COLLOIDS

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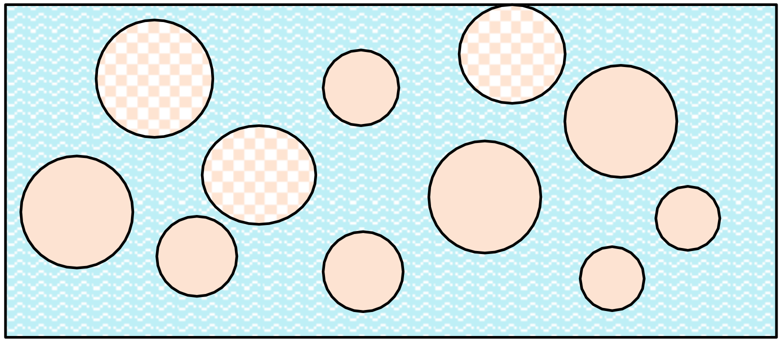
Colloids

- A **colloid** is a dispersion in which the dispersed matter has dimensions in the range from about 1 nm to 1000 nm.
- A suspension is a temporary dispersion of a material

Dispersion system: One or several substances disperse in another substance serving as medium.



Domain: **dispersed phase**

Continuous phase: **dispersion medium**

Classification of dispersed systems

According to the size of dispersed phase

d / m	Atom number	name	Phase number	uniformity
< 10^{-9} m	< 10^{3}	Molecular dispersion	Single phase	uniform
10^{-7}~10^{-9} m	10^{3}~10^{9}	Colloidal dispersion	multiphase	uniform
10^{-7}~10^{-4} m	> 10^{9}	Coarse dispersion	multiphase	nonuniform

Classification of colloids

Dispersion medium	Dispersed phase	name	Examples
Gas	liquid	Liquid aerosol	Fog, liquid sprays
	Solid	Solid aerosol	Smoke, dust
liquid	Gas	foam	Whipped cream
	Liquid	Emulsion	Milk
	solid	sol	Paint, mud
solid	gas	Solid foam	Expanded PS
	liquid	gel	Jellies, opal
	solid	Solid suspension	Colored glass Smoky crystal

Solutions, colloids, and heterogeneous mixtures

Wine is a solution of dissolved molecules

Milk is a colloid with fine particles that do not separate out on standing.

An aerosol spray, by contrast, is a heterogeneous mixture of small particles visible to the naked eye.

Colloidal Systems

- Particle Size Range

  $10\,\mathring{A} - 5000\,\mathring{A}$

  $1\,\mathring{A} = 10^{-8}\ \text{cm} = 10^{-10}\ \text{m}$

- Small particle size means a large interfacial area and a system in which interfacial properties are important.

Definitions

- Sol
  - general term used primarily for dispersions of solids in liquids, but also for dispersions in solid or gaseous media
    - hydrosol - dispersion in water
    - alcosol - dispersion in alcohol
    - aerosol - dispersion in air

Definitions

- Gel
  - a colloidal system which under a set of conditions of concentration and temperature, "sets" into a solid or semisolid
  - the rigidity of a gel is due to an intertwining network which traps the dispersion medium

Definitions

- Lyophobic Colloid
  - thermodynamically unstable systems
  - little interaction between dispersed phase and dispersion medium
    - low adhesional forces

Definitions

- Lyophilic Colloids
  - thermodynamically stable systems
  - strong and extensive interactions between dispersed phase and dispersion medium

Definitions

- Association Colloids
  - thermodynamically stable systems in which the dispersed phase consists of aggregates of amphiphilic molecules or ions (micelles)
    - at low concentration, these molecules exist in true solution
    - at higher concentrations, they aggregate to form micelles

Some probable shapes of micelles

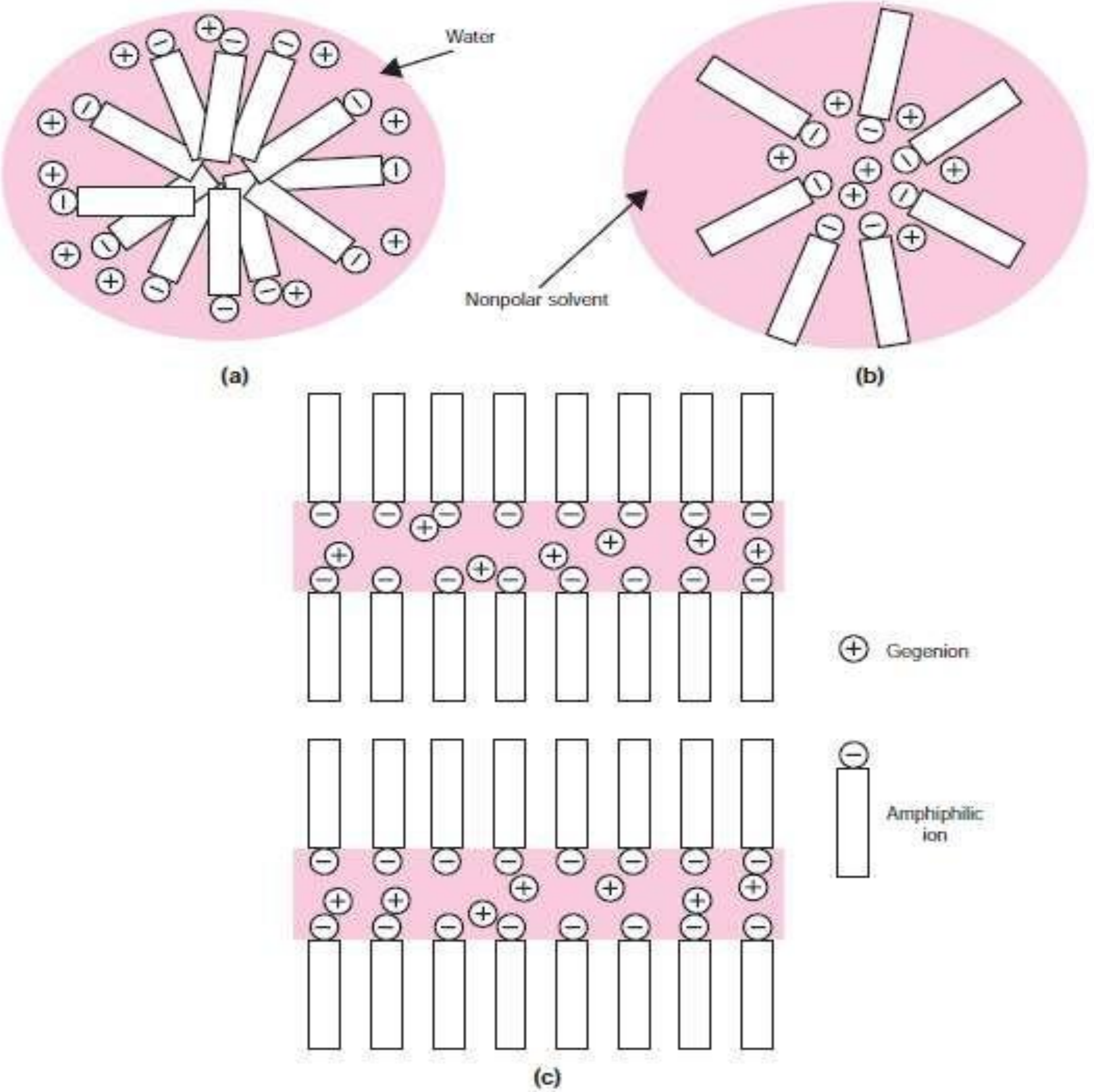


Fig. 16–4. Some probable shapes of micelles: (*a*) spherical micelle in aqueous media, (*b*) reversed micelle in nonaqueous media, and (*c*) laminar micelle, formed at higher amphiphile concentration, in aqueous media.

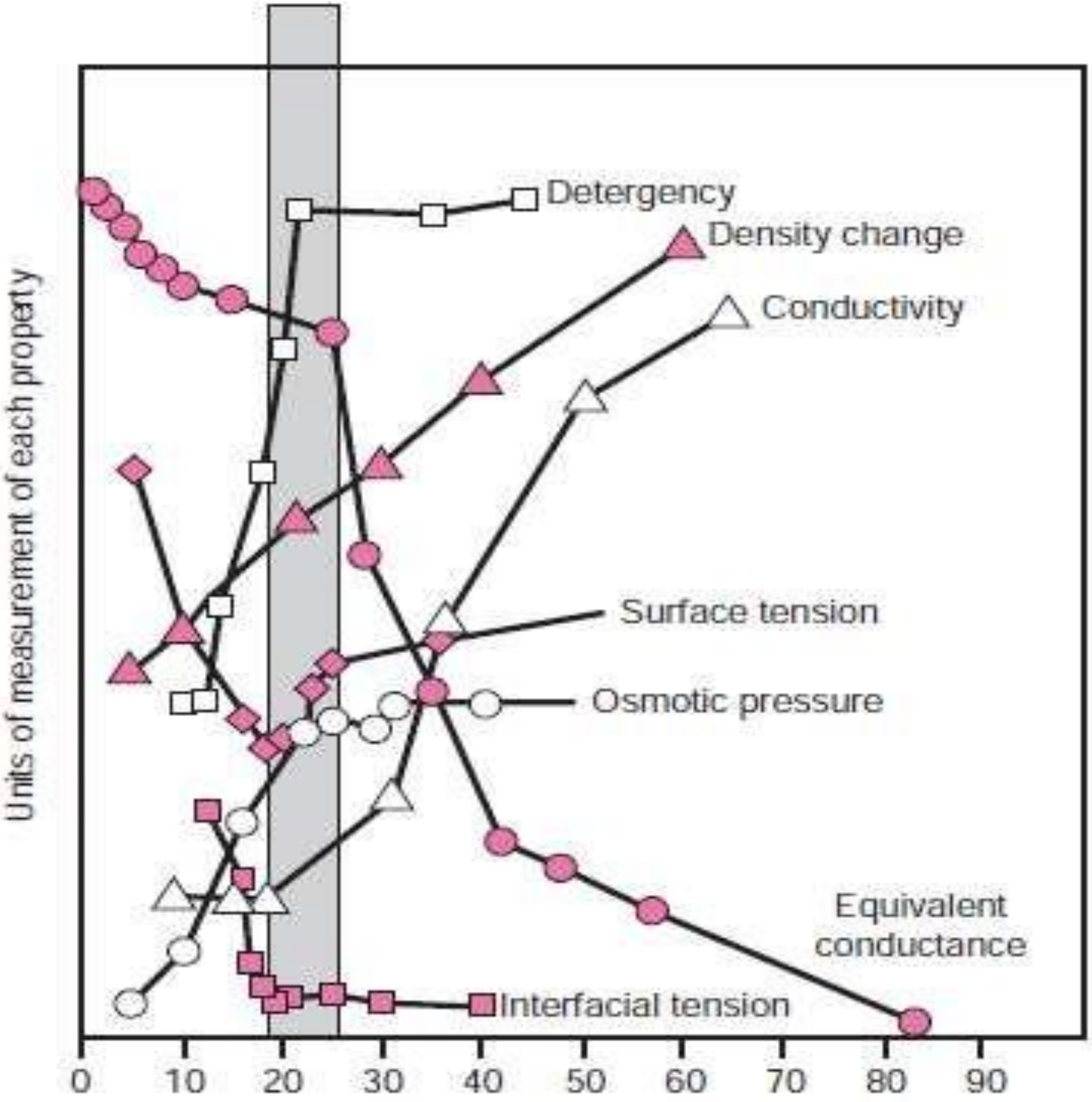


Fig. 16–3. Properties of surface-active agents showing changes that occur sharply at the critical micelle concentration. (Modified from W. J. Preston, Phys. Coll. Chem. **52**, 85, 1948.)

Classification of Colloidal Systems

Classification	Lyophilic (Hydrophilic)	Lyophobic (Hydrophobic)	Association
Dispersed Phase	Single Macro -molecule	Large collection of ions	Collection of surfactant molecules (micelle)
Interaction with Dispersion Medium	Strong	Weak	Strong
Formation	Spontaneous Reversible	Special technique	Spontaneous above cmc.

Classification of Colloidal Systems

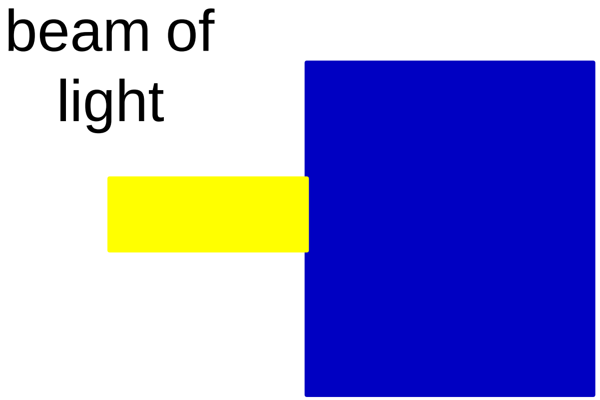
Classification	Hydrophilic	Hydrophobic	Association
Stabilizing Mechanism	Hydration Electrical repulsion	Electrical repulsion	Hydration/ Hydrophobic interactions
Viscosity	Dramatic increase	No change	Little change; can increase at high conc.
Examples	Gelatin Methyl-cellulose	Silver Iodide Gold Sols	Tween 80 Bile Salts

Properties of Colloids

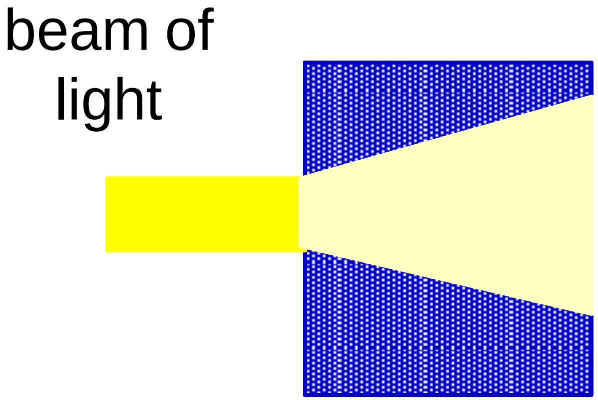
- Optical Properties
- Electrical Properties
- Kinetic Properties

Properties of Colloids

- Optical Properties
  - Tyndall Effect
    - light may be absorbed, scattered, or transmitted by the dispersed phase of a colloid



solution



colloid

Tyndall Effect

- Colloidal suspensions can scatter rays of light.
- This phenomenon is known as the Tyndall effect.

Tyndall Effect

A Solution
Does not
Scatter light

Colloidal
Iron(III) Oxide
Scatters light

Properties of Colloids

- Brownian Movement
  - particles are generally small enough to be influenced by the collision with molecules of the dispersion medium
  - when particles are observed, they are seen to move in a random, erratic manner

Properties of Colloids

- Consequences of Brownian movement
  - Stable colloids are systems in which the dispersed particles do not settle, because the force of gravity is counteracted by Brownian movement
  - Colloidal sols will **diffuse** from a region of high concentration to a region of low concentration
  - Colloidal sols show **colligative properties**

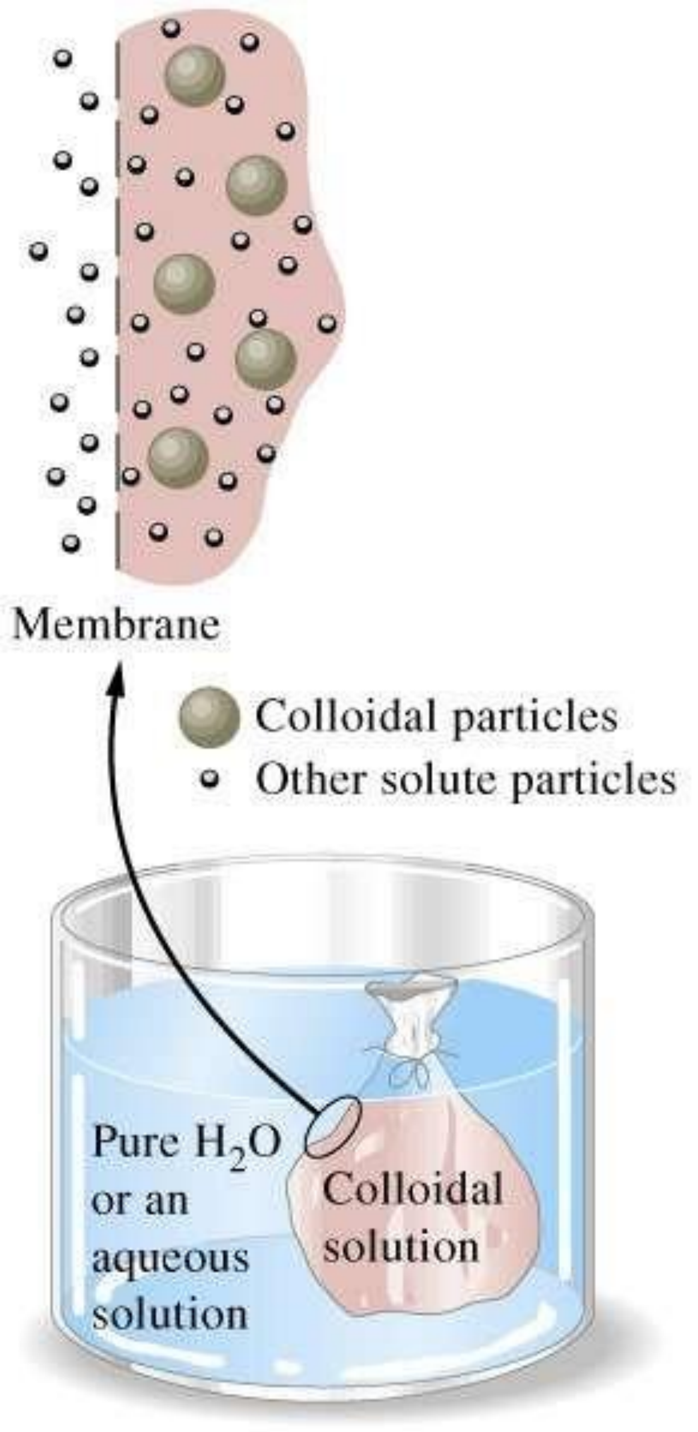
A **colligative property** is a physical property of a solution that depends on the concentration of solute in the solution but not on the identity of the solute.

Colloidal Diffusion

- Fick's Law

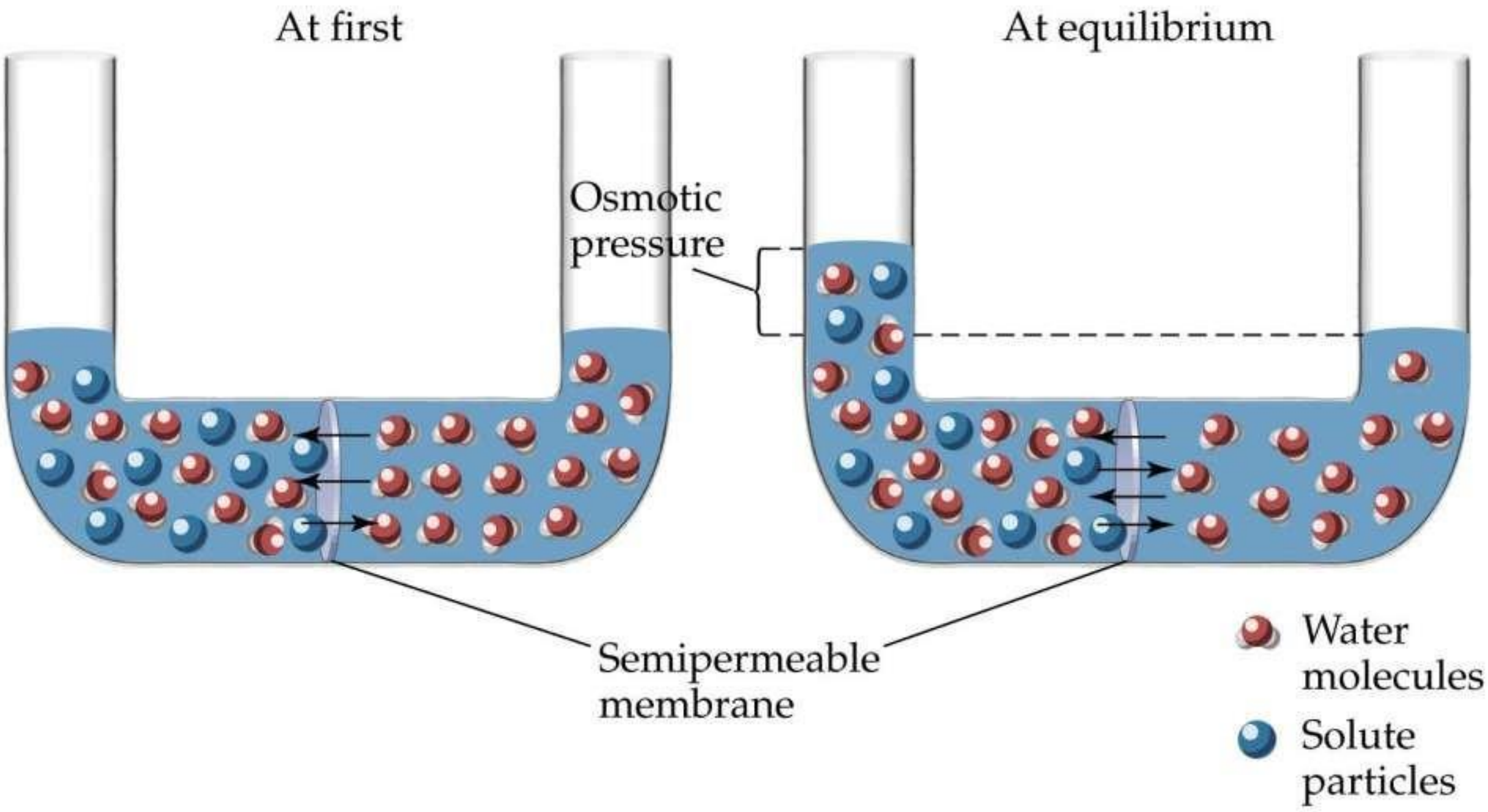
  $-dM/dt = D\,A\,[dc/dx]$

$$D = \frac{R\,T}{6\,\pi\eta r\,N}$$



- In dialysis, molecules and ions always diffuse from areas of higher concentration to areas of lower concentration.

Osmosis

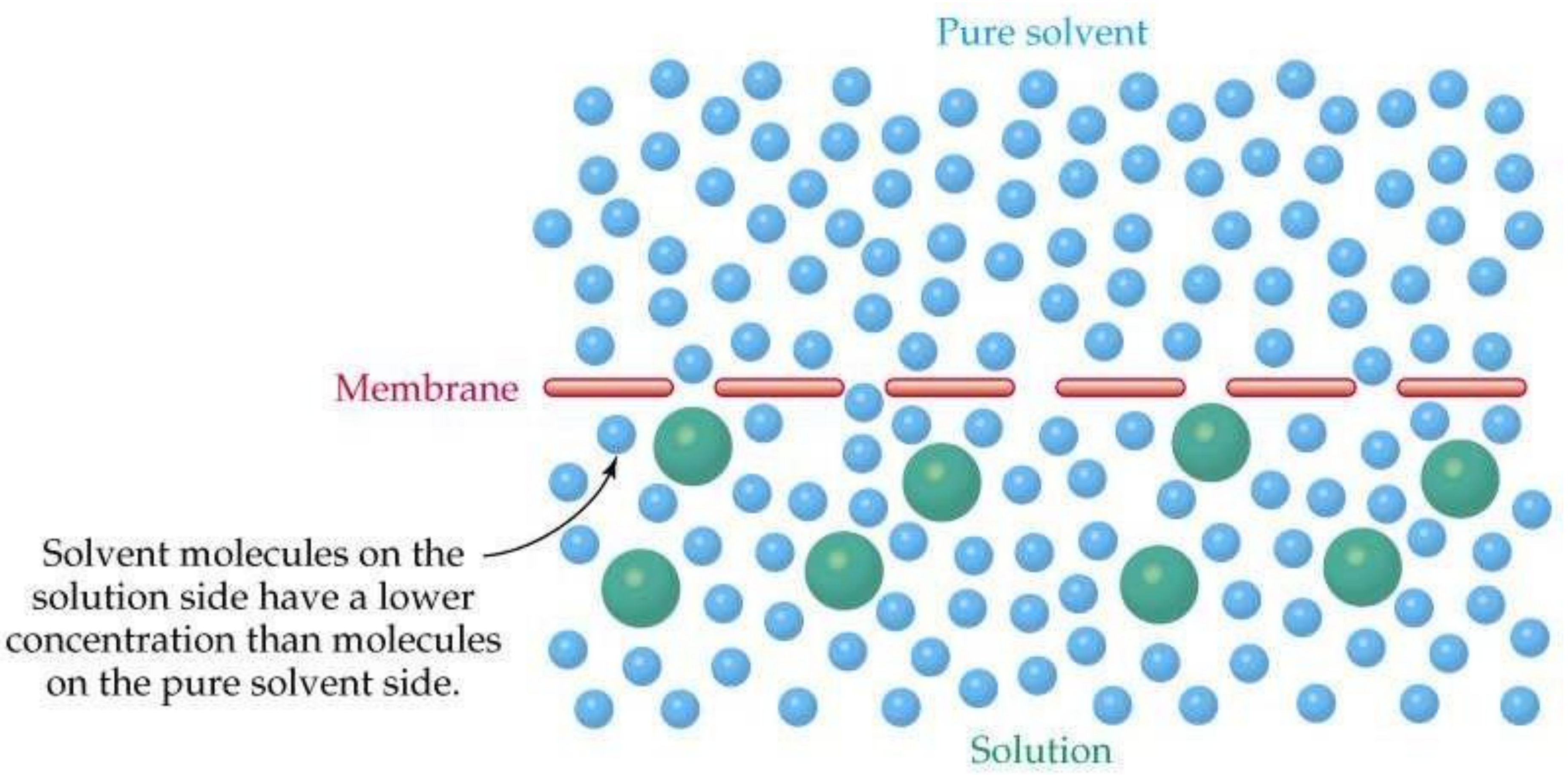

At first
At equilibrium
Osmotic pressure
Semipermeable membrane
Water molecules
Solute particles

Semi permeable membranes

- A semi permeable membrane only lets the solvent molecules through

- Examples
  - Cell walls
  - Parchment
  - Cellophane

Osmosis



Solvent molecules on the solution side have a lower concentration than molecules on the pure solvent side.

Osmotic Pressure

The **osmotic pressure** of a solution is the pressure that must be applied to the solution to prevent the flow of solvent molecules into the solution when the solution and pure solvent are separated by a semipermeable membrane.

The higher the osmolarity the greater the osmotic pressure

Equation for Calculation of Mol. weight of Colloid

- Van’t Hoff equation

$$\Pi = \mathbf{cRT} \ldots .1$$

Where c= molar conc. of Solute

Equation used for calculation of dilute solution.

Replace $C = c_g/M$ in equation 1

$$\Pi = \mathbf{c_g/M\ RT} \ldots ..2$$

Cont…

- Rearranging equation…2

$$\Pi/c_g = RT \div M \ldots\ldots 3$$

which applies in a very dilute solution.

If polymer having a molecular weight of, say, 50,000 is often a linear function of the concentration

$$\Pi/c_g = RT\,(1 \div M + Bc_g) \quad \ldots.4$$

Osmotic pressure Cont….

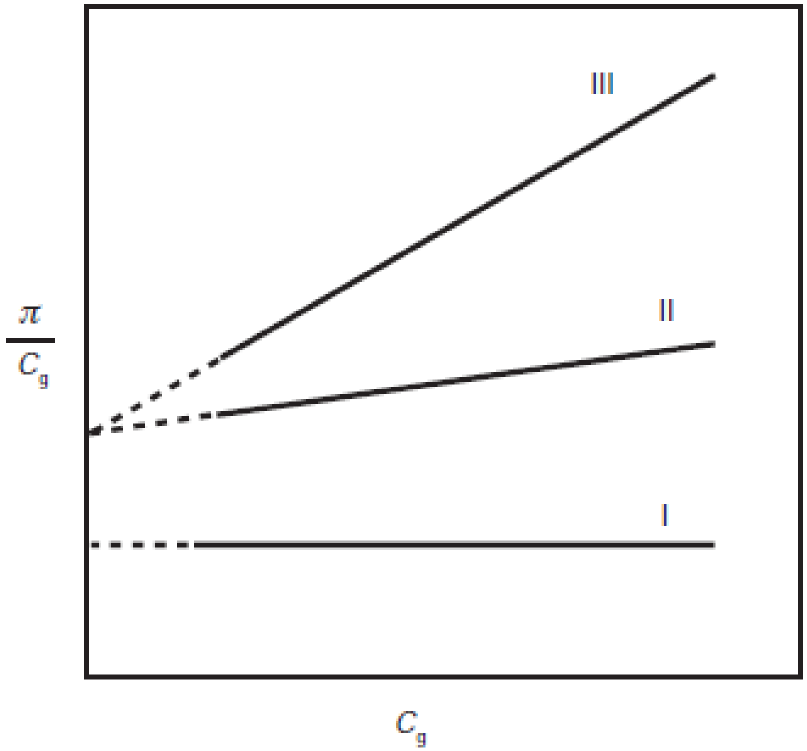


Fig. 16–8. Determination of molecular weight by means of the osmotic pressure method. Extrapolation of the line to the vertical axis where $c_g = 0$ gives RT/M, from which M is obtained. Refer to text for significance of lines I, II, and III. Lines II and III are taken to represent two samples of a species of hemoglobin.

Viscosity

Viscosity – resistance to flow of liquids

Related to

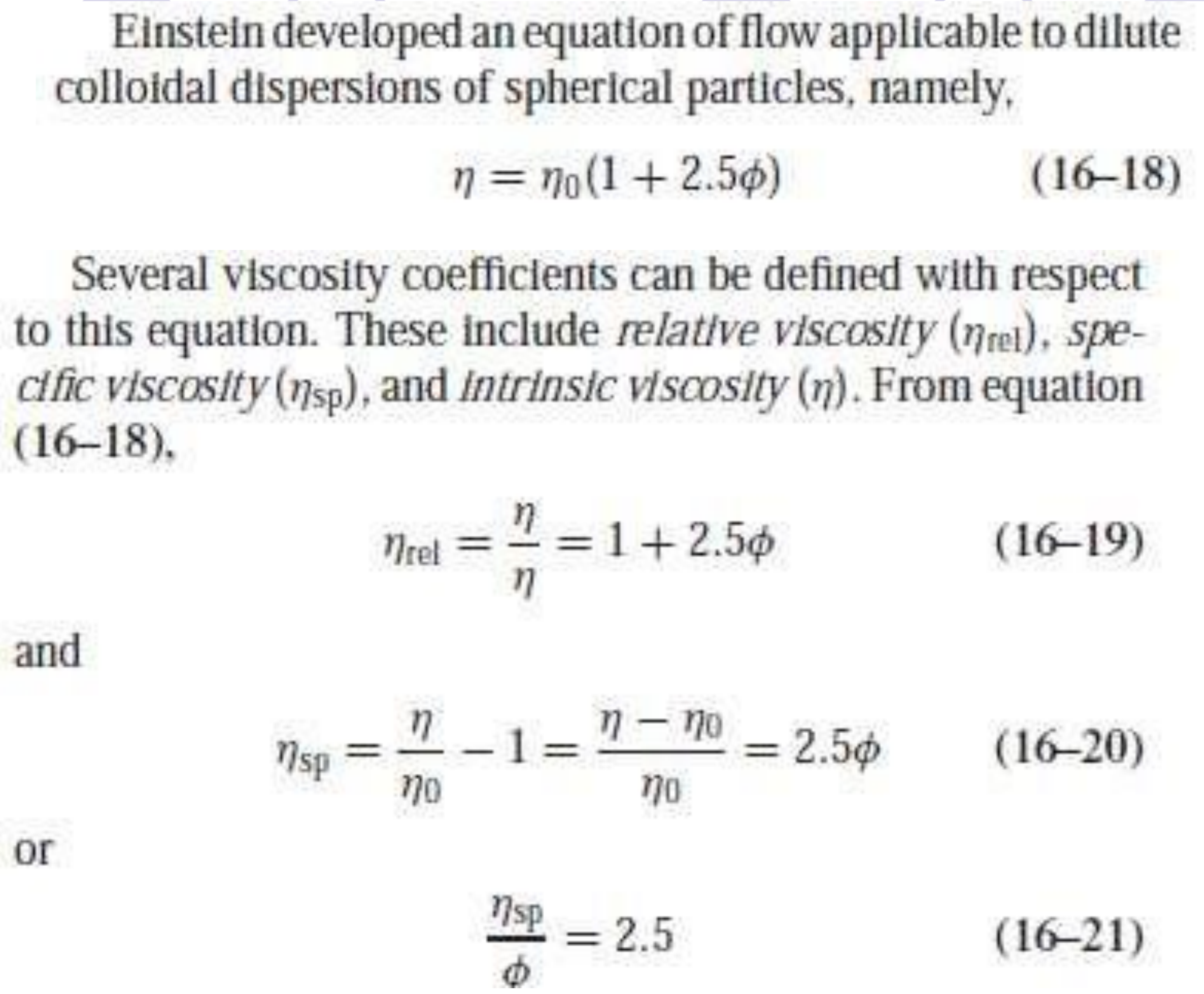
- -Intermolecular forces of attraction
- -Size and shape of constituent particles

Low viscosity (this easily flowable liquids)

- weak intermolecular forces
- - small symmetrical molecules
- **-Ex: Spherical colloids**

High Viscosity (difficult to flow liquids)

- -Strong intermolecular forces
- - large or unsymmetrical molecules
- **- Ex: linear colloids**



Einstein developed an equation of flow applicable to dilute colloidal dispersions of spherical particles, namely,

$$\eta = \eta_0(1 + 2.5\phi) \tag{16–18}$$

Several viscosity coefficients can be defined with respect to this equation. These include *relative viscosity* (η_{rel}), *specific viscosity* (η_{sp}), and *intrinsic viscosity* (η). From equation (16–18),

$$\eta_{\text{rel}} = \frac{\eta}{\eta} = 1 + 2.5\phi \tag{16–19}$$

and

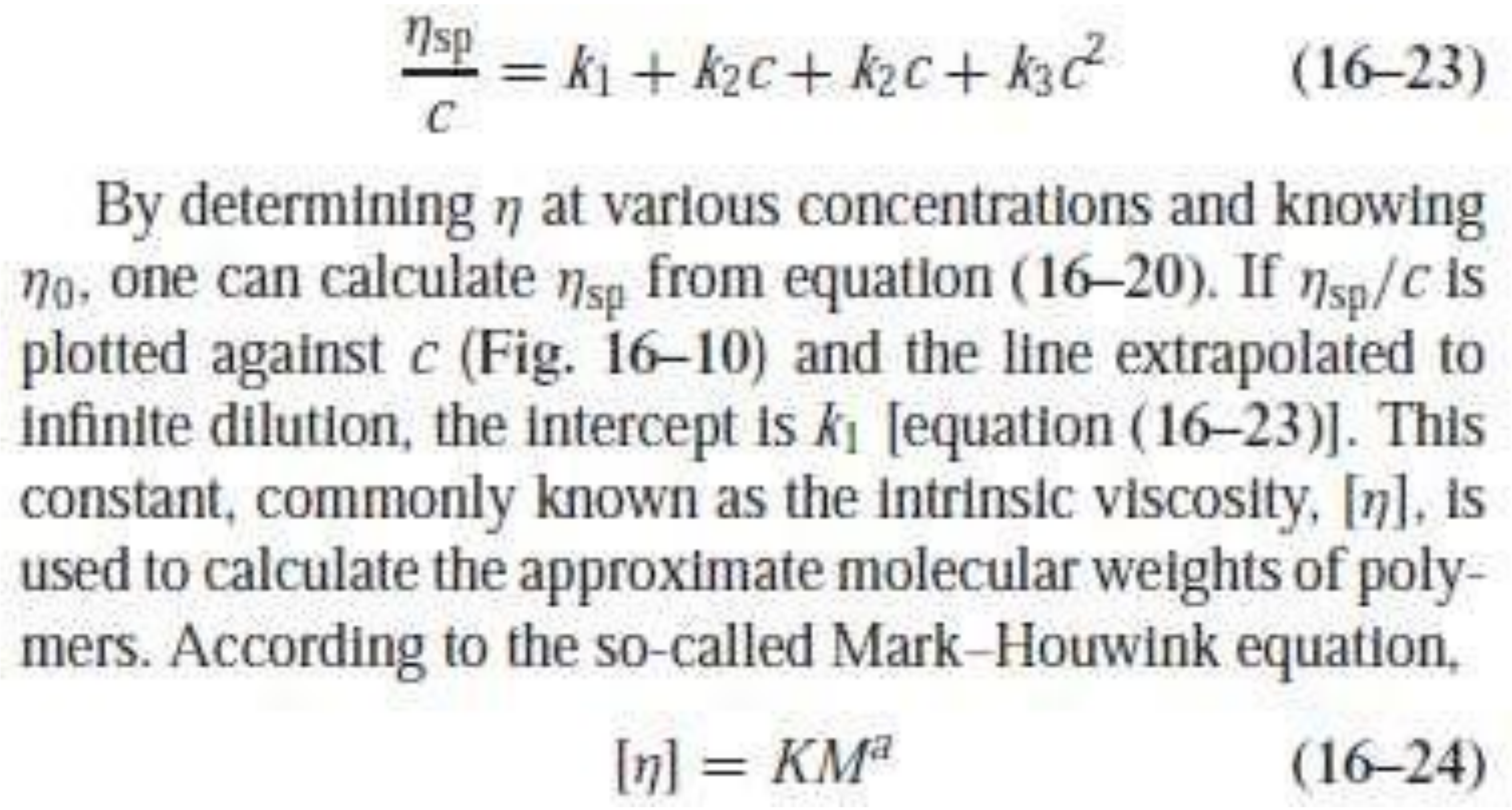
$$\eta_{\text{sp}} = \frac{\eta}{\eta_0} - 1 = \frac{\eta - \eta_0}{\eta_0} = 2.5\phi \tag{16–20}$$

or

$$\frac{\eta_{\text{sp}}}{\phi} = 2.5 \tag{16–21}$$

η_0 is the viscosity of the dispersion medium and η is the viscosity of the dispersion when the volume fraction of colloidal particles present is ϕ. The volume fraction is defined as the volume of the particles divided by the total volume of the dispersion; it is therefore equivalent to a concentration term.

$$\frac{\eta_{\mathrm{sp}}}{c} = k \qquad (16\text{–}22)$$



$$\frac{\eta_{sp}}{c} = k_1 + k_2c + k_2c + k_3c^2 \qquad (16\text{–}23)$$

By determining η at various concentrations and knowing η_0, one can calculate η_{sp} from equation (16–20). If η_{sp}/c is plotted against c (Fig. 16–10) and the line extrapolated to infinite dilution, the intercept is k_1 [equation (16–23)]. This constant, commonly known as the intrinsic viscosity, $[\eta]$, is used to calculate the approximate molecular weights of polymers. According to the so-called Mark–Houwink equation,

$$[\eta] = KM^a \qquad (16\text{–}24)$$

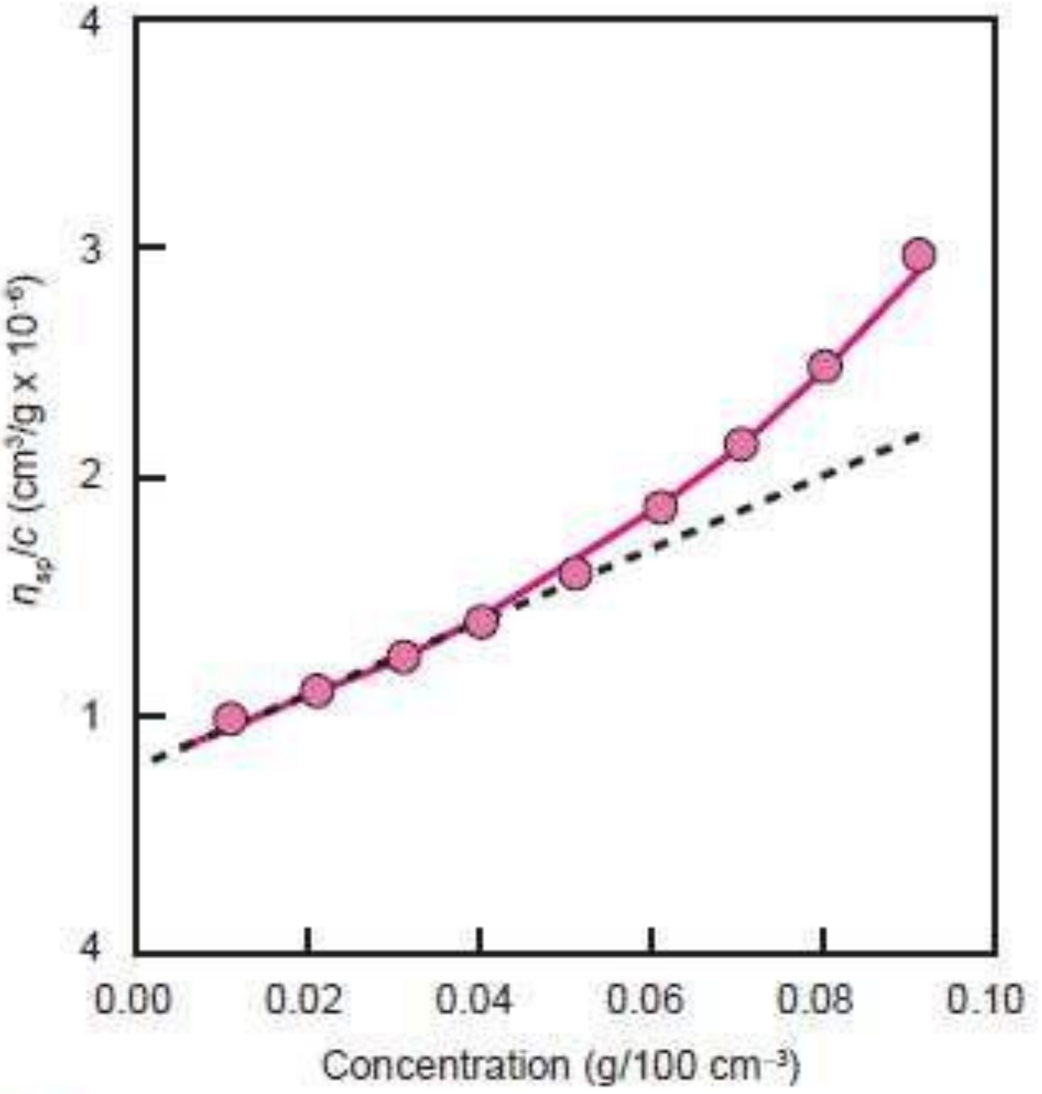


Fig. 16–10. Determination of molecular weight using viscosity data. (Replotted from D. R. Powell, J. Swarbrick, and G. S. Banker, J. Pharm. Sci. **55**, 601, 1966. With permission.)

Sedimentation

- Stock’s low

$$v = \frac{2r^2(\rho - \rho_0)g}{9\eta_0}$$

- In centrifuge, the acceleration of gravity is replaced by angular velocity ….W^2x

$$v = \frac{dx}{dt} = \frac{2r^2(\rho - \rho_0)\omega^2 x}{9\eta_0}$$

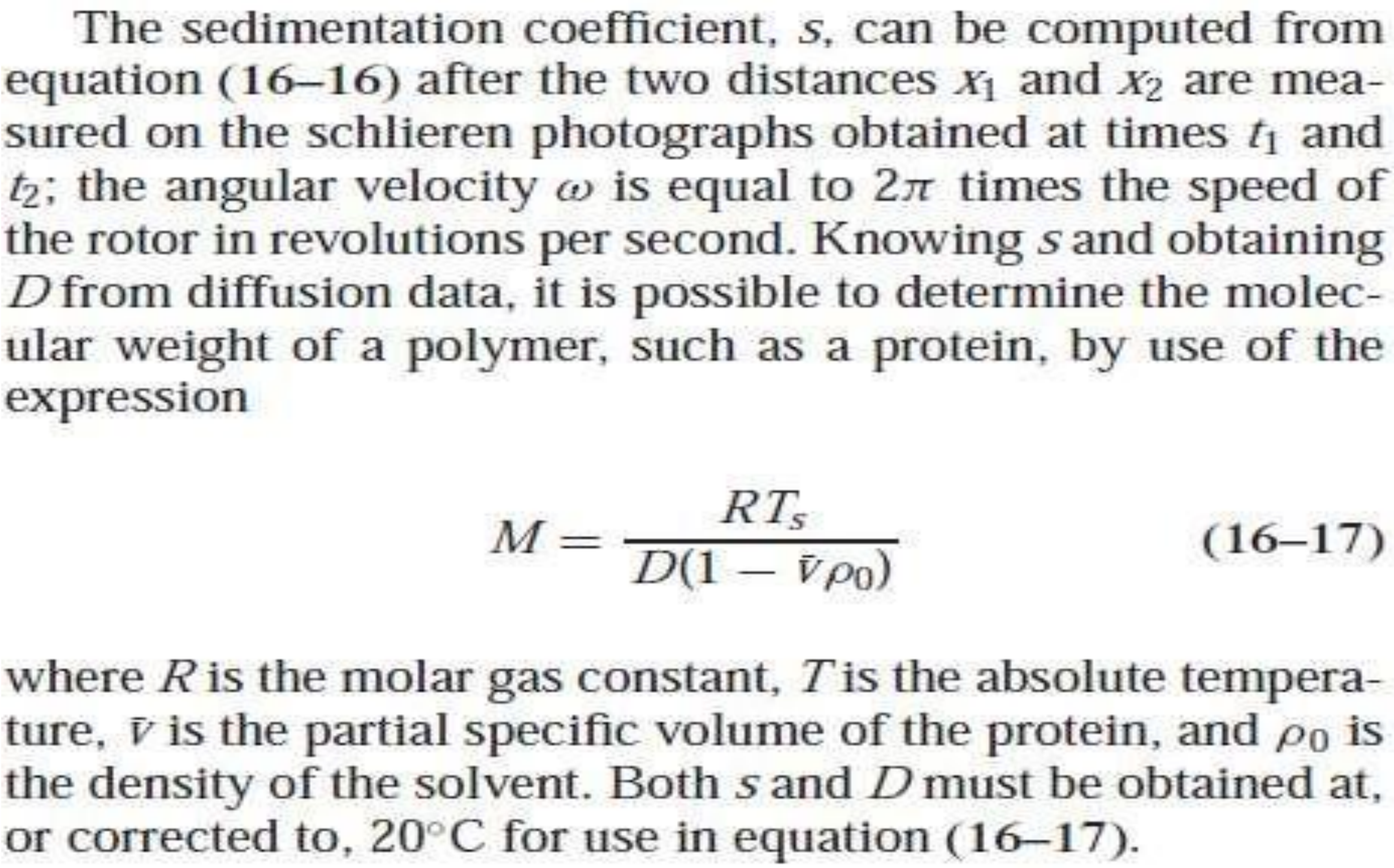
Cont…

- The velocity, v of sedimentation of spherical particles having a density ρ in a medium of density ρ_0 and viscosity η_0 is given by stock's law

$$s = \frac{dx/dt}{\omega^2 x}$$

- Sedimentation co-efficient obtain by integrating above equation….

$$s = \frac{\ln(x_2/x_1)}{\omega^2(t_2 - t_1)}$$



The sedimentation coefficient, s, can be computed from equation (16–16) after the two distances x_1 and x_2 are measured on the schlieren photographs obtained at times t_1 and t_2; the angular velocity ω is equal to 2π times the speed of the rotor in revolutions per second. Knowing s and obtaining D from diffusion data, it is possible to determine the molecular weight of a polymer, such as a protein, by use of the expression

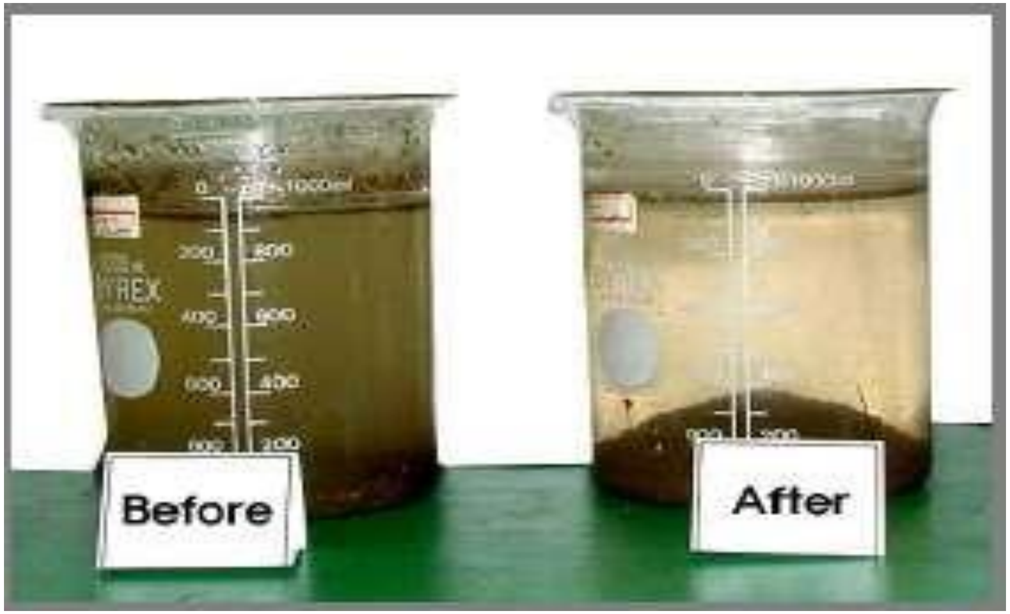
$$M = \frac{RT_s}{D(1 - \bar{v}\rho_0)} \qquad (16\text{–}17)$$

where R is the molar gas constant, T is the absolute temperature, $\bar{v}$ is the partial specific volume of the protein, and ρ_0 is the density of the solvent. Both s and D must be obtained at, or corrected to, 20°C for use in equation (16–17).

Ref: Martin's Physical Pharmacy

sedimentation of colloids:

M=R*T*S/D(1-V*Po)



Properties of Solutions, Colloids, and Suspensions

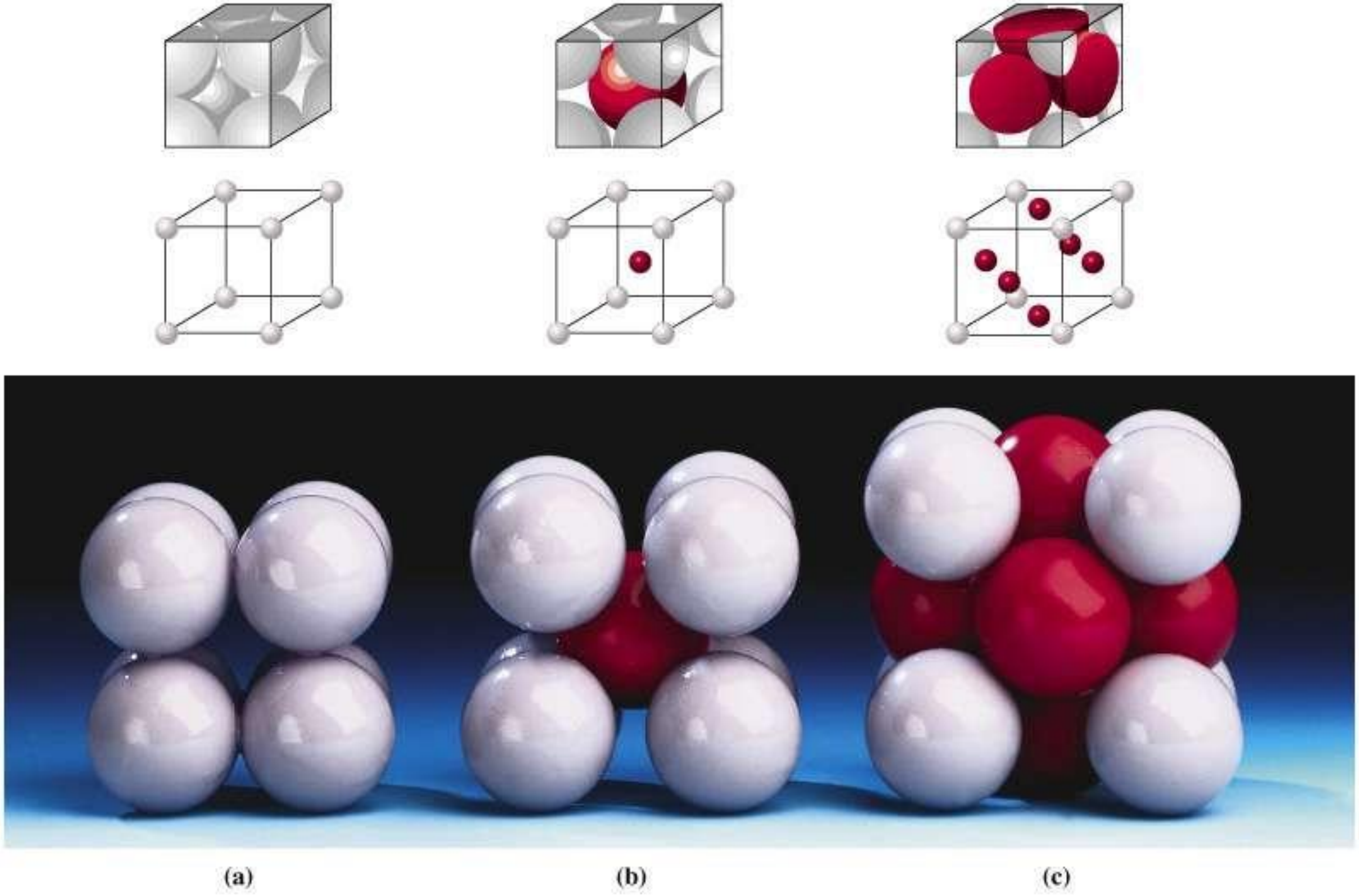
Property	Solution	Colloid	Suspension
Particle Size	0.1-1.0 nm	1-1000 nm	>1000 nm
Settles on Standing?	No	No	Yes
Filter with Paper?	No	No	Yes
Separate by Dialysis?	No	Yes	Yes
Homogeneous?	Yes	Borderline	No

ELECTRICAL PROPERTIES

Origin of Surface Charge

- ionizable functional groups
- crystal lattice extension

Crystal Lattice Structure 3D

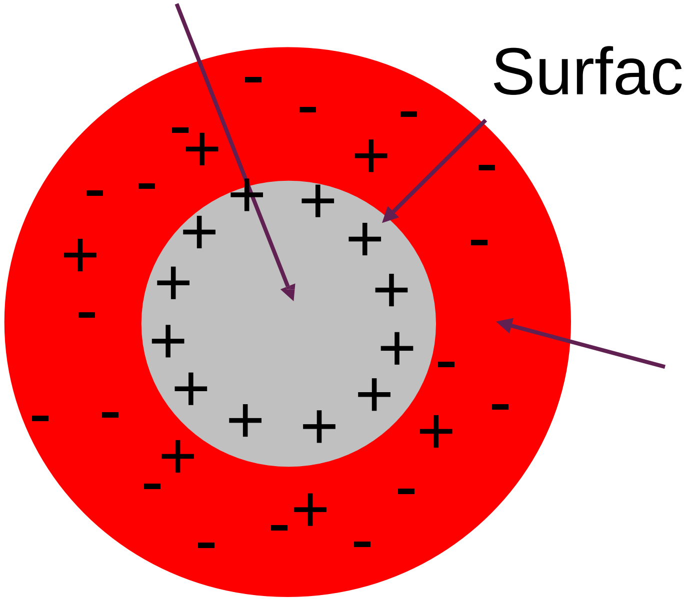


Cubic

Body Centered Cubic

Face Centered Cubic

Double Layer Theory



Colloidal Particle

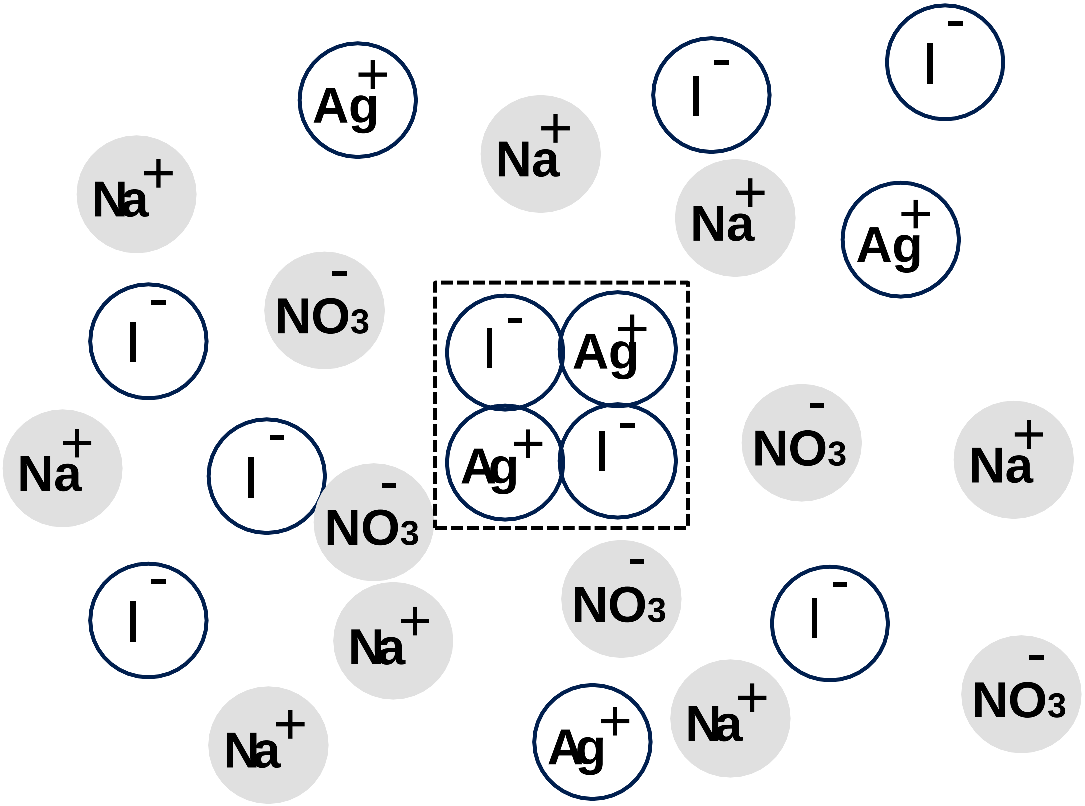
Surface Charge

Diffuse Region with excess "counterions"

Aqueous Dispersion Medium (Electrically Neutral)

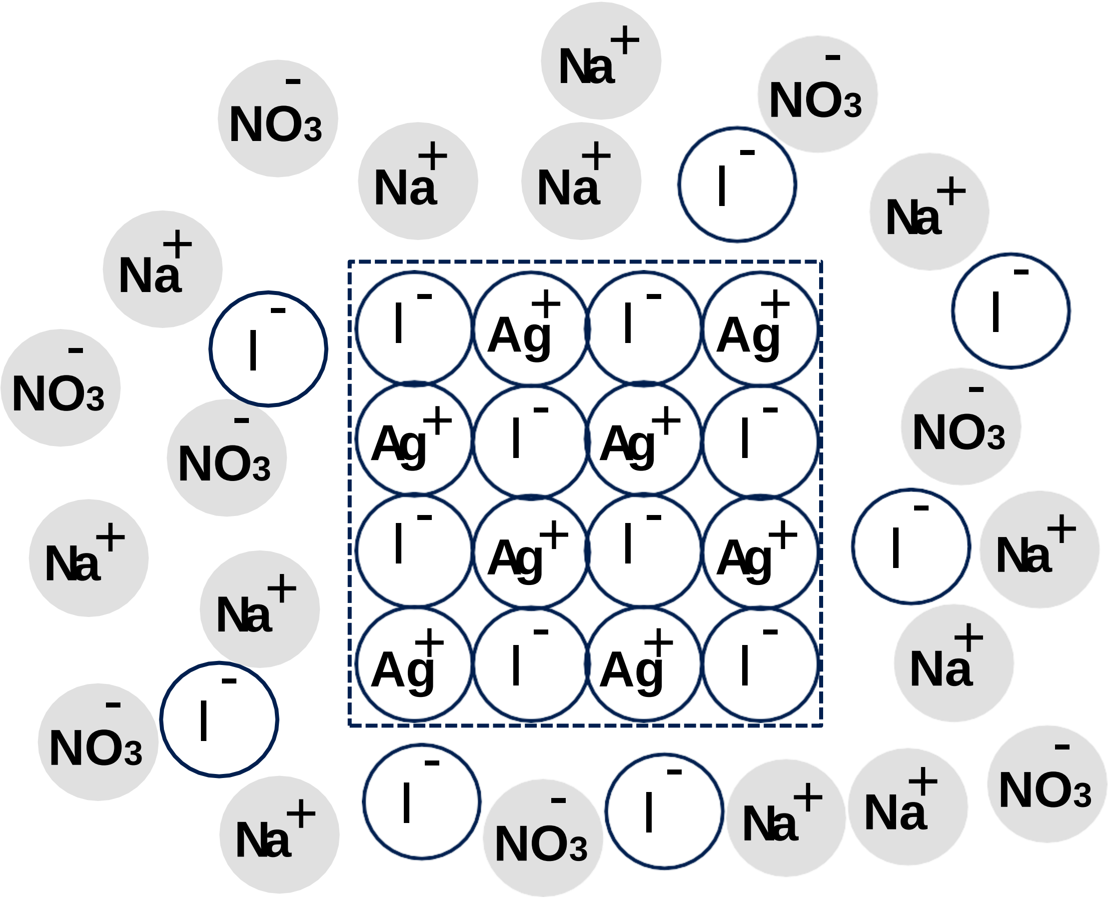
Early Stage Crystal Growth

$$NaI_{excess} + AgNO_3 \longrightarrow AgI\downarrow + Na^+ + NO_3^-$$



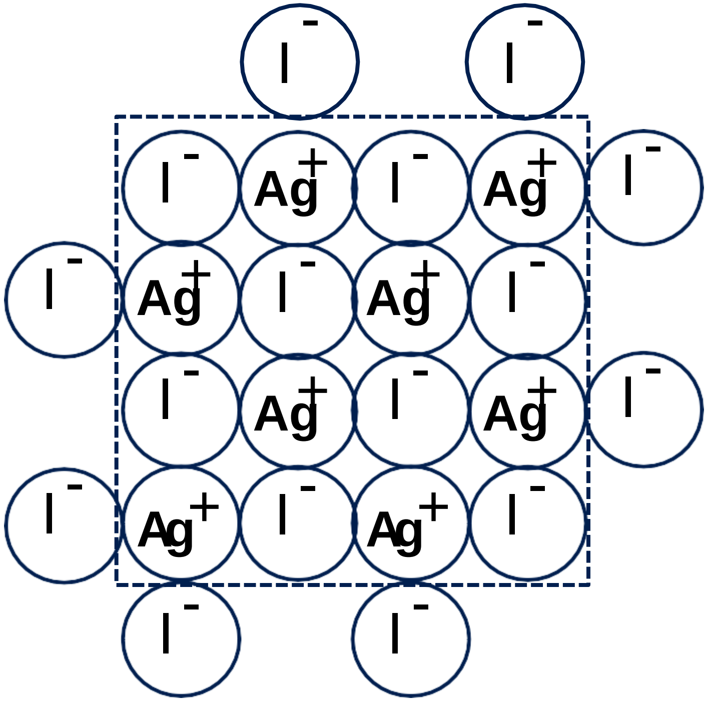
Crystal Growth

$$NaI_{\text{excess}} + AgNO_3 \rightarrow AgI \downarrow + Na^+ + NO_3^-$$



Crystal Lattice Extension

$$NaI_{excess} + AgNO_3 \longrightarrow AgI\downarrow + Na^+ + NO_3^-$$



Crystal Growth

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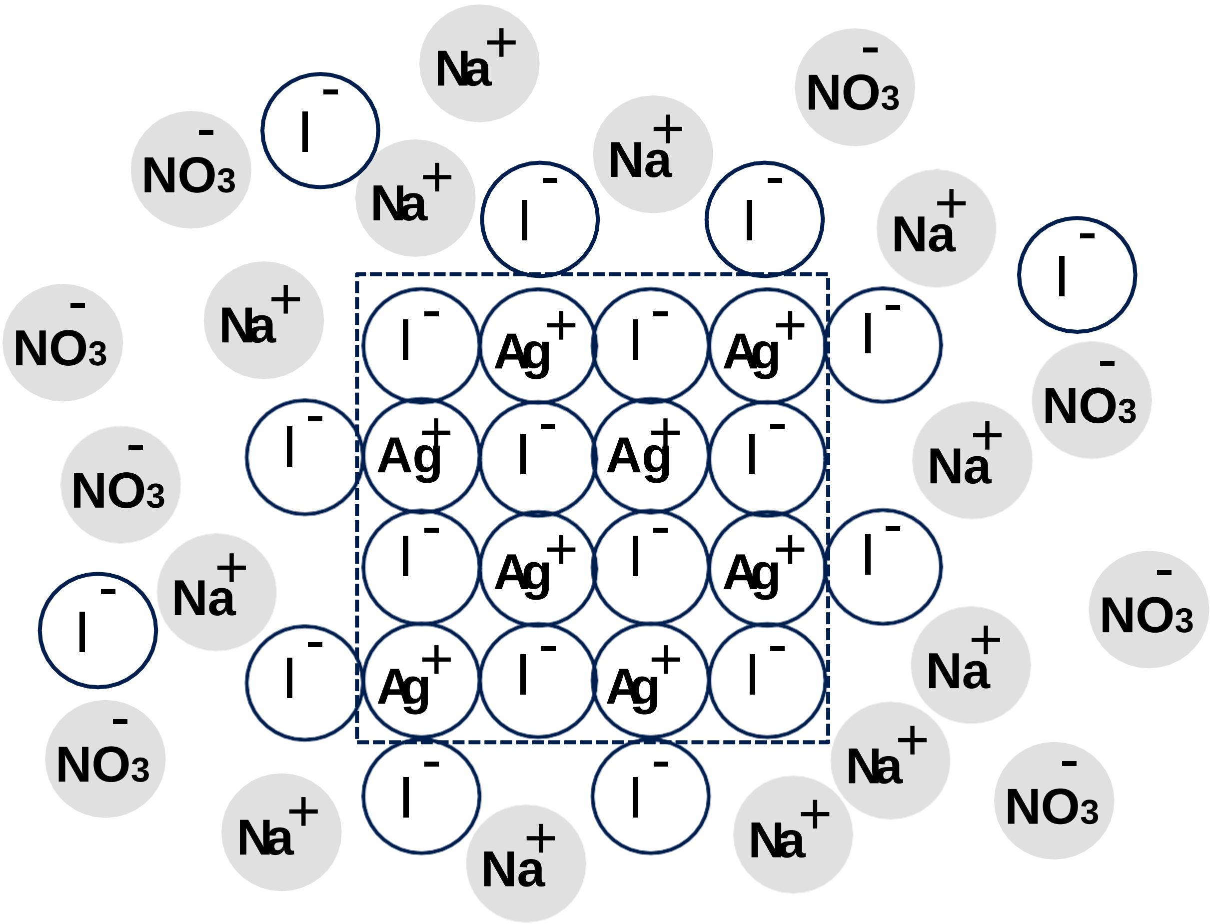

Crystal Growth

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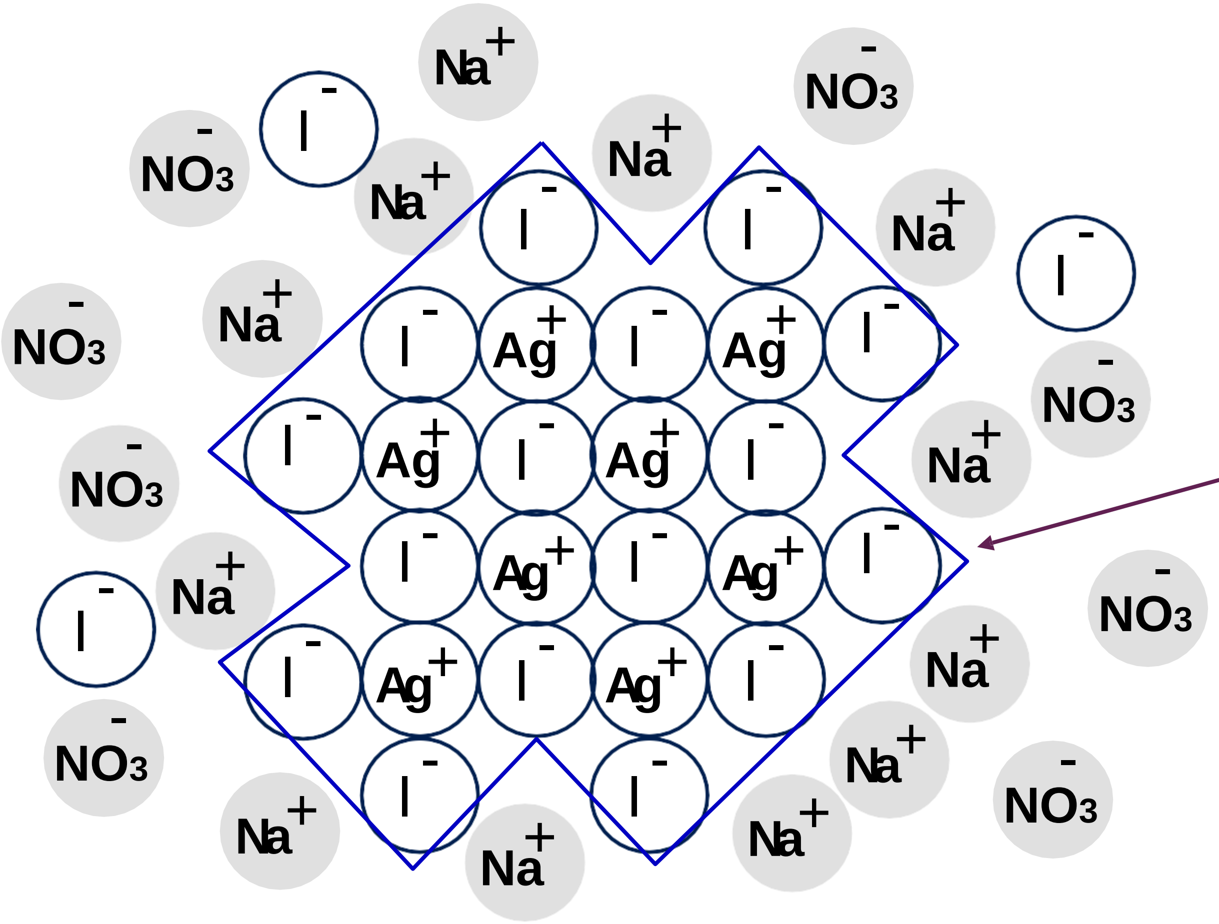
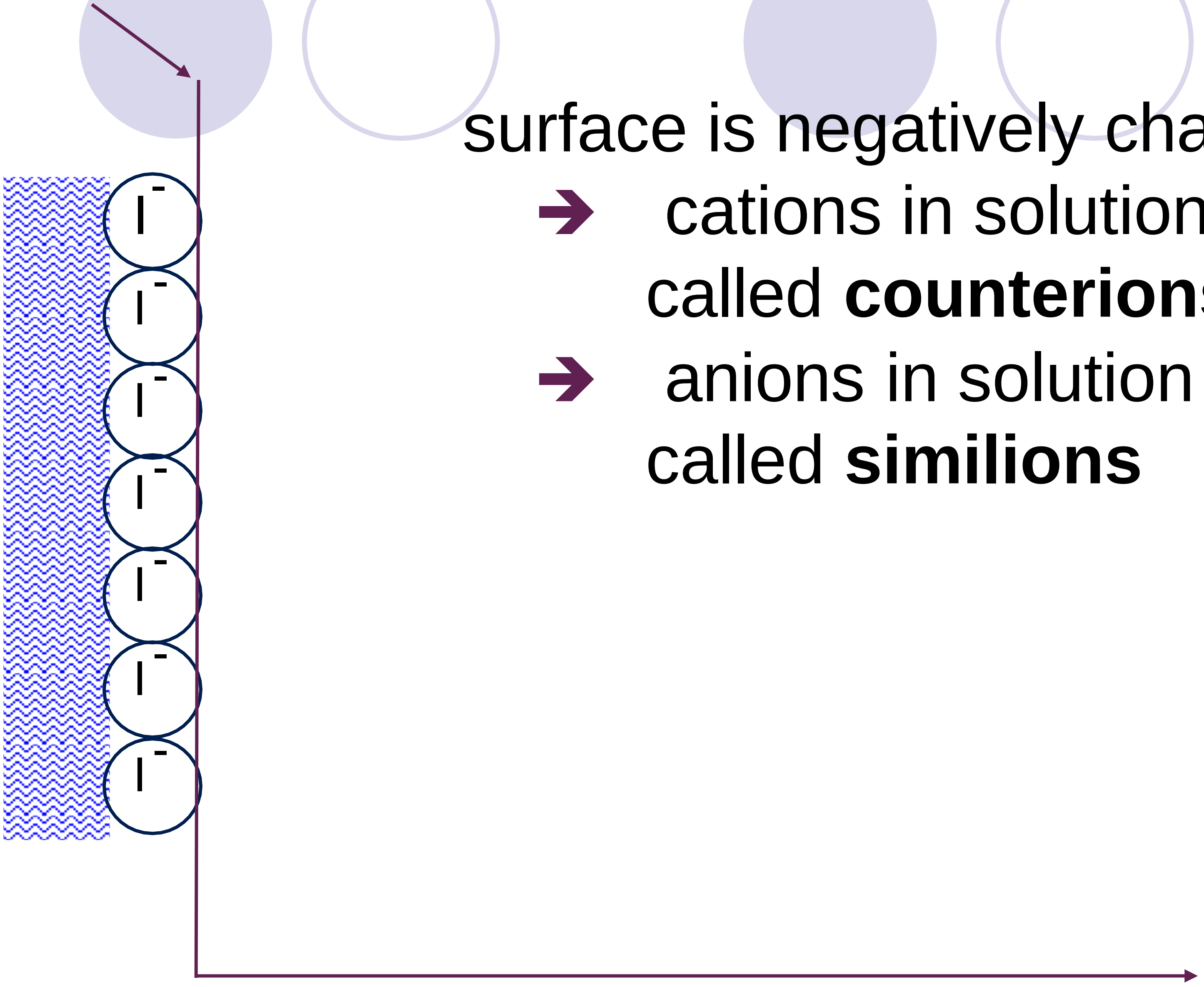


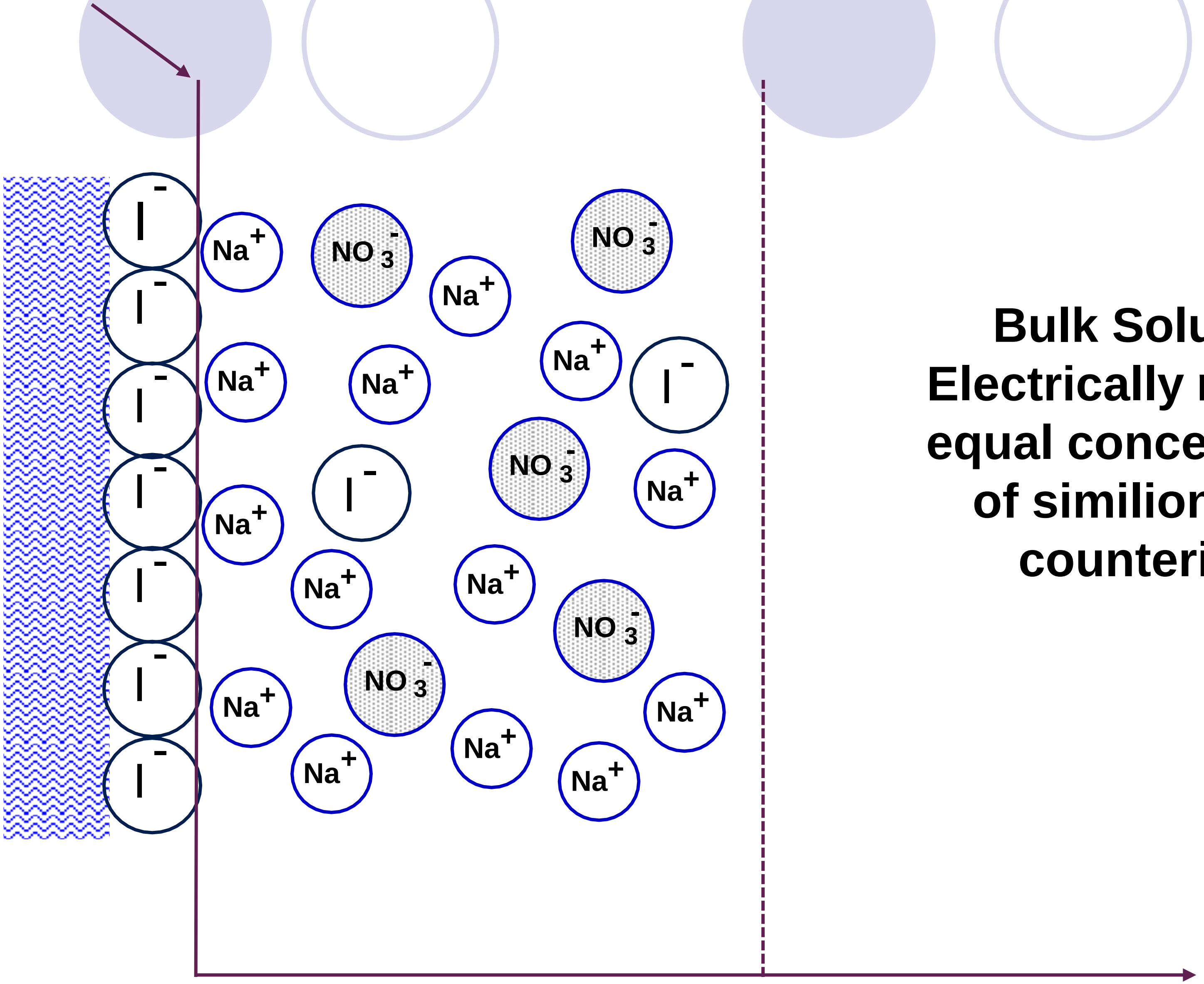
negatively charged colloidal particle



surface is negatively charged

- ➔ cations in solution are called **counterions**
- ➔ anions in solution are called **similions**

Particle Surface

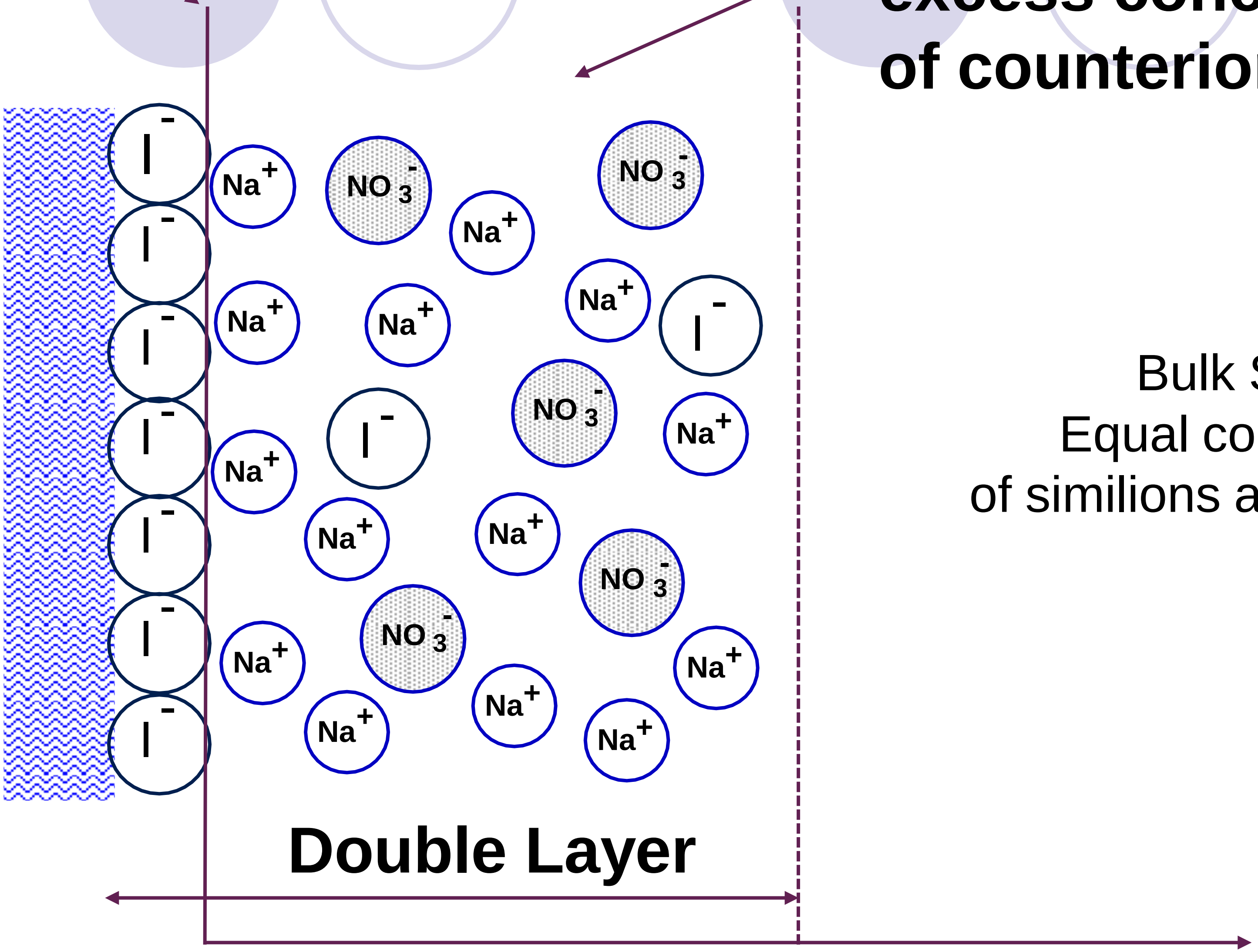


Bulk Solution: Electrically neutral - equal concentration of similions and counterions

Distance from particle surface

Particle Surface

Diffuse region with excess concentration of counterions



Bulk Solution
Equal concentration
of similions and counterio

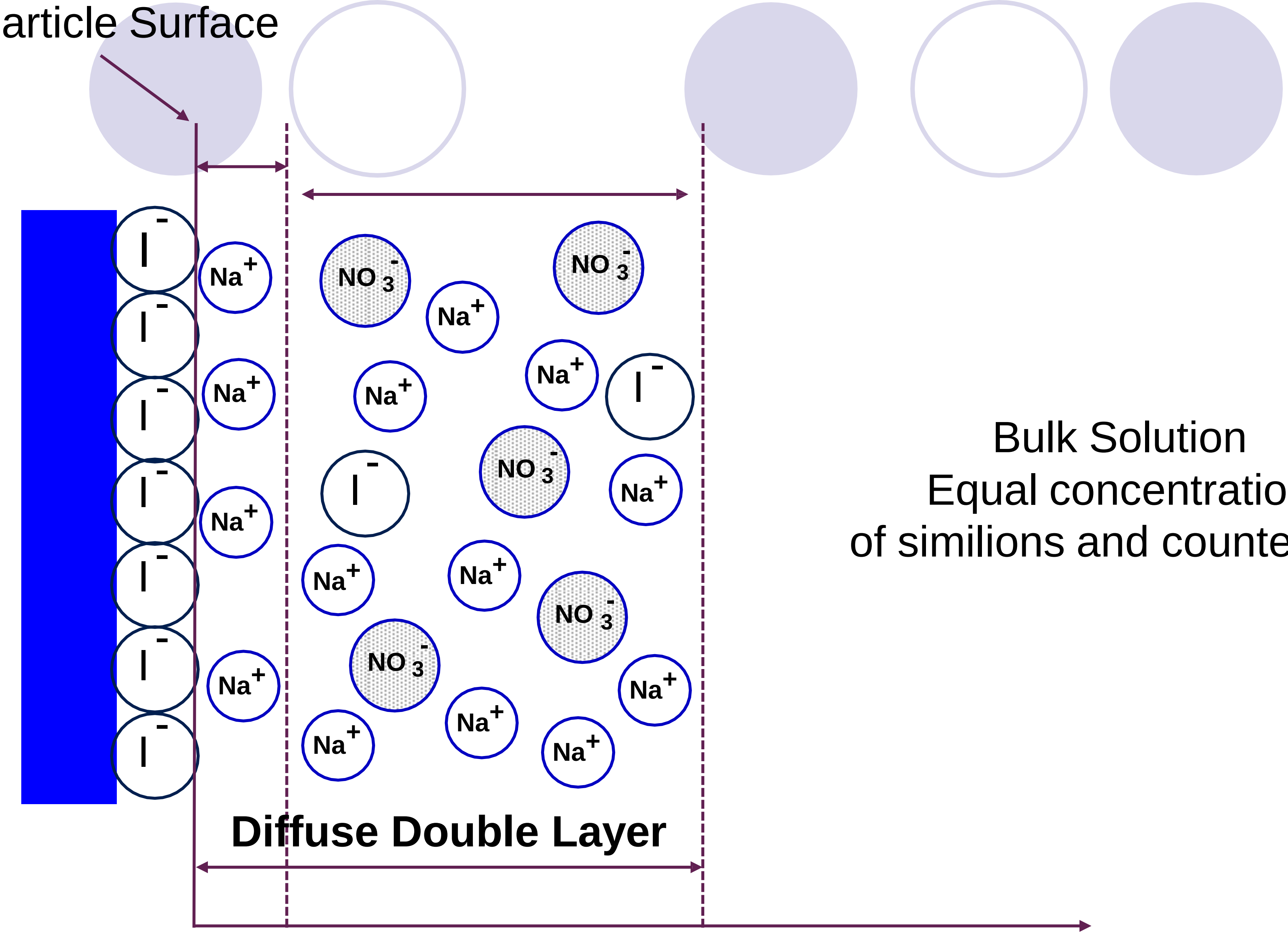
Double Layer

Distance from particle surface

Double Layer

- "Adsorbed" ions on the surface of the extended crystal.
- Diffuse Layer with an excess of counterions to neutralize surface charge.

Particle Surface



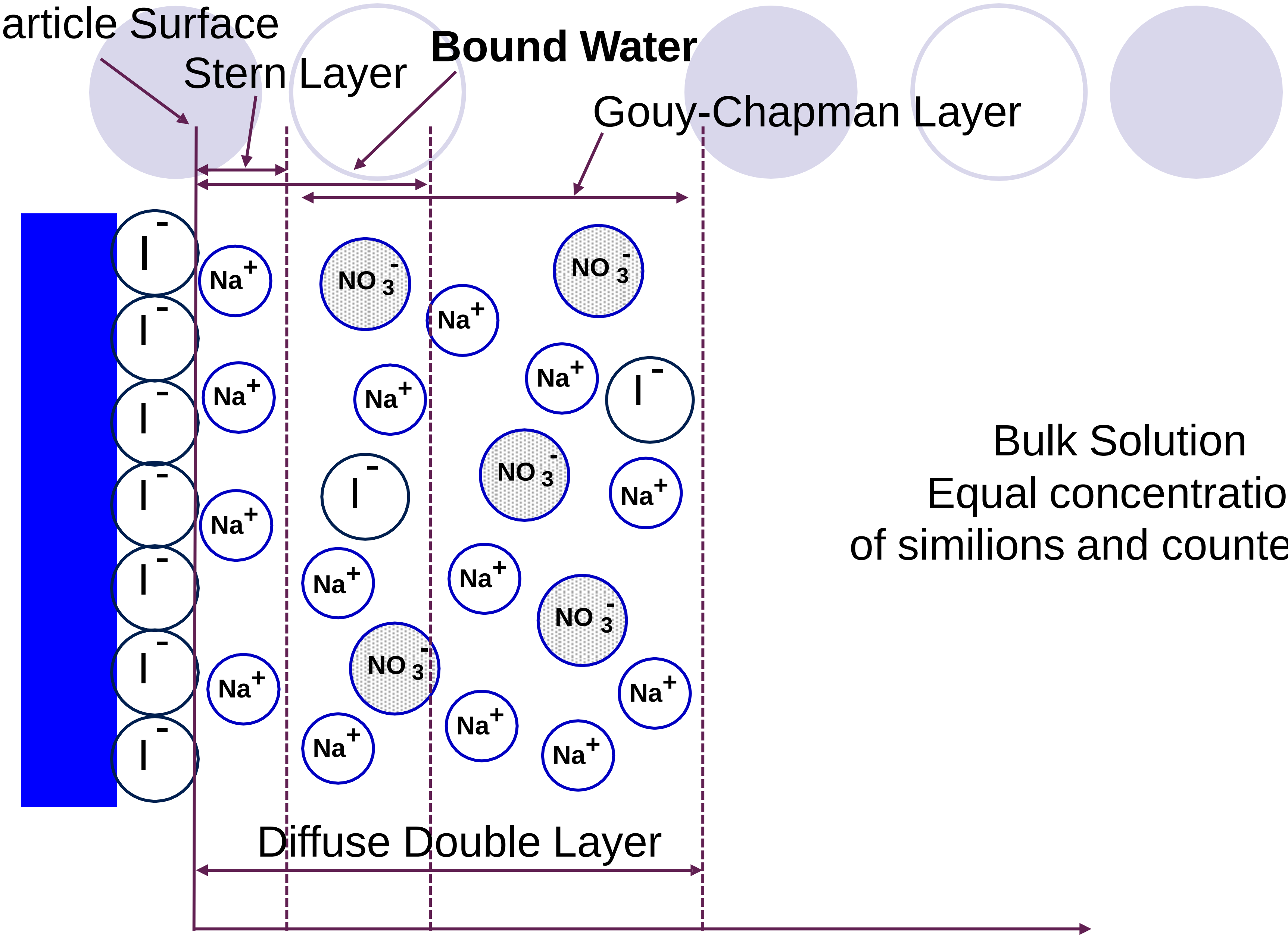
Bulk Solution
Equal concentration
of similions and counterio

Diffuse Double Layer

Distance from particle surface

Diffuse Double Layer

- Stern Layer
  - compact layer adjacent to the particle surface
  - almost exclusively counterions
  - most of the surface charge is neutralized
- Gouy-Chapman Layer
  - more diffuse region
  - counterions and similions



Particle Surface

Stern Layer

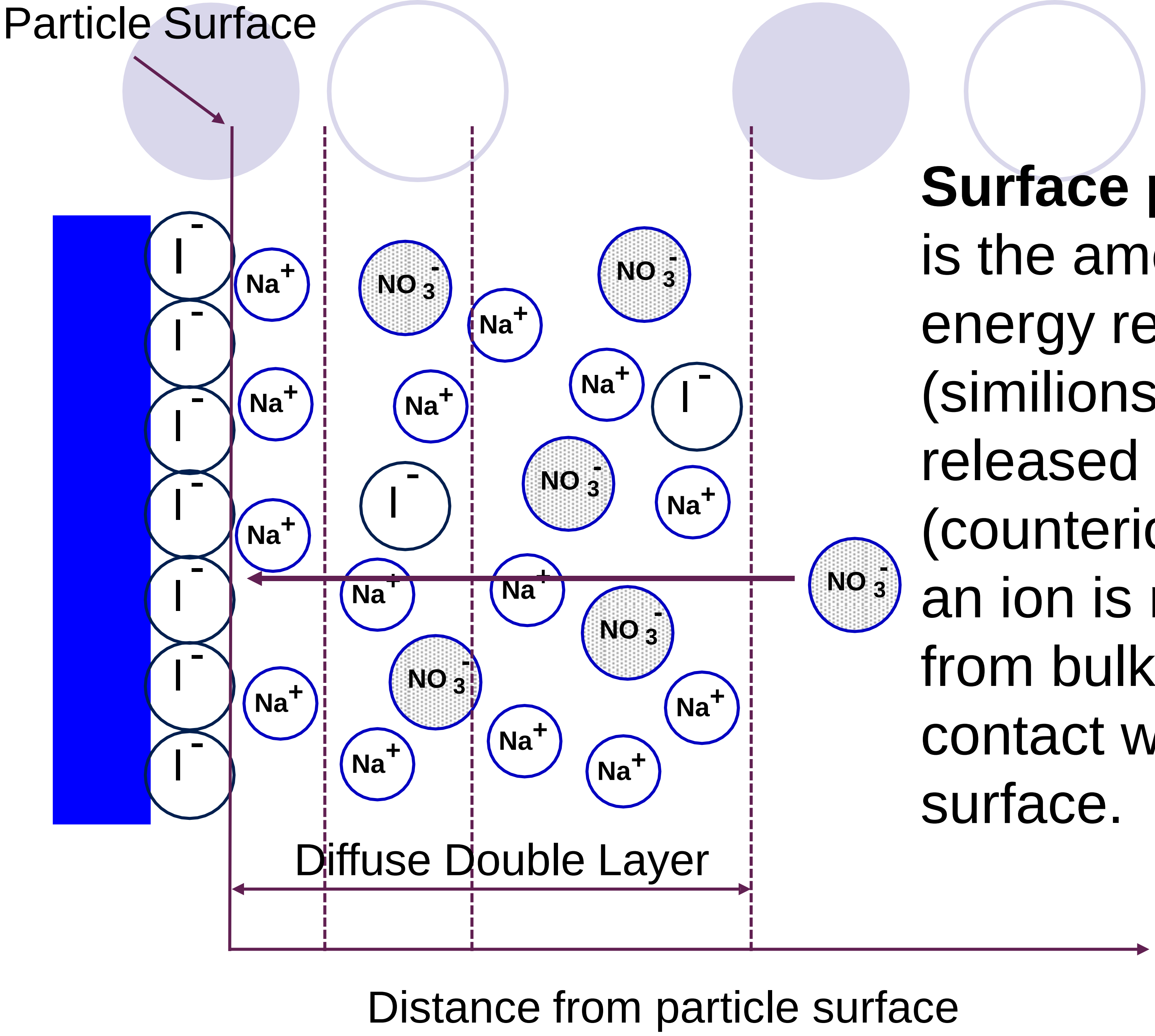
Bound Water

Gouy-Chapman Layer

Diffuse Double Layer

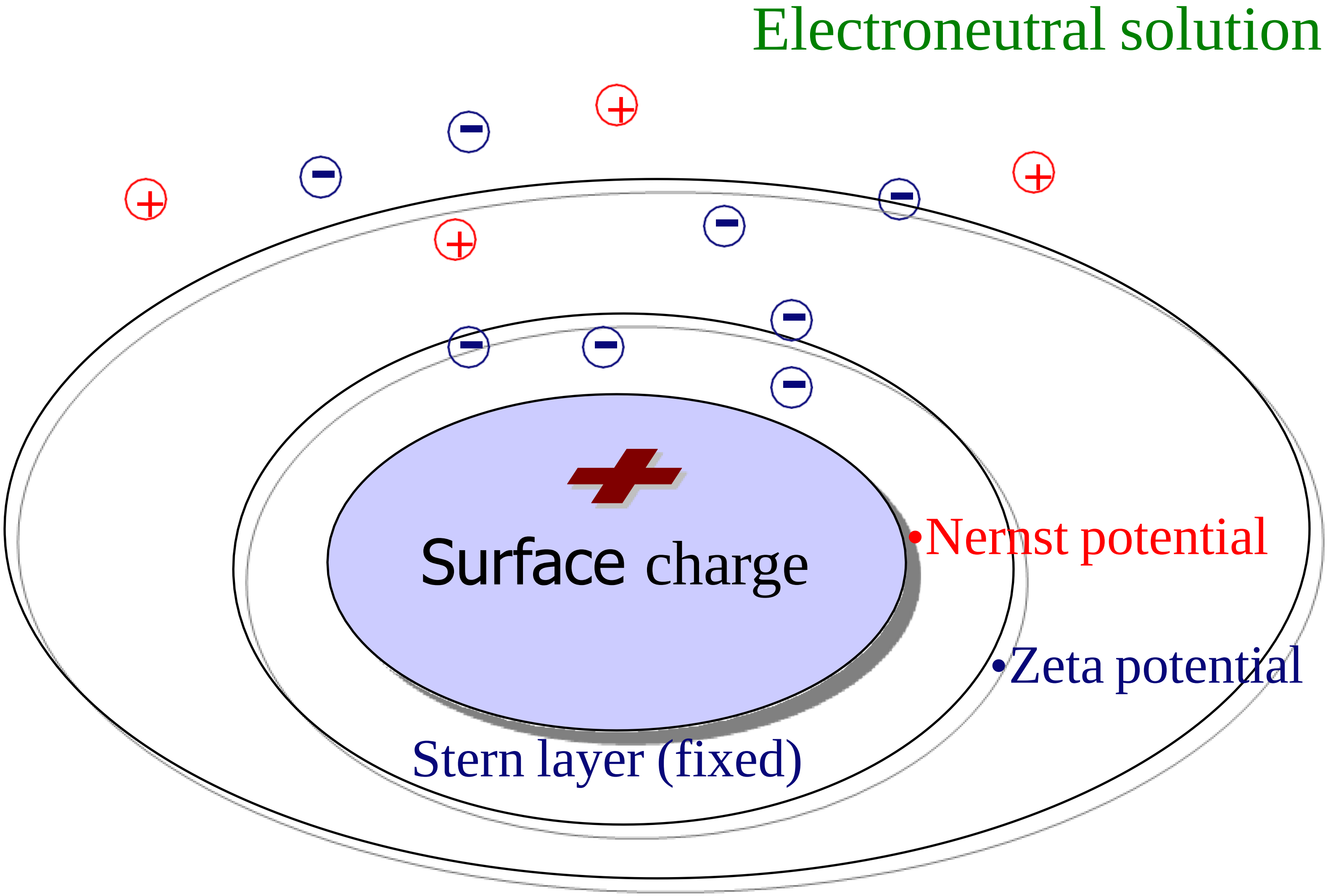
Bulk Solution
Equal concentration
of similions and counterio

Distance from particle surface



Surface potential is the amount of energy required (similions) or released (counterions) when an ion is moved from bulk into contact with the surface.

Electrical Double Layer



Electroneutral solution

Surface charge

- Nernst potential
- Zeta potential

Stern layer (fixed)

Electrokinetic Phenomena

Electrophoresis - Movement of particle in a stationary fluid by an applied electric field.

Electro-osmosis - Movement of liquid past a surface by an applied electric field

Streaming Potential - Creation of an electric field as a liquid moves past a stationary charged surface

Sedimentation Potential - Creation of an electric field when a charged particle moves relative to stationary fluid

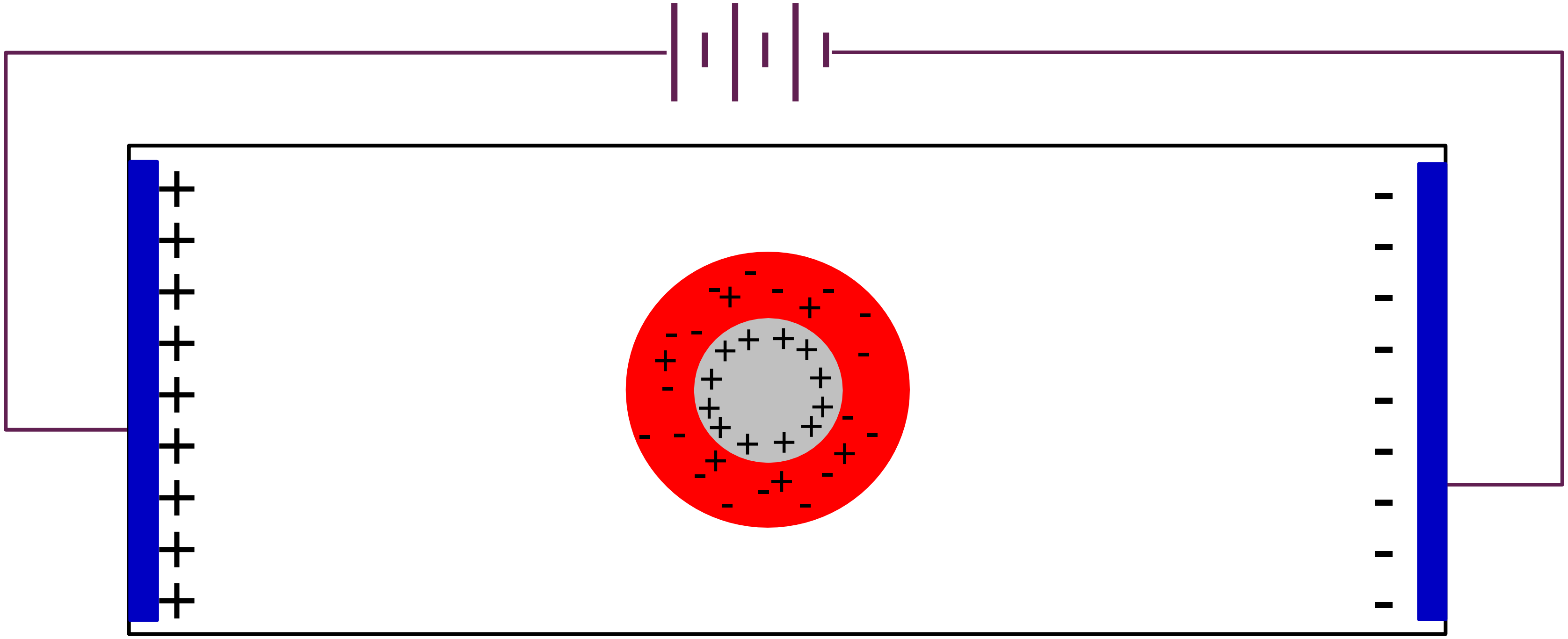
Zeta Potential Measurements

- Electrophoresis - ζ determined by the rate of diffusion (electrophoretic mobility) of a charged particle in a applied DC electric field.

- Streaming Potential - ζ determined by measuring the potential created as a fluid moves past macroscopic surfaces or a porous plug

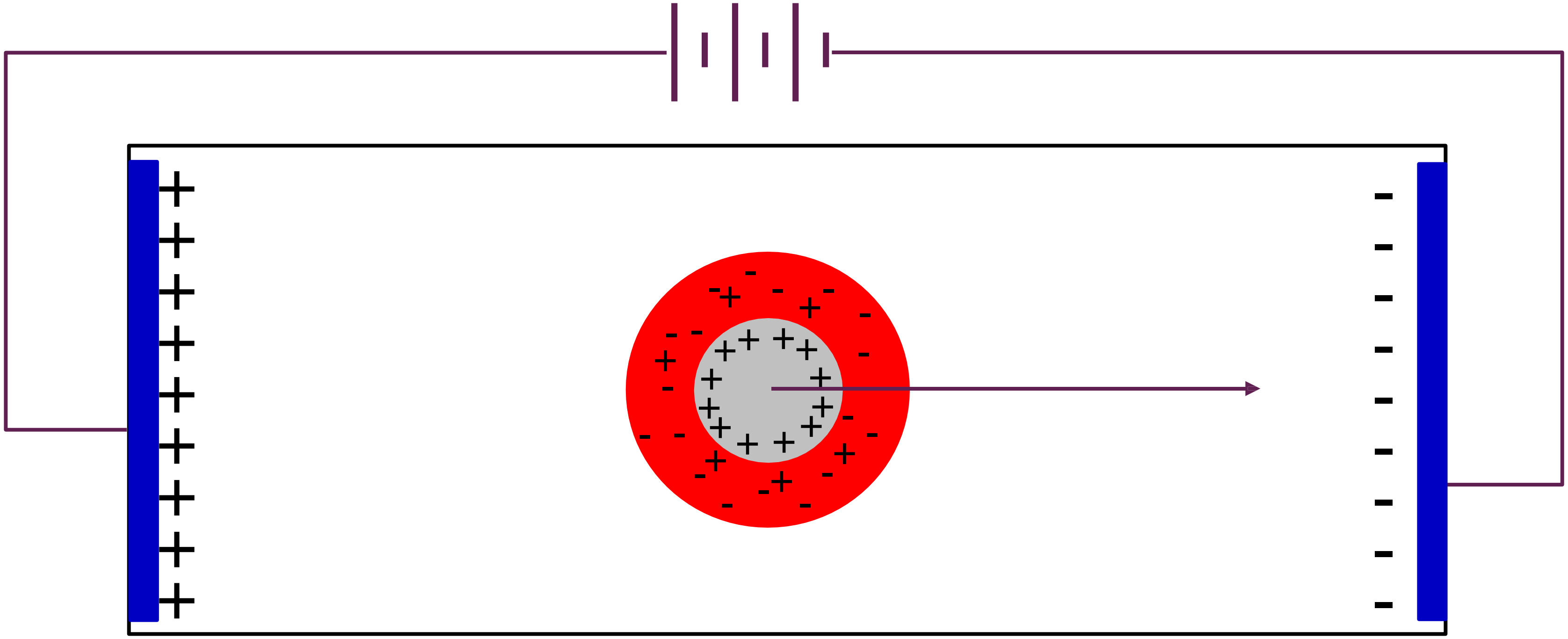
What happens when a charged colloid is placed in an electrical field?

Voltage Source



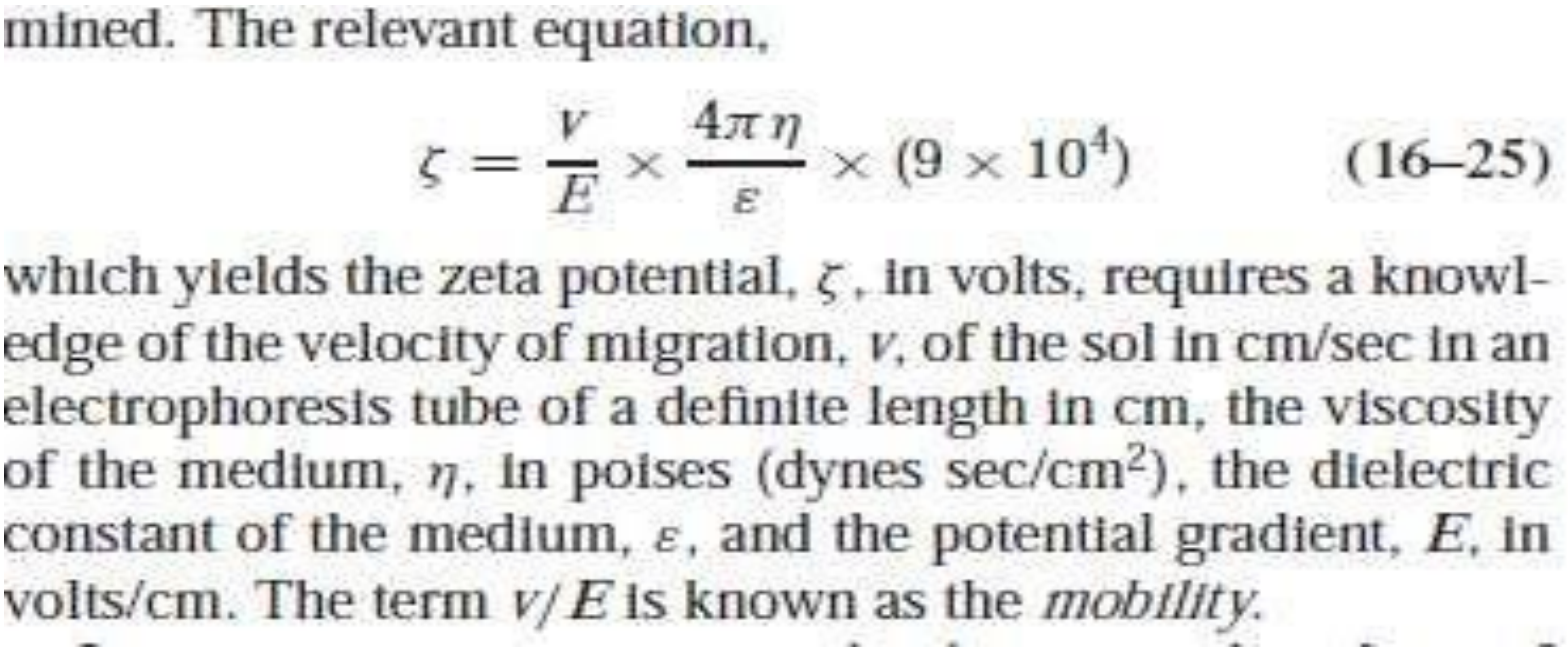
Electrophoresis

Voltage Source



Elektrophoresis:

Movement of charged particles in an electrical field. The background medium does not need to be a simple liquid, it may be also highly viscous: elelectrophoresis. The charged particles may be ordinary colloids or charged macromolecules (e.g. proteins).



mined. The relevant equation,

$$\zeta = \frac{v}{E} \times \frac{4\pi\eta}{\varepsilon} \times (9 \times 10^4) \qquad (16\text{–}25)$$

which yields the zeta potential, ζ, in volts, requires a knowledge of the velocity of migration, v, of the sol in cm/sec in an electrophoresis tube of a definite length in cm, the viscosity of the medium, η, in poises (dynes sec/cm^2), the dielectric constant of the medium, ε, and the potential gradient, E, in volts/cm. The term v/E is known as the *mobility*.

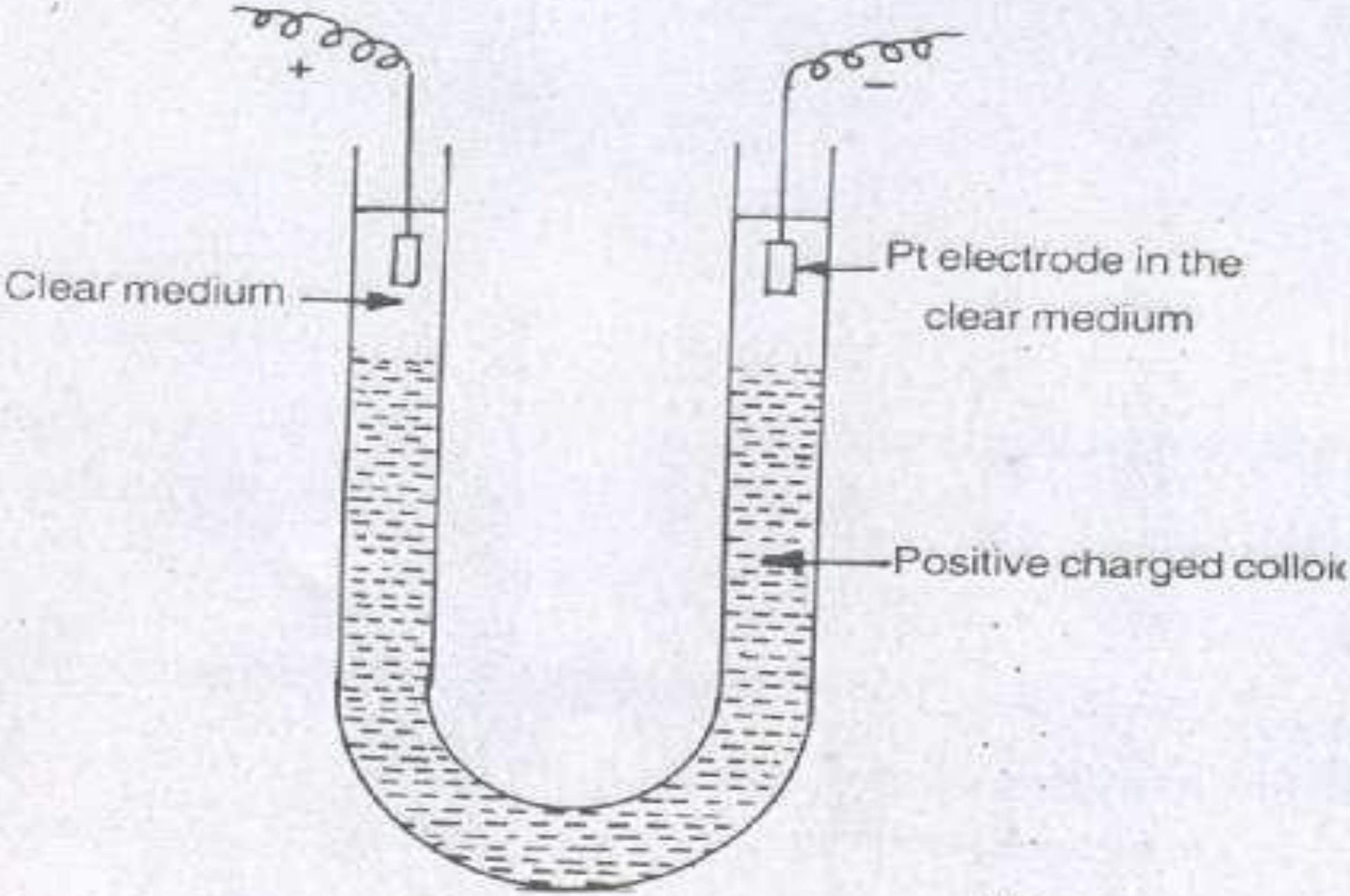


Fig. 5.6. Electrophoretic cell.

Electroosmosis:

An electrolyte is moved relative to a charged surface. This applies to capillaries, membranes or powders.

The effect relies on the fact, that the electrical field supplied exerts a force on the electrochemical double layer. The mobile layer drags on the electrolyte which results in a liquid stream through the apparatus.

Electro osmosis

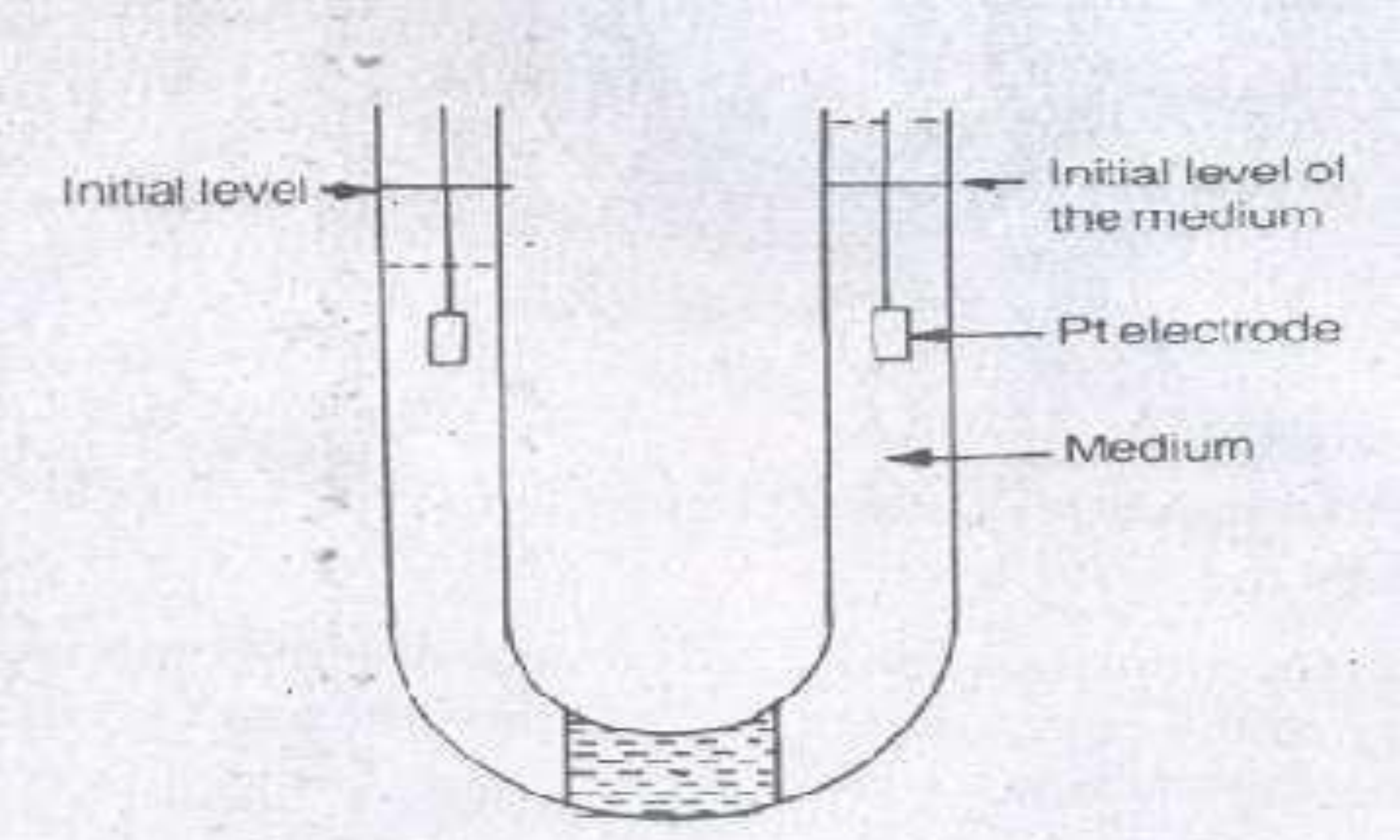


Fig. 5.7. Electro-osmotic cell.

Sedimentation potential:

This is the potential difference set up between top and bottom of a suspension of solid particles in a liquid when the particles settle under the influence of gravity.

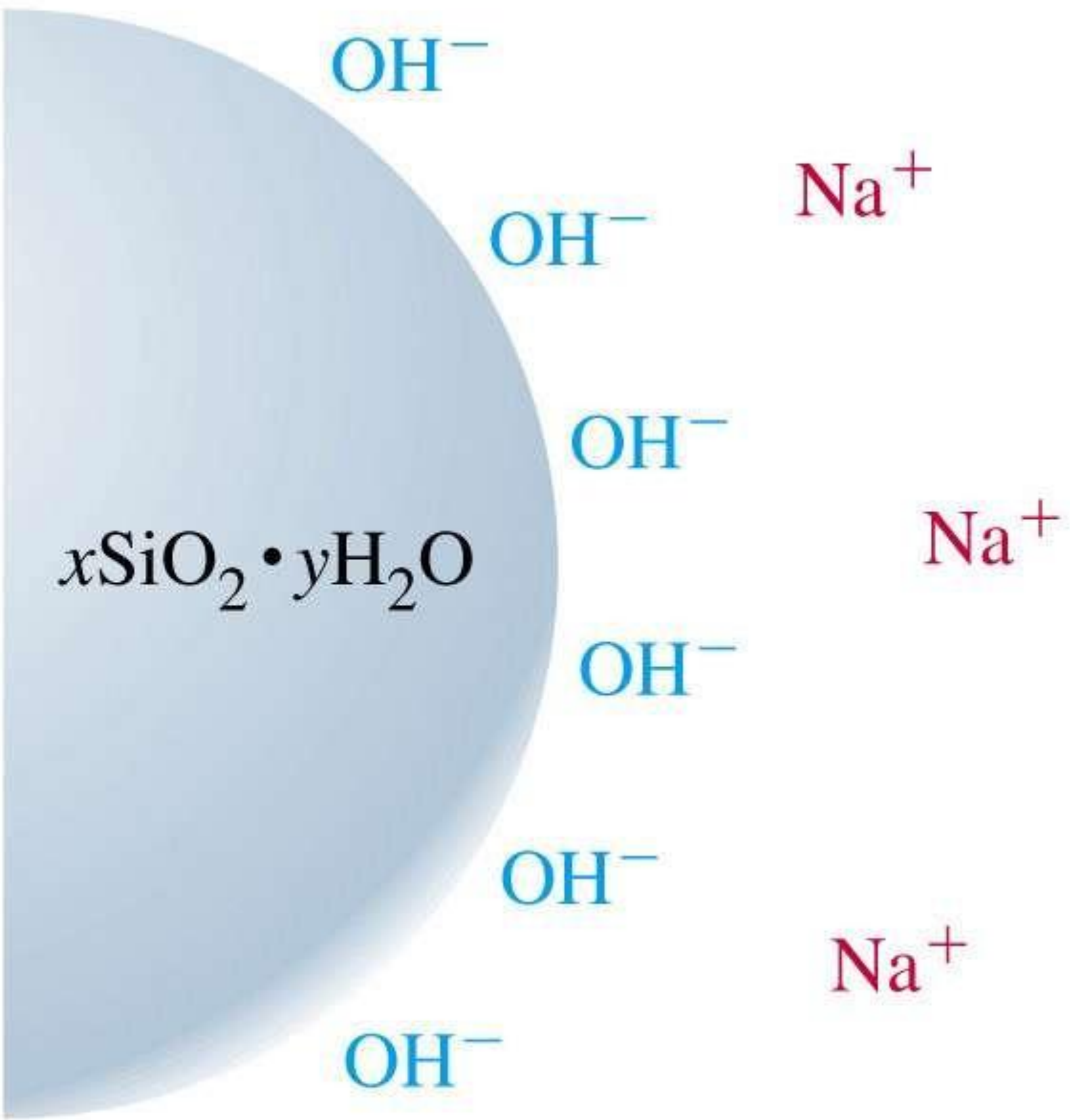
Streaming potential:

1. This is the converse of electro-osmosis. If the electrodes in the electro-osmosis apparatus, are replaced by a galvanometer in the circuit.
2. if the liquid is forced through the tube, the galvanometer will indicate a current. This streaming potential is due to the displacement of the charges equilibrated in the double layer around the solid.

Stabilization of Colloids

- The stability of a colloidal dispersion depends on two factors,
- The presence of charge on the dispersed colloidal particles
- The presence of a solvent sheath surrounding each dispersed particle

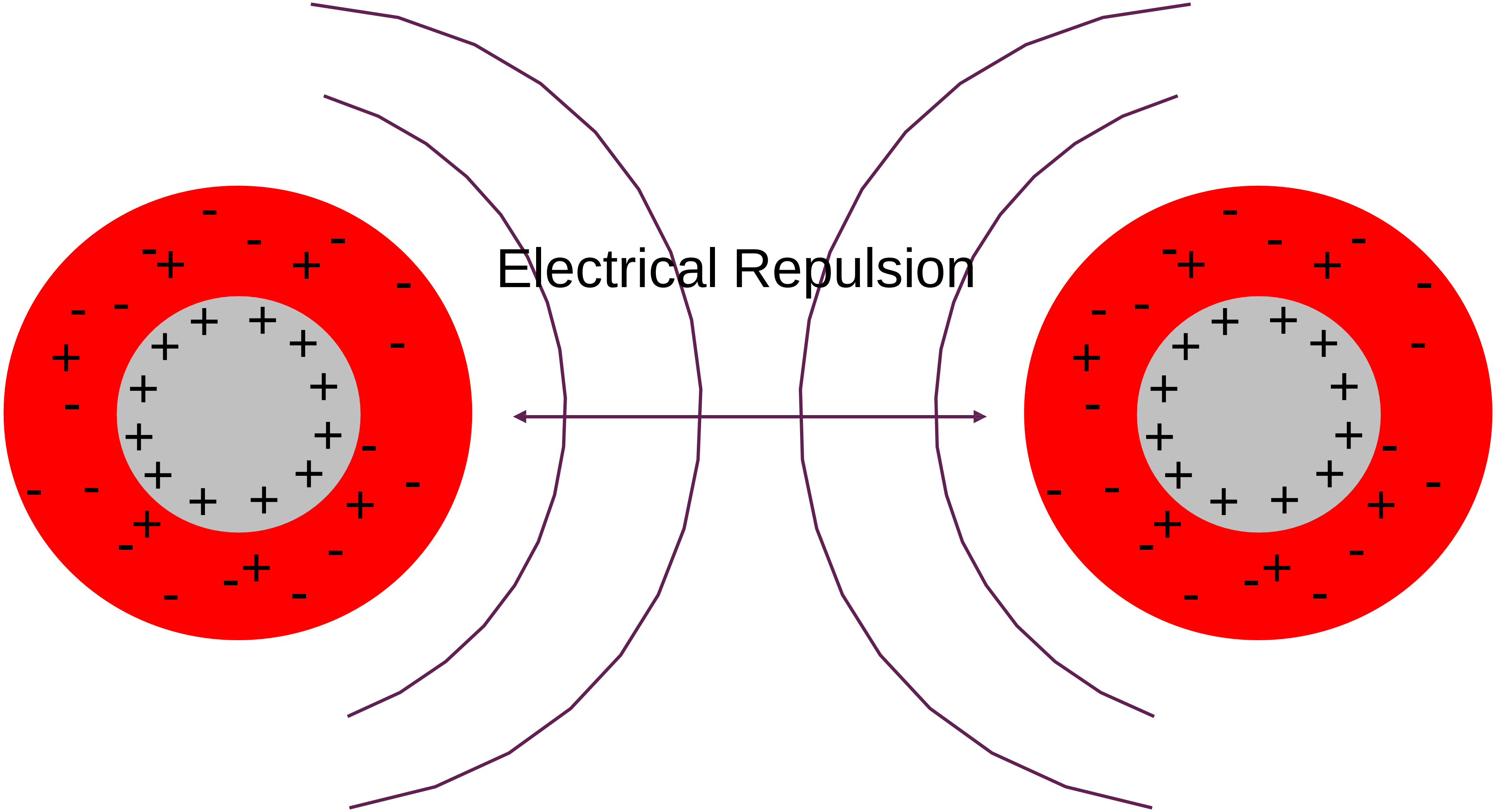
Stabilization of Colloids



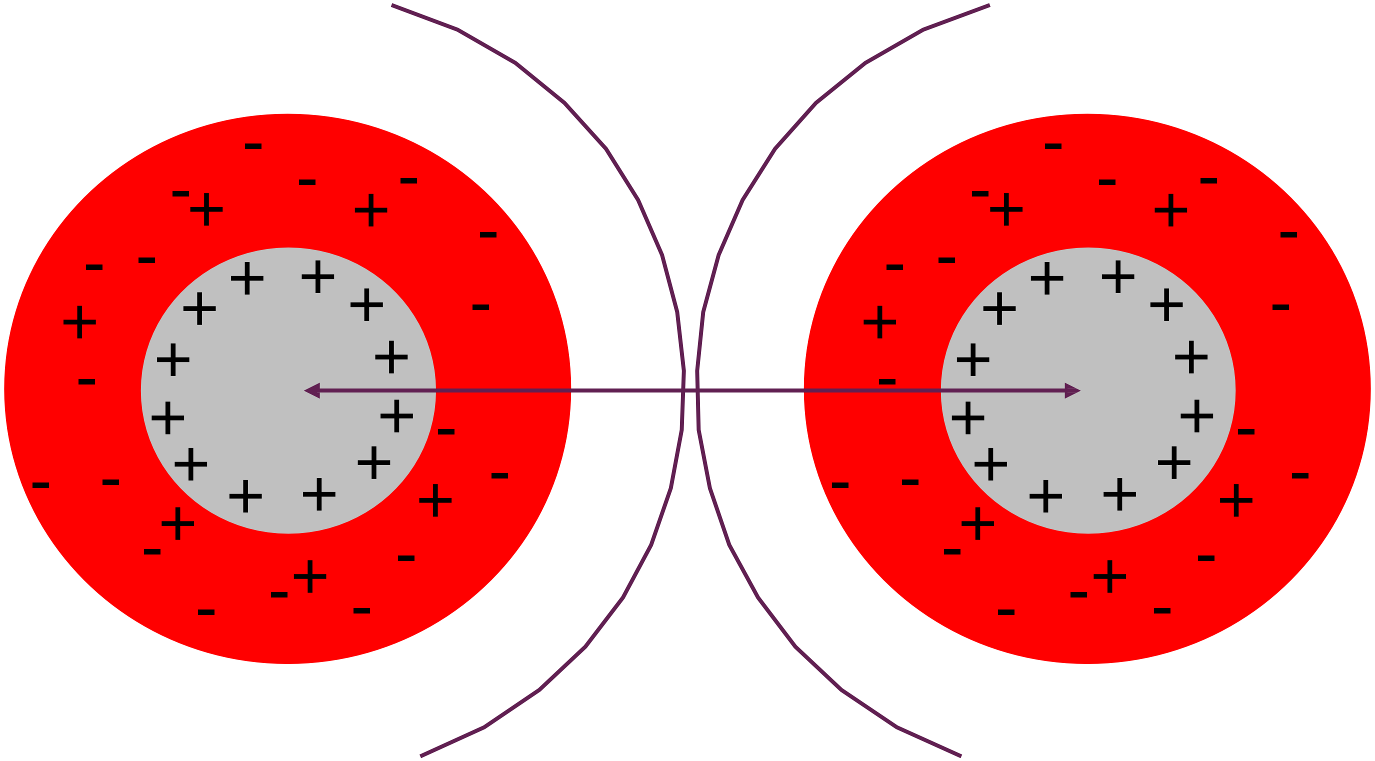
- Colloids can be stabilized by surface interactions

- It may be say that the stability:
- Lyophobic colloid is largely due to the electric charges on the surface of the dispersed particles,
- Lyophilic sols it is the solvent sheath that is significant in stabilizing the system

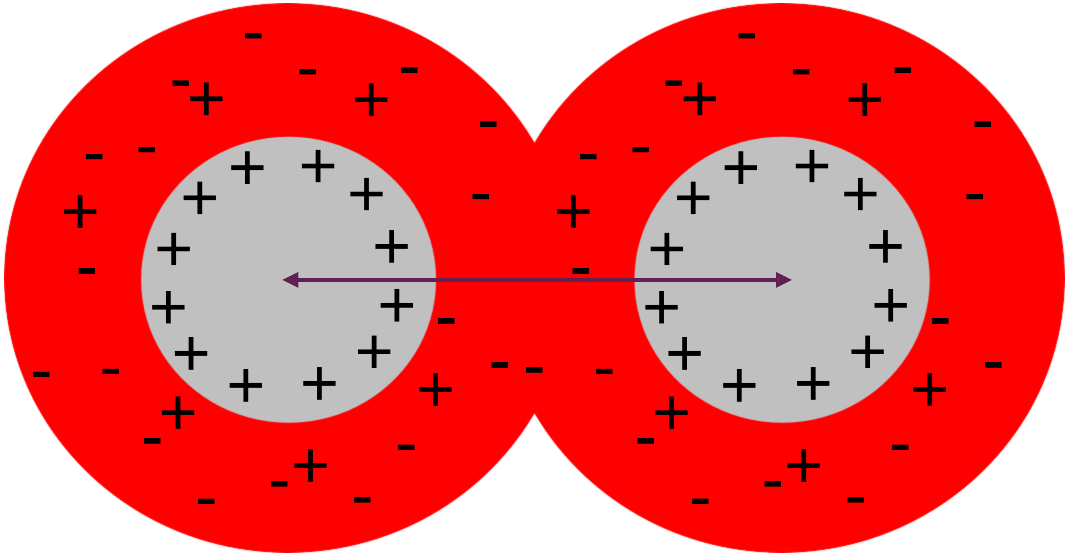
Electrical Repulsion



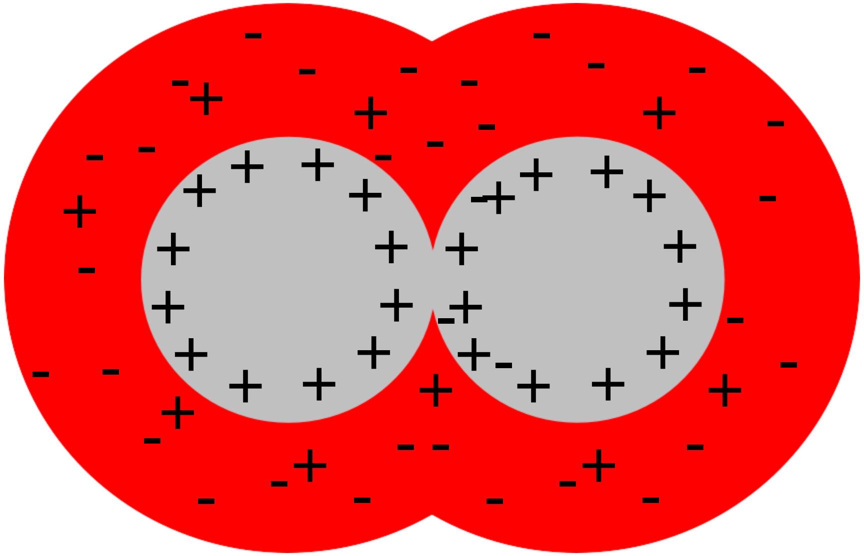
Electrical Repulsion



Interpenetration of the Diffuse Double Layers



Coagulation



Attractive forces overwhelm repulsive forces.

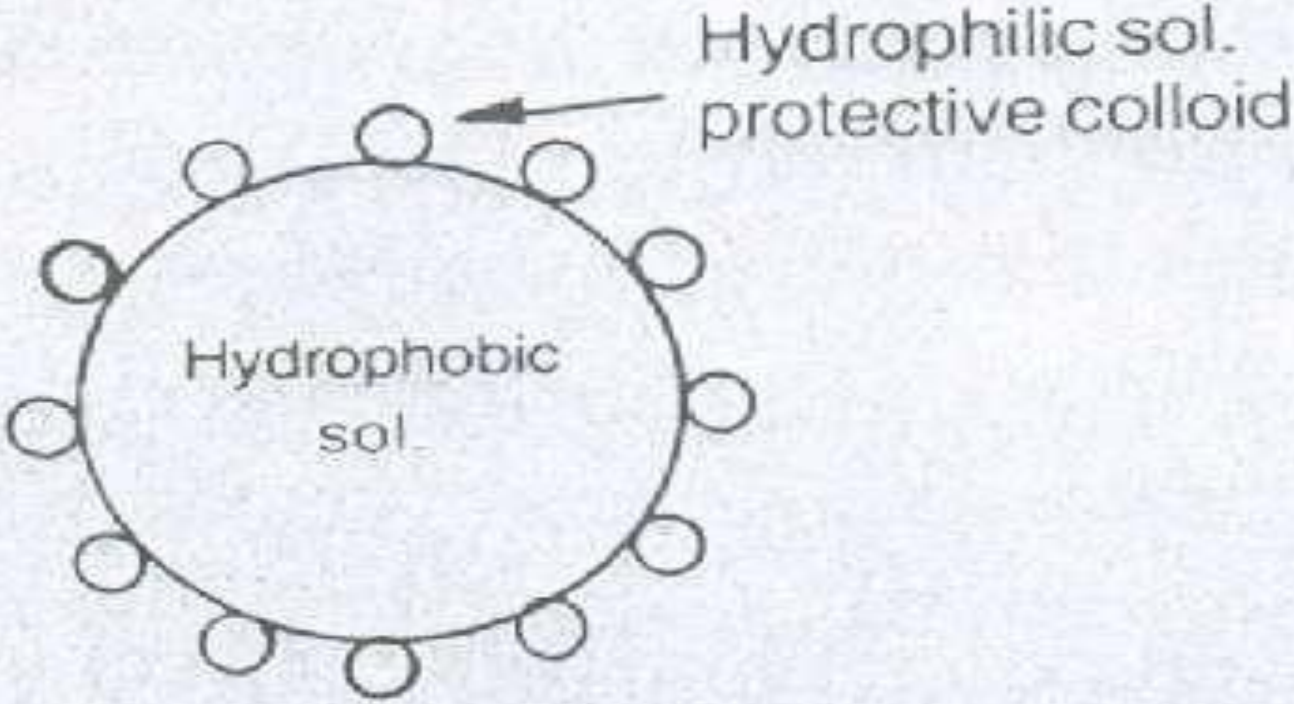
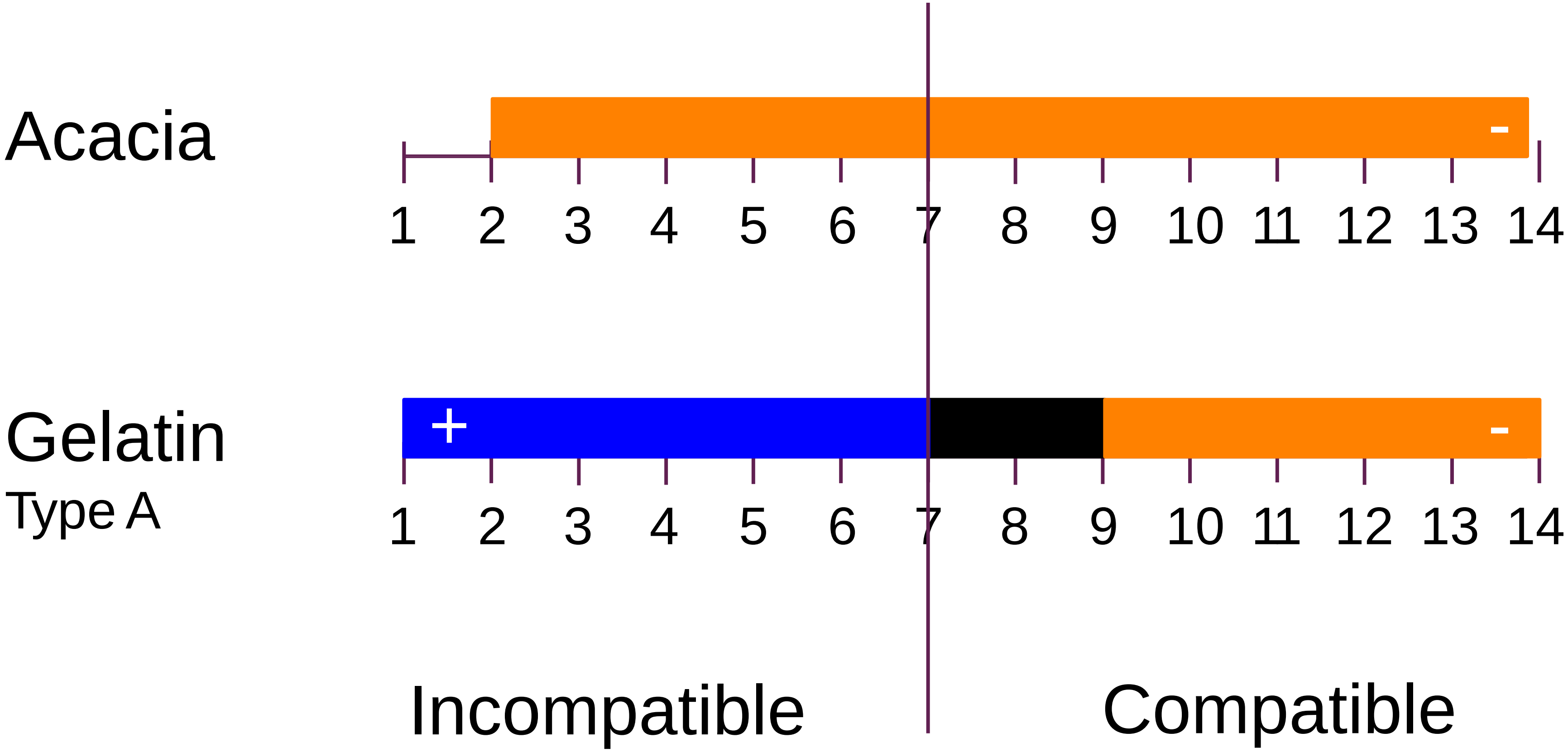


Fig. 5.8. Principle of protection by a protective colloid.

Net Charge Profiles for Acacia and Gelatin (Type A)



- Coagulation of colloidal dispersions can be brought about by the addition of electrolytes which reduce the zeta potential. The effectiveness of an electrolyte to cause precipitation depends not only on the concentration but also on the valence of the active ion (ion causing coagulation).

- The higher the valency of the ion, the greater is the precipitating power. This is known as the *Schulze-Hardy* rule.

- Generally hydrophobic colloids need very small amount of electrolyte for coagulation whereas hydrophilic colloids need a larger amount because the hydration layer surrounding the dispersed particles has to be removed.

Hardy and Schulze made systematic investigation on the precipitation of sols by adding electrolytes and summarized rules latterly named as Hardy-Schulze rules.

Precipitating value of different electrolytes towards the same colloids

	As_2S_3 (-)		$Al(OH)_3$
LiCl	58	NaCl	43.5
NaCl	51	KCl	46
KCl	49.5	KNO_3	60
$CaCl_2$	0.65	K_2SO_4	0.30
$MgCl_2$	0.72	$K_2Cr_2O_7$	0.63
$MgSO_4$	0.81	$(KOOC)_2$	0.69
$AlCl_3$	0.093	$K_3[Fe(CN)_6]$	0.08
$Al(NO_3)_3$	0.095		

The ion which is effective in causing precipitation of a sol is the one whose charge is of opposite sign to that of the colloidal particles, i.e., counterions

Gold number:

the number of milligrams of the protective colloid that just prevents the change of color when 1 cm^3 of the standard salt solution (10 % NaCl) is added to 10 cm^3 of the standard gold sol (0.006 %). (By Zsigmondy)

Protective colloids	Gold number / mg
Gelatin	0.005-0.01
Albumin	0.1-0.2
Gum arabic	0.15-0.5
Dextrin	6.0-20.0
Potato starch	25

Red number: Congo red

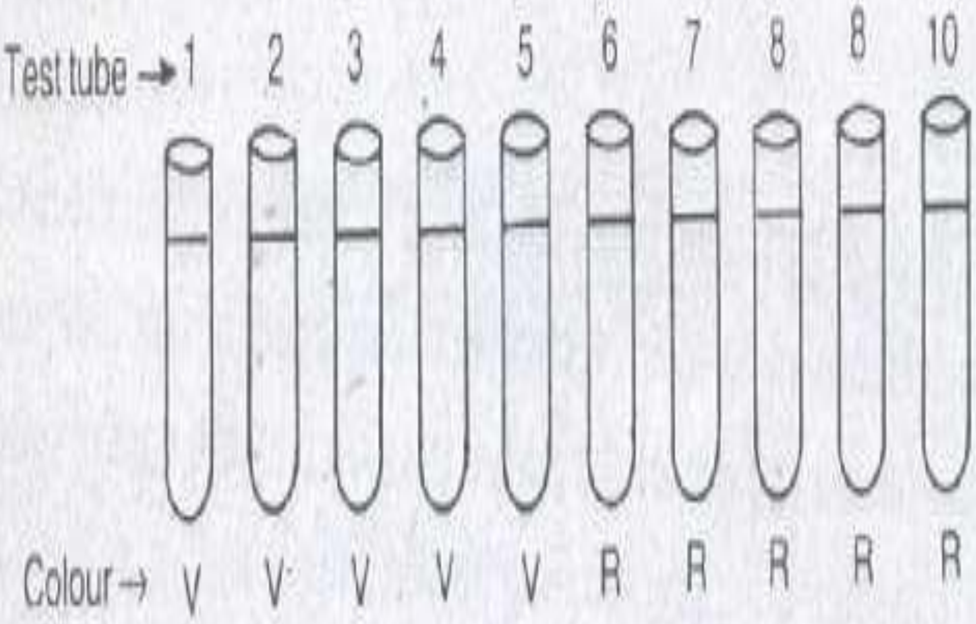
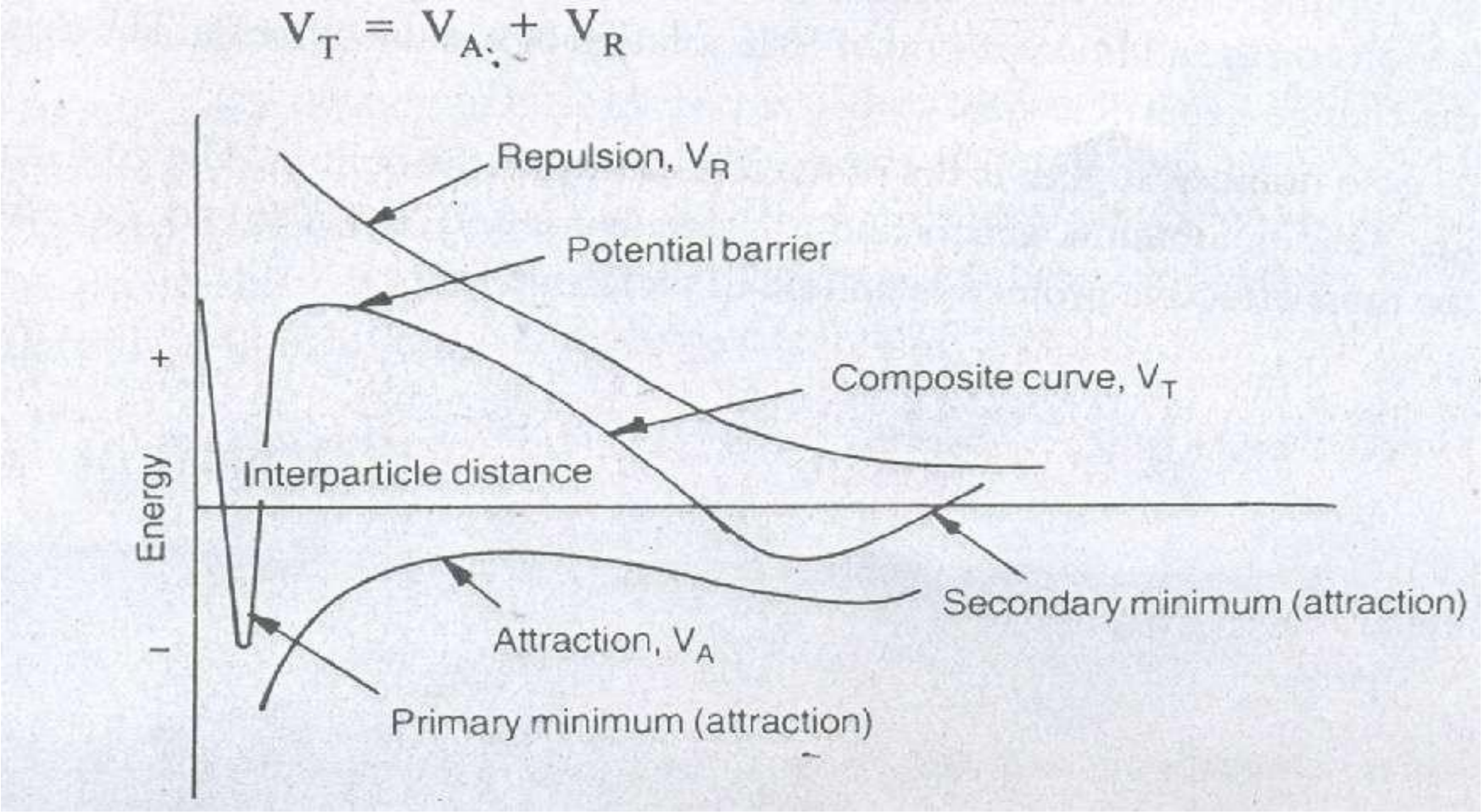


Fig. 5.9. Assembly for determination of Gold number, V = Violet, R = Red. Test tube number 6 gives number.

DLVO theory


$V_T = V_A + V_R$
Repulsion, V_R
Potential barrier
Composite curve, V_T
+
Energy
Interparticle distance
–
Secondary minimum (attraction)
Attraction, V_A
Primary minimum (attraction)

Effect of Added Electrolyte

Coagulation of Hydrophilic Colloids Follows the Hofmeister Series

Decreasing hydration →

$SO_4^{-2} > CH_3COO^- > Cl^- > NO_3^- > Br^- > I^- >$

$Mg^{+2} > Ca^{+2} > Ba^{+2} > Li^+ > Na^+ > K^+$

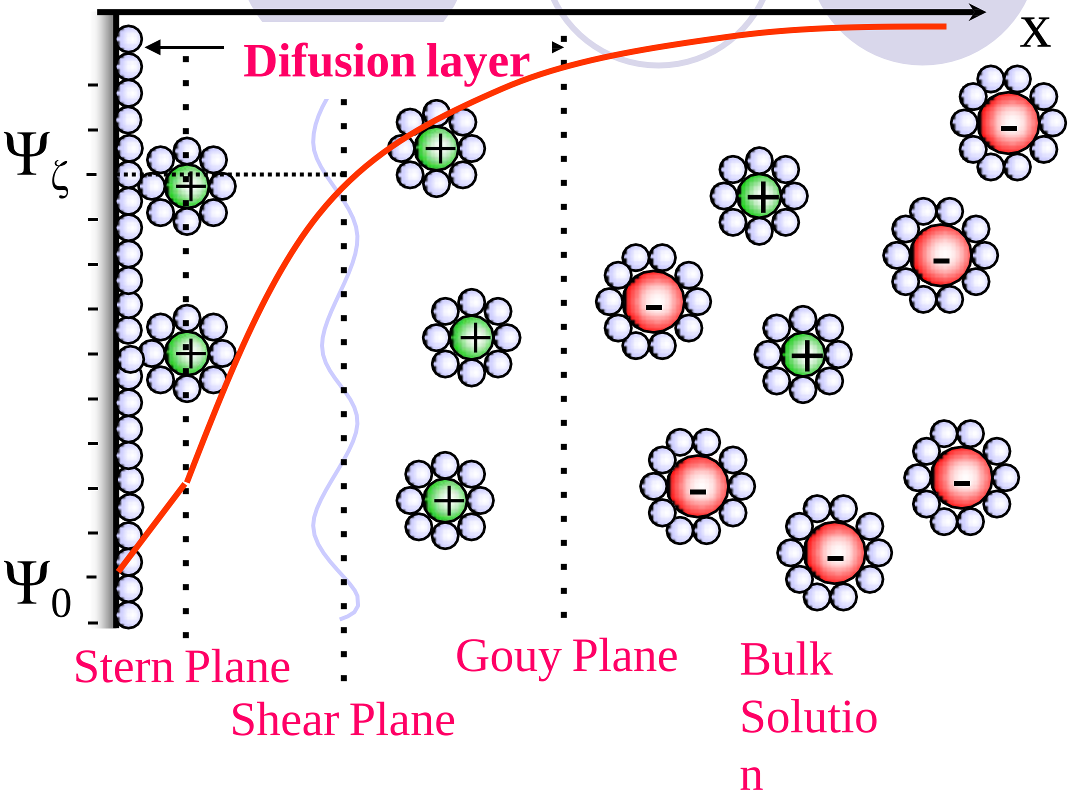
Hydration and Electrolytes

- increasing concentration and hydration ability of ions in the dispersion medium correlates with increasing effectiveness "salting out" hydrophilic colloids
- increasing concentration and presence of extensively hydrated ions makes it more difficult to hydrate added solid colloidal material

Zeta Potential

The value of the potential at the ***shear plane*** is called ***zeta potential*** and it is representative of the surface charge.

It is measured in *mV*.



Remember: Positive value does not mean that there are only positive sites on the surface. Means that there are more positive than negative sites.

Equipment for Measuring Zeta Potential

Electrophoresis - **Zeta Mark 21** particles ~ .10 microns- 300 µm

Equipment for Measuring Zeta Potential

Electroacoustic - **Colloidal Dynamics Acoustosizer** powders/slurries < 10nm - up to 50 weight%

Equipment for Measuring Zeta Potential

Photocorrelation Spectroscopy - **Brookhaven Zeta Plus** dilute msuspensions <5microns light scattering technique

Equipment for Measuring Zeta Potential

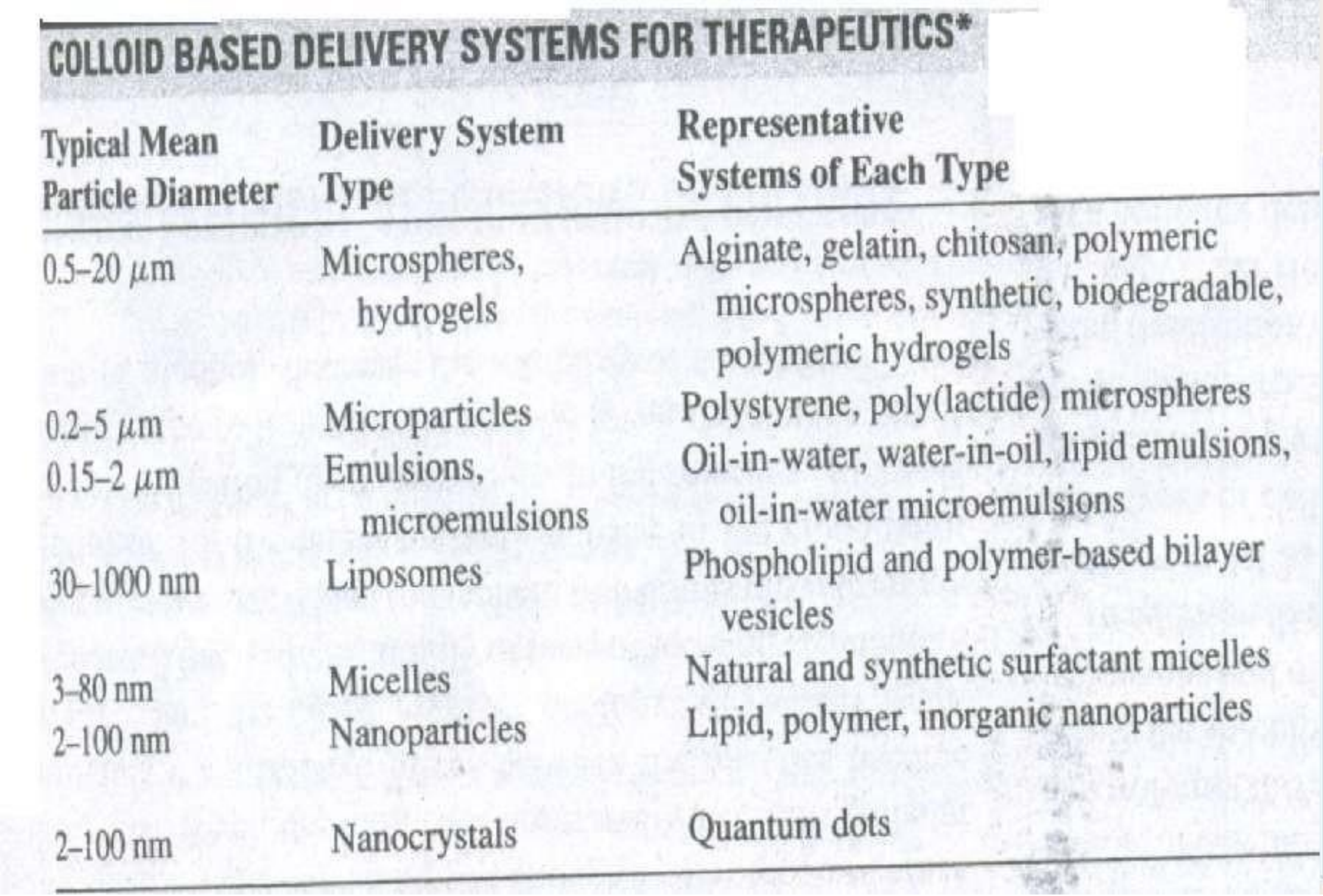
Streaming Potential – **Paar Physica EKA** granular particles, surfaces

Colloidal Stability and the Diffuse Double Layer

- Generally, the larger the diffuse double layer the greater the repulsive force and the more stable the colloid.

Application Fields of Colloids

Area	Example
Industrial	Paints, Adhesives, Floor polishes, Print inks, Carpet backing, Paper sizing, Water/sewage treatment, Secondary oil recovery, Rubberized concrete
Research	Size standard for electron microscopy High resolution chromatography column packing
Medical	Magnetic particles targeted drug delivery Immunodiagnostics Controlled released drugs
Chemical	Catalysts, Colloids & surface chemistry, Coagulation kinetics Model liquid crystals, Rheology, Dielectric spectroscopy Particle interaction *Dispersion forces *Electrostatics *Steric stabilization

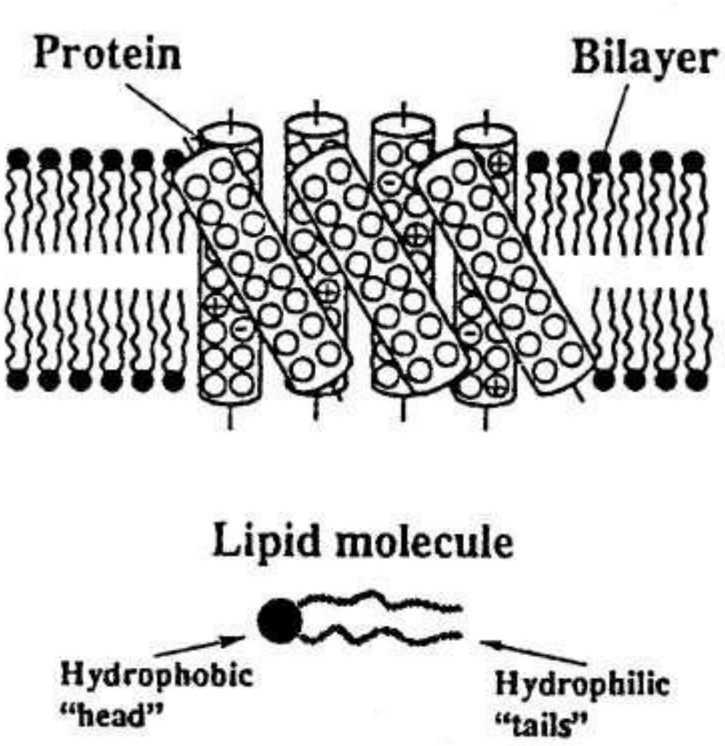


COLLOID BASED DELIVERY SYSTEMS FOR THERAPEUTICS*

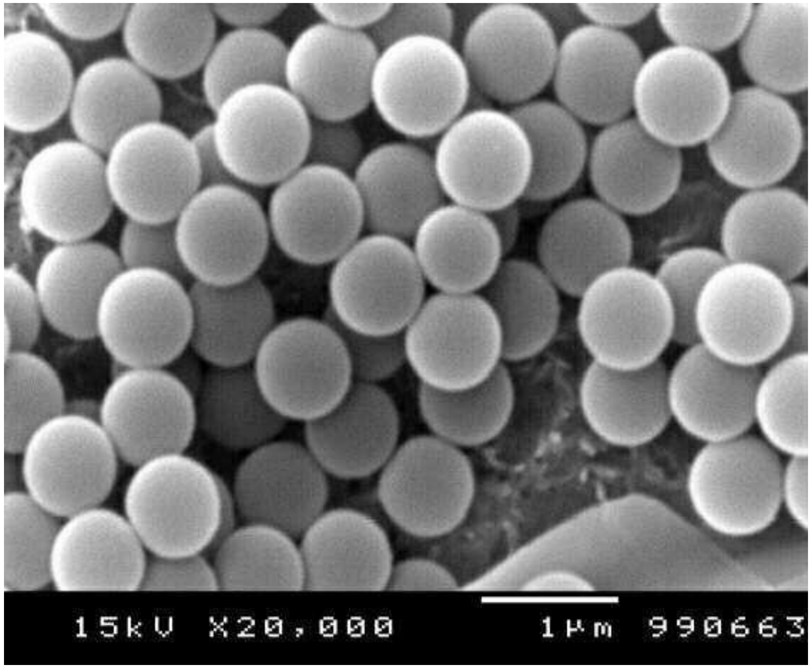
Typical Mean Particle Diameter	Delivery System Type	Representative Systems of Each Type
0.5–20 μm	Microspheres, hydrogels	Alginate, gelatin, chitosan, polymeric microspheres, synthetic, biodegradable, polymeric hydrogels
0.2–5 μm	Microparticles	Polystyrene, poly(lactide) microspheres
0.15–2 μm	Emulsions, microemulsions	Oil-in-water, water-in-oil, lipid emulsions, oil-in-water microemulsions
30–1000 nm	Liposomes	Phospholipid and polymer-based bilayer vesicles
3–80 nm	Micelles	Natural and synthetic surfactant micelles
2–100 nm	Nanoparticles	Lipid, polymer, inorganic nanoparticles
2–100 nm	Nanocrystals	Quantum dots

Biological and life science:

Biological membranes and cells



Microspheres



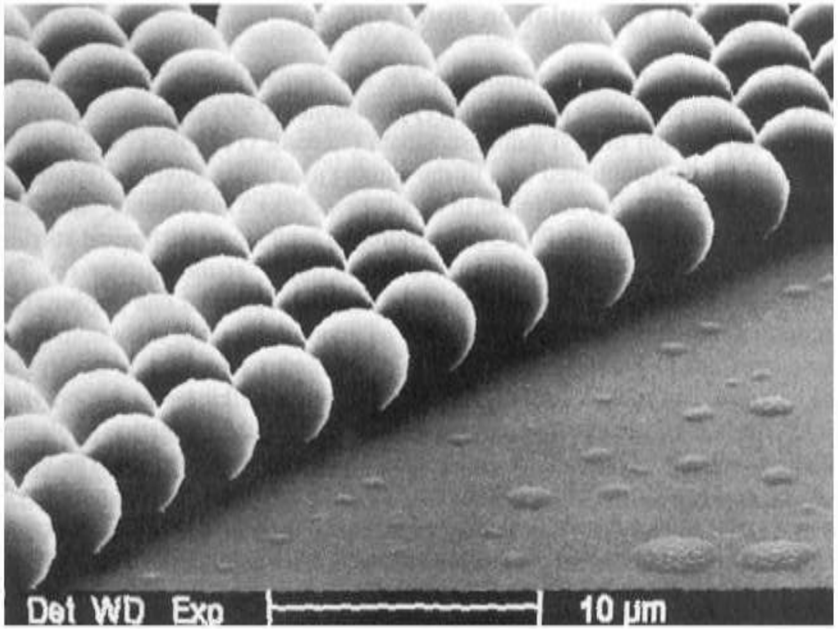
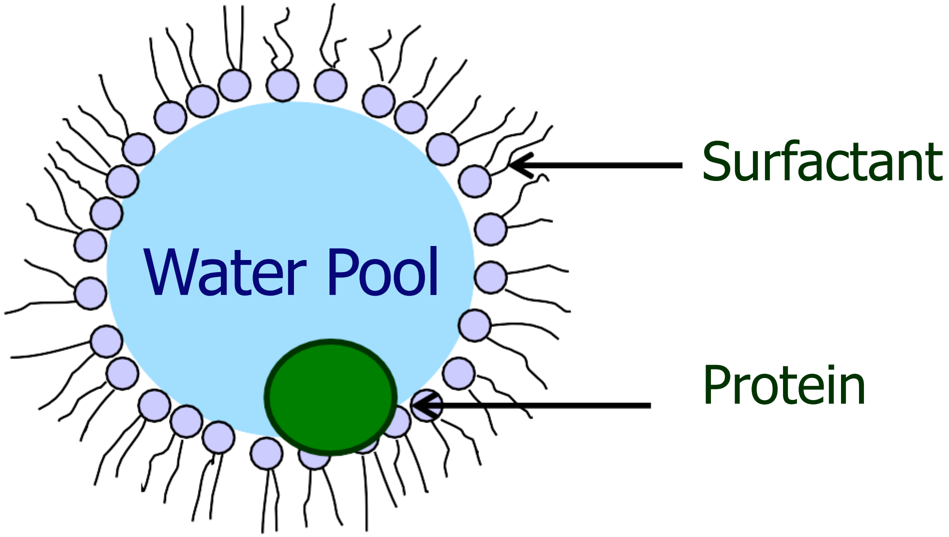


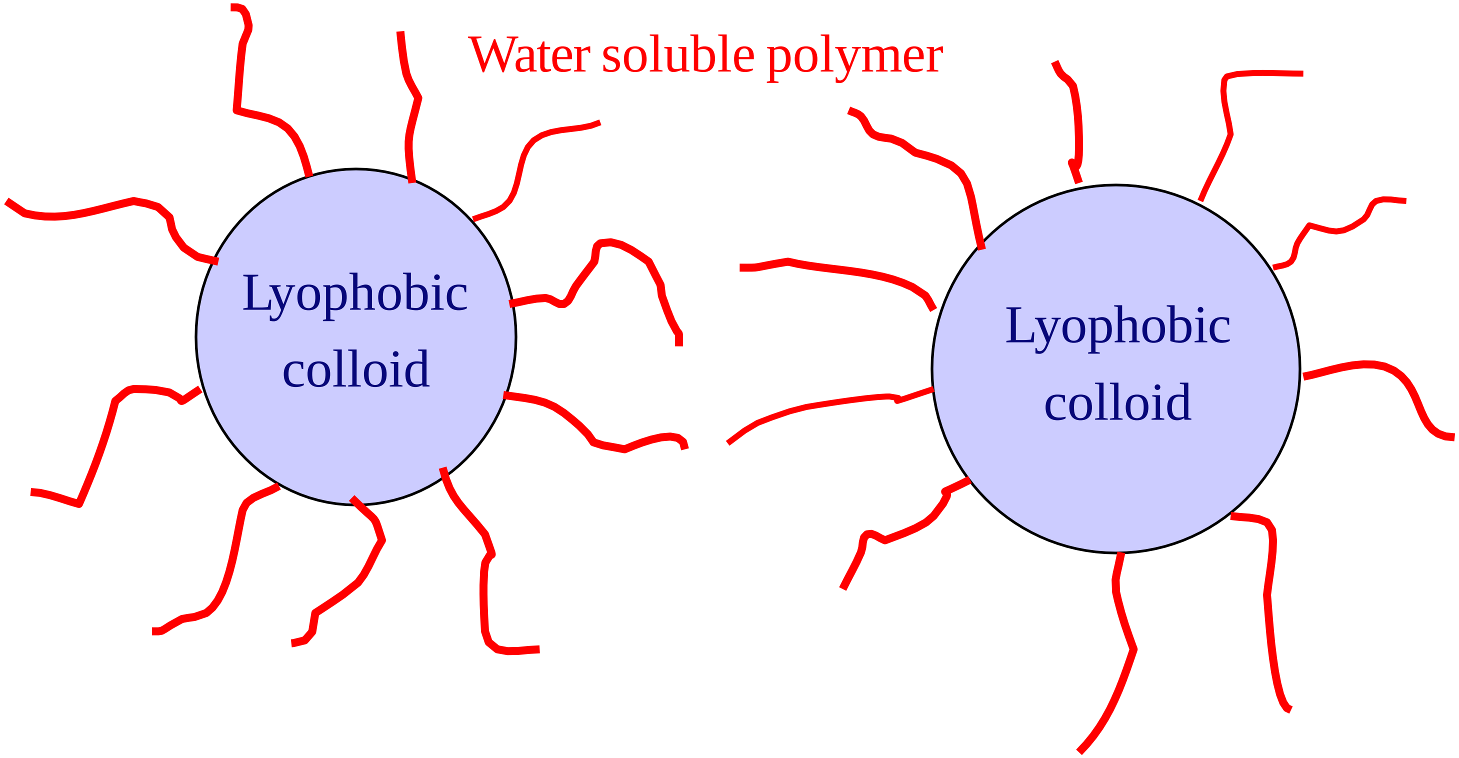
Figure 22.1 Scanning *electron micrograph* of polystyrene microspheres prepared by *dispersion polymerization.* (Photomicrograph courtesy of T. Groves/A. Rowley, Ilford Ltd)

Microemulsion



Organic Solvent

Structure-Mechanical Barrier



"Stealth" Liposomes

Nanoparticles

Nanoparticles

NanoMill™-01

1-10g API Batch Sizes

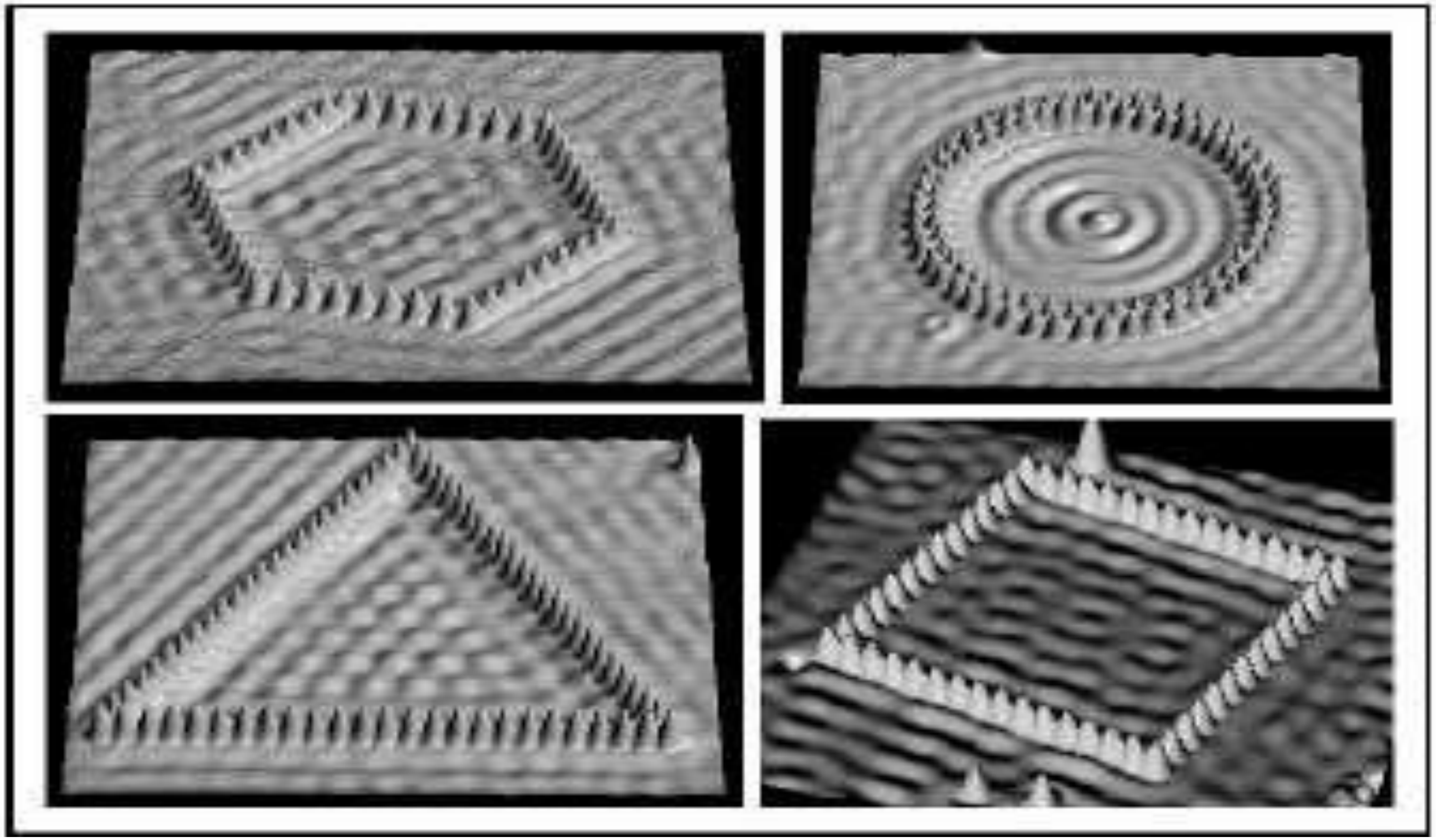
OLEY

élan NanoSystems

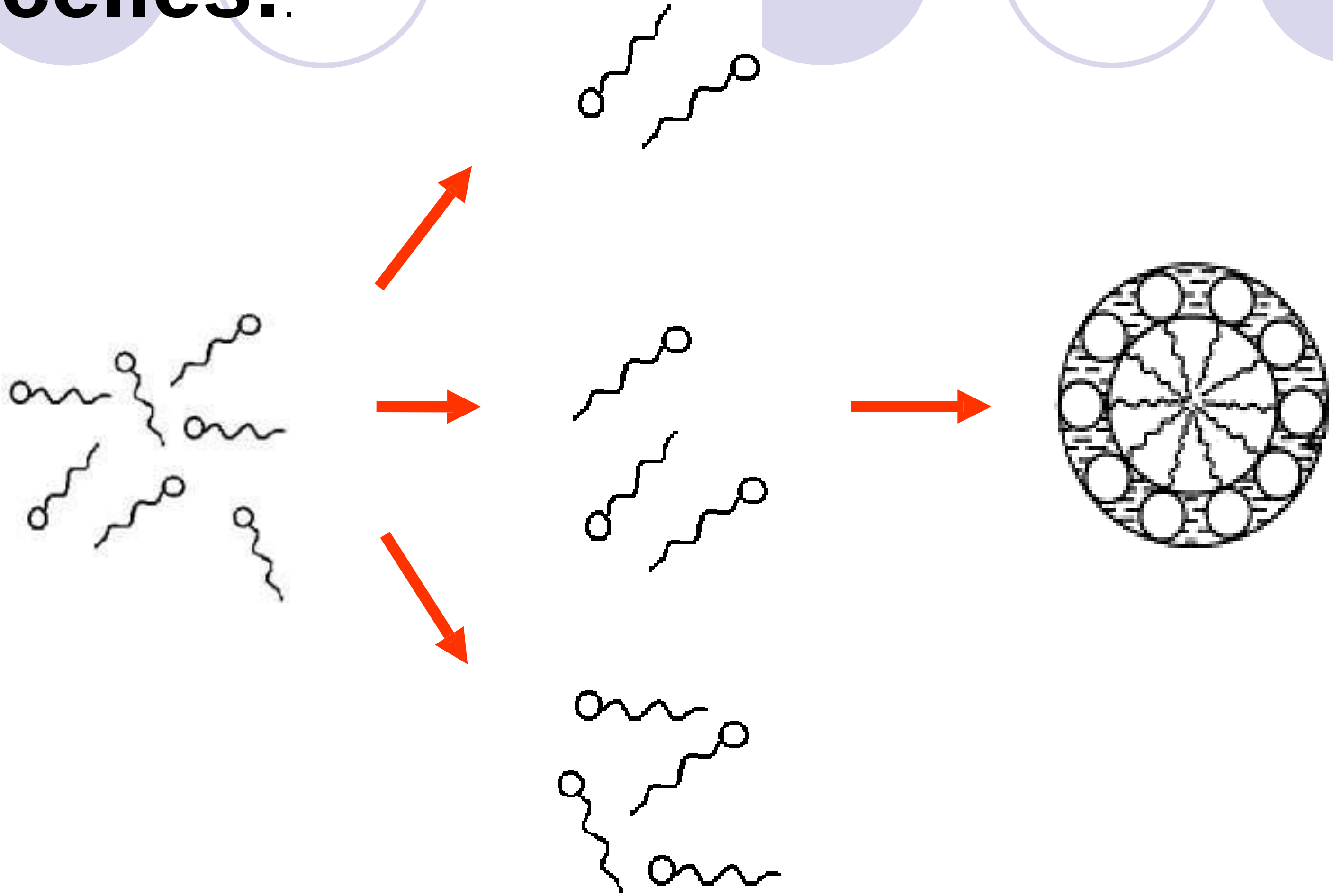
Nanoparticles products

Rapamune® Commercial Products

Quantum dots (Q-dots)

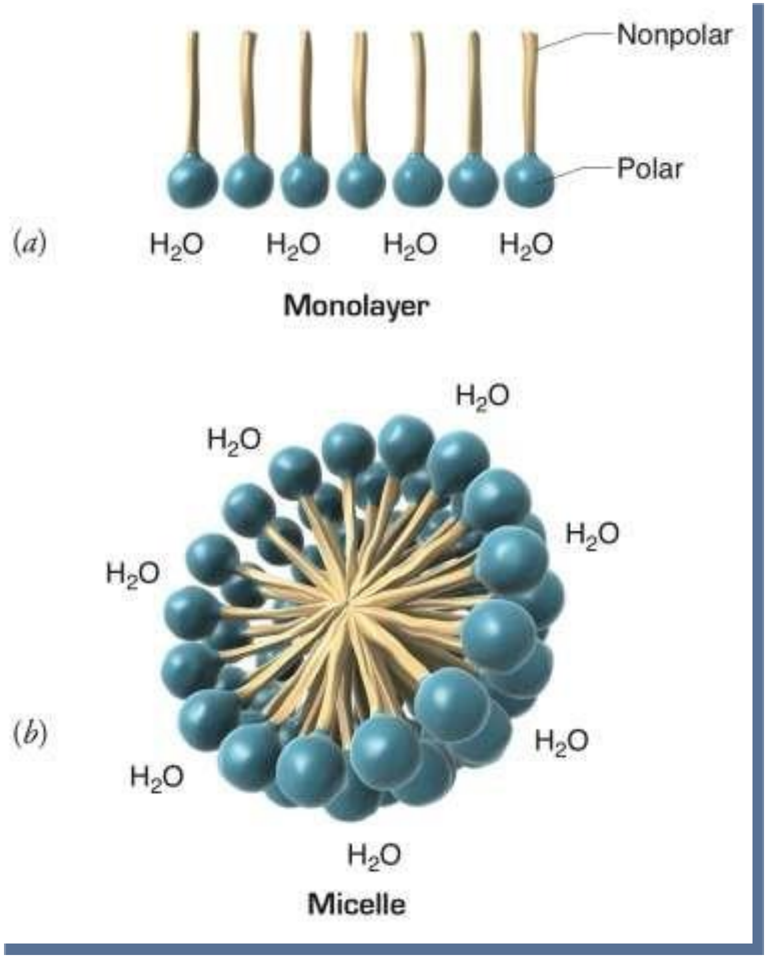


Micelles::

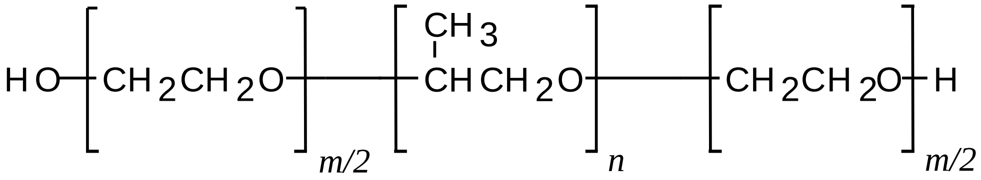


Micelles:

When placed in water, amphipathic molecules, form structures, such as micelles,
which attempt to address the conflict.

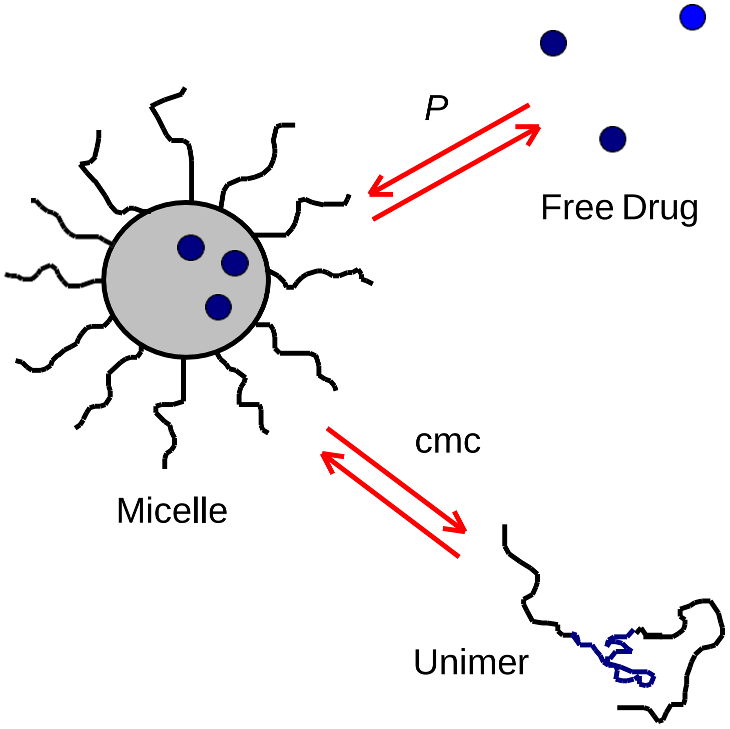


Block Copolymer Micelle



$$HO\left[CH_2CH_2O\right]_{m/2}\left[\overset{\overset{\displaystyle CH_3}{|}}{CH}CH_2O\right]_{n}\left[CH_2CH_2O\right]_{m/2}H$$

- Pluronic



P

Free Drug

cmc

Micelle

Unimer