SOLUBILITY OF DRUG

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INTRODUCTION

- Slow absorption leading to inadequate bioavailability

- Solubility of a compound depends on the physical and chemical properties of the components

- A solute is any substance which can be either solid or liquid or gas dissolved in a solvent. For ex. Sodium Chloride, Sugar.

- A solvent is a substance that dissolves a solute. The solvent is the component of a solution that is present in higher concentration. For ex. Water, Ethanol.

DEFINITION

- Solubility can be defined in two ways

     quantitative way

     qualitative way.

- Quantitatively solubility is defined as the maximum amount of a substance that will dissolve in a given amount of solvent at a specified temperature.

- Qualitatively solubility can be defined as spontaneous interaction between solute and solvent to form homogeneous solution.

- Solubility is usually expressed as grams of solute per litre of solvent.

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SOLUTION

- **Solution:** The homogeneous mixture formed after mixing of solute and solvent. It can also be termed as molecular dispersion. For ex. Solution of sugar in water.

Solute   Solvent   Solution

SOLUTION (continued)

- **Types of Solution:**

  - Depending upon the dissolution of the solute in the solvent

  i) Saturated Solution: These are the solution in which a solvent is not capable of dissolving any more solute at a given temperature.

  ii) Unsaturated solution: In this type of solution a solvent is capable of dissolving any more solute at a given temperature.

  iii) Supersaturated Solution: Supersaturated solution is defined as solution which contains more amount of solute than saturated solution.

  - Depending upon physical state of solute and solvent

  i) Homogeneous solutions are solutions with uniform composition and properties throughout the solution.

  ii) Heterogeneous solutions are solutions with non-uniform composition and properties throughout the solution.

SOLUBILITY EXPRESSION

- **Qualitatively** USP gives solubility as part of solvents required to dissolve one part of solute.

Solubility expression	Part of solvent required to dissolve one part of solute
Very soluble	Less than 1 part
Freely soluble	1 to 10 parts
Soluble	10 to 30 parts
Sparingly soluble	30 to 100 parts
Slightly soluble	100 to 1000 parts
Very slightly soluble	1000 to 10,000 parts
Insoluble or practically insolule	More than 10,000 parts

- **Quantitatively** solubility can be expressed by using following terms Molarity, Normality, Molality, Mole fraction, Mole percent, Percent by Weight, Percent by Volume, Percent weight-in volume, Milligram percent

BIOPHARMACEUTICAL CLASSIFICATION SYSTEM

- **Using solubility and permeability**

Class 1: High permeability - High solubility Drugs

The drugs of this class exhibit high absorption number and high dissolution number.

Class 2: High permeability - Low solubility Drugs

The drugs of this class have a high absorption number but a low dissolution number.

Class 3: Low permeability - High solubility Drugs

These drugs exhibit a high variation in the rate and extent of drug absorption. If the formulation does not change the permeability or gastrointestinal duration time, then Class I criteria can be applied.

Class 4: Low permeability - Low solubility Drugs

These compounds have poor bioavailability. They are usually not well absorbed through the intestinal mucosa, and a high variability is expected.

SOLUTE SOLVENT INTERACTION

- Dissolution and phase joining.
- Solubility is a characteristic property of a specific solute–solvent interaction.
- "like dissolves like"
- The intermolecular interaction between the solvent and the solute molecules.

Solute A	Solvent B	Interaction			Solubility of A in B
		A-A	B-B	A-B	
Nonpolar	Nonpolar	weak	weak	weak	Highly soluble
Nonpolar	Polar	weak	strong	weak	Sparingly soluble
Polar	Nonpolar	strong	weak	weak	Sparingly soluble
Polar	Polar	strong	strong	strong	Highly soluble

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SOLUTE SOLVENT INTERACTION

(continued)

- On the basis of the types of forces that may be dominant in solute-solvent interaction, solvents may be divided into three families.

- **Protic solvent or Polar Solvent:** Protic solvents (like water) have dipole moments, thus enabling them to dissolve polar solutes i.e. ionic compounds, covalent compounds which ionize, organic and inorganic salts.

- **Dipolar aprotic solvents:** They have no protons to be involved in hydrogen bonding neverthless, their lone pairs can act as hydrogen bond acceptors in any hydrogen bond formation between solvent and solute and they can take part in donor-acceptor (charge transfer) complex formation.

- **Aprotic solvents:** Apolar aprotic solvents have low dipole moments and dielectric constants, hence they cannot dissolve polar or ionic solutes. These solvents dissolve Apolar aprotic compounds by keeping them in solution by forces like Van der Waals-London forces.

SOLUTE SOLVENT INTERACTION

(continued)

- **Step 1: The breaking of bonds within the solute**
- **Step 2: The breaking of intermolecular attractive forces within the solvent**
- **Step 3: The formation of new attractive solute-solvent bonds in solution**
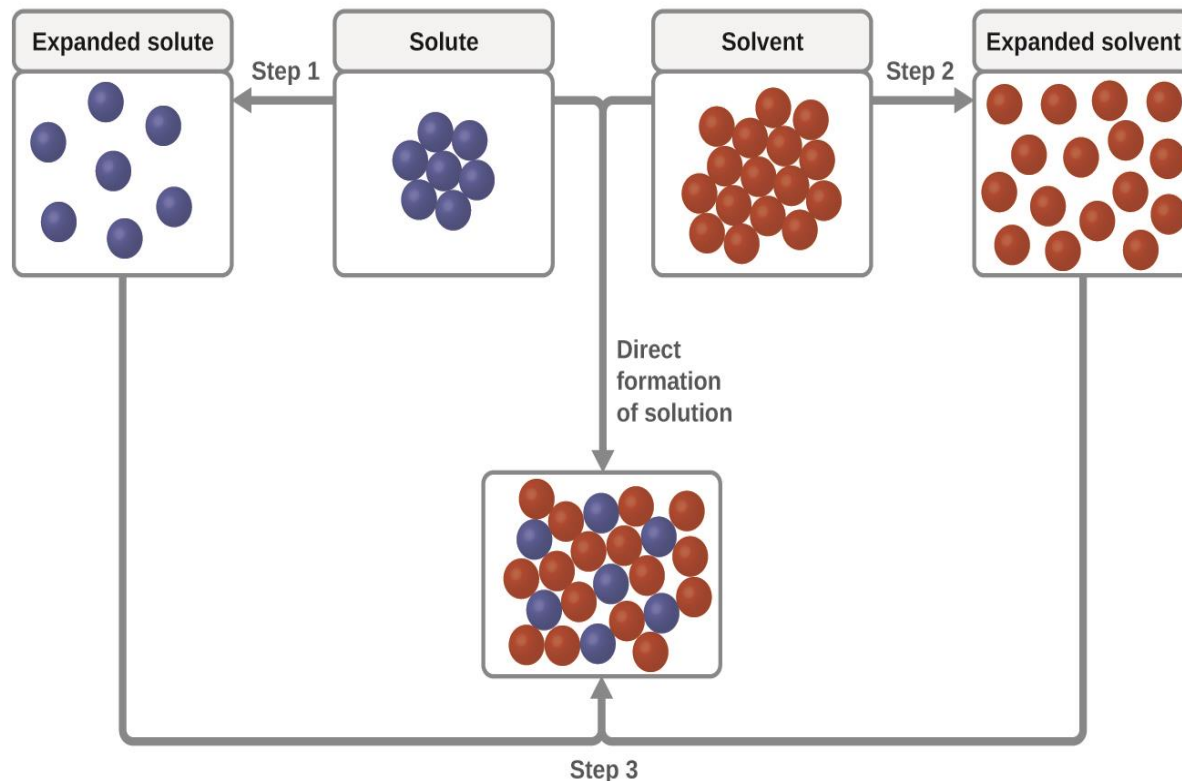
IDEAL SOLUBILITY PARAMETER

- Solubility parameter provides numerical method to predict interaction between materials.

- It is used for estimation of whether substance will dissolve in another substance or not.

- If values of solubility parameter are same then we can say that one substance is soluble in another.

- Two types of solubility parameter
    - Hildebrand solubility parameter
    - Hansen solubility parameters

HILDEBRAND SOLUBILITY PARAMETER

- Theory of solubility parameters

  - Scatchard in 1931

  - Joel H. Hildebrand in 1936

- It indicates relative solvency behavior of specific solvent.

- The Hildebrand solubility parameter describes the degree of solubility for nonpolar or slightly polar substances without hydrogen bonding.

- The Hildebrand solubility is defined as the square root of the cohesive energy density, which is a characteristic for the intermolecular interactions in a pure liquid or solid.

$$\delta = \sqrt{C}$$

- **Cohesive energy density(C)** is the forces of attraction per unit volume of solvent.

$$C = \frac{\Delta H - RT}{V_m}$$

- The cohesive energy density of a liquid is a numerical value that indicates the energy of vaporization in calories per cubic centimeter.

- **Heat of vaporization** is the amount of heat required to convert boiling liquid into gas.

- To convert any boiling liquid into gas, heat of vaporization must be supplied which is an amount of energy required to overcome Van-der Waal forces of attraction between molecules of solvent i.e. cohesive forces, i.e. solubility parameter δ.

$$\delta = \sqrt{C} = \sqrt{\frac{E}{V}} = \sqrt{\frac{\Delta H_V - RT}{V_m}}$$

- Cohesive energy density is directly related to "heat of vaporization".

- Solubility parameter (δ) is commonly expressed in units of $(cal/cm^3)^{1/2}$.

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HANSEN SOLUBILITY PARAMETER

- Charles M. Hansen in 1967

- Based on the idea that like dissolves like

- Each molecule is given three Hansen parameters.

   δ_d = The energy from dispersion forces between molecules

   δ_p = The energy from dipolar intermolecular force between molecules

   δ_h = The energy from hydrogen bonds between molecules.

- Hansen solubility parameters may be useful for preparing emulsions and to estimate their miscibility

SOLVATION

- Solvent strongly interacts with solute molecules or ions causing stabilization of solute species in solution.

- Solvent shell

- Solute molecules gradually disappear during the dissolving process

- Disappearing intermolecular forces are to be replaced by the new intermolecular forces

- Solvation complex

- Solvation by water molecules is called as hydration.

- Solvation due to ion-dipole interactions : strong ion-dipole attractions between the ions and the water molecules

- Solvation due to hydrogen bonding

ASSOCIATION

- Association refers to the attraction between the ions having opposite charges.

- ion pairs or ion triplets

- Dilelectric constant

- Attraction between the two opposite charges is described by Coulomb's law

$$F = \frac{q_1 q_2}{er^2}$$

Where,

F is force of attraction

q_1 and q_2 are magnitude of electric charges present on ions

e is dielectric constant of solvent

r is distance between the ions.

FACTORS INFLUENCING SOLUBILITY OF DRUGS

- Temperature

- pH

- Pressure

- Solvent Nature

- Co-solvent

- Particle Size And Surface Area

- Molecular Structure Modification

- Common Ion Effect

- Effect Of Complex Formation

- Effect Of Surfactants

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TEMPERATURE

Effect of Temperature on solubility of solids

- **Le Chatelier's principles:** Le Chatelier said that equilibrium adjusts the forward and backward reactions in such a way to accept the changes affecting the equilibrium conditions.

- Solids which dissolve with absorption of heat, the solubility of such solids increases as the temperature increases while solids which dissolve with the evolution of heat, increase in temperature causes a decrease in solubility

- The effects of temperature on the solubility of solids differ depending on whether the reaction is endothermic or exothermic.

- For an endothermic reaction ($\Delta H_{solvation} > 0$) - stress on the reactants side

- For an exothermic reaction ($\Delta H_{solvation} < 0$) - stress on the products side

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TEMPERATURE

Effect of Temperature on solubility of Liquids:

- No defined trends for the effects of temperature on the solubility of liquids.
- Basically, solubility increases with temperature

Effect of Temperature on solubility of Gas:

- With increase of the temperature gases became less soluble in each other and in water, but more soluble in organic solvents.
- Le Chatelier's principle

Solubility curve is used to indicate effect of temperature on solubility. Solubility curves are the curves drawn as solubility versus temperature.

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pH

- Depends on the pKa
- The relationship between pH, solubility and pKa value of drugs is expressed as,

Acidic Drug	$pH = pKa + log\dfrac{S-S_o}{S_o}$
Basic Drug	$pH = pKa + log\dfrac{S_o}{S-S_o}$

- Where,

  pKa is the dissociation constant

  So is the solubility of unionized form in moles/litre

  S is the overall solubility of drug in moles/litre

- The ionized form of acidic or basic drug is considered as soluble whereas unionized form is insoluble.

- A weakly basic drug is more soluble in acidic medium and an acidic drug is more soluble in basic medium

- Basic drug will be precipitated from aqueous solution, if the pH of solution is raised by the addition of strong base.

PRESSURE

- Significant in affecting the solubility of gases in liquids
- For solids and liquids the pressure dependence of solubility is typically weak
- Combination of henry's law and le chatelier principle

SOLVENT NATURE

- Like dissolves like'

CO-SOLVENT

- Solutes are more soluble in mixture of solvents
- Co-solvents are the solvents which are the solvent in combination which increase the solubility of the solute and the phenomenon is called as cosolvency.

PARTICLE SIZE AND SURFACE AREA

- The surface area in contact with the medium increases rapid dissolution is obtained.

MOLECULAR STRUCTURE MODIFICATION

- Slight modification may lead to marked changes in their solubility in given solvent. For example, Acetic Acid is converted into its salt (sodium acetate), its ionic dissociation in water increases which ultimately leads to an increase in the solubility.

- Solubility can also be decreased by modifications such as esterification. For example, Chloramphenicol (soluble) by esterfication converts into Chloramphenicol palmitate (Poor Soluble).

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COMMON ION EFFECT

- The common-ion effect is a term that describes the decrease in solubility of an ionic compound when a salt that contains an ion that already exists in the chemical equilibrium is added to the mixture.

EFFECT OF COMPLEX FORMATION

- The solubility of some solutes in a liquid may be increased or decreased by the addition of a substance that forms a complex which is either more or less soluble.

EFFECT OF SURFACTANTS

- Micelle and micellar solublization
- Orientation of hydrophilic and lipophilic groups

DIFFUSION PRINCIPLES IN BIOLOGICAL SYSTEMS
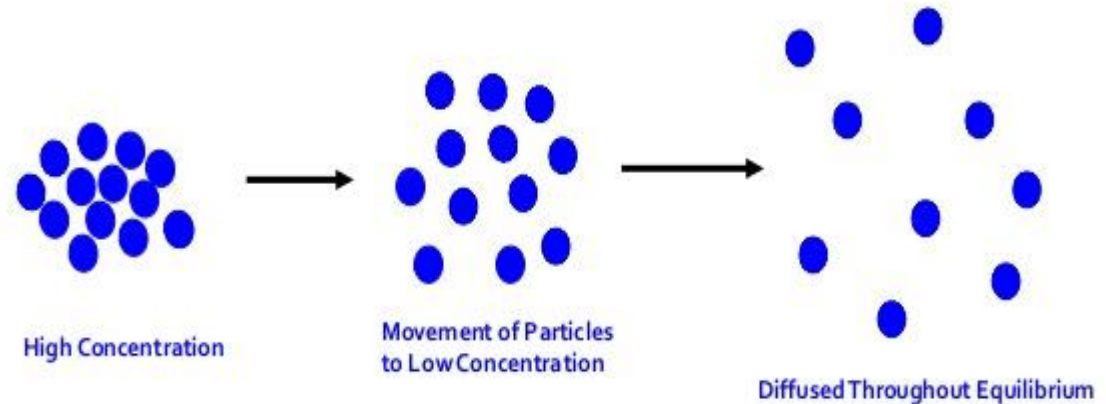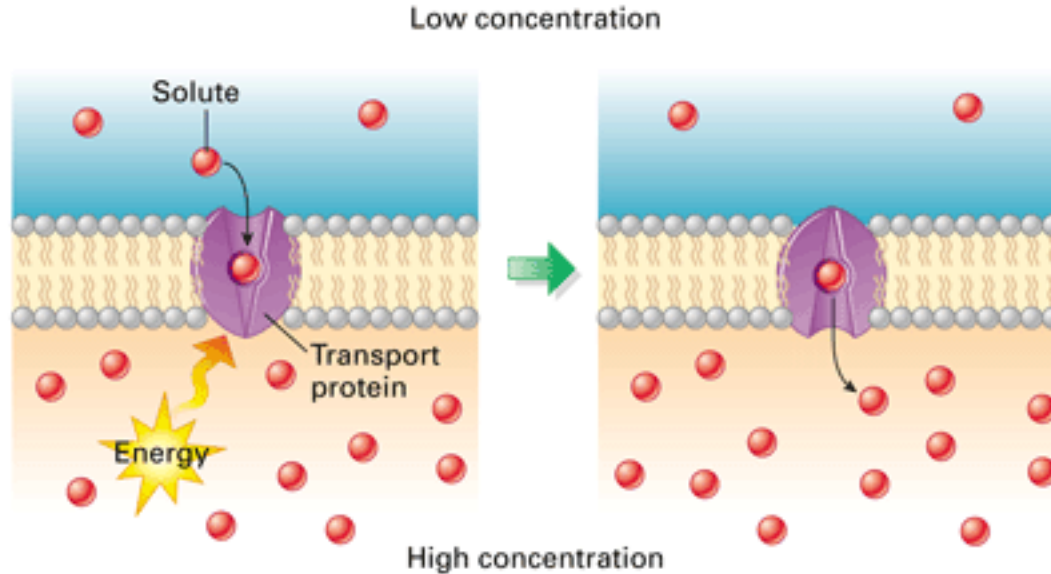
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- The movement of solute particles or mass transfer of individual molecule by random molecular motion is called as diffusion.

- The rate of diffusion is dependent on temperature, size of the particles and size of the concentration gradient.

- Time dependent process

- Concentration gradient as a cause of diffusion

- Importance of Diffusion

MECHANISM OF DRUG TRANSPORT

- **Passive Diffusion**

- **Facilitated Diffusion**

- **Ionic or electrochemical diffusion**

- **Ion Pair transport**

- **Active Transport**

- **Pore Transport**

- **Endocytosis**

MECHANISM OF DRUG TRANSPORT

- **Passive Diffusion and Facilitated Diffusion:**
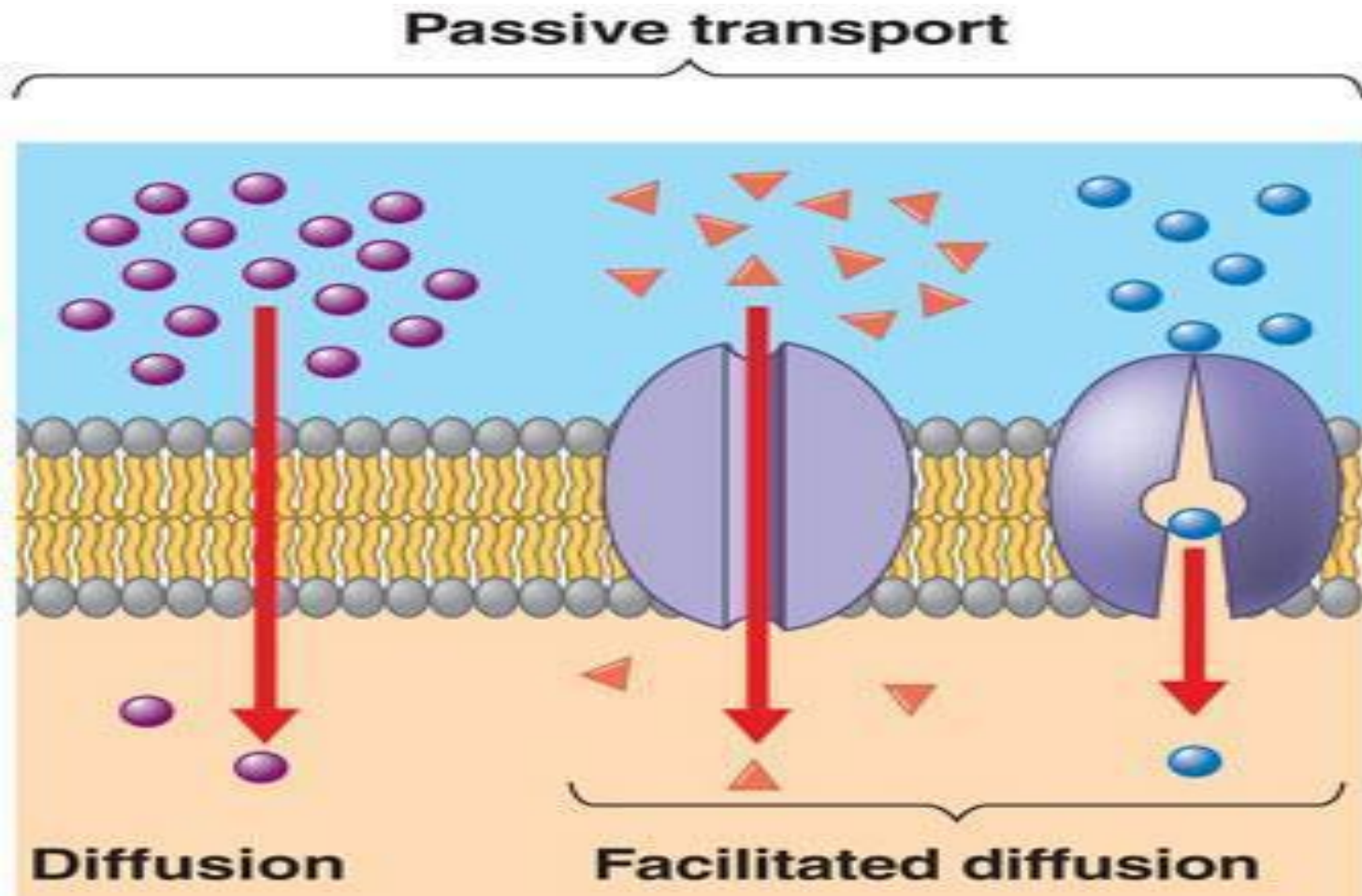
- **Passive Diffusion:**

  - The transport of molecule from high concentration to low concentration

  - The driving force for this process is concentration or electrochemical gradient.

Passive Transport

Diffusion | Facilitated diffusion
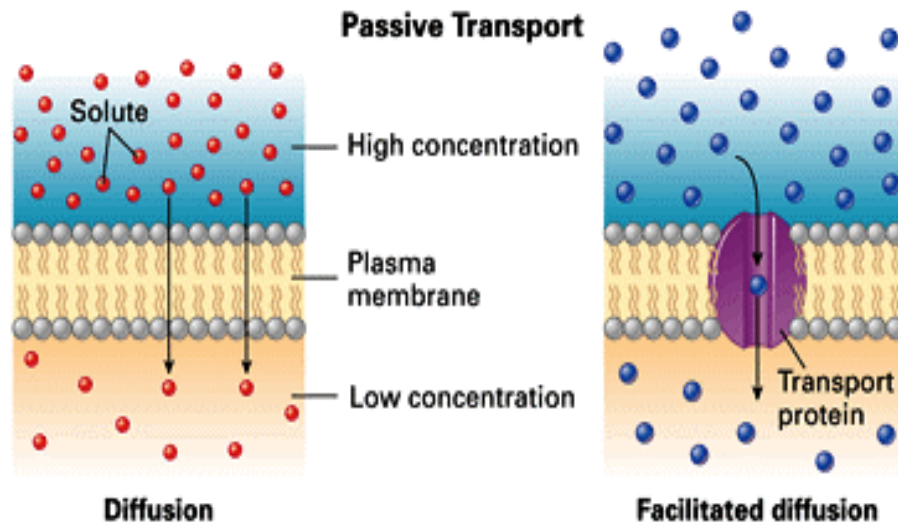
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- **Facilitated Diffusion:**

  - It is a carrier mediated transport system

  - Concentration gradient is the driving force and no energy expenditure is involved.

- **Pore Transport:**

  - The process is important in the absorption of low molecular weight, low molecular size and generally water soluble drugs through narrow, aqueous filled channel or pores in the membrane structure.

  - Osmotic differences across the membrane or hydrostatic pressure is the driving force for pore transport.

- **Active Transport:**

  - The drug is transported from a region of lower to higher concentration i.e. against the concentration gradient

  - Energy is required in the work done by the carrier. Such process is called as active transport.

  - Some molecules do require energy for their transport across the membrane.

Continued…

- **Active Transport and Pore Transport:**
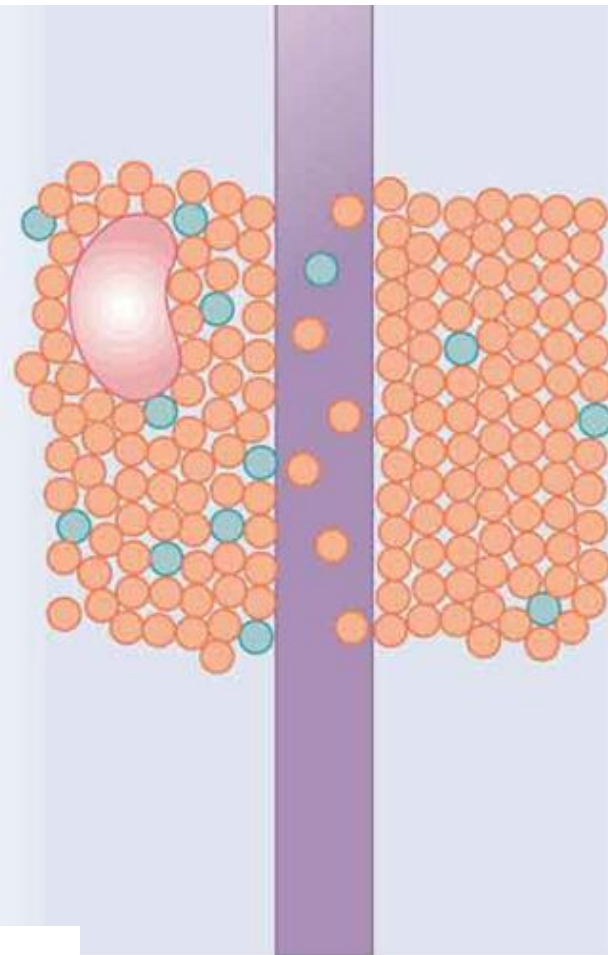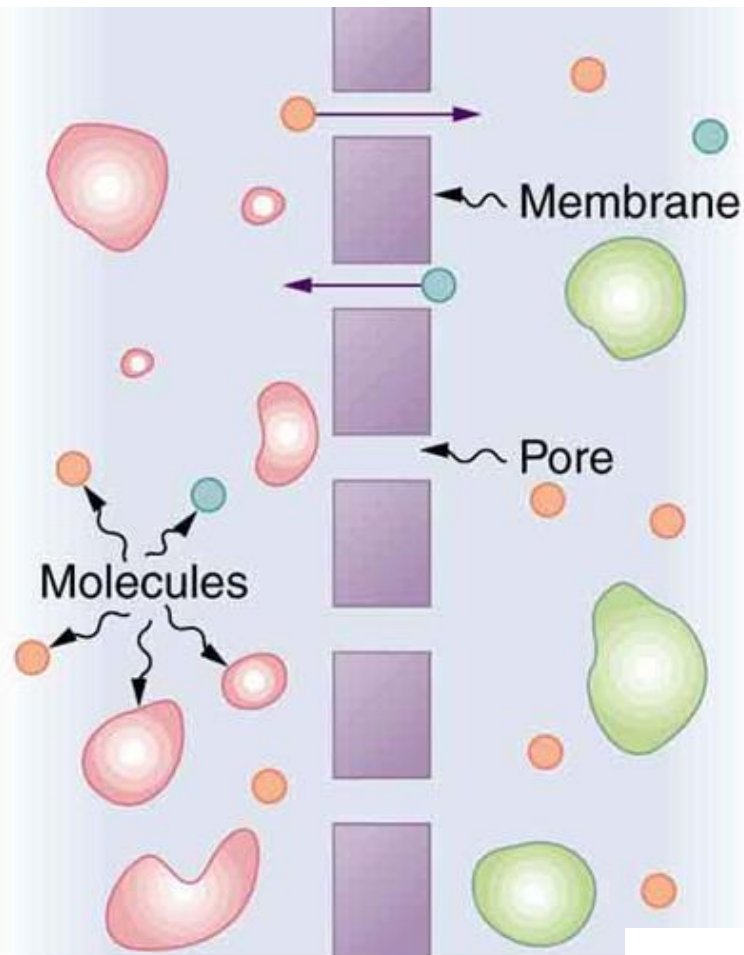
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- **Ionic or electrochemical diffusion:**

  - Effect of the charge on the membrane

  - Molecular forms and ionic forms.

  - The anionic solute permeates faster than the cationic form in the following order – unionized molecule > anions > cations.
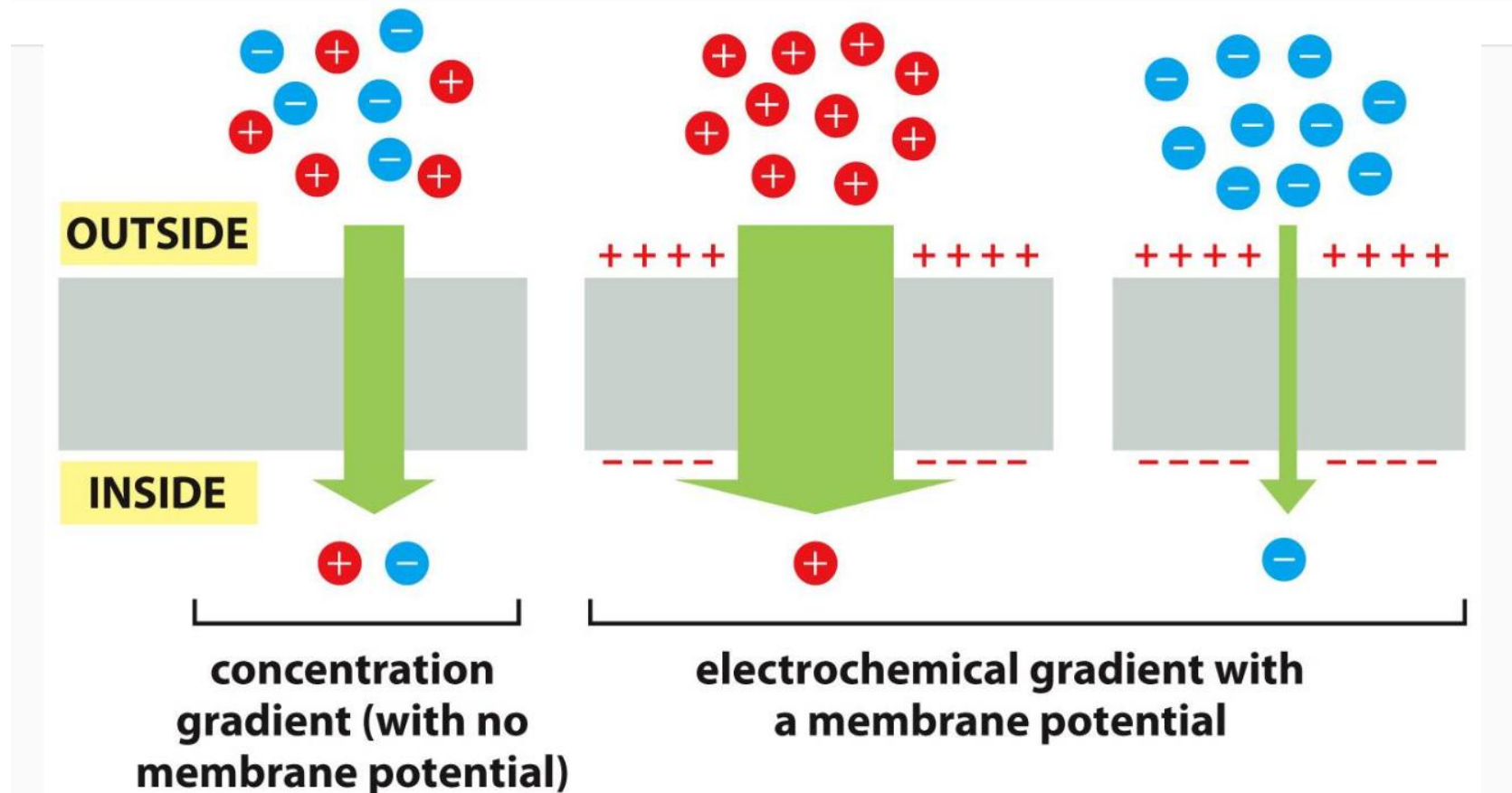
- **Ion Pair transport:**

  - Beneficial for the drugs which ionize under all pH conditions.

- **Endocytosis:**

  - Involves engulfing extracellular materials within a segment of the cell membrane to form a vesicle which is then pinched off intracellularly.

Continued…

- **Ionic or electrochemical diffusion**

- **Ion Pair transport:**

OUTSIDE

INSIDE

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concentration gradient (with no membrane potential)

electrochemical gradient with a membrane potential

DIFFERENCE BETWEEN ACTIVE AND PASSIVE TRANSPORT

Active Transport	Passive Transport
Requires cellular energy.	Do not require cellular energy.
Transport occurs from region of lower concentration to higher concentration	Transport occurs from a region of higher concentration to lower concentration
Required in the transportation of all the molecules such as proteins, large cells, complex sugars, ions, etc.	Required in the transportation all the soluble molecules which include oxygen, water, carbon dioxide, lipids, monosaccharides, etc.
Active transport is a dynamic process.	Passive Transport is a physical process.
It is highly selective.	It is partly non-selective
Active transport is a rapid process.	Passive transport is a comparatively slow process.
One directional.	Bidirectional.

FICK's LAWS OF DIFFUSION

- **Adolf Fick in the 19th century**

  - The molar flux due to diffusion is proportional to the concentration gradient.

  - The rate of change of concentration at a point in space is proportional to the second derivative of concentration with space.

- **Fick's Laws of Diffusion:**

  - Ficks's first law of diffusion

  - Fick's second law of diffusion

FICK's FIRST LAW OF DIFFUSION

- Molecules travel from one compartment to other compartment over period of time. This rate of mass transfer over the period of time can be expressed as flux.

$$J = \frac{1}{S}\frac{dM}{dt}$$

……. (1)

- Fick's first law of diffusion states that flux is directly proportional to the concentration gradient.

$$J = -D\frac{dc}{dx}$$

…….. (2)

- From above two equation we get,

$$\frac{dM}{dt} = -DS\frac{dc}{dx}$$

……. (3)

FICK's SECOND LAW OF DIFFUSION

This law states that change in concentration with time in particular region is proportional to the change in concentration gradient at that point of time.

$$\frac{dc}{dt} = -\frac{dj}{dx}$$

…… (4)

From Fick's first law of diffusion,

$$J = -D\frac{dc}{dx}$$

….. (5)

Differentiating above equation with respect to x we get,

$$-\frac{dj}{dx} = D\frac{d^2c}{d^2x}$$

….. (6)

Continued…

As we know that,

$$\frac{dc}{dt} = -\frac{dj}{dx}$$

Hence equation (6) can be written as

$$\frac{dc}{dt} = D\frac{d^2c}{d^2x}$$

….. (7)

Above equation (7) represent diffusion in x direction only, converting this equation to the 3 coordinates x, y and z, we get,

$$\frac{dc}{dt} = D\left[\left(\frac{d^2c}{d^2x}\right) + \left(\frac{d^2c}{d^2y}\right) + \left(\left(\frac{d^2c}{d^2z}\right)\right]$$

….. (8)

SOLUBILITY OF GAS IN LIQUID

- **Effect of Pressure**

- **Effect of temperature**

- **Addition of salt**

- **Chemical reaction**

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EFFECT OF PRESSURE
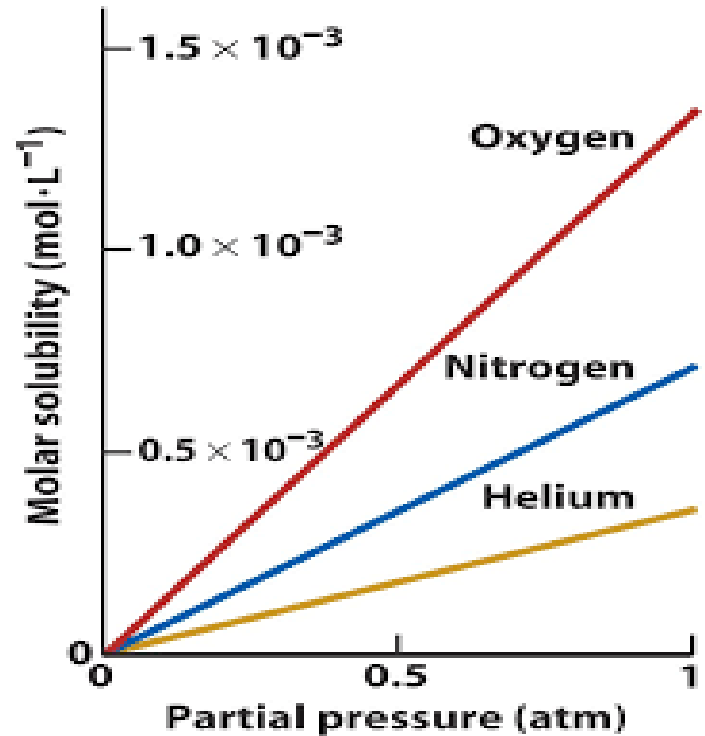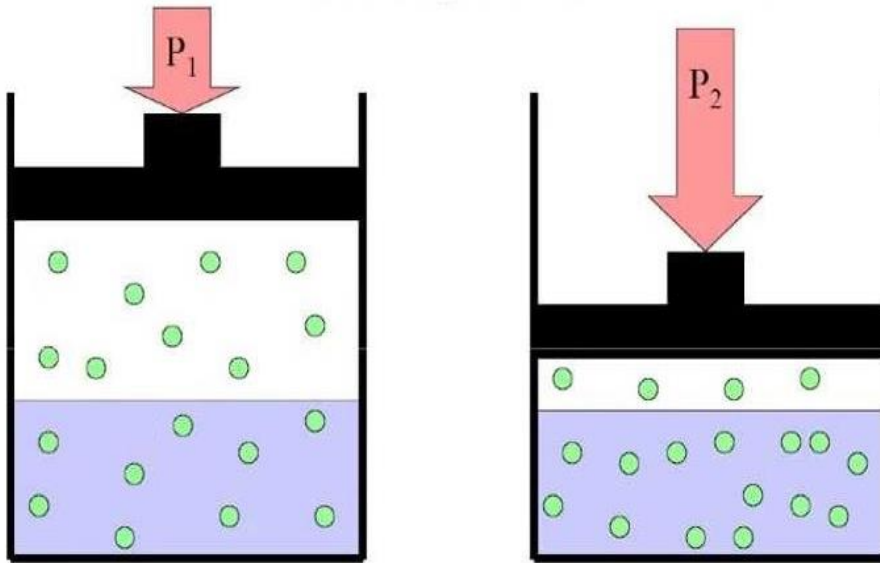
Henry's law

$$C = \sigma P$$

C is concentration of dissolved gas, (mol/lit)

P is partial pressure of undissolved gas above the solution, (kPa)

σ is solubility coefficient, (mol/l.kPa)

Henry's law

• Henry's law states that "in very dilute solution at constant temperature, the concentration of dissolved gas(C) is proportional to the partial pressure (P) of undissolved gas present above the solution.

$$C=\sigma P$$

• Solubility of a gas in a liquid is directly proportional to the pressure of that gas above the surface of the solution.

• If pressure is reduced the solubility of gas decreases which can be observed as effervescence in liquid.

EFFECT OF TEMPERATURE
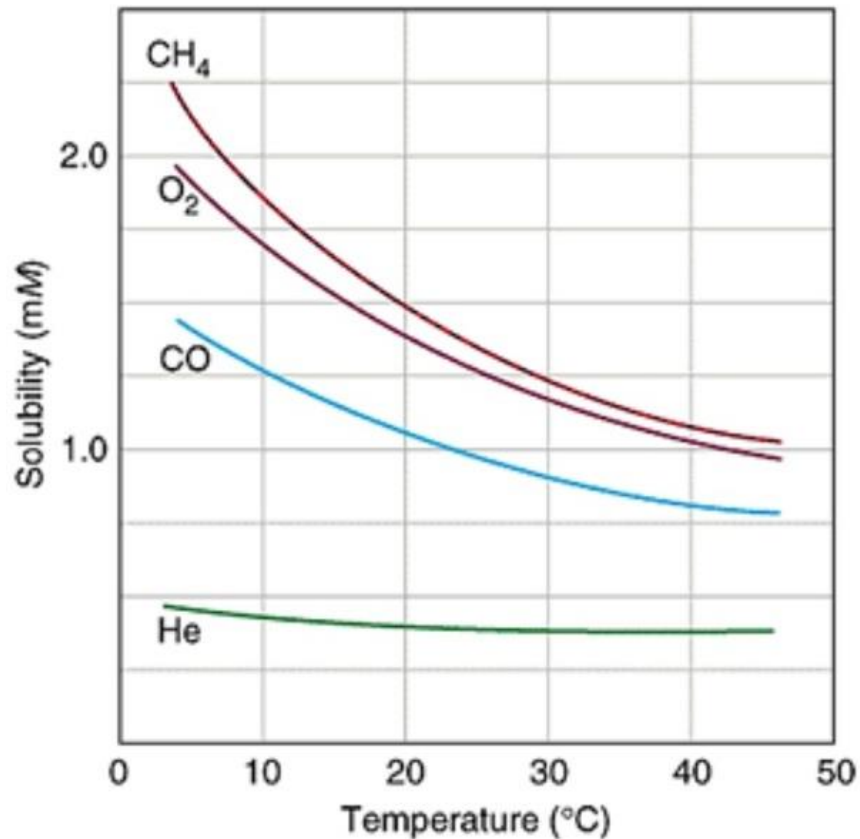
As temperature is increased solubility of gases in liquid decreases.

continued…

Why? Solubility decreases with increase in temperature

- It is first important to remember that temperature is a measure of the average kinetic energy.

- As temperature increases, kinetic energy increases.

- The greater kinetic energy results in greater molecular motion of the gas particles. As a result, the gas particles dissolved in the liquid are more likely to escape to the gas phase and the existing gas particles are less likely to be dissolved. As temperature is increased solubility of gases in liquid decreases.

ADDITION OF SALT
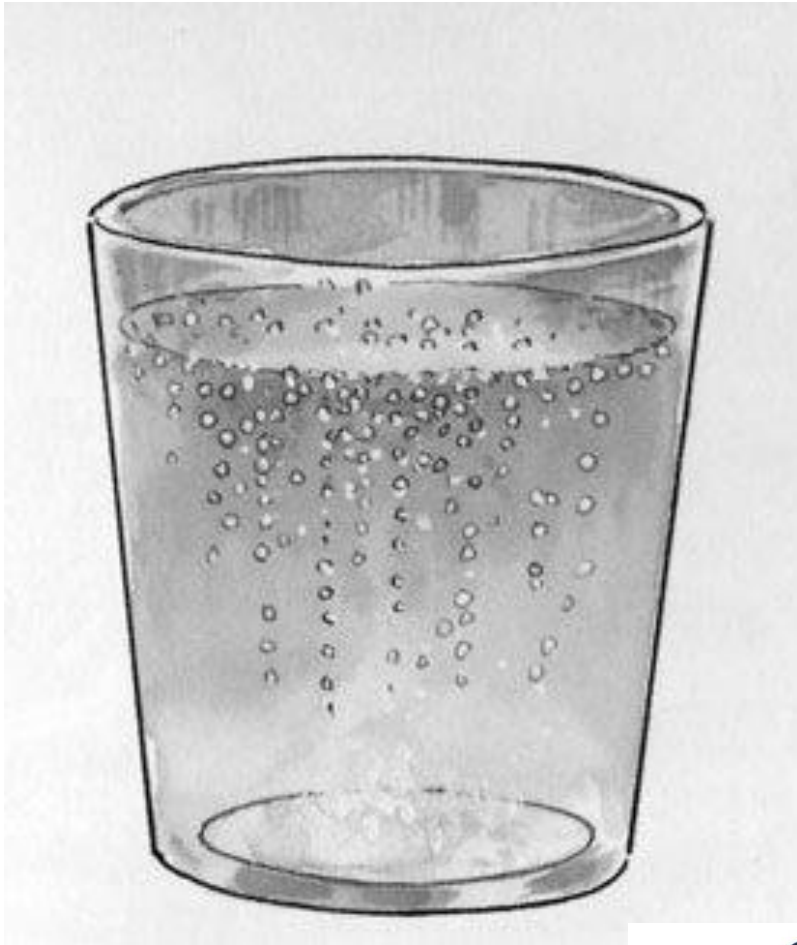
Solubility of gas in liquid decreases drastically because of salting out effect.

continued…

• Solubility of gas in liquid decreases drastically because of salting out effect.

• Because addition of an electrolyte liberation of gas from solution occurs. This effect is called as salting out effect.

• This occurs because adhesive force between salt and liquid molecule is far more than gas and water molecule. The difference in the adhesive forces permits liquid to leave gas molecule and combine with salt molecule and solubility of gas molecule decreases.

CHEMICAL REACTION

- When any type of chemical reaction occurs between gaseous solute and liquid solvent, then solubility of gas in liquid increases.

- The change is by means of change in pressure and temperature of system

- Henry's law is not applicable to these systems

MISCIBILITY IN LIQUIDS

- **Miscibility**

- **Completely Miscible Systems**

- **Partially Miscible Systems**

- **Immiscible Systems**

MISCIBILITY

• Miscibility refers to the ability of a liquid to completely dissolve in another liquid solution.

•Two liquids that combine in any ratio to form a homogeneous solution.

• Depends on the forces of attraction

• Liquid liquid system can be classified in following types depending upon miscibility of liquid into another.

- Completely miscible systems

- Partially miscible systems

- Immiscible systems

continued…

Oil
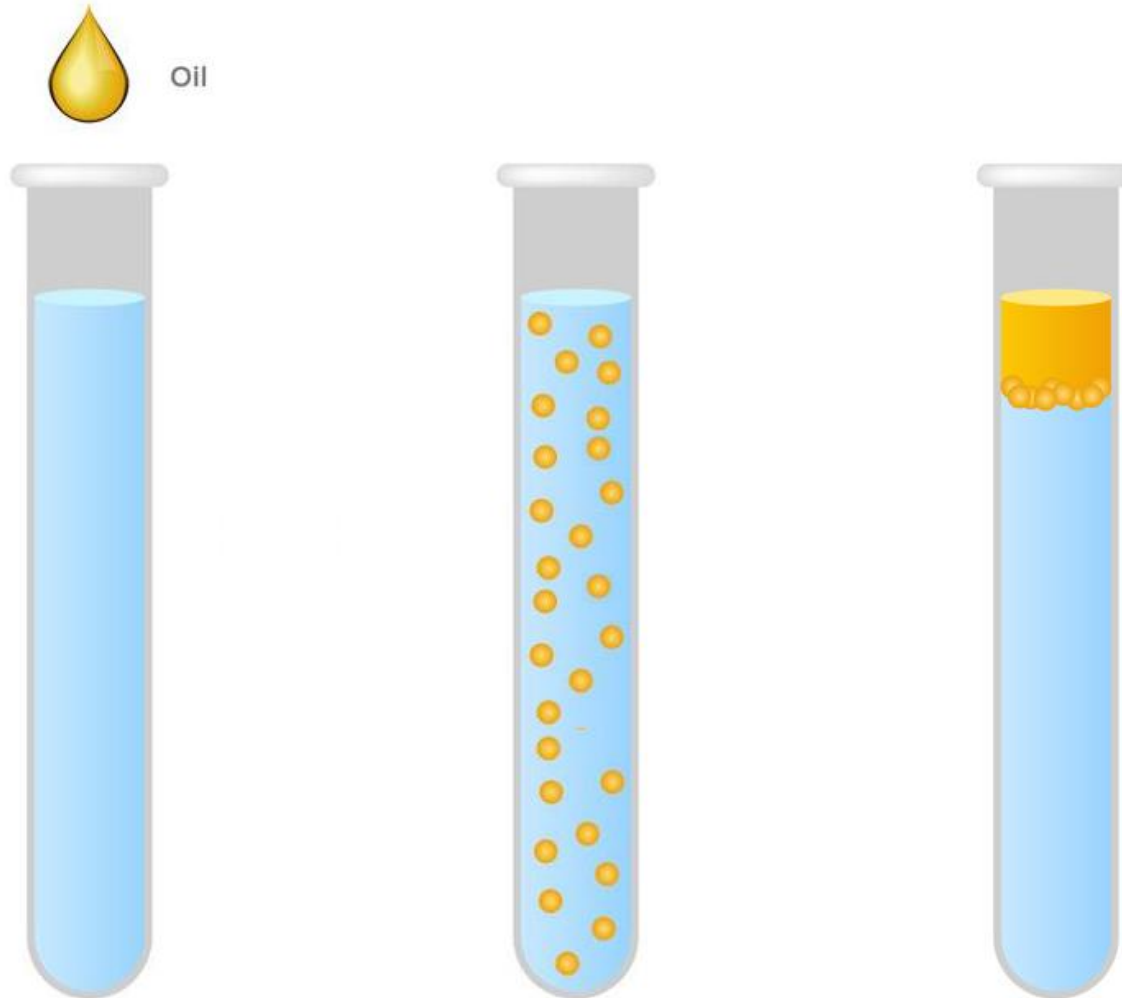
COMPLETELY MISCIBLE SYSTEMS

continued…

- A distinct layer between two liquids will not form when you have a solution that is labeled miscible.

- This type of system consists of liquid pair which is completely miscible with each other in all proportions.

- This class of liquid represents complete miscibility of polar and non polar solvents in all proportions.

- This kind of system is also called as binary system.

PARTIALLY MISCIBLE SYSTEMS
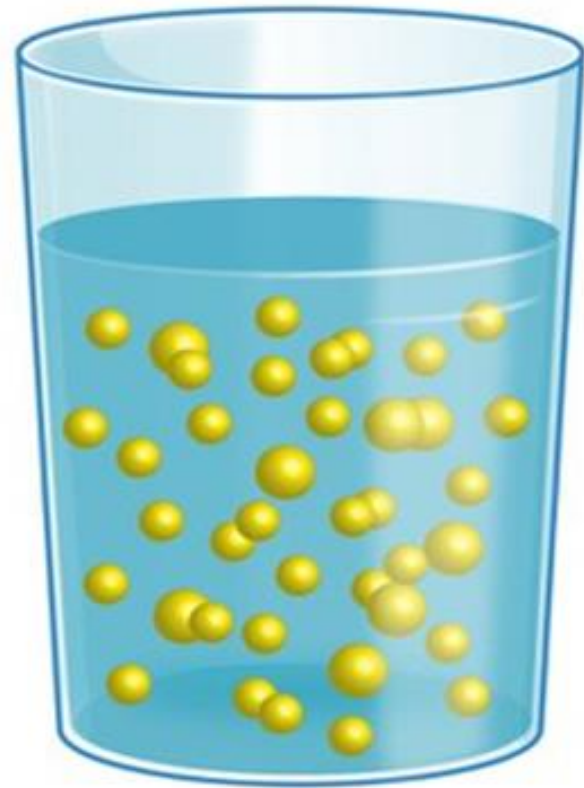
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• A liquid-liquid system is said to be partially miscible when their mutual solubility in one another is limited.

• They are miscible only in a fixed proportion.

• In some extent this two liquid phases becomes homogeneous with change in temperature.

• The plot showing the conditions of pressure and temperature under which two or more physical states can exist together in dynamic equilibrium is called as phase diagram.

IMMISCIBLE SYSTEMS

continued…

• A liquid system is said to be immiscible when the components do not mix at all, at any proportion.

• In immiscible liquids, cohesion forces among the same molecules are stronger than those between different molecules.

• When two immiscible liquid phases are brought into contact, the following three events may occur per unit surface area: adhesion, cohesion, and spreading.

• The work of adhesion presents the energy that appears when two surfaces, formerly in contact, become separated, and each of them establishes a contact with a third phase.

• The work of cohesion presents the energy that is required for doubling the interface area. Now, it follows that the energy required for dispersion of a light liquid phase into a heavy liquid phase—that is, the energy needed for emulsification—increases as the interfacial tension increases.

• The work of spreading presents the energy that appears when emulsified light liquid phase droplet contact, the heavy liquid phase interface and spread over the surface.

PHASE RULE

- **Phase Rule**

- **Applications of Phase Rule**

- **Reduced Phase Rule ad Extended Phase Rule**

- **Phase Diagram**

- **One Component System**

- **Two Component System**

- **Three Component System**

PHASE RULE

- 1875 - J. Willard Gibbs

- 1884 - J. W. B. Roozeboom

- The phase rule is a general principle governing systems in thermodynamic equilibrium.

$$F = C - P + 2$$

- C is the number of components

- F is the number of degree of freedom

- P is the number of phases

APPLICATIONS of PHASE RULE

REDUCED and EXTENDED PHASE RULE

- **Reduced Phase Rule :** Constancy of one of the variables reduces the phase rule equation to following form

$$F = C - P + 1$$

- **Extended Phase Rule:**

$$F = C - P + x$$

Where,

x is the number of intensive variables like pressure, temperature, concentration and possibly magnetic and electric fields that can be changed independently without loss of a phase.

PHASE DIAGRAM

- The plot showing the conditions of pressure and temperature
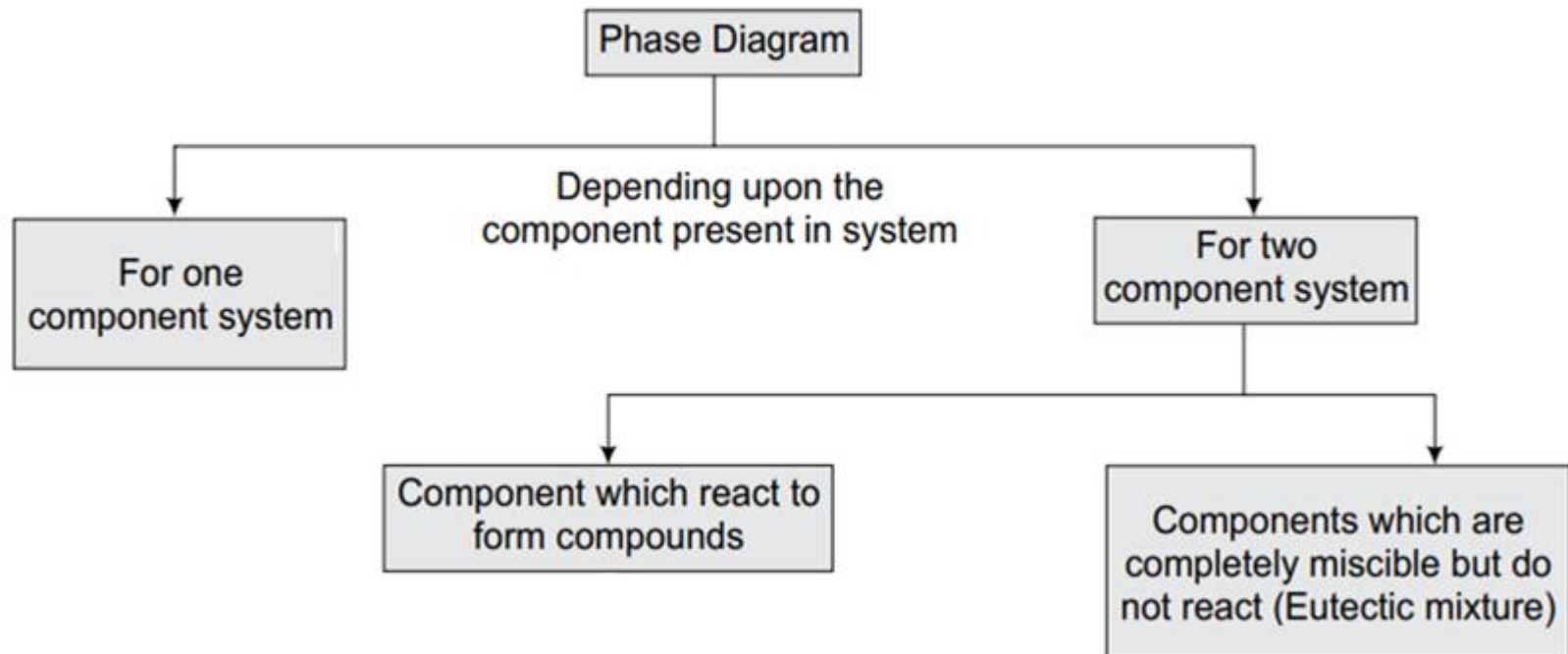
ONE COMPONENT SYSTEM

e.g. Water (H2O)
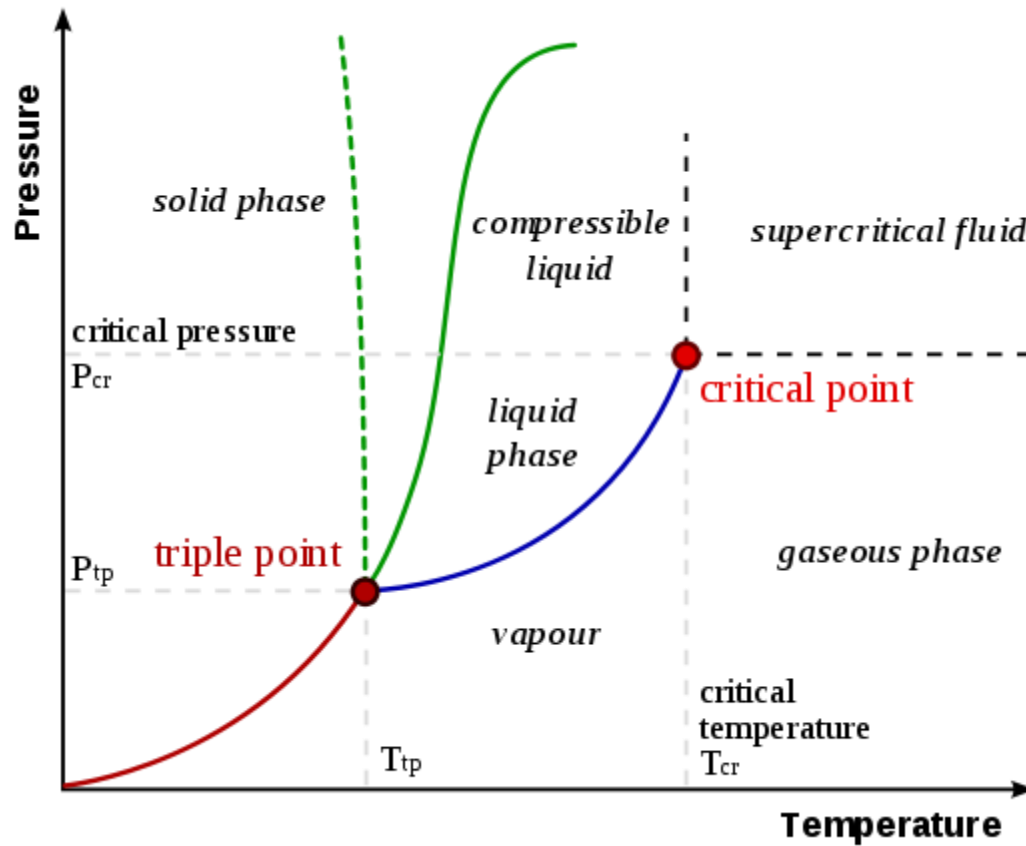
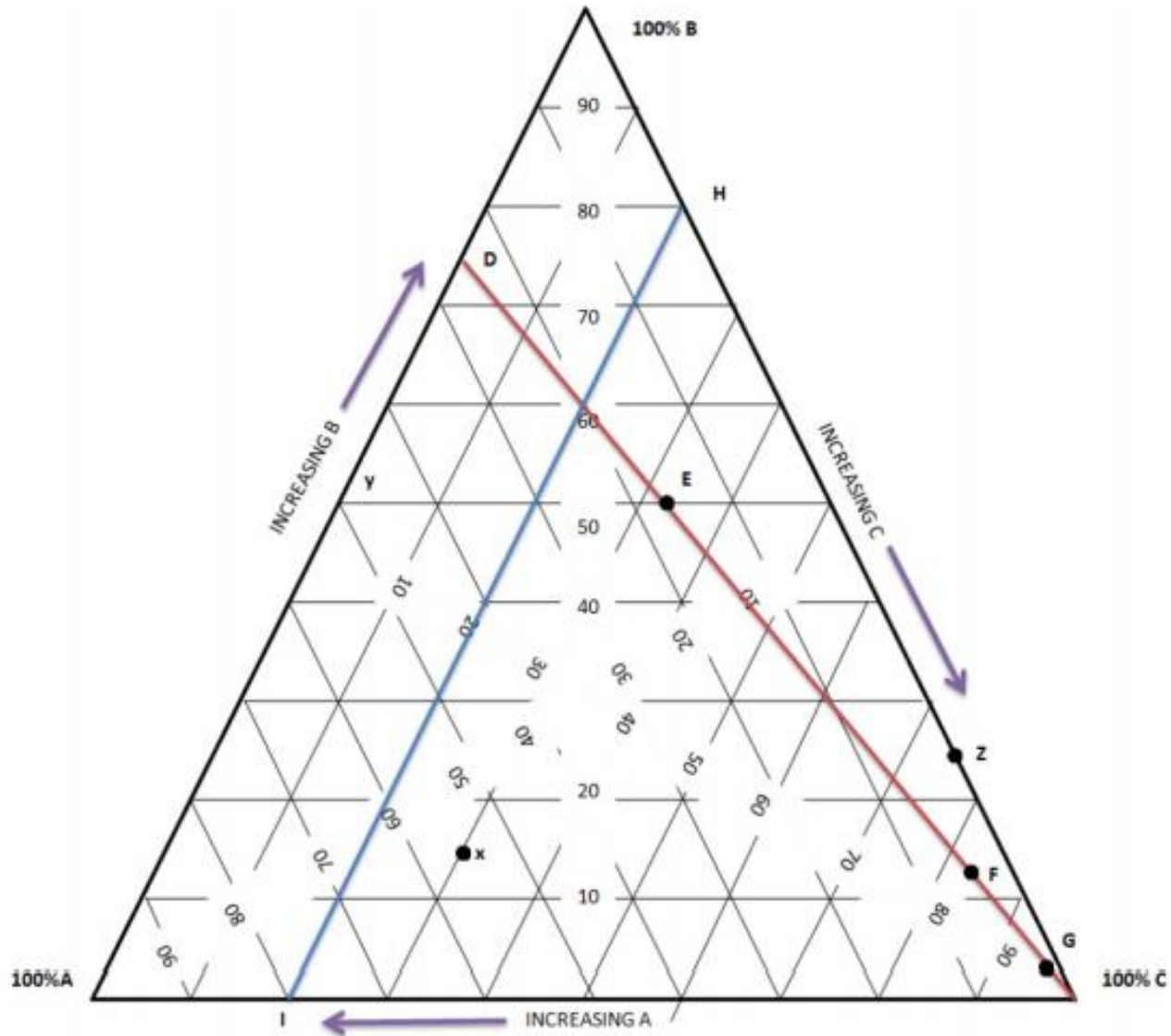# TWO COMPONENT SYSTEM
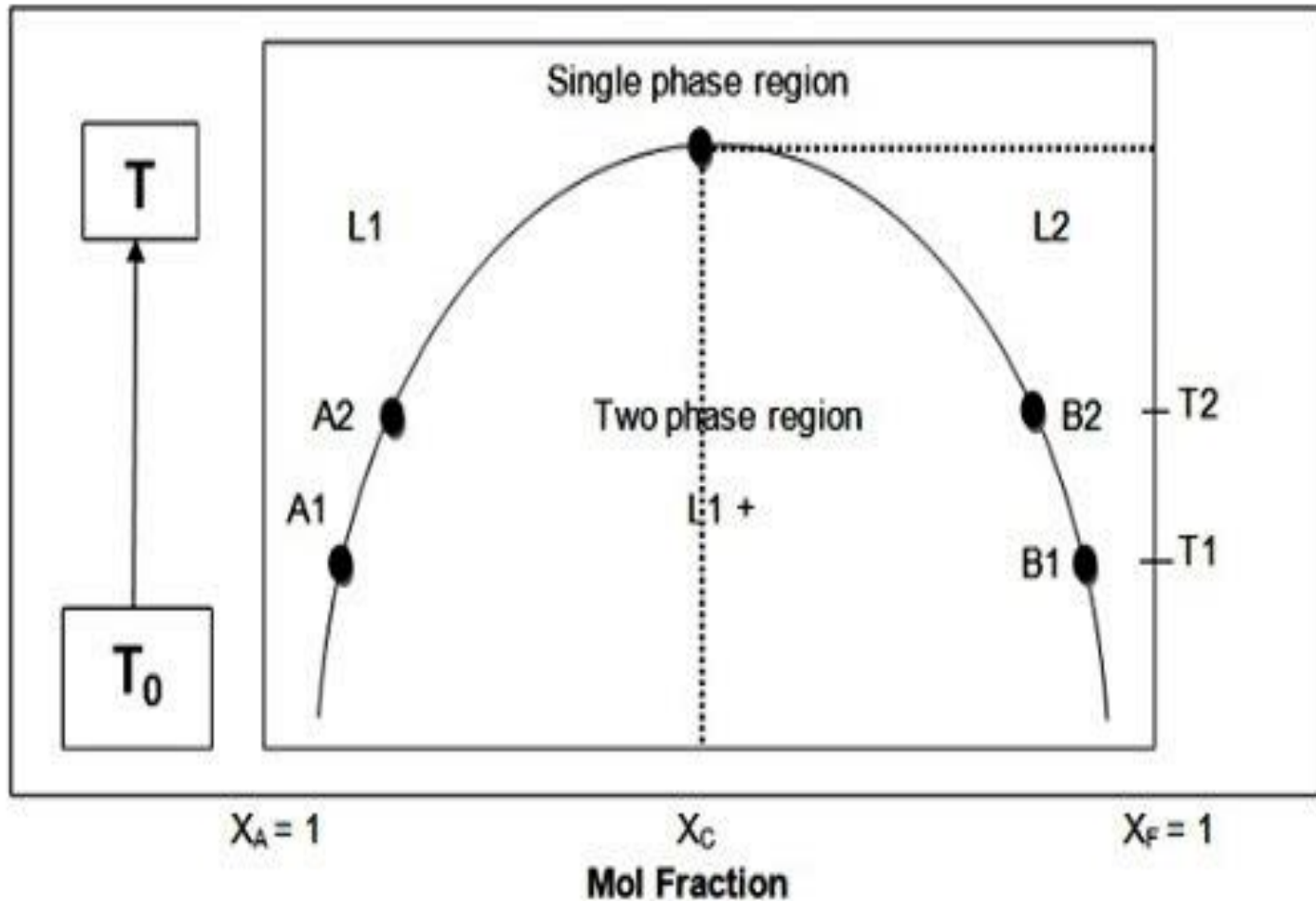
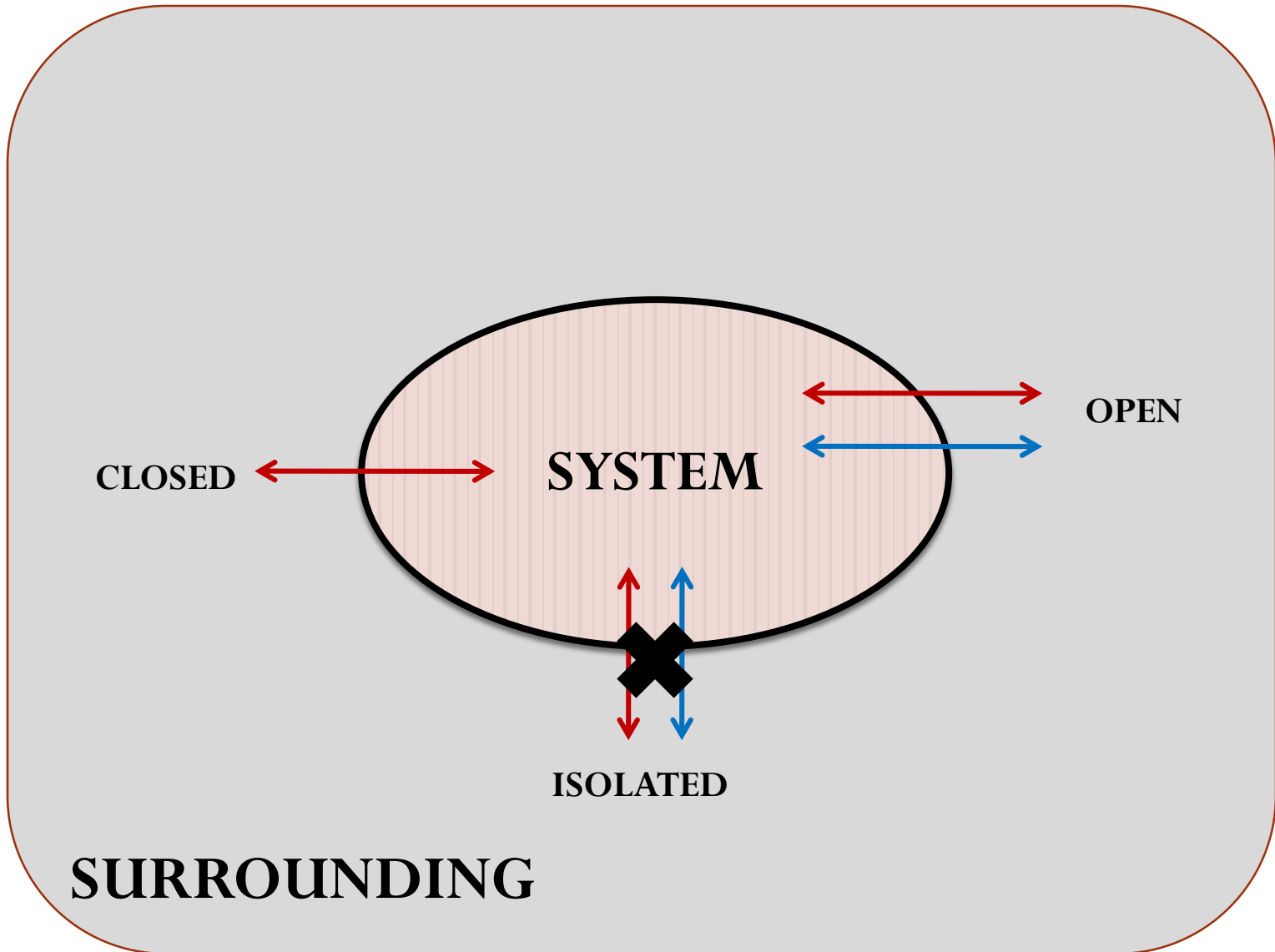# Partially Miscible Liquid System e.g. Phenol Water
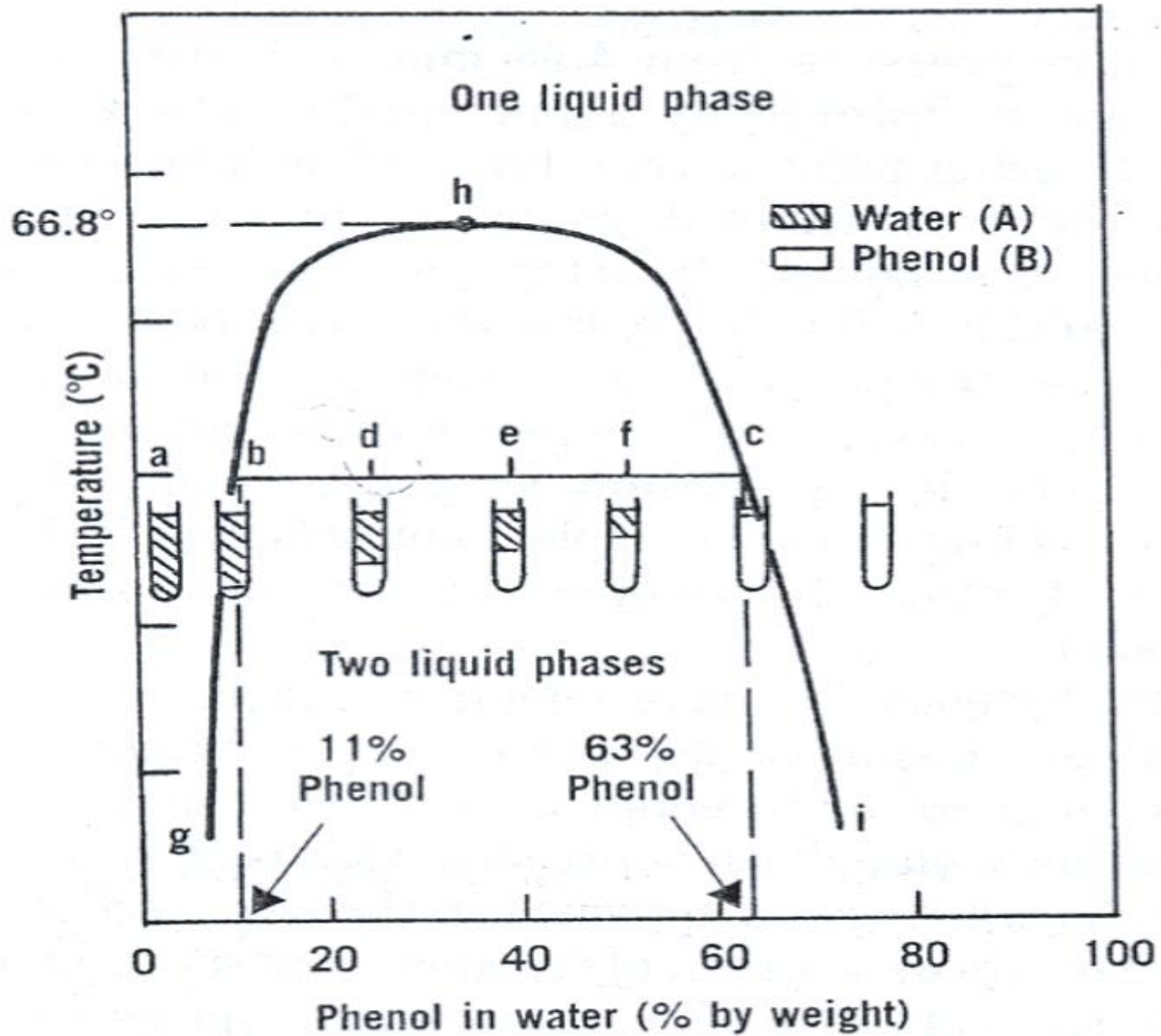
Miscible System e.g. eutectic mixture
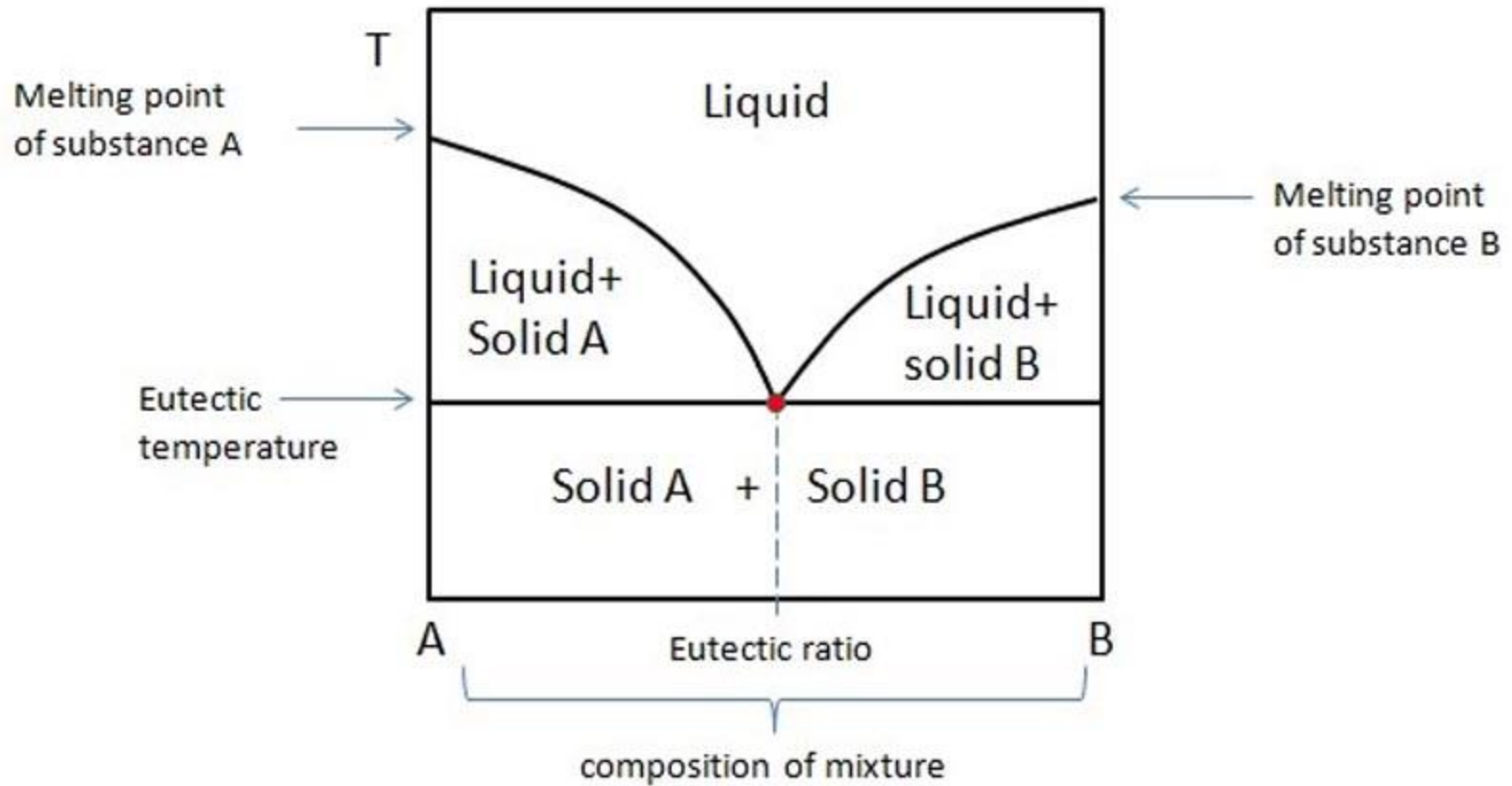
# THREE COMPONENT SYSTEM

THERMODYNAMIC SYSTEM

MOLE FRACTION

• Mole fraction is simply the number of moles of a particular substance compared to the total number of moles.

• The mole fraction for a substance always ranges between 0 (none) and 1 (all).

• The mole fraction is typically given the symbol X.

$$X = \frac{n_1}{n_1 + n_2}$$

Where,

n_1 is the number of mole of component and $n_1 + n_2$ is the total number of moles of all the substances in the mixture.

BOILING POINT DIAGRAM
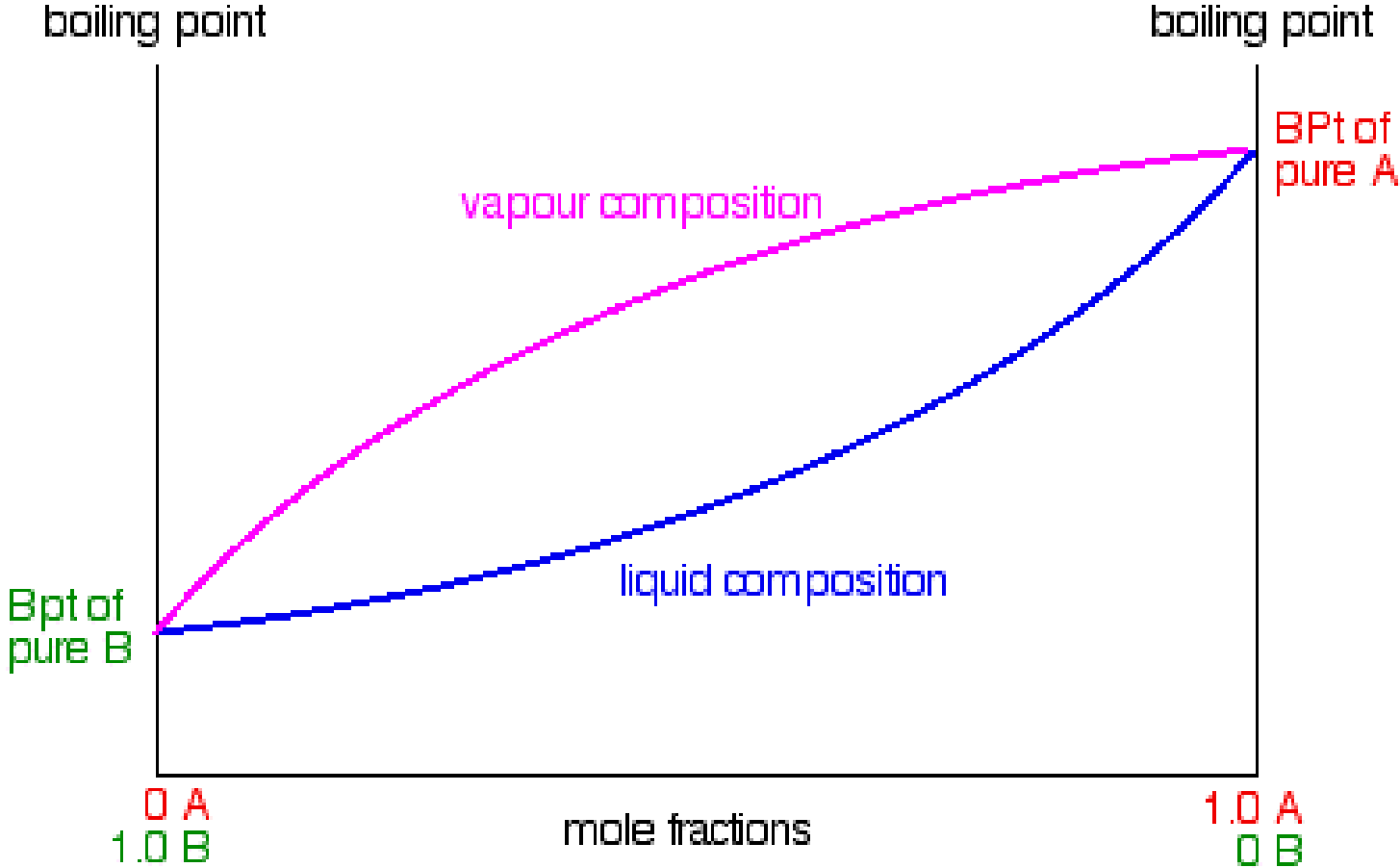
RAOULT's LAW

- In 1986 - French Chemist - Francois Marte Raoult

- Relationship between partial pressure and mole fraction of liquids.

 Raoult's law states that,

at definite temperature, The partial vapor pressure (P) of each volatile component of a solution, at any temperature, is equal to the product of the vapor pressure of pure component (P^0) and its mole fraction (X).

$$P = P^0 X$$

Consider a binary solution which is made up of two completely miscible components A and B,

then as per Raoult's law,

$$P_A = P^0_A X_A \quad\quad \ldots\ldots\ldots\ldots (01)$$

And $\quad\quad\quad\quad\quad P_B = P^0_B X_B \quad\quad \ldots\ldots\ldots\ldots (02)$

Where,

P_A and P_B is the Partial vapor pressure of component A and B

P^0_A and P^0_B is the Vapor pressure of pure component A and B

X_A and X_B is the Mole fraction of component A and B

The total vapor pressure of system

$\therefore$ $\qquad$ $P = P_A + P_B$ $\qquad$ ………… (03)

$\therefore$ from equation 01 and 02, equation 03 can be written as

$\therefore$ $\qquad$ $P = (P^0_A X_A) + (P^0_B X_B)$ $\qquad$ ………… (04)

Now,

According to definition of Mole fraction

$$X_A = \frac{n_A}{n_A + n_B} \qquad ………… (05)$$

$$X_B = \frac{n_B}{n_A + n_B} \qquad ………… (06)$$

As mole fraction is unitless

$$X_A + X_B = 1$$

$$X_A = 1 - X_B \qquad \qquad \text{…….……… (07)}$$

Now, considering equation 07, equation 04 can be written as

$$P = [P^0_A (1 - X_B)] + (P^0_B X_B)$$

$$P = P^0_A - P^0_A X_B + (P^0_B X_B)$$

Rearranging the equation, we have

$$\therefore \qquad P = P^0_B X_B + P^0_A - P^0_A X_B$$

$$\therefore \qquad P = P^0_B X_B - P^0_A X_B + P^0_A$$

$$\therefore \qquad P = (P^0_B - P^0_A) X_B + P^0_A \qquad \text{……….…….. (08)}$$

Equation (08) gives total vapor pressure in terms of vapor pressure of two pure components and mole fraction of one component.

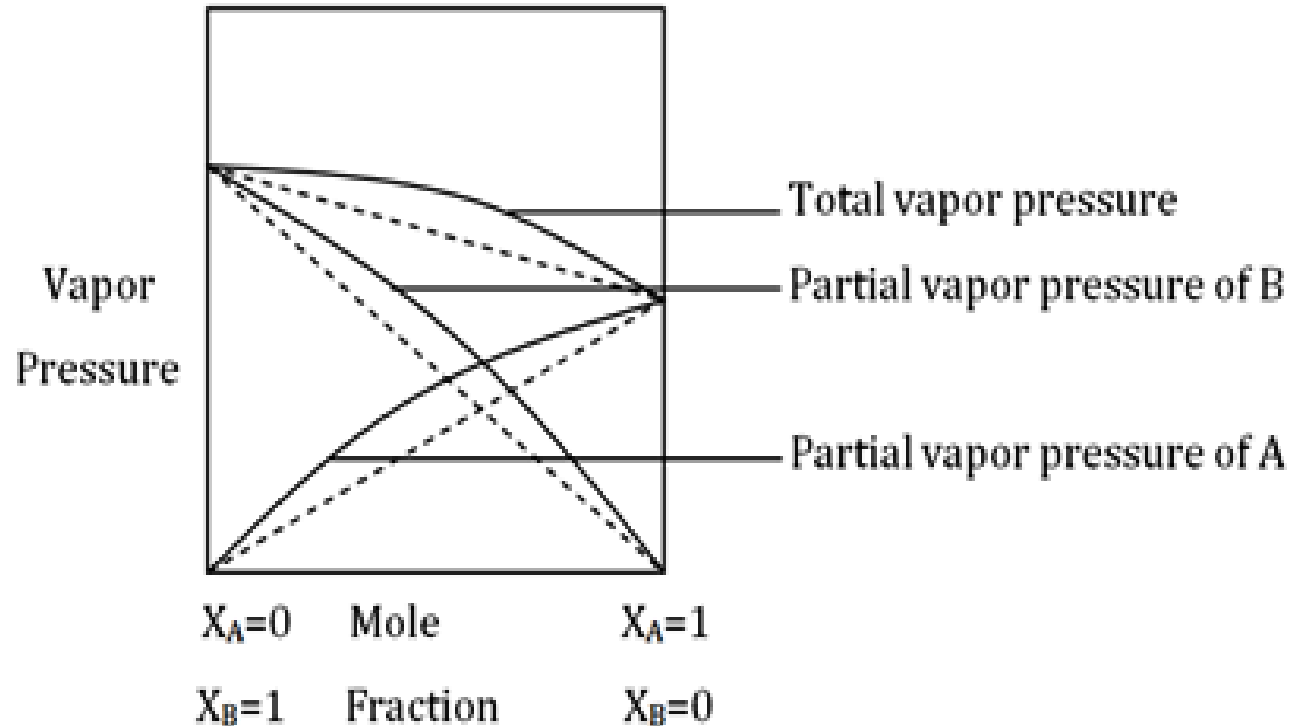Since, P^0_A and P^0_B are constant at definite temperature;

$\therefore$ plot of Vapor Pressure (P) Vs Mole Fraction (X) should be straight line with slope $(P^0_B - P^0_A)$
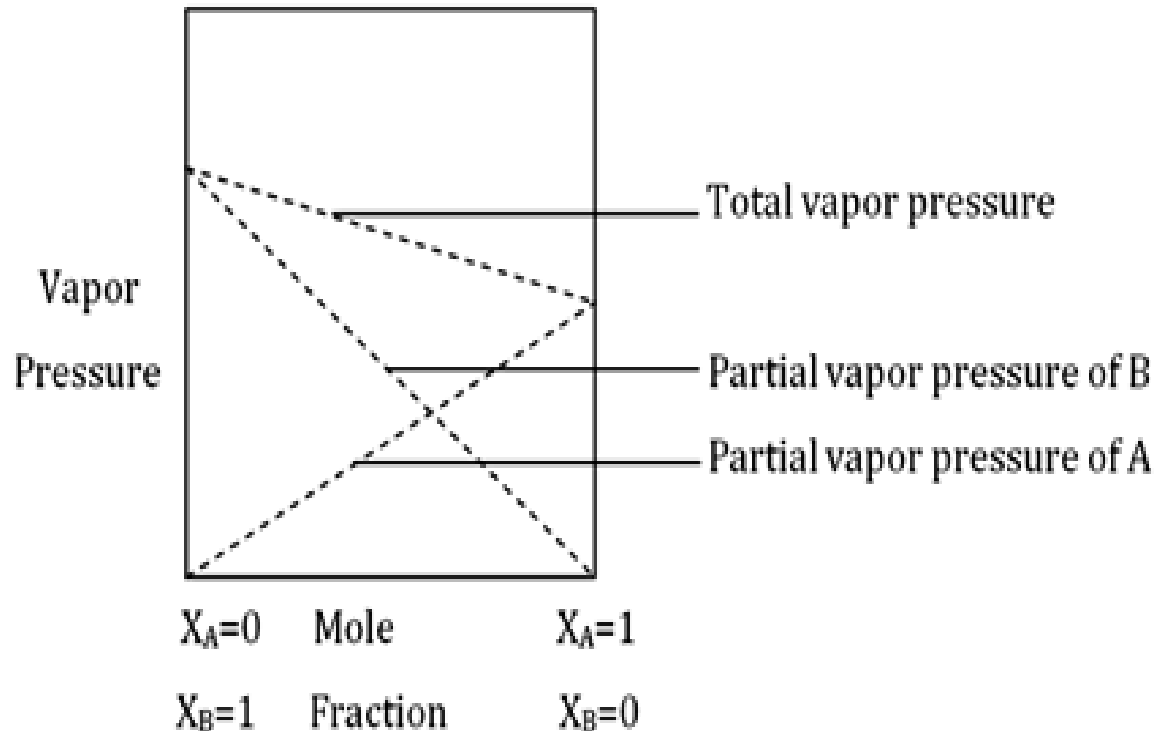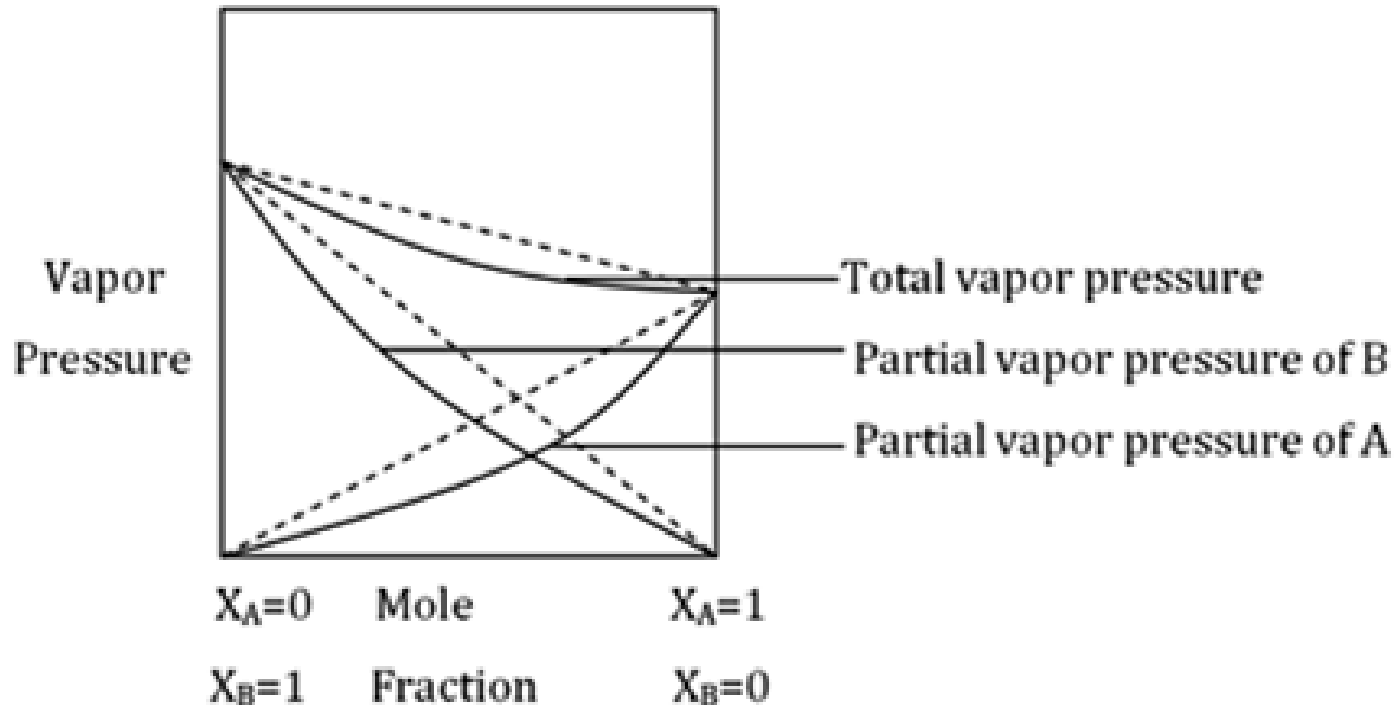
DEVIATIONS FROM RAOULTS LAW

If adhesive forces are less than cohesive forces B

i.e. A - A > A - B or B - B > A – B

then presence of component B reduces the interaction of component A and similar with presence of component A reduces the interaction of component

DEVIATIONS FROM RAOULTS LAW

If adhesive forces are more than cohesive forces
 i.e A – B > A – A or A – B > B – B then total vapor pressure is less than sum of partial vapor pressure of each component then it is called as negative deviation from Raoult's law.

| IDEAL SOLUTION	REAL SOLUTION
Obeys Raoult's Law	Deviated From Raoult's Law
Linear Relation in physical properties as like pure component	Non Linear Relation in physical properties with pure component
Same adhesive and cohesive forces for all molecules .	Difference in adhesive and cohesive forces for all molecules .
No change in properties of individual liquid after formation of solution	Change in properties of individual liquid after formation of solution
The concept of an ideal solution is fundamental to chemical thermodynamics	The concept of a real solution is not fundamental to chemical thermodynamics
During mixing of ideal solution no heat is evolved or absorbed.	Heat is evolved or absorbed during mixing.
$\Delta H_{solution} = 0$	$\Delta H_{solution} \neq 0$

NERNST's DISTRIBUTION LAW

• 1891 – Nernst

• It is related to the distribution of a solute in mixture of two non-miscible solvents. However, it dissolves in both of them.

•The Law States That,

" at constant temperature, the ratio of the concentrations of a solute distributed between two non-miscible solvents is a constant quantity "

$$\frac{c_1}{c_2} = K$$

Solute
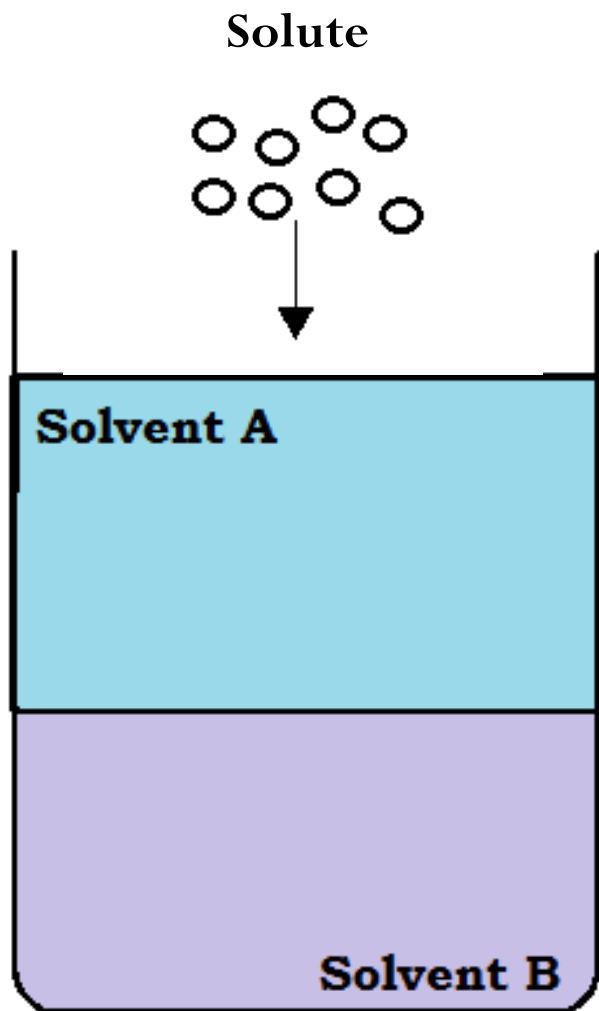
Solvent A

Solvent B

Before Distribution
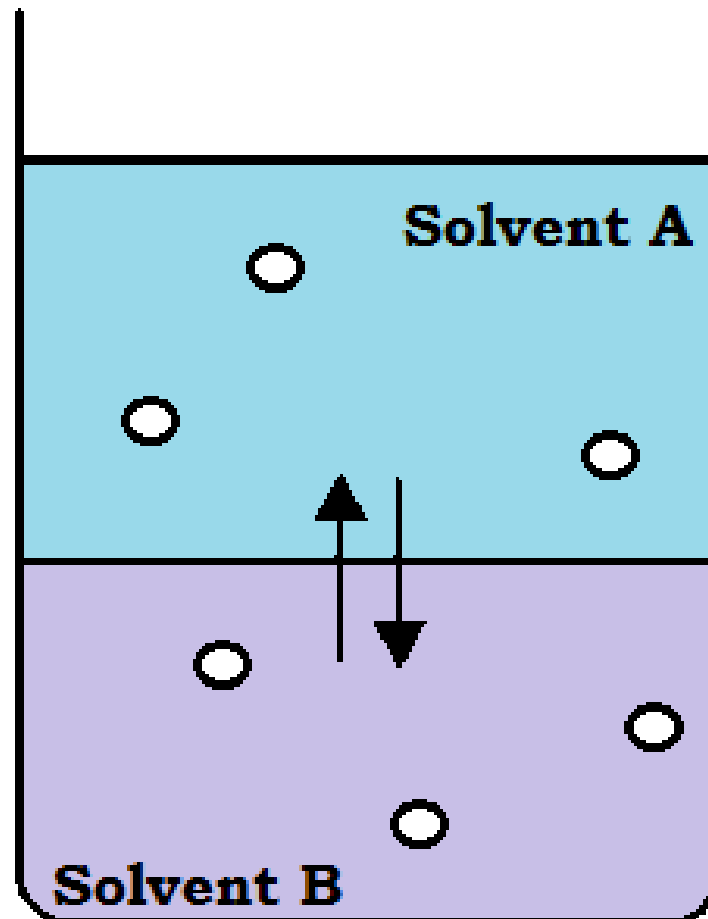
Solvent A

Solvent B

After Distribution

When the distribution of the solute X has reached dynamic equilibrium, the rate (R_1) at which molecule (X) pass from solvent A to B is proportional to its concentration (C_1) in solvent.

$$R_1 \propto C_1$$

$$R_1 = K_1 \times C_1 \qquad \text{where } K_1 \text{ is a constant}$$

Again

$$R_2 \propto C_2$$

$$R_2 = K_2 \times C_2 \qquad \text{where } K_2 \text{ is a constant}$$

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At equilibrium, the rate of migration of solute from one solvent to the other is equal.

Thus we have,

$$R_1 = R_2$$

$$K_1 \times C_1 = K_2 \times C_2$$

$$\frac{C_1}{C_2} = \frac{K_2}{K_1} = K_D$$

Equation gives mathematical expression of the Nernst's Distribution law.

Since K_1 and K_2 are constants at the same temperature, the distribution coefficient K_D is also constant if temperature is fixed.

LIMITATIONS

• The solute is to be distributed should not rest with any of the solvents.

•Solute should neither dissociate nor associate in the solvents.

•The solute that is being distributed shall not be reactive towards the solvents being used.

•Nernst distribution law is applicable if low concentration of solute is present in the two immiscible solvents.

•The temperature should be kept stable during the experiment.

APPLICATIONS

•This phenomenon is used for separation of organic solutions from aqueous solutions.

•Extraction of one substance from a solution containing various substances by using a suitable solvent.

•The solubility of drugs in water and other solvents and in a mixture of solvents can be predicted.

•For Desilverization of lead (Parke's Process)

•Also useful for determination of association and dissociation.

•The degree of hydrolysis of substance can be studied.

•For removal of solvent.

•Used for confirmatory test of bromide and iodide.

PARTITIONING

$$\frac{C_{org}}{C_{aq}} = K$$
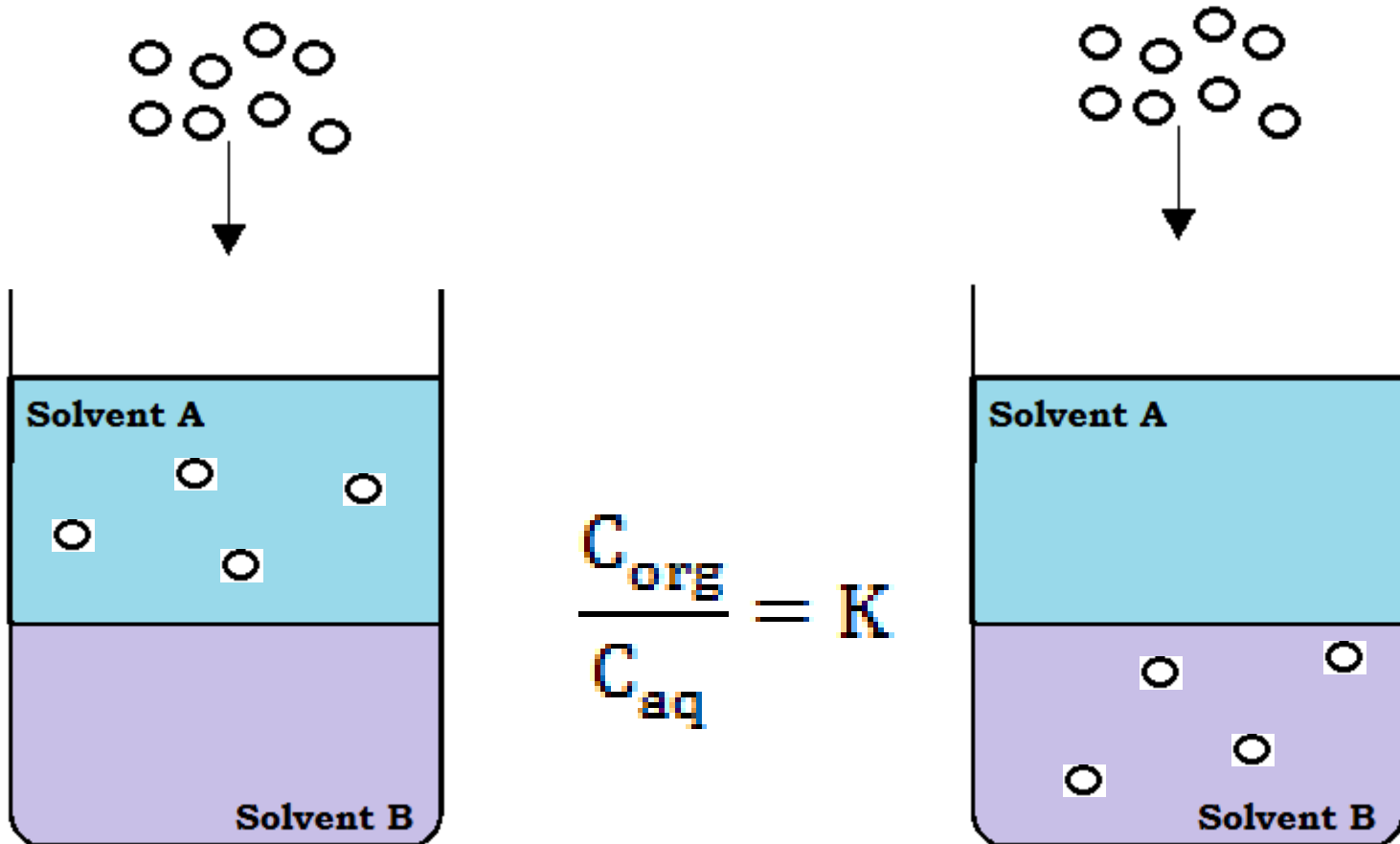
THANK YOU!

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