Physical Pharmacy

Colloids

Khalid T Maaroof
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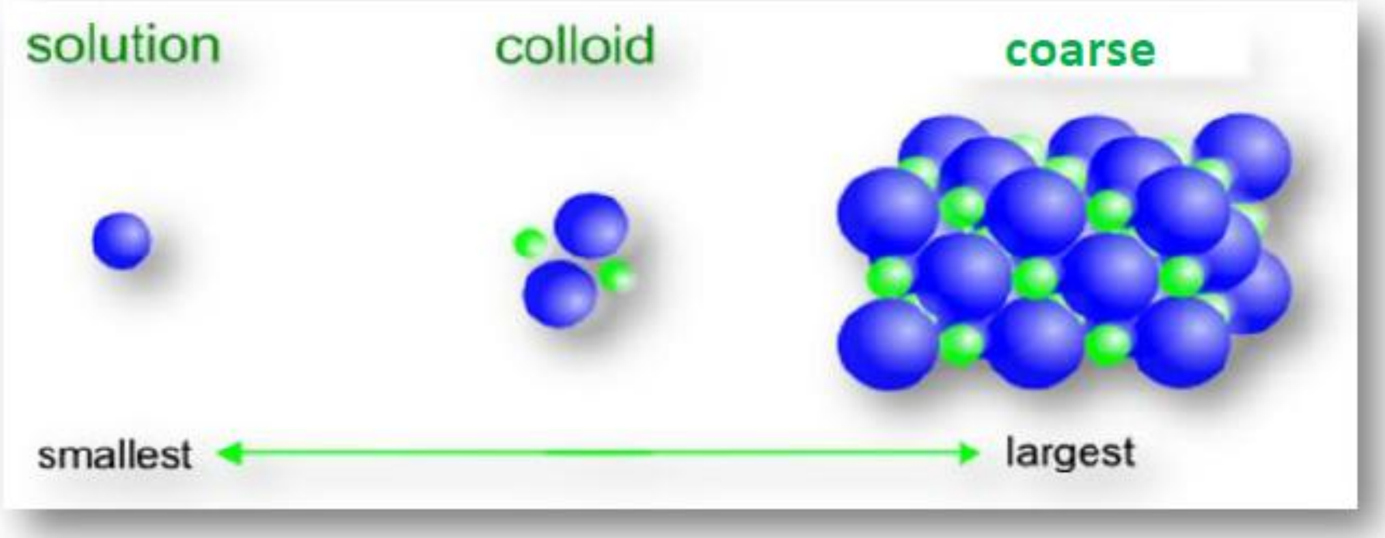
Introduction

- When two materials are mixed, one becomes dispersed in the other
- There are three types of dispersions according to the particle size:

Dispersions (mixtures)
- **True solutions (<1nm)**
- **Colloidal dispersions (1nm-500nm)**
- **Course dispersions (>500nm)**



Types of dispersions

Properties	**Molecular Dispersion**	**Colloidal Dispersion**	**Coarse Dispersion**
Size	< 1 nm	1-500 nm	> 500 nm
Diffusion	Fast	Slow	Don't diffuse
Microscope	Particles invisible in electron microscope	Particles resolved by electron microscope.	Particles are visible under ordinary microscope.
Filtration	Pass through semipermeable membranes and filter paper.	Pass through filter paper but not pass through semipermeable membrane.	Do not pass through filter paper or semipermeable membrane.
Example	O_2, glucose in water	Polymer and protein in water	Suspension and emulsion

Colloidal dispersions

Dispersed Phase	Dispersion Medium	Colloid Type	Examples
Solid	Solid	Solid sol	Stained glass, colored gemstones
Liquid	Solid	Solid emulsion	Aged cheese, solidified chocolate
Gas	Solid	Solid foam	Styrofoam, aerogel
Solid	Liquid	Sol, gel	Hair gel, silica gel
Liquid	Liquid	Emulsion	Cream in coffee, vinaigrette
Gas	Liquid	Foam	Soap foam, beer foam
Solid	Gas	Solid aerosol	Ash from a volcano, particulate pollutants
Liquid	Gas	Liquid aerosols	Spray perfume, aerosol deodorants
Gas	Gas	---	None (A gas in a gas always produces a solution)

Colloidal dispersions (Sols)

- Particles in the colloidal size range possess a surface area that is enormous compared with the surface area of an equal volume of larger particles.

- The possession of a large **specific surface** results in many of the unique properties of colloidal dispersions.

- The most important property of colloidal dispersions is that they are **stable** compared to coarse dispersions

Classification

- Colloidal systems are best classified into three groups on the basis of the interaction of the dispersed phase with the the dispersion medium.

- Lyophilic colloids

- Lyophobic colloids

- Amphiphilic colloids

Lyophilic (Solvent-loving) Colloids

- Systems containing colloidal particles that readily **interact** with the dispersion medium

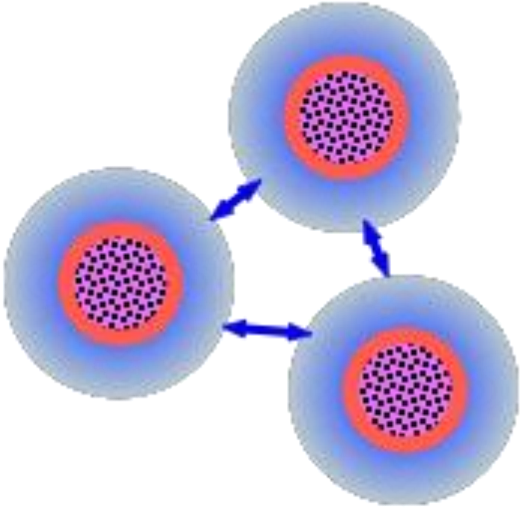
- Due to their **affinity** for the dispersion medium, such materials can easily form colloidal dispersions; simply by **dissolving** the material in the solvent being used.

- Most lyophilic colloids are **organic** molecules, for example, gelatin, acacia, insulin, albumin, rubber, and polystyrene.

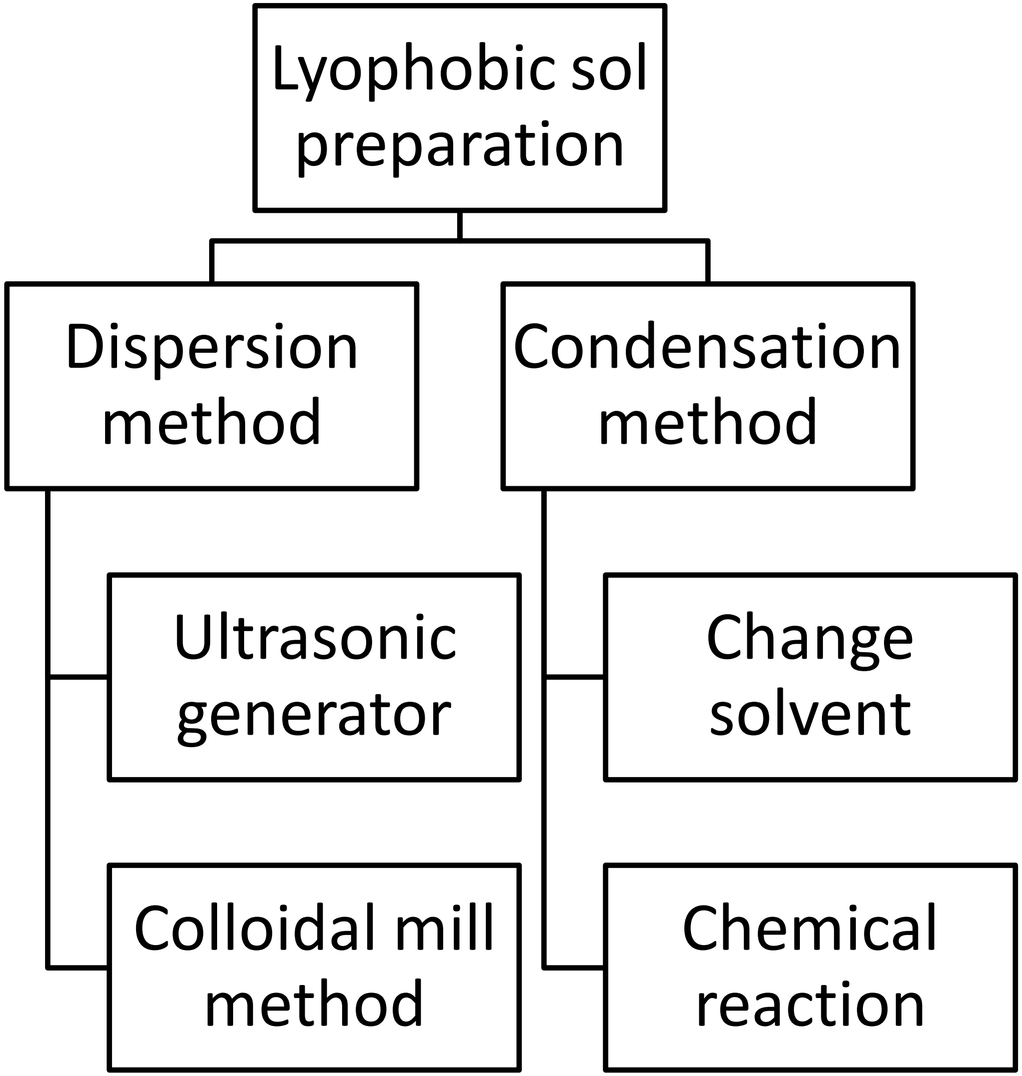
- According to the type of dispersion media, this type is also subdivided into:
  - **Hydrophilic** colloids: the dispersion medium is water. Examples: starch, gelatin and acacia in water.
  - **Lipophilic** or **oleophilic**: the dispersion media are oils or solvent of low polarity or low dielectric constant. Example: polystyrene in benzene; magnesium stearate in cottonseed oil.

Lyophobic (Solvent-hating) Colloids

- Systems composed of materials that have **little attraction**, if any, for the dispersion medium
- It is necessary to use **special** methods to prepare lyophobic colloids.
- They are generally composed of **inorganic** particles dispersed in water. Examples of such materials are gold, silver, sulfur, arsenous sulfide, and silver iodide.
- These colloids are easily precipitated on the addition of small amounts of **electrolytes**, by **heating** or by **shaking**.
- Once precipitated, it is **not** easy to reconstitute the sol by simple mixing with the dispersion medium. Hence, these sols are called **irreversible** sols.



Preparation technique of lyophobic colloids

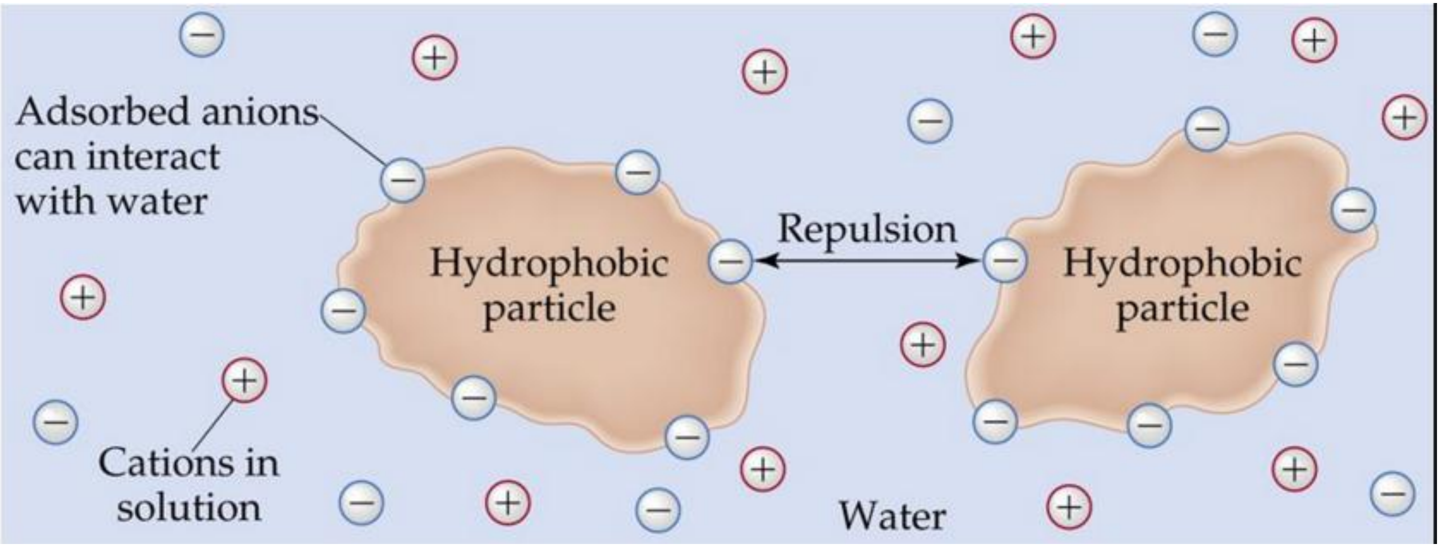


Lyophobic sol preparation

- Dispersion method
  - Ultrasonic generator
  - Colloidal mill method
- Condensation method
  - Change solvent
  - Chemical reaction

Stability of lyophobic colloids

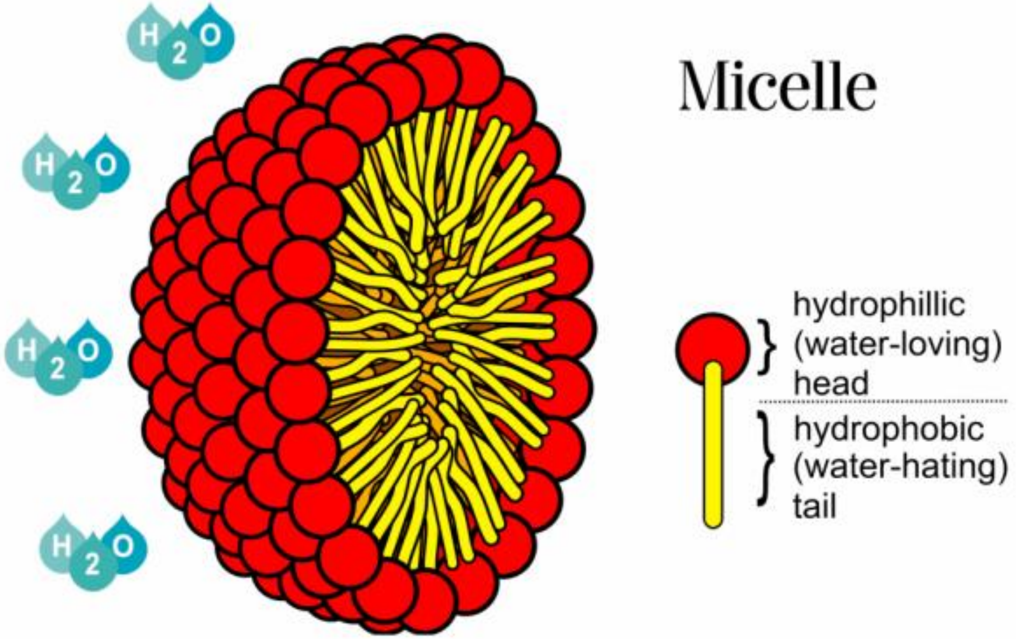
- Lyophobic colloids precipitate by addition of electrolytes to the dispersion, because they have initially been stabilized by charges.
- When they precipitate lyophobic colloids can not be re-dispersed by agitation or shaking.



- Lyophilic colloids do not precipitate by addition of electrolytes.
- If for any reason a lyophilic colloidal dispersion precipitate (for example by centrifuge) is can be re-dispersed by agitation.

Amphiphilic Colloids

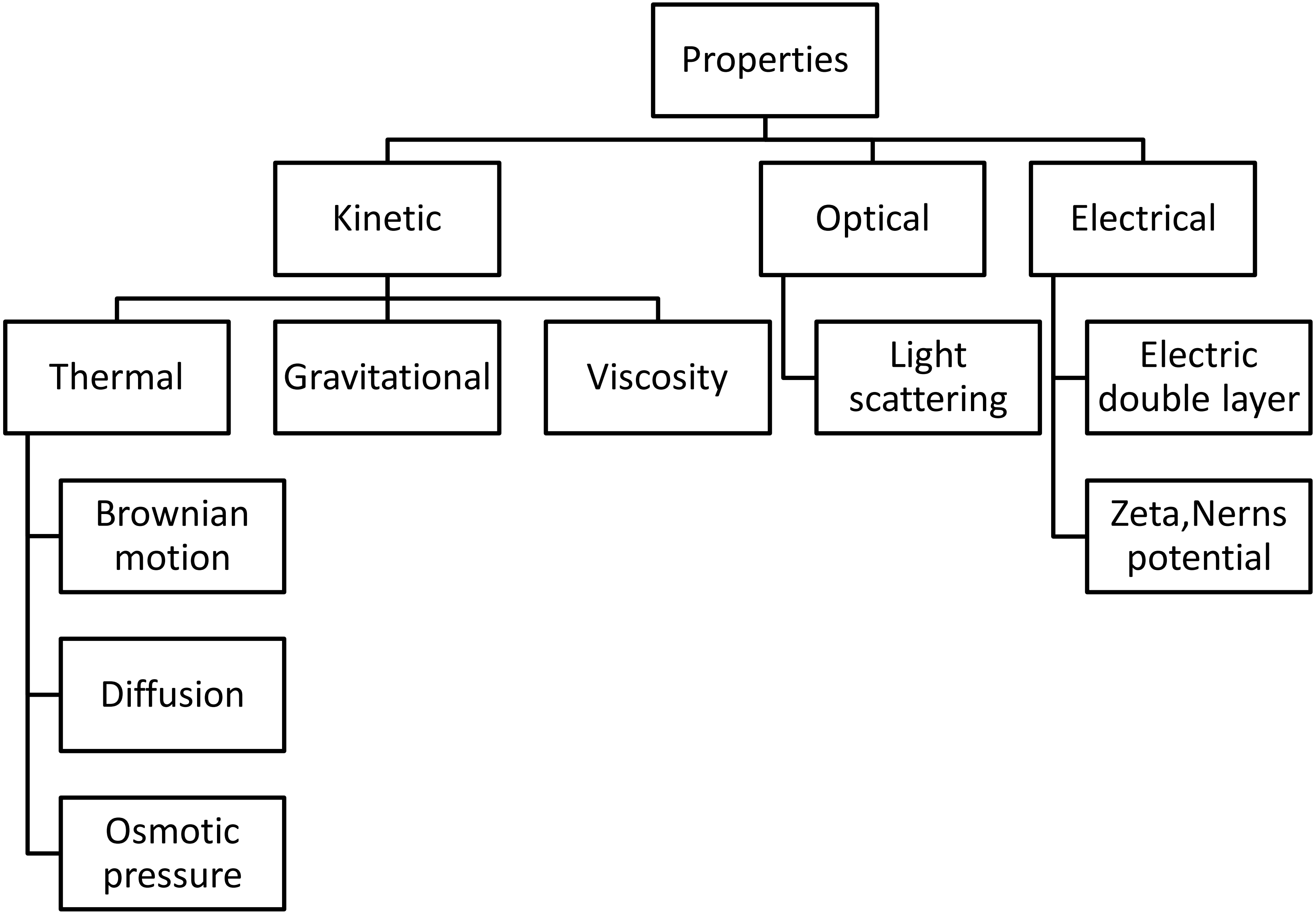
- Systems composed of **amphiphiles** or **surface-active agents**, When present in a liquid medium at low concentrations (below the **CMC**), the amphiphiles exist separately and are of subcolloidal size
- As the concentration is increased (above the CMC), micelles are formed which may contain **50** or more monomers, the diameter of each micelle is around **5** nm (colloidal size).
- The formation of amphiphilic colloids is **spontaneous**, if the concentration of the amphiphile **exceeds** the CMC.



Comparison

Property	**Lyophilic (solvent-loving)**	**Lyophobic (solvent-hating)**	**Association (amphiphilic)**
Dispersed phase	Large organic molecules lying within colloidal size	Inorganic particles such as gold or silver	Aggregates (micelles) of small organic molecules or ions whose size is below the colloidal size
Solvation	Solvated	Little solvation	Hydrophilic or lipophilic portion of the molecules is solvated depending on the medium
Preparation	Spontaneous by dissolving in solvent	Needs special procedure	Spontaneous when conc. of amphiphiles exceeds CMC
Viscosity	Viscosity increased as the conc. increases. At certain conc., gel-sol formation.	Not greatly increased due to unsolvation	Increased as conc. of amphiphile increases, as micelles no increase & become asymmetric.
Effect of electrolytes	Stable in presence of electrolytes. Desolvation and salting out in high conc.	Unstable due to neutralization of charges on particles;	CMC is reduced and salting out occur at high salt conc. (ionic SAAs)

Properties of colloidal dispersions



Properties

Kinetic

Optical

Electrical

Thermal

Gravitational

Viscosity

Light scattering

Electric double layer

Brownian motion

Diffusion

Osmotic pressure

Zeta,Nerns potential

Optical properties: Faraday-Tyndall Effect

- When a strong beam of light is passed through a colloidal sol, a visible cone, resulting from the scattering of light by the colloidal particles, is formed. This is the Faraday-Tyndall

Optical properties: Light scattering

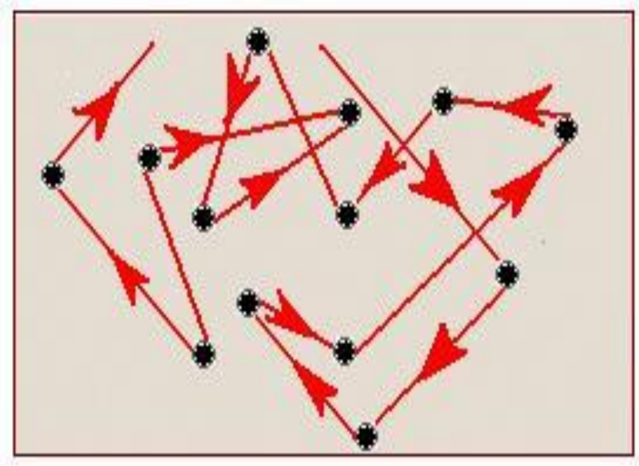
- This property depends on the Faraday-Tyndall effect and is used for determining the molecular weight of colloids, in addition to the shape and size of these particles.
- Scattering can be described in terms of the turbidity, τ, which is the intensity of light scattered I_s, divided by the intensity of the incident light, I.
- At a given concentration of dispersed phase, the turbidity is proportional to the molecular weight of the colloid, which can be obtained from the following equation:

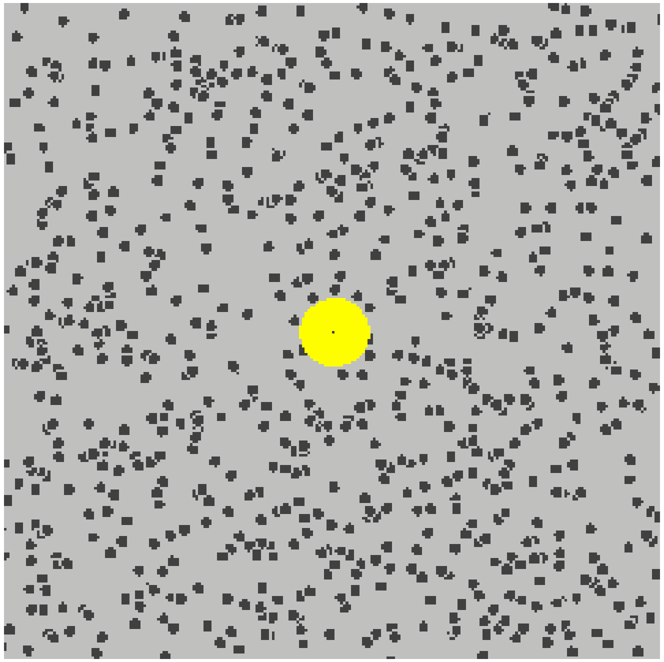
- H = optical constant; c = concentration of the solute; M = molecular weight; τ = turbidity; B = interaction constant

$$\frac{Hc}{\tau} = \frac{1}{M} + 2Bc$$

Kinetic properties: Brownian motion

- **Random movement** of colloidal particles resulting from the **bombardment of the particles by the molecules of the dispersion medium**.
- The velocity of the particles increases with decreasing **particle size**.
- Increasing the viscosity of the medium decreases and finally stops the Brownian movement.
- Brownian motion play the **major role** in stabilizing colloidal dispersions.





Kinetic properties: Diffusion

- Particles diffuse spontaneously from a region of higher concentration to one of lower concentration until the concentration of the system is uniform.
- Diffusion is a direct result of Brownian movement.
- According to Fick's first law, the amount of substance diffusing per unit time (flux, J) across a plane of area, S, is directly proportional to the change in concentration, dc, with distance traveled, dx.

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

Kinetic properties: Diffusion

- Assuming particles are spherical, diffusion coefficient can be used in Stokes-Einstein equation to obtain the radius of the particle :

$$D = \frac{RT}{6\pi\eta r N}$$

R = molar gas constant; T = absolute temperature; η = viscosity of the solvent; r = radius of the spherical particle; N = Avogadro's number.

- Diffusion coefficient can also be used to obtain the molecular weight of approximately spherical molecules, such as egg albumin and hemoglobin, by use of the equation:

$$D = \frac{RT}{6\pi\eta N} \sqrt[3]{\frac{4\pi N}{3M\bar{v}}}$$

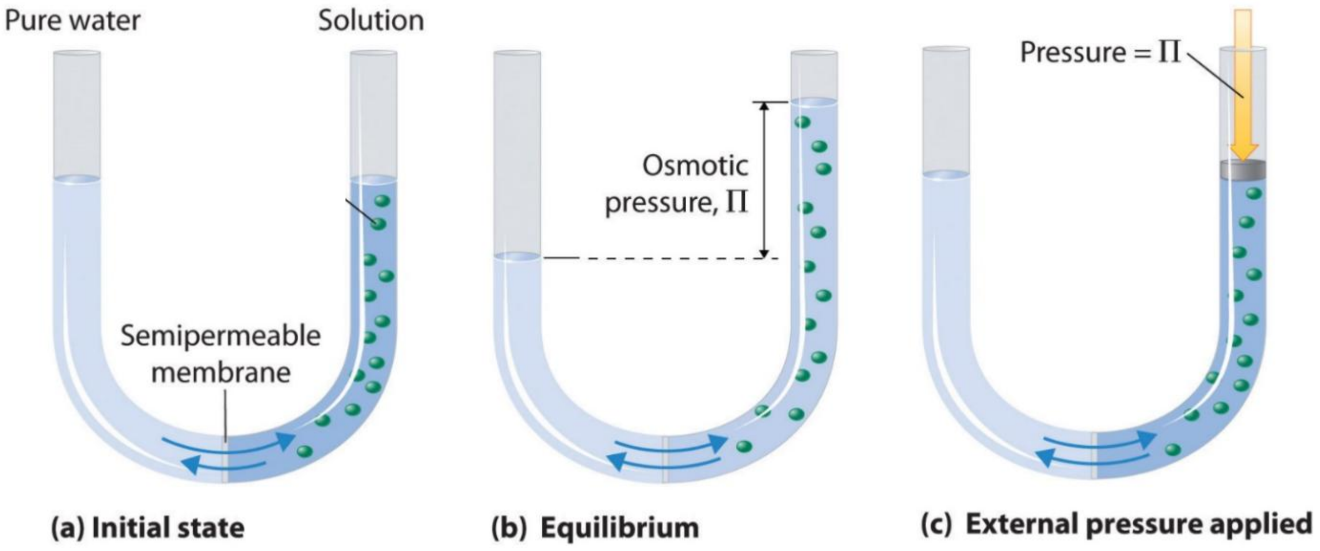
$\bar{v}$ = partial specific volume (volume of 1 g of the solute)

Kinetic properties: Osmotic pressure

The osmotic pressure π can be used to obtain the molecular weight using a modified van’t Hoff equation:

$$\frac{\pi}{c_g} = RT\left(\frac{1}{M} + Bc_g\right)$$

c_g = concentration of solute (g/L); B = a constant for any particular solvent/solute system



Kinetic properties: Sedimentation

The velocity of sedimentation (v) of spherical particles having a density (p) in a medium of density (P_o) and a viscosity (ŋ) is given by Stokes's law'.

$$v = \frac{r^2\,(p - p_0)g}{18\,\eta_0}$$

g = acceleration due to gravity

r = radius of particles

The equation is used to determine particle size larger than 0.5 µm. Particles lower than 0.5 µm in size don't obey Stokes's equation because Brownian movement becomes significant and tends to offset gravity sedimentation. Stronger force (ultracentrifugation) must be applied to generate the sedimentation of colloidal particles in a measurable manner.

Stokes's equation is modified to:

$$v = \frac{r^2\,(p - p_0)\omega^2 x}{18\,\eta_0}$$

Where gravity g is replaced by w^{2x}

w = angular velocity

X = distance of particles from the center of rotation

Kinetic properties: Viscosity

- Viscosity is the resistance of a system to flow under an applied stress. The more viscous a liquid is, the greater is the applied force required to make it flow at a particular rate.
- Einstein developed an equation of flow applicable to dilute colloidal dispersions of spherical particles:

$$ŋ = ŋ_0(1 + 2.5\varphi)$$

$ŋ_0$= viscosity of the dispersion medium

ŋ = intrinsic viscosity of the dispersion when the volume fraction of colloidal particles present is ϕ

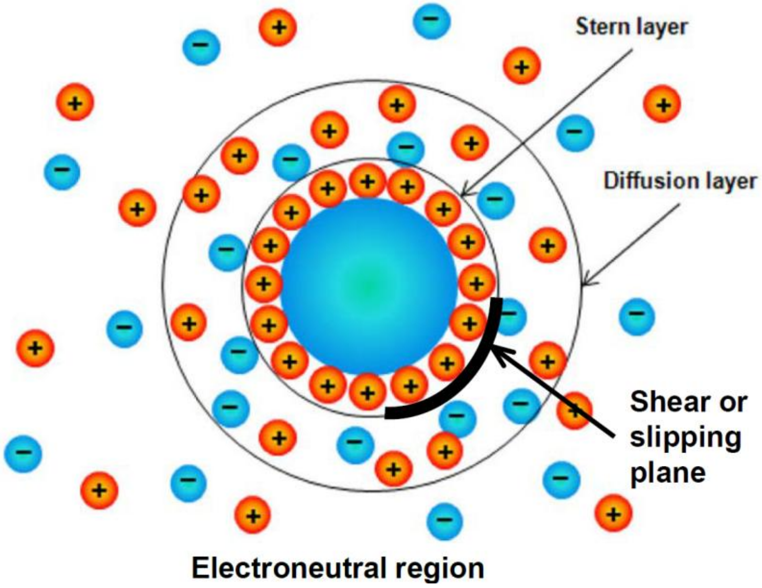
- Viscosity can be used to obtain the molecular weight (M) of material forming the dispersed phase according to Mark-Houwink equation:

$$\eta = KM^a$$

K & a =constants for each particular dispersion

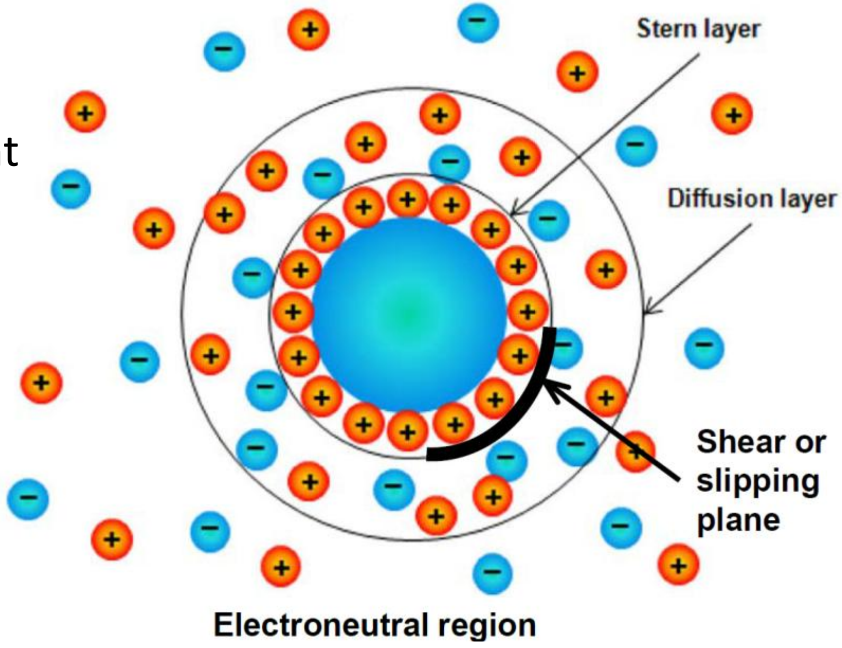
Electrical properties: Electric Double Layer

- Particles dispersed in liquid may become charged as a result of:
  - Adsorption of a particular ionic species present in solution.
  - Ionization of groups (such as COOH) that may be substituted at the surface of the particle. In this case, the charge depends on pK and pH.
- As a result, dispersed particles usually are surrounded by a double layer of electric charge made of ions from the dispersion medium.



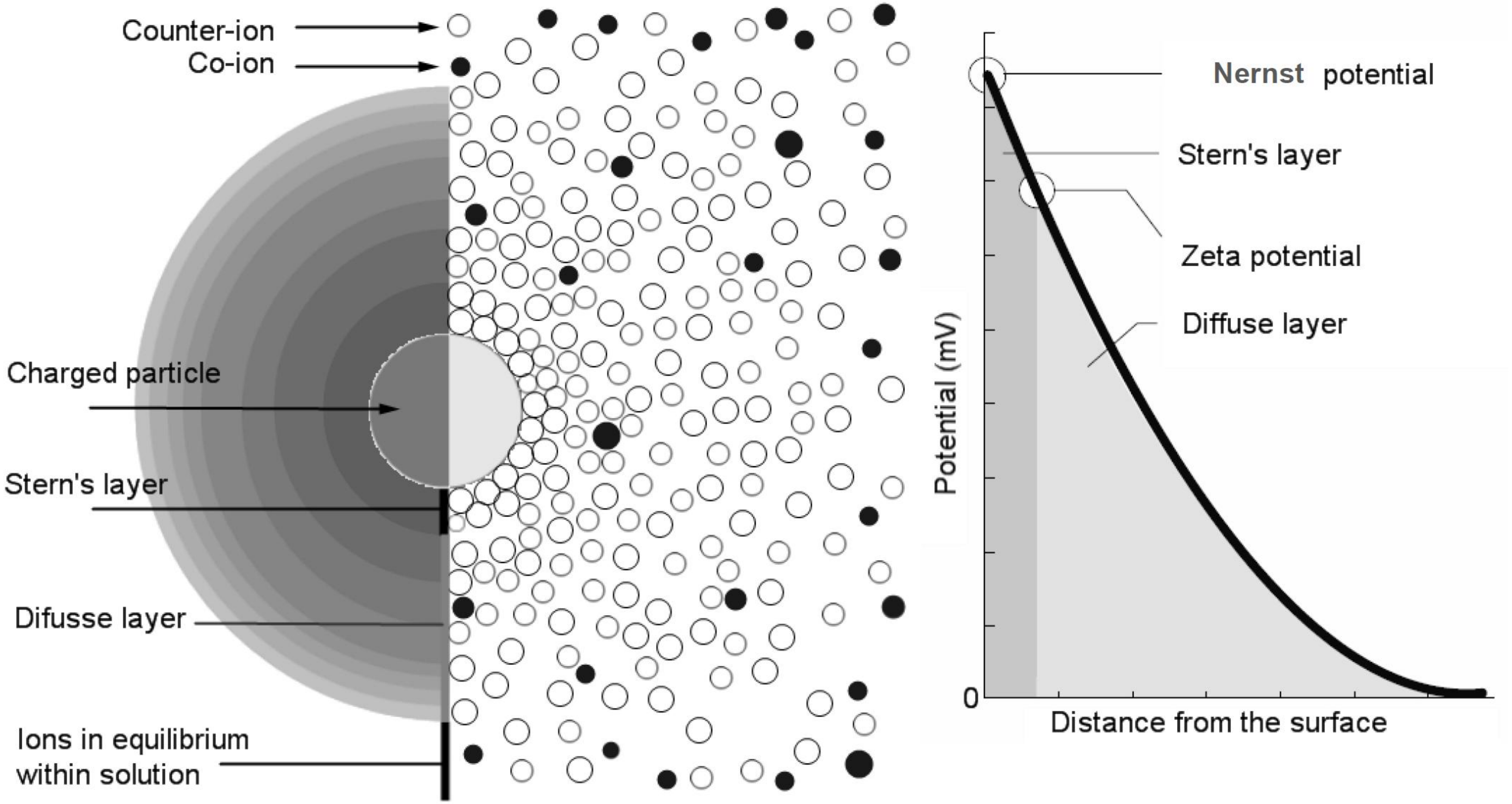
Electrical properties: Electric Double Layer

- The electric double layer consists of a Layer of ions bounded firmly to the surface called **Stern layer**, surrounded by oppositely charged ions that form a loose **diffusion layer** in the adjacent liquid phase.
- The surface separating the two layers is called (shear or slipping plane).
- The region outside the double layer with equal distribution of anions and cations is called **electroneutral region**.



Electrical properties: Nernst and Zeta Potentials

- The **electro-thermo-dynamic (Nernst) potential (E)** is the difference in potential between the actual surface and the electroneutral region of the solution.
- the **electrokinetic zetapotential ζ** is the difference in potential between the surface of the stern layer and the electroneutral region of the solution.
- The zeta potential is measured to monitor and predict the **stability** of dispersion systems



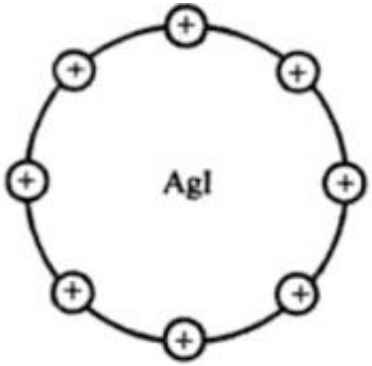
Stability of colloidal dispersions

- **The mechanism behind stability of colloidal dispersions:**

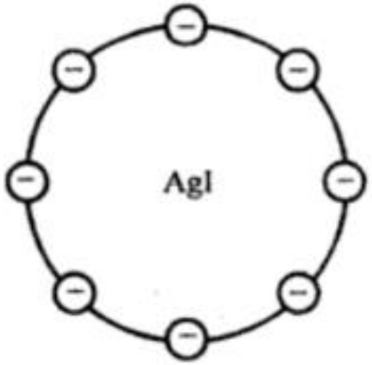
– The main reason of colloidal dispersion stability is their particle size which is very small that they can be kept dispersed by Brownian motion

– But we should avoid aggregation of these small particles to form larger particles and this done by:

- **Steric stabilization**: Particles are surrounded by a protective solvent sheath that prevents mutual adherence when they collide as a result of Brownian movement (in case of lyophilic and association colloids).
- **Electrostatic stabilization:** Dispersed particles are stabilized by charges (in case of lyophobic colloids)



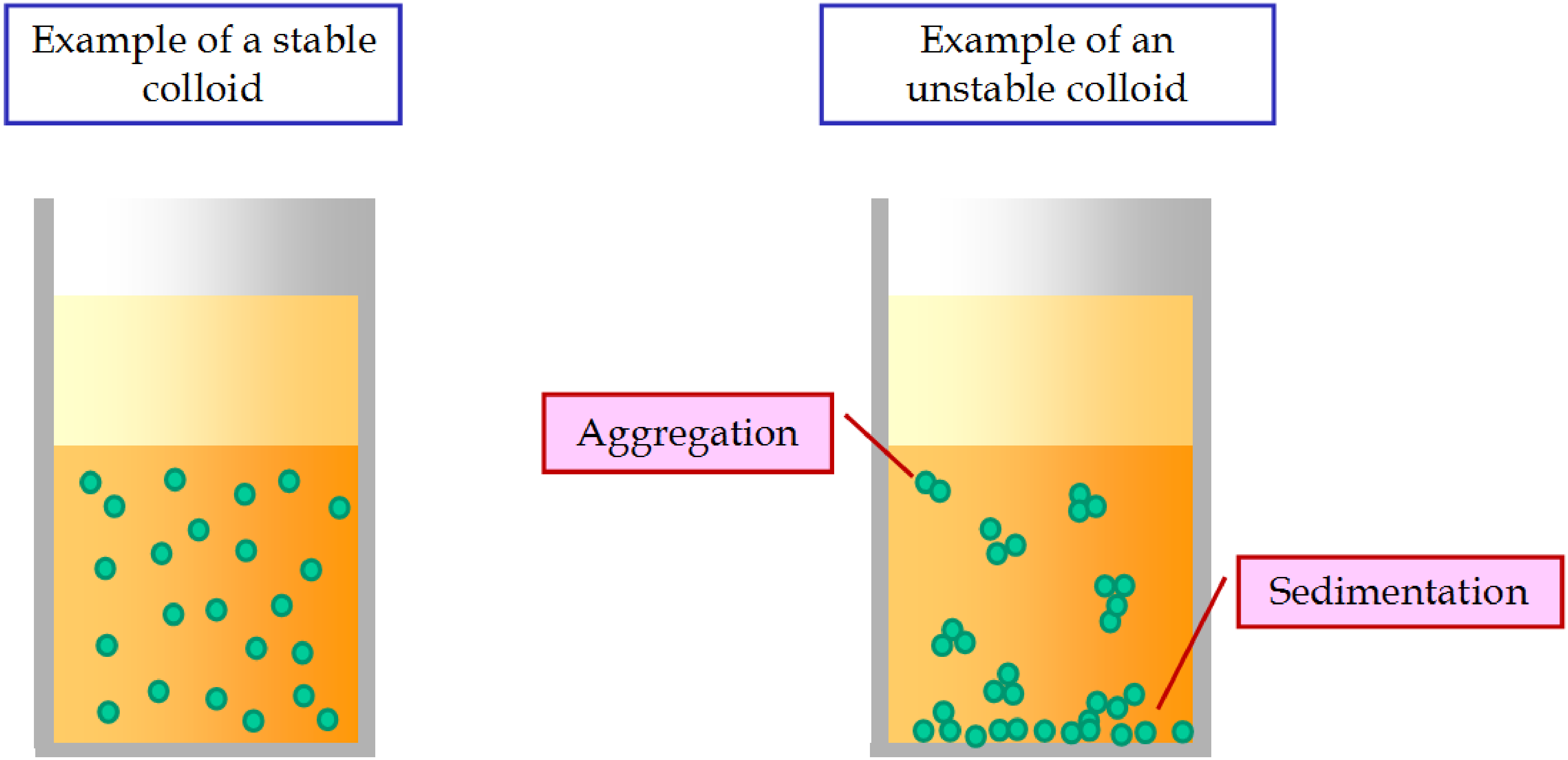
(a) Positively charged colloidal particle



(b) Negatively charged colloidal particle

Stability of colloidal dispersions

- If colloidal particle aggregate they from larger particles and sedimentation occurs over time
- Aggregation of particle is called **flocculation**



Example of a stable colloid

Example of an unstable colloid

Aggregation

Sedimentation

Pharmaceutical applications of colloids

- Effect: e.g. aluminum hydroxide as antacid.
- Dosage from development: e.g. nanoparticles
- Modifying solubility & stability of drugs.
- Modifying drug release: e.g. (Sustained drug delivery systems).
- Targeted delivery.

Pharmaceutical applications of colloids- some examples

- Colloidal silver iodide, silver chloride & silver protein are effective germicides & not cause irritation as ionic silver salts.
- Colloidal copper used in cancer.
- Colloidal gold used as diagnostic agent.
- Colloidal mercury used in syphilis.
- Association colloids (SAA) are used to increase solubility & stability of certain compounds in aqueous & oily pharmaceutical preparations.
- Blood plasma substitutes as dextran, PVP & gelatin are hydrophilic colloids used to restore or maintain blood volume.
- Iron - dextran complex form non-ionic hydrophilic sols used for treatment of anemia.

Questions?