Decomposition is fast.



Competitive adsorption and bimolecular surface kinetics.



Catalyst surface

2 different gas phase reactants compete for adsorption sites S.

$$A(g) + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} A_{ads}$$

$$B(g) + S \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} B_{ads}$$

$$A_{ads} + B_{ads} \xrightarrow{k} C_{ads}$$

Bimolecular surface reaction

Assuming an adsorption/desorption equilibrium for each gas we get:

$$\frac{\theta_A}{1-\theta_A-\theta_B} = K_A p_A$$

$$\frac{\theta_B}{1-\theta_A-\theta_B} = K_B p_B$$

$$\theta_A = \frac{K_A p_A}{1+K_A p_A + K_B p_B}$$

$$\theta_B = \frac{K_B p_B}{1+K_A p_A + K_B p_B}$$

$$K_A = \frac{k_1}{k_{-1}}$$

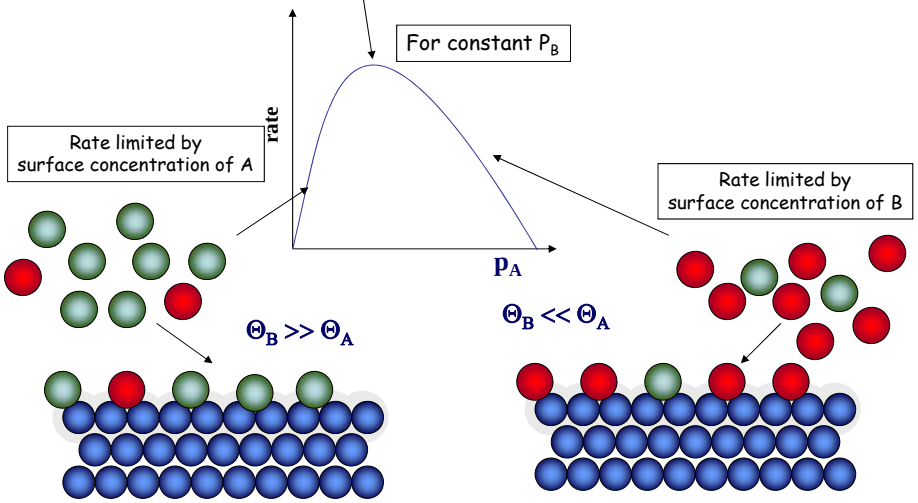
$$K_B = \frac{k_2}{k_{-2}}$$

$$R_\Sigma = \frac{dc}{dt} = k\theta_A\theta_B = \frac{kK_A K_B p_A p_B}{(1+K_A p_A + K_B p_B)^2}$$

LH model bimolecular reaction

$$R_{\Sigma} = \frac{dc}{dt} = k\theta_A\theta_B = \frac{kK_AK_Bp_Ap_B}{(1+K_Ap_A+K_Bp_B)^2}$$

Maximum rate occurs where
$\theta_A = \theta_B = 0.5$

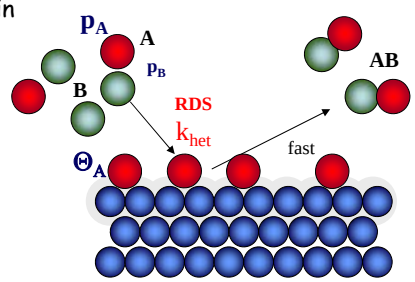


Eley-Rideal Mechanism.

Mechanism describes a surface reaction in which one reactant is adsorbed while the other is in the gas phase.

$$A(g) \rightarrow A_{ads}$$
$$A_{ads} + B(g) \rightarrow P(g)$$

An adsorbed molecule may react directly with an impinging gas molecule by a collisional mechanism



Reaction rate R is dependent on the pressure of B p_B, and the surface coverage of A θ_A.

We assume that B and product P do not competitively bind for surface sites with A.

$$R = k\theta_A p_B = \frac{kK_Ap_Ap_B}{1+K_Ap_A}$$

Rate always 1st order wrt p_B.
2 limiting cases for reaction order wrt p_A.
When K_A (ΔH_{ads}) is small or p_A is small then K_Ap_A <<1 and R = $kK_Ap_Ap_B$.
Rate is 1st order wrt p_A.
When K_A (ΔH_{ads}) is large or p_A is large then K_Ap_A >>1 and R = kp_B.
Rate is zero order wrt p_A.
Competitive adsorption of products can complicate the kinetics.

Diagnosis of mechanism

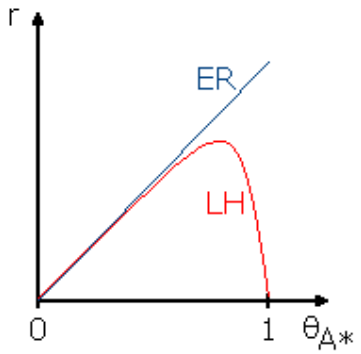
If we measure the reaction rate as a function of the coverage by A, the rate will initially increase for both mechanisms.

Eley-Rideal: rate increases until surface is covered by A.

Langmuir-Hinshelwood: rate passes a maximum and ends up at zero, when surface covered by A.

The reaction B + S ⇔ B-S

cannot proceed when A blocks all sites.



Catalyst Preparation

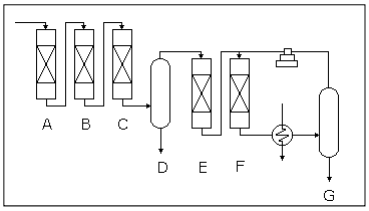
For a catalyst the desired properties are

- high and stable activity
- high and stable selectivity
- controlled surface area and porosity
- good resistance to poisons
- good resistance to high temperatures and temperature fluctuations.
- high mechanical strength
- no uncontrollable hazards

Once a catalyst system has been identified, the parameters in the manufacture of the catalyst are

- If the catalyst should be supported or unsupported.
- The shape of the catalyst pellets. The shape (cylinders, rings, spheres, monoliths) influence the void fraction, the flow and diffusion phenomena and the mechanical strength.
- The size of the catalyst pellets. For a given shape the size influences only the flow and diffusion phenomena, but small pellets are often much easier to prepare.
- Catalyst based on oxides are usually activated by reduction in H_2 in the reactor.

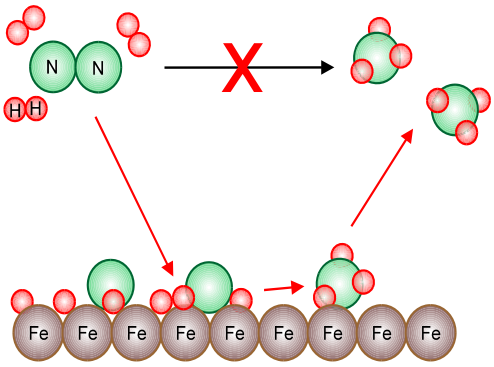
Ammonia synthesis



A: Steam reforming
B: High temperature water-gas shift
C: Low temperature water-gas shift
D: CO_2 absorption
E: Methanation
F: Ammonia synthesis
G: NH_3 separation.

Ammonia Synthesis

$N_2 + 3H_2 \rightarrow 2NH_3$



Fe/K catalyst

exothermic

Mechanism

1	$N_2(g) + *$	⇌	N_2*
2	$N_2* + *$	⇌	$2N*$
3	$N* + H*$	⇌	$NH* + *$
4	$NH* + H*$	⇌	$NH_2* + *$
5	$NH_2* + H*$	⇌	$NH_3* + *$
6	NH_3*	⇌	$NH_3(g) + *$
7	$H_2(g) + 2*$	⇌	$2H*$

Step 2 is generally rate-limiting. Volcano curve is therefore apparent with d-block metals as catalysts.

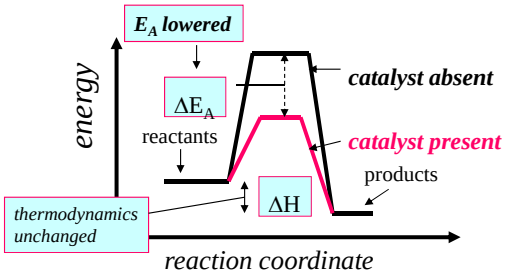
Ru and Os are more active catalysts, but iron is used.

Biocatalysis: Kinetics of enzyme reactions.

Enzymes are very specific biological catalysts.
A catalyst is a substance that increases the rate of a reaction without itself being consumed by the process.

This material is described in most Biochemistry texts.

• A catalyst lowers the Gibbs energy of activation $\Delta G^{\ddagger}$ by providing a different mechanistic pathway by which the reaction may proceed. This alternative mechanistic path enhances the rate of both the forward and reverse directions of the reaction.
• The catalyst forms an intermediate with the reactants in the initial step of the reaction (a binding reaction), and is released during the product forming step.
• Regardless of the mechanism and reaction energetics a catalyst does not effect ΔH or ΔG of the reactants and products. Hence catalysts increase the rate of approach to equilibrium, but cannot alter the value of the thermodynamic equilibrium constant.



A reactant molecule acted upon by an enzyme is termed a substrate. The region of the enzyme where the substrate reacts is called the active site. Enzyme specificity depends on the geometry of the active site and the spatial constraints imposed on this region by the overall structure of the enzyme molecule.

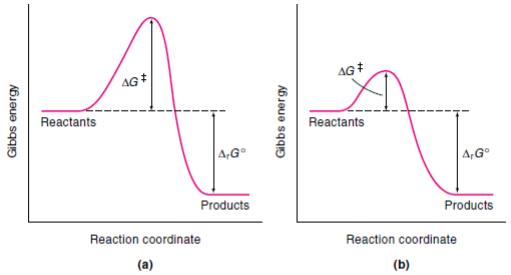


Figure 10.1
Gibbs energy change for (a) an uncatalyzed reaction and (b) a catalyzed reaction. A catalyzed reaction must involve the formation of at least one intermediate (between the reactant and the catalyst). The $\Delta_r G^\circ$ is the same in both cases.

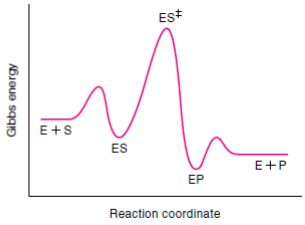
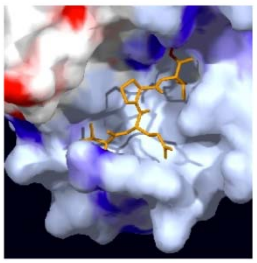


Figure 10.4
Plot of Gibbs energy versus reaction coordinate for an enzyme-catalyzed reaction.

Enzyme reactions - background



- An enzyme is a protein that catalyses a specific (bio)chemical reaction by lowering the activation energy.
- The reactant molecule (the substrate) binds to the active site on the enzyme.
- Binding shifts the substrate geometry closer to that of the transition state for the reaction, lowering the activation energy.

- Enzyme-catalysed reactions are millions of times faster than uncatalyzed reactions, and virtually every chemical reaction in biology requires an enzyme in order to occur at a significant rate.
- Many drugs work by binding to a carefully targeted enzyme in place of the normal substrate, thereby blocking its action.

Enzyme lock/key mechanism : natural molecular recognition.

Space filling models of the two conformations of the enzyme hexokinase. (a) the active site is not occupied. There is a cleft in the protein structure that allows the substrate molecule glucose to access the active site. (b) the active site is occupied. The protein has closed around the substrate.

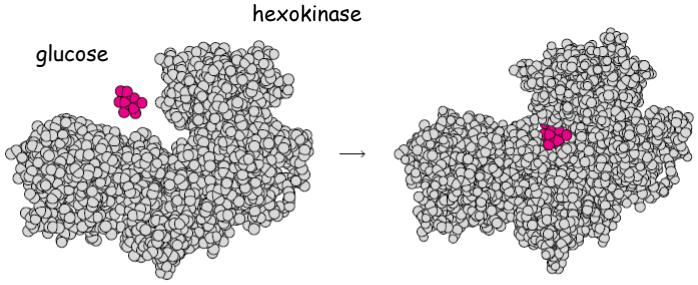
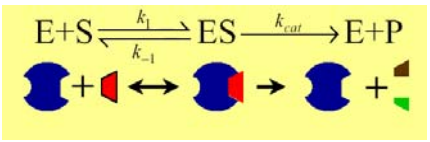


Figure 10.3
The conformational change that occurs when glucose binds to hexokinase, which is an enzyme in the metabolic pathway. [From W. S. Bennet and T. A. Steitz, *J. Mol. Biol.* **140**, 211 (1980).]

Classification of enzymes.



Oxidoreductases	Transfer electrons
Transferases	Transfer functional groups
Hydrolases	Transfer functional groups to water
Lyases	Transfer groups to or from double bonds
Isomerases	Transfer groups within molecules
Ligases	Transfer by joining groups

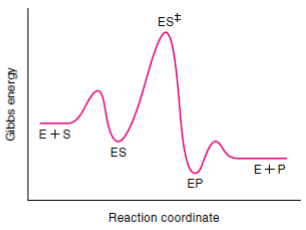


Figure 10.4
Plot of Gibbs energy versus reaction coordinate for an enzyme-catalyzed reaction.

Amperometric Glucose Sensors

- Enzymes are very specific biological catalysts.
- They interact with substrates via the Michaelis/Menten mechanism.
- If enzymes can be incorporated and immobilized within a matrix located next to an electrode surface, then it is possible to combine the specificity of enzyme catalysis with the many advantages of amperometric detection.
- We focus attention of glucose oxidase and the amperometric detection of blood glucose, since the glucose sensor is well developed commercially.

- A. Heller, B. Feldman, Electrochemical glucose sensors and their applications in diabetes management. Chem. Rev. 2008, in press.
- J. Wang, Electrochemical glucose biosensors. Chem. Rev., 108 (2008) 814-825.
- J. Wang, Glucose biosensors: 40 years of advances and challenges. Electroanalysis, 13 (2001) 983-988.
- J. Wang, In vivo glucose monitoring: towards 'sense and act' feedback loop individualized medical systems. Talanta, 75 (2008) 636-641.

Redox enzymes.

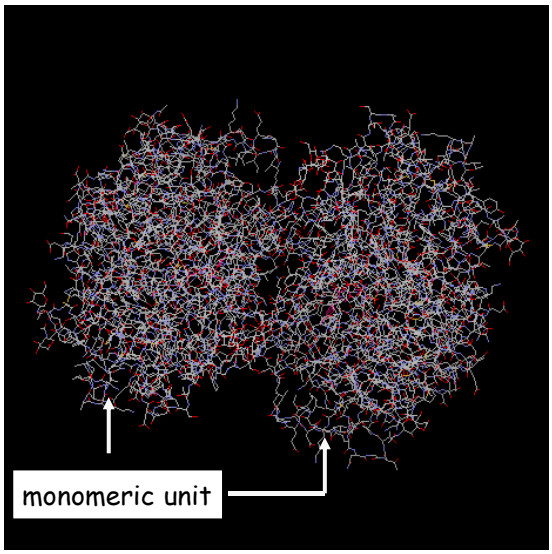
- Redox enzyme contains tightly bound redox active prosthetic group (e.g. flavin, haem, quinone) that remains bound to the protein throughout redox cycle.
  - Prosthetic group = non amino acid component of conjugated protein.
- Redox enzymes exist in both oxidised and reduced forms.
- Redox enzymes can be subclassified in terms of the redox centres present in the enzyme.
- Flavoproteins are most often studied.
- They consist of ca. 80 different enzymes containing either
  - Flavin adenine dinucleotide (FAD)
  - Flavin mononucleotide (FMN)

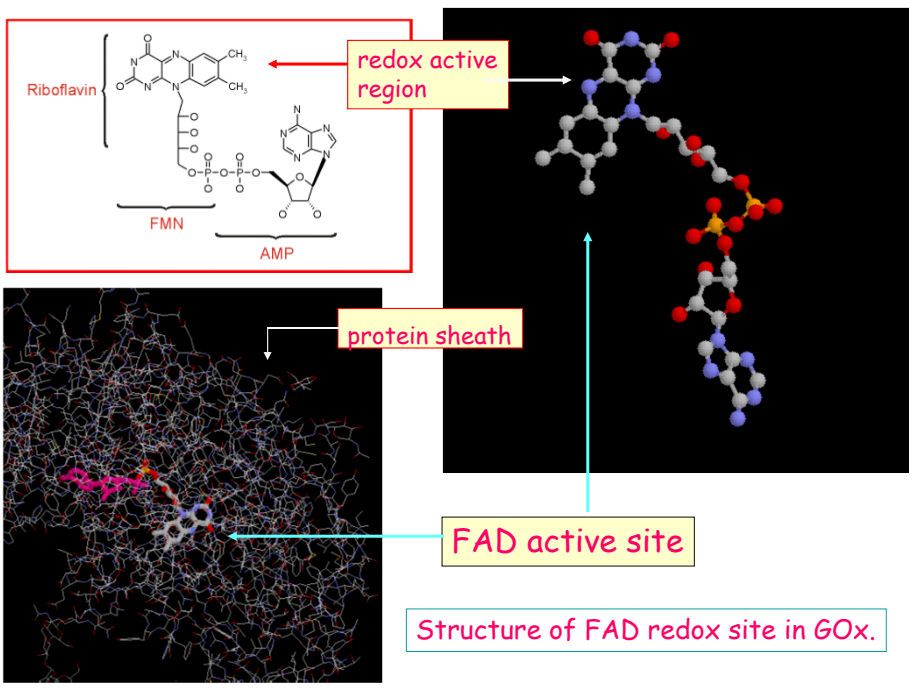
  at the active site.
- The flavin unit is strongly associated with the protein structure and is sometimes covalently bound to the amino acid residues in enzyme.

Dimeric structure of glucose oxidase GOx.

Glucose oxidase
b-D-glucose: oxygen 1-oxidoreductase EC1.1.3.4) : **GOx** .

GOx is a dimeric protein with MW = 160 kDa. Contains one tightly bound flavin adenine dinucleotide FAD unit per monomer as cofactor. FAD is not covalently bound and can be released from the holo protein following denaturation.
FAD exhibits redox activity. Gox exhibits a very high degree of specificity for β-D-glucose.

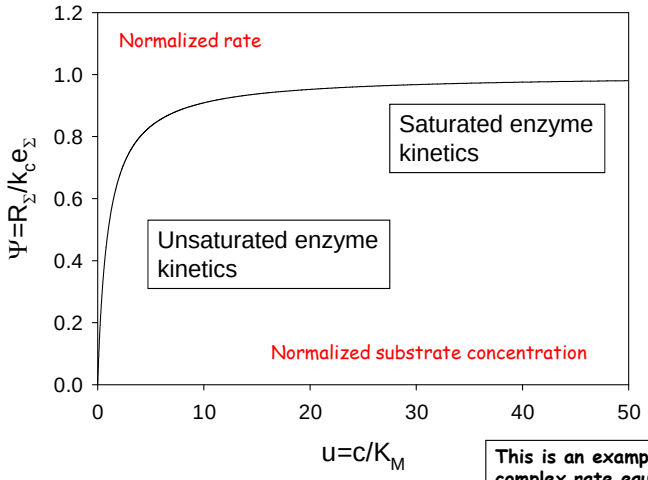




Structure of FAD redox site in GOx.

Enzyme catalysed reaction:
Variation of reaction rate with substrate (reactant) concentration.

Rate variation adopts shape of rectangular hyperbola.



This is an example of a complex rate equation, where the reaction rate varies with reactant concentration in a non linear way.

In electrochemical biosensor output have current (rate) vs substrate concentration.

The relationship between reaction rate and substrate concentration

When an enzyme is first mixed with a large excess of substrate, the initial period, called the pre-steady state, involves build-up of ES.

Within microseconds, the reaction achieves a steady state in which [ES] remains essentially constant over time. The measured V_o generally reflects the steady state - hence the analysis of initial reaction rates under saturating substrate conditions is called **steady-state kinetics**.

Leonor Michaelis
1875–1949

Maud Menten
1879–1960

Enzyme reactions - experimental data

Any kinetic model for enzyme action must explain the following:

- For many enzyme reactions, the rate is found to follow the Michaelis-Menten equation.

$$v = \frac{v_{max}[S]}{K_M + [S]}$$

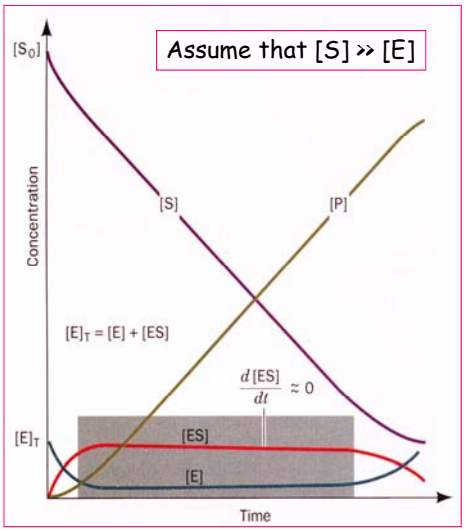
(v_{max}: maximum rate; $[S]$: substrate concentration; K_M: Michaelis constant)

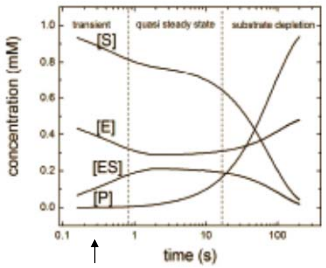
- The maximum rate is found to be proportional to the total concentration of enzyme, [E], even though there is no net change in this quantity over the course of the reaction.

$$v_{max} = k_{cat}[E]_0$$

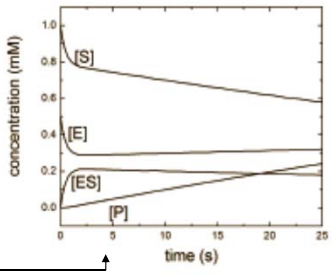
'turnover number' - maximum number of substrate molecules that each enzyme can convert into products per second

Time course of enzyme catalyzed reaction.





Note logarithmic timescale.



Note linear timescale.

Single substrate Michaelis-Menten Kinetics.

Enzyme-substrate complex

Rate

$$v = k_2[\mathrm{ES}]$$

Also termed k_c or turnover number = max number of enzymatic reactions catalyzed per second.

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

Substrate binding | Catalytic step

k_c/K_M measures catalytic efficiency of enzyme. Maximum value corresponds to Diffusion control reaction between S and E in solution (10^{10} $M^{-1}s^{-1}$).

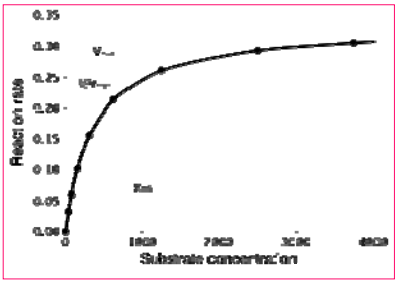
$$\frac{d}{dt}[\mathrm{ES}] = k_1[\mathrm{E}][\mathrm{S}] - k_2[\mathrm{ES}] - k_{-1}[\mathrm{ES}] \approx 0.$$

$$[\mathrm{E}]_{\mathrm{tot}} \stackrel{\mathrm{def}}{=} [\mathrm{E}] + [\mathrm{ES}]$$

$$K_m \stackrel{\mathrm{def}}{=} \frac{k_2 + k_{-1}}{k_1} \approx \frac{[\mathrm{E}][\mathrm{S}]}{[\mathrm{ES}]}$$

$$[\mathrm{ES}] \approx \frac{[\mathrm{E}]_{\mathrm{tot}}[\mathrm{S}]}{[\mathrm{S}] + K_m}$$

$$v = k_2[\mathrm{ES}] = \frac{k_2[\mathrm{E}]_{\mathrm{tot}}[\mathrm{S}]}{[\mathrm{S}] + K_m} = \frac{V_{\max}[\mathrm{S}]}{[\mathrm{S}] + K_m}.$$



Enzyme reactions - trial mechanism

Try a very simple trial mechanism.

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

E = enzyme
S = substrate
ES = enzyme-substrate complex
P = product

Can we use the steady state approximation?

- [ES] is not much less than the reactant concentration [E], so we may think not...
- ....but, because [E] is regenerated in the second step, both [E] and [ES] change much more slowly than [S] and [P], so the SSA is valid and we can apply it to [ES].

$$\frac{d[ES]}{dt} = 0 = k_1[E][S] - k_{-1}[ES] - k_2[ES] \quad \Rightarrow \quad [ES] = \frac{k_1[E][S]}{k_{-1}+k_2}$$

- The total enzyme concentration is $[E]_0 = [E] + [ES]$, so $[E] = [E]_0 - [ES]$.

$$[ES] = \frac{k_1([E]_0-[ES])[S]}{k_{-1}+k_2} \quad \Rightarrow \quad [ES] = \frac{k_1[E]_0[S]}{k_{-1}+k_2+k_1[S]}$$

Enzyme reactions - trial mechanism

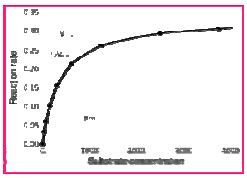
$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} P + E \qquad [ES] = \frac{k_1[E]_0[S]}{k_{-1}+k_2+k_1[S]}$$

- The overall rate of formation of products is then

$$\nu = \frac{d[P]}{dt} = k_2[ES] = \frac{k_2k_1[E]_0[S]}{k_{-1}+k_2+k_1[S]}$$

- If we define

$$K_M = \frac{k_2+k_{-1}}{k_1}$$



then we can write the rate as

$$\nu = \frac{k_2[S][E]_0}{K_M+[S]} = k\,[E]_0 \quad \text{with} \quad k = \frac{k_2[S]}{K_M+[S]}$$

- Our mechanism predicts the Michaelis-Menten equation, with $k_2 = k_{cat}$.

Enzyme reactions - analysis of the Michaelis-Menten equation

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} P + E \qquad \nu = \frac{k_2[S][E]_0}{K_M+[S]} = k\,[E]_0 \quad \text{with} \quad k = \frac{k_2[S]}{K_M+[S]}$$

- Rate of enyzyme-catalysed reaction depends linearly on [E], and in a more complicated way on [S]. This dependence simplifies in two cases:

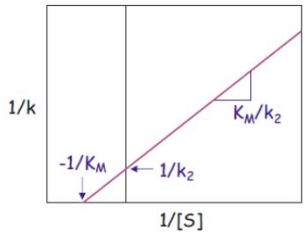
1. $[S] \ll K_M$
   - The rate is $\nu = (k_2/K_M)[E]_0[S]$, and the rate is first order in both [E] and [S].
2. $[S] \gg K_M$
   - The rate is $\nu = k_2[E]_0 = k_{cat}[E]_0$ and is independent of [S]
   - There is so much substrate present that [S] is essentially constant, the enzyme is saturated with substrate and the rate is a maximum, $\nu = \nu_{max}$.

Enzyme reactions - rate constants from experimental data

- We can rewrite our expression for the rate constant by inverting it.

$$k = \frac{k_2[S]}{K_M+[S]} \quad \Rightarrow \quad \frac{1}{k} = \frac{K_M}{k_2[S]} + \frac{1}{k_2}$$

- A plot of 1/k against 1/[S] (a Lineweaver-Burke plot) has a slope of K_M/k_2 and an intercept of $1/k_2$.



k_2/K_M measures catalytic efficiency of enzyme. Maximum value corresponds to Diffusion control reaction between S and E in solution (10^{10} $M^{-1}s^{-1}$).

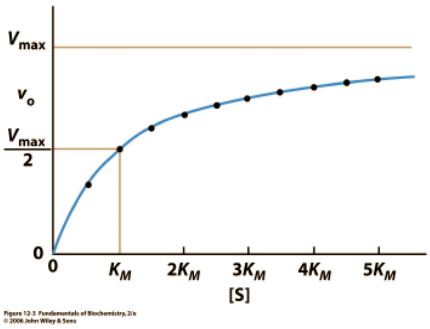
- Usually use the initial rates method to measure k to prevent complications due to secondary reactions of the products.

Note: Biochemistry texts use v as symbol for reaction rate (velocity).

$$v = k_2[\mathrm{ES}] = \frac{k_2[\mathrm{E}]_{\mathrm{tot}}[\mathrm{S}]}{[\mathrm{S}] + K_m} = \frac{V_{\max}[\mathrm{S}]}{[\mathrm{S}] + K_m}$$

$$v = \frac{V_{\max}[\mathrm{S}]}{K_m + [\mathrm{S}]}$$

$$\frac{1}{v} = \frac{K_m}{V_{\max}[\mathrm{S}]} + \frac{1}{V_{\max}}$$



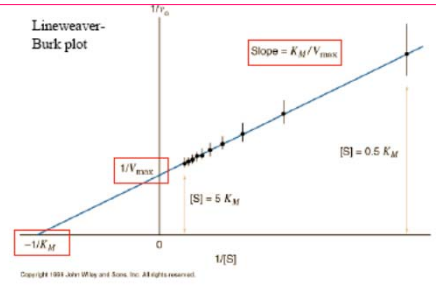


TABLE 6–7 Turnover Numbers, k_{cat}, of Some Enzymes

Enzyme	Substrate	k_{cat} (s^{-1})
Catalase	H_2O_2	40,000,000
Carbonic anhydrase	HCO_3^-	400,000
Acetylcholinesterase	Acetylcholine	14,000
β-Lactamase	Benzylpenicillin	2,000
Fumarase	Fumarate	800
RecA protein (an ATPase)	ATP	0.4

TABLE 6–8 Enzymes for Which k_{cat}/K_m Is Close to the Diffusion-Controlled Limit (10^8 to 10^9 $M^{-1}s^{-1}$)

Enzyme	Substrate	k_{cat} (s^{-1})	K_m (M)	k_{cat}/K_m ($M^{-1}s^{-1}$)
Acetylcholinesterase	Acetylcholine	1.4×10^4	9×10^{-5}	1.6×10^8
Carbonic anhydrase	CO_2	1×10^6	1.2×10^{-2}	8.3×10^7
	HCO_3^-	4×10^5	2.6×10^{-2}	1.5×10^7
Catalase	H_2O_2	4×10^7	1.1×10^0	4×10^7
Crotonase	Crotonyl-CoA	5.7×10^3	2×10^{-5}	2.8×10^8
Fumarase	Fumarate	8×10^2	5×10^{-6}	1.6×10^8
	Malate	9×10^2	2.5×10^{-5}	3.6×10^7
β-Lactamase	Benzylpenicillin	2.0×10^3	2×10^{-5}	1×10^8

Source: Fersht, A. (1999) *Structure and Mechanism in Protein Science*, p. 166, W. H. Freeman and Company, New York.

Competitive Inhibition

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In classical competitive inhibition the inhibitor occupies the active site on the enzyme, blocking out the substrate. If the enzyme has already bound with a substrate the inhibitor is blocked out. Hence the inhibitor species I reacts with the free enzyme E but not with the enzyme- substrate complex ES. Hence both Substrate S and inhibitor I compete for same active site.

Net rate equation (Derived using QSSA)

$$R_\Sigma = \frac{k_c [E]_\Sigma [S]}{K_M \{1 + [I]/K_I\} + [S]}$$

$$E + S \rightleftharpoons ES \rightarrow E + P$$
$$E + I \rightleftharpoons EI$$

EI does not react with S to form Products.

$$\frac{1}{R_\Sigma} = \frac{1}{(k_c/K_M)[E]_\Sigma}\{1 + [I]/K_I\}\frac{1}{[S]} + \frac{1}{k_c[E]_\Sigma}$$

$$\frac{R_\Sigma}{R_{\Sigma,inh}} = 1 + \frac{K_M[I]}{K_M K_I + K_I[S]} \xrightarrow{\text{large } [S]} 1 + \frac{K_M[I]}{K_I[S]} \cong 1$$

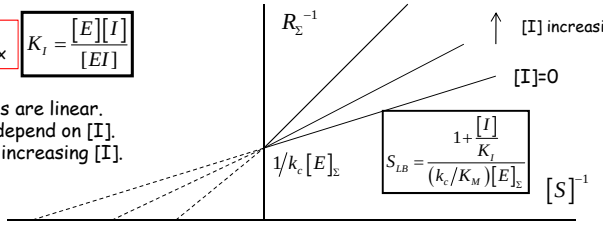
Total enzyme concentration

$$[E]_\Sigma = [E] + [ES] + [EI] + [ESI]$$

To overcome competitive inhibition we need to increase [S] relative to [I].

Equilibrium constant for dissociation of EI complex

$$K_I = \frac{[E][I]}{[EI]}$$



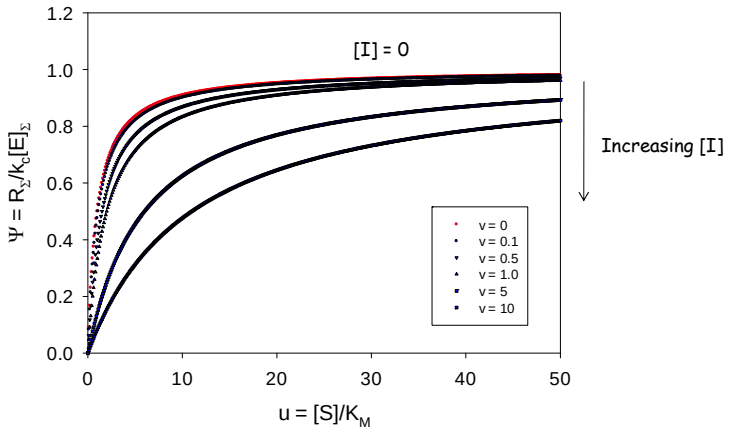
Lineweaver-Burk Plots are linear.
Slope and intercept depend on [I].
Slope increases with increasing [I].

Net rate equation

Competitive Inhibition

$$u = \frac{[S]}{K_M} \quad v = \frac{[I]}{K_I} \quad \Psi = \frac{R_\Sigma}{k_c[E]_\Sigma} = \frac{R_\Sigma}{R_{\max}}$$

$$\Psi = \frac{u}{1+u+v}$$



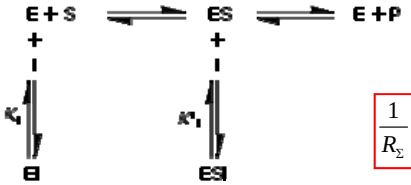
Noncompetitive Inhibition

A noncompetitive inhibitor binds to the enzyme at a site that is distinct from the substrate binding site; therefore it can bind to both the free enzyme and the enzyme/substrate complex. The enzyme's function is inhibited by inhibitor binding by perturbing the 3-D structure of the protein so that the active site does not catalyze the substrate reaction.
Inhibition occurs both at E and ES sites, and S and I bind independently to E. Because I does not interfere with ES formation, noncompetitive inhibition cannot be reversed by increasing substrate concentration.

Net rate equation (Derived via QSSA)

$$R_\Sigma = \frac{k_c[E]_\Sigma[S]}{(K_M+[S])\{1+[I]/K_I\}} = \frac{\frac{k_c[E]_\Sigma}{(1+[I]/K_I)}[S]}{K_M+[S]}$$

Note that $R_m = k_c[E]_\Sigma$ is reduced by the factor $(1+[I]/K_I)$ but K_M is unchanged.



$$\frac{1}{R_\Sigma} = \frac{1}{k_c[E]_\Sigma/K_M}\{1+[I]/K_I\}\frac{1}{[S]} + \frac{1}{k_c[E]_\Sigma}\{1+[I]/K_I\}$$

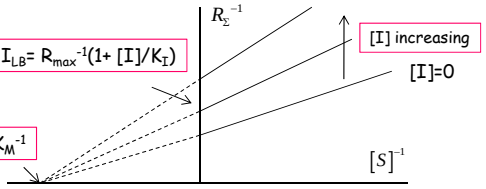
$$E+S \rightleftharpoons ES \rightarrow E+P$$
$$E+I \rightleftharpoons EI$$
$$ES+I \rightleftharpoons ESI$$

$$\frac{R_\Sigma}{R_{\Sigma,inh}} = 1+[I]/K_I$$

$I_{LB} = R_{max}^{-1}(1+[I]/K_I)$

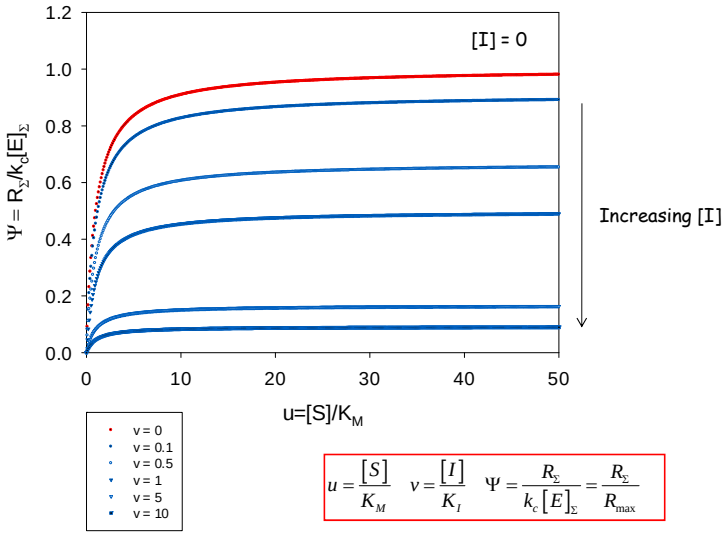
$$K_I = \frac{[E][I]}{[EI]} \qquad K_I' = \frac{[ES][I]}{[ESI]} \qquad K_I = K_I'$$

$-K_M^{-1}$



Non competitive Inhibition

$$\Psi = \frac{u}{(1+u)(1+v)}$$



$$u = \frac{[S]}{K_M} \quad v = \frac{[I]}{K_I} \quad \Psi = \frac{R_\Sigma}{k_c[E]_\Sigma} = \frac{R_\Sigma}{R_{max}}$$

Uncompetitive Inhibition

In uncompetitive inhibition the inhibitor I binds to the ES complex only to form the adduct ESI.
Inhibition occurs because ESI reduces concentration of active adduct ES. Because I does not interfere with the formation of ES, uncompetitive inhibition cannot be reversed by increasing substrate concentration.

$$E + S \rightleftharpoons ES \rightarrow E + P$$
$$ES + I \rightleftharpoons ESI$$

$$K'_I = \frac{[ES][I]}{[ESI]}$$

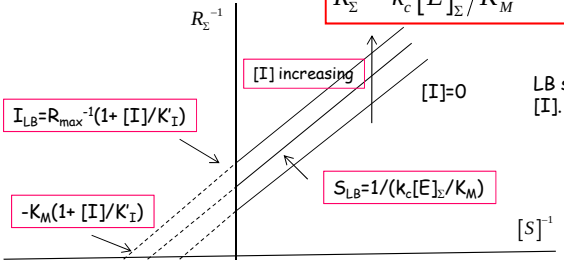
Equilibrium constant for dissociation of ESI complex

Net rate equation (QSSA)

$$R_\Sigma = \frac{k_c[E]_\Sigma[S]}{K_M + \{1+[I]/K'_I\}[S]} = \frac{\frac{k_c[E]_\Sigma}{(1+[I]/K'_I)}[S]}{\frac{K_M}{(1+[I]/K'_I)} + [S]}$$

Both K_M and $R_{max}=k_c[E]_\Sigma$ are reduced by the factor $1+K_I[I]$.

$$\frac{1}{R_\Sigma} = \frac{1}{k_c[E]_\Sigma/K_M}[S]^{-1} + \frac{1}{k_c[E]_\Sigma}\left\{1+\frac{[I]}{K'_I}\right\}$$

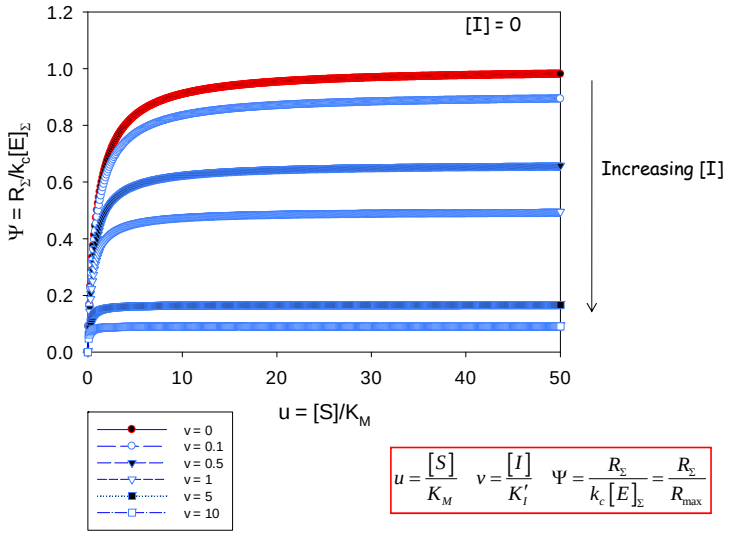


LB slope independent of [I].

Uncompetitive Inhibition

$$R_\Sigma = \frac{k_c[E]_\Sigma[S]}{K_M + \{1+[I]/K_I'\}[S]} = \frac{\frac{k_c[E]_\Sigma}{(1+[I]/K_I')}[S]}{\frac{K_M}{(1+[I]/K_I')}+[S]}$$

$$\Psi = \frac{u}{1+u(1+v)}$$



$$u = \frac{[S]}{K_M} \quad v = \frac{[I]}{K_I'} \quad \Psi = \frac{R_\Sigma}{k_c[E]_\Sigma} = \frac{R_\Sigma}{R_{max}}$$

Very useful chapter on enzyme kinetics. www.uscibooks.com/changten.pdf

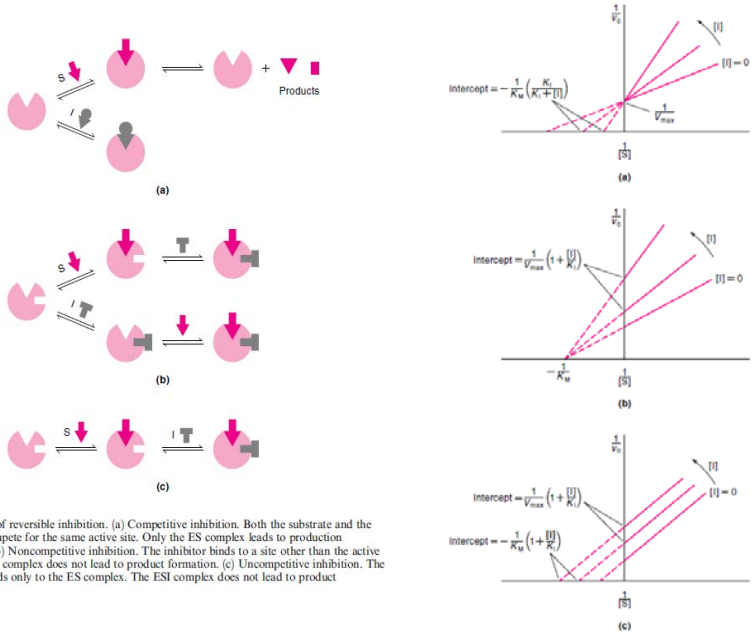


Figure 10.13
Three types of reversible inhibition. (a) Competitive inhibition. Both the substrate and the inhibitor compete for the same active site. Only the ES complex leads to production formation. (b) Noncompetitive inhibition. The inhibitor binds to a site other than the active site. The ESI complex does not lead to product formation. (c) Uncompetitive inhibition. The inhibitor binds only to the ES complex. The ESI complex does not lead to product formation.