

CHEMICAL KINETICS

Chemical kinetics is the study of the rates of chemical reactions, the factors that affect these rates, and the reaction mechanisms by which the reactions occur.

Chemical Reaction Rate

This is the change in concentration of a product per unit of time (rate of formation of product). Also it can be viewed as negative change in the concentration of reactant per unit time (rate of disappearance of reactant).



$$rate = -\frac{d[A]}{dt} = \frac{d[B]}{dt}$$



$$rate = -\left[\frac{1}{a} * \frac{d[A]}{dt}\right] = \left[\frac{1}{b} * \frac{d[B]}{dt}\right]$$

Unit of rate of reaction = MS^{-1} or $ML^{-1}S^{-1}$

Factors that Affect Reaction Rates

1. Concentration of reactants- the rate of reaction increases as the concentration of reactant increases.
2. Temperature- reaction rates increase rapidly as temperature increases.
3. Surface area- as surface area increases, reaction rate increases.
4. Catalysts- speed up reaction rate by decreasing the activation energy.
5. Inhibitors- slow down the rate of chemical reaction.
6. Pressure- this affects the rate of chemical reaction in a gaseous phase.

Rate Law of Chemical Reaction

This is a mathematical expression that relates that rate of reaction to the concentrations of reactants.



$$\text{Rate law} = k[A]^m[B]^n$$

k = rate constant, it is the ratio of rate of reaction to concentration of reactant.

m and n- are reaction orders derived from experimental analysis; they are not stoichiometric coefficients.

Order of Chemical Reaction

This is the sum of powers of concentrations of reactants in rate law expression. The values can be:

- Zero- concentration of reactants does not affect the rate of reaction.
- Negative integer value- concentration of reactant is inversely proportional to rate of reaction.
- Positive integer value- concentration of reactants is directly proportional to the rate of reaction.
- Fractional integer value- indicates a complex relationship between the reactant concentration and the rate.

Types of Reaction Orders

1. Zero order- reaction does not depend on the concentration of reactants. It means change in the concentration of reactants does not affect the rate of reaction.
 $R = k$
2. First order reaction- rate depends on the concentration of one of the reactants.
 $R = k[A]$ or $R = k[B]$
3. Second order reaction- rate depends on the concentrations of two different reactants or square of concentration of one reactant.

$$R = k[A][B] \text{ or } R = k[A]^2$$

4. Third order- rate depends on the concentrations of three reactants.

$$R = k[A][B][C] \text{ or } R = [A][B]^2 \text{ or } R = [A]^2[B]$$

Overall Order of Reaction

This is the sum of individual orders in a chemical reaction.

$$R = k[A][B]^{1/2}[C]^2 \text{ Overall order} = 1 + \frac{1}{2} + 2 = 3.5 = \frac{7}{2} \text{ seven-half order}$$

Units of k of Reaction Orders

$$R = k[\text{Conc.}]$$

$$R = k = \text{MS}^{-1} \quad \text{Zero order}$$

$$k = \frac{R}{\text{conc.}} = \frac{\text{MS}^{-1}}{\text{M}} = \text{S}^{-1} \quad \text{First order}$$

$$k = \frac{R}{\text{conc.}} = \frac{\text{MS}^{-1}}{\text{M}^2} = \text{M}^{-1}\text{S}^{-1} \quad \text{Second order}$$

$$k = \frac{R}{\text{conc.}} = \frac{\text{MS}^{-1}}{\text{M}^3} = \text{M}^{-2}\text{S}^{-1} \quad \text{Third order}$$

Reaction Mechanism

This is the step by step sequence of elementary reactions by which overall chemical process occurs. A mechanism describes in details exactly what takes place at each of an overall transformation. It also describes each reaction intermediate, activated complex, transition state and which bonds are broken and formed.

Rate Limiting Step

This is the crucial step in establishing the rate of the overall in biological system.

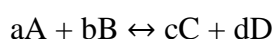
CHEMICAL EQUILIBRIUM

Chemical equilibrium refers to a state in which the rates of forward and reverse reactions are equal and the concentrations of the reactants and products remain constant.

Equilibrium is a dynamic process- the conversion of reactants to products and products to reactants are still going on, although there is no net change in the number of reactant and product,

Equilibrium Constant

The equilibrium constant, K_c , is the ratio of the equilibrium concentrations of products over the equilibrium concentrations of reactants each raised to the power of their stoichiometric coefficient.



$$\frac{[C]^c [D]^d}{[A]^a [B]^b} = K_c$$

K_c - remains the same

K_c - does not depend on the temperature

K_c - does not depend on the initial concentrations of reactants and products.

Information from K_c

It shows the direction of chemical reaction

- If K_c value is large ($K_c \gg 1$); the equilibrium lies to the right and the reaction mixture contains mostly products.
- If K_c value is small ($K_c \ll 1$); the equilibrium lies to the left and the reaction mixture contains mostly reactants.
- If K_c value is 1, the mixture contains appreciable amounts of both reactants and product. This implies equilibrium state.

Factors that Affect Chemical Equilibrium

Le Chatelier's principle: If a system at equilibrium is disturbed by external stress/constraints, the system adjusts to partially offset the stress as the system attains new equilibrium position.

These external constraints are: concentration, temperature, pressure, volume, catalyst

THERMODYNAMICS

This studies the energy flow, heat and movement, in structures among the universe. When the study concerns a living system, i.e. a cell, it is usual to refer to open system thermodynamics or non-equilibrium thermodynamics. That is mainly because the concepts of flow, growth and change are not static, not in equilibrium.

Laws of thermodynamics

First law states that for any physical or chemical change, the total amount of energy in the universe remains constant; energy may change form or it may be transported from one region to another, but it cannot be created or destroyed.

The second law states that in all natural processes, the entropy of the universe increases.

The reacting system is the collection of matter that is undergoing a particular chemical or physical process; it may be an organism, a cell, or two reacting compounds. The reacting system and its surroundings together constitute the universe.

Definition of three thermodynamic quantities that describe the energy changes occurring in a chemical reaction:

Gibbs free energy, G , expresses the amount of energy capable of doing work during a reaction at constant temperature and pressure. When a reaction proceeds with the release of free energy (that is, when the system changes so as to possess less free energy), the free-energy change, ΔG , has a negative value and the reaction is said to be **exergonic**. In **endergonic** reactions, the system gains free energy and ΔG is positive.

ΔG is a measure of how far a chemical reaction is from equilibrium.
 ΔG represents the amount of work that can be done by a chemical reaction.

You get more useful work (ΔG) out of a chemical reaction if it is far from equilibrium.

| | | |
|----------------------|----------------|---|
| | $\Delta G = 0$ | Reaction is at equilibrium, and the concentrations of products and reactants equal the equilibrium concentrations. |
| Exergonic reaction: | $\Delta G < 0$ | Reaction happens in the direction written. Reactant concentrations are <i>higher</i> than the equilibrium concentration. |
| Endergonic reaction: | $\Delta G > 0$ | Reaction happens in the direction opposite to that written. Product concentrations are higher than the equilibrium concentration. |

$$\Delta G = \Delta G^0 + RT \ln \frac{[P][Q]}{[A][B]}$$

Enthalpy, H , is the heat content of the reacting system. It reflects the number and kinds of chemical bonds in the reactants and products. When a chemical reaction releases heat, it is said to be **exothermic**; the heat content of the products is less than that of the reactants and ΔH has, by convention, a negative value. Reacting systems that take up heat from their surroundings are **endothermic** and have positive values of ΔH .

Entropy, S , is a quantitative expression for the randomness or disorder in a system. When the products of a reaction are less complex and more disordered than the reactants, the reaction is said to proceed with a gain in entropy.

The units of ΔG and ΔH are joules/mole or calories/mole (recall that 1 cal = 4.184 J); units of entropy are joules/mole .Kelvin (J/mol.K)

Under the conditions existing in biological systems (including constant temperature and pressure), changes in free energy, enthalpy, and entropy are related to each other quantitatively by the equation

$$\Delta G = \Delta H - T \Delta S$$

Sources of Free Energy

Heterotrophic cells acquire free energy from nutrient molecules, and photosynthetic cells acquire it from absorbed solar radiation. Both kinds of cells transform this free energy into ATP and other energy-rich compounds capable of providing energy for biological work at constant temperature.

Relationship between Standard Free-Energy Change and Equilibrium Constant

At the equilibrium concentration of reactants and products, the rates of the forward and reverse reactions are exactly equal and no further net change occurs in the system. The concentrations of reactants and products *at equilibrium* define the equilibrium constant, K_{eq} . In the general reaction $aA + bB \leftrightarrow cC + dD$, where a , b , c , and d are the number of molecules of A, B, C, and D participating, the equilibrium constant is given by

$$K_{eq} = \frac{[C]^c [D]^d}{[A]^a [B]^b}$$

$$\Delta G'^{\circ} = -RT \ln K_{eq}^{\circ}$$

Difference between $\Delta G'^{\circ}$ and ΔG ,

The standard transformed free-energy change, $\Delta G'^{\circ}$, is a physical constant that is characteristic for a given reaction and can be calculated from the equilibrium constant for the reaction:

$$\Delta G'^{\circ} = -RT \ln K_{eq}^{\circ}$$

The actual free-energy change, ΔG , is a variable that depends on $\Delta G'^{\circ}$ and on the concentrations of reactants and products:

$$\Delta G = \Delta G'^{\circ} + RT \ln ([\text{products}]/[\text{reactants}]).$$

When ΔG is large and negative, the reaction tends to go in the forward direction; when ΔG is large and positive, the reaction tends to go in the reverse direction; and when $\Delta G = 0$, the system is at equilibrium.

The criterion for spontaneity of a reaction is the value of ΔG , not $\Delta G'^{\circ}$. A reaction with a positive $\Delta G'^{\circ}$ can go in the forward direction *if ΔG is negative*. This is possible if the term $RT \ln ([\text{products}]/[\text{reactants}])$ in equation above is negative and has a larger absolute value than $\Delta G'^{\circ}$.

The free-energy change for a reaction is independent of the pathway by which the reaction occurs; it depends only on the nature and concentration of the initial reactants and the final products. Enzymes cannot, therefore, change equilibrium constants; but they can and do increase the *rate* at which a reaction proceeds in the direction dictated by thermodynamics.

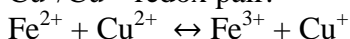
OXIDATION-REDUCTION REACTIONS

These reactions involve the loss of electrons by one chemical species, which is thereby oxidized, and the gain of electrons by another, which is reduced. The electron-donating molecule in an oxidation-reduction reaction is called the reducing agent or reductant; the electron-accepting molecule is the oxidizing agent or oxidant. The flow of electrons in oxidation-reduction reactions is responsible, directly or indirectly, for all work done by living organisms. In non-photosynthetic organisms, the sources of electrons are reduced compounds (foods); in photosynthetic organisms, the initial electron donor is a chemical species excited by the absorption of light.

Electrons move from various metabolic intermediates to specialized electron carriers (such as NADH, NADPH, FMN and FADH₂) in enzyme-catalyzed reactions. The carriers in turn donate electrons to acceptors with higher electron affinities, with the release of energy. Cells contain a variety of molecular energy transducers, which convert the energy of electron flow into useful work.

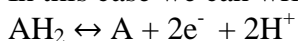
Electrons are transferred from one molecule (electron donor) to another (electron acceptor) in one of four different ways:

1. Directly as electrons. For example, the Fe²⁺/Fe³⁺ redox pair can transfer an electron to the Cu⁺/Cu²⁺ redox pair:



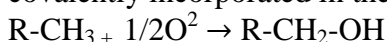
2. As hydrogen atoms. Recall that a hydrogen atom consists of a proton (H⁺) and a single electron (e⁻).

In this case we can write the general equation



3. As a hydride ion (:H⁻), which has two electrons. This occurs in the case of NAD-linked dehydrogenases, described below.

4. Through direct combination with oxygen. In this case, oxygen combines with an organic reductant and is covalently incorporated in the product, as in the oxidation of a hydrocarbon to an alcohol:



The hydrocarbon is the electron donor and the oxygen atom is the electron acceptor.

OXIDO-REDUCTASES

Enzymes involved in oxidation and reduction are called **oxidoreductases** and are classified into four groups: **oxidases, dehydrogenases, hydroperoxidases, and oxygenases.**

OXIDASES- use Oxygen as a Hydrogen Acceptor

Oxidases catalyze the removal of hydrogen from a substrate using oxygen as a hydrogen acceptor. They form water or hydrogen peroxide as a reaction product.

Examples of oxidases include: Cytochrome oxidase, Flavoprotein enzymes contain flavin mononucleotide (FMN) or flavin adenine dinucleotide (FAD) as prosthetic groups. Examples of flavoprotein oxidases include L-amino acid oxidase, an FMN-linked enzyme found in kidney with general specificity for the oxidative deamination of the naturally occurring L-amino acids; xanthine oxidase, which contains molybdenum and plays an important role in the conversion of purine bases to uric acid and aldehyde dehydrogenase, an FAD-linked enzyme present in mammalian livers, which contains molybdenum and non-haem iron and acts upon aldehydes and N-heterocyclic substrates.

DEHYDROGENASES- cannot use oxygen as a hydrogen acceptor

There are a large number of enzymes in this class. They perform two main functions:

(1) Transfer of hydrogen from one substrate to another in a coupled oxidation-reduction reaction

(2) As components in the **respiratory chain** of electron transport from substrate to oxygen

Some of these dehydrogenases use **nicotinamide adenine dinucleotide (NAD⁺)** or **nicotinamide adenine dinucleotide phosphate (NADP⁺)** whereas **others depend on** the flavin groups similar to FMN and FAD occurring in oxidases.

HYDROPEROXIDASES- use hydrogen peroxide or an organic peroxide as substrate

Two types of enzymes found both in animals and plants fall into this category: **peroxidases** and **catalase**.

Hydroperoxidases protect the body against harmful peroxides. Accumulation of peroxides can lead to generation of free radicals, which in turn can disrupt membranes and perhaps cause cancer and atherosclerosis. Peroxidases reduce peroxides using various electron acceptors; catalase uses hydrogen peroxide as electron donor & electron acceptor

OXYGENASES- catalyze the direct transfer & incorporation of oxygen into a substrate molecule

Oxygenases are concerned with the synthesis or degradation of many different types of metabolites. They catalyze the incorporation of oxygen into a substrate molecule in two steps: (1) oxygen is bound to the enzyme at the active site, and (2) the bound oxygen is reduced or transferred to the substrate. Oxygenases may be divided into two subgroups, as follows.

- **Dioxygenases incorporate both atoms of molecular oxygen into the substrate eg Homogentisate dioxygenase (oxidase) and 3-hydroxyanthranilate dioxygenase (oxidase),**
- **Monooxygenases (mixed-function oxidases, hydroxylases) incorporate only one atom of molecular oxygen into the substrate**
- **Cytochromes P450 are monooxygenases important for the detoxification of many drugs and for the hydroxylation of steroids. Both NADH and NADPH donate reducing equivalents for the reduction of these cytochromes, which in turn are oxidized by substrates in a series of enzymatic reactions collectively known as the hydroxylase cycle.**