

**MUNI**  
PHARM

# **Interfacial Phenomena**

Physical chemistry

# Basic concepts

**Phase** – a homogeneous part of a heterogeneous system separated from other phases by the phase interface (the system's properties are step-changed to the phase interface).

The properties of the phase interface are influenced by the properties of the two interconnecting phases.

Phase interfaces are divided according to the state of the matter of the phases in contact:

- **interface liquid/gas (l/g)**
  - **interface liquid /liquid (l/l)**
  - **interface solid/gas (s/g)**
  - **interface solid /liquid (s/l)**
  - **interface solid /solid (s/s)**
- } **mobile interfaces**

Phase interfaces liquid/gas and solid/gas are known as **surfaces**.

# Phase interface from a molecular perspective

The **phase interface size determines the effect of the phase interface on the system properties** (i.e. ratio of the number of molecules at the interface to the number of molecules in the bulk phase).

**Large specific surface are common in:**

- Heterogeneous colloidal dispersion systems (particle size 1 nm - 1  $\mu\text{m}$ )
- Microporous solid substances

**Interface phenomena:**

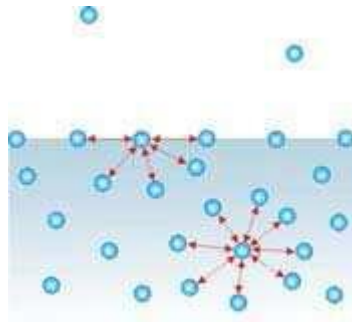
- Surface tension
- Spreading and wetting (capillary phenomena)
- The stability of dispersion systems
- Adsorption
- Micelles and cell membrane formation

These phenomena are influenced by forces that originate in **interatomic or intermolecular interactions**.

# Phase interface gas-liquid

Interactions between molecules different from interactions in the phases take place on the phase interfaces – difference most obvious in the case of pure interface liquid / vapor – **surface tension**

$$\sigma = F / \ell \quad [\text{N.m}^{-1}]$$



Surface tension is the force acting in the plane of the liquid surface. It causes the liquid to try to reduce its surface area – **spherical shape** (droplet formation).

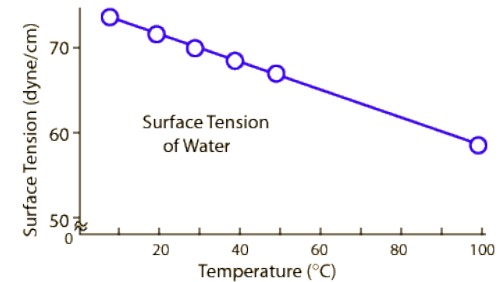
When the surface of the fluid increases, some molecules have to get from the inside to the surface – work needs to be done, so called **surface energy**.

$$\gamma = dW / dS \quad [\text{J.m}^{-2} = \text{N.m.m}^{-2} = \text{N.m}^{-1}]$$

# Phase interface gas-liquid

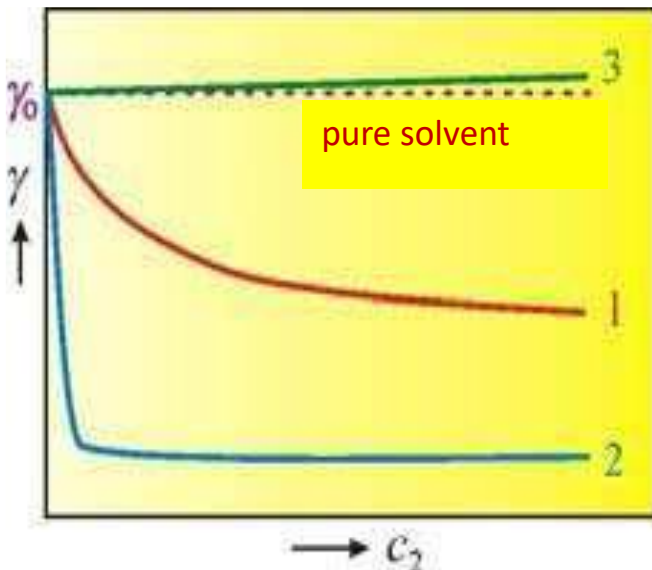
The surface tension depends on the **temperature**:

- with increasing temperature the surface tension always decreases.



## The surface tension of solutions:

- varies with concentration and type of added compounds



1 – simple organic compounds

**2 – surfactants**

3 – inorganic electrolytes (increase surface tension)

dash line - no effect on surface tension (e.g. sugar solutions in water)

# Phase interface gas-liquid

## Practical consequences of surface tension

Surface tension is responsible for the formation of droplets. The **droplet size** depends on the size of surface tension and hence on the liquid used.

Example:

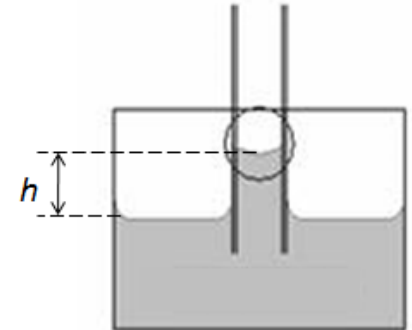
If we have two medicinal products (e.g. solutions) with the same content of active substance and different content of solvent (e.g. ethanol), **we have to dispense a different number of drops to achieve the same dose** of active substance.



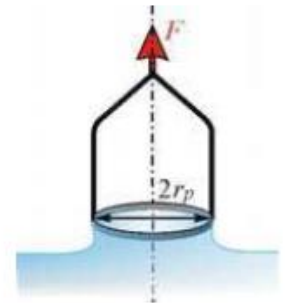
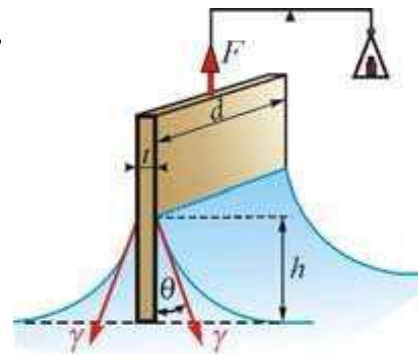
# Methods for measuring surface tension

Static methods – monitoring the steady state of equilibrium

- The method of capillary elevation  $\frac{\sigma_1}{\sigma_2} = \frac{\rho_1 \times h_1}{\rho_2 \times h_2}$



- Wilhelmy plate method:  $F = 2d \sigma$
- Du Noüy Ring method:  $F = 4\pi r \sigma$

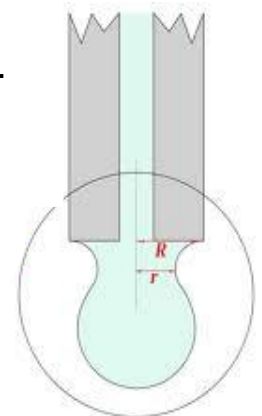


Semi-static methods – achieved equilibrium is unstable

- Method of weighting a drop of liquid (stalagmometry):  $mg = 2\pi r \sigma$

$$\frac{m_1}{\sigma_1} = \frac{m_2}{\sigma_2}$$

$$\sigma = \sigma_{H_2O} \times \frac{m}{m_{H_2O}}$$



# Heterogeneous dispersion

## Classification of heterogeneous systems:

L	L	emulsion
S	L	suspension
G	L	foam
S/L	G	aerosols (dust / fog)
G/L/S	S	solid foam / gel / mixture

The phase interface size determines the total effect on the system properties:

**Colloidal dispersion** 1-1000 nm

**Coarse dispersion**  $> 1 \mu\text{m}$

Large interface energy = these systems need to be **stabilized**.



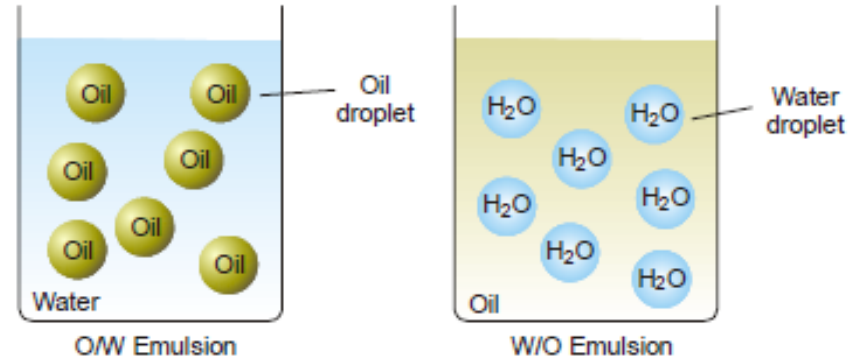
# Phase interface liquid-liquid

**Emulsions:** are formed by dispersion medium and dispersed substance.

The systems of immiscible or limited miscible liquids.

**Types of emulsions:** a) **oil in water** (O/W)

b) **water in oil** (W/O)



**Applications in pharmacy** – creams (O/W, W/O)

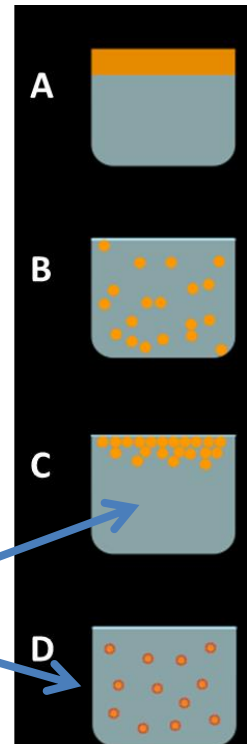
– injections, infusions (O/W)

– ointments (W/O)

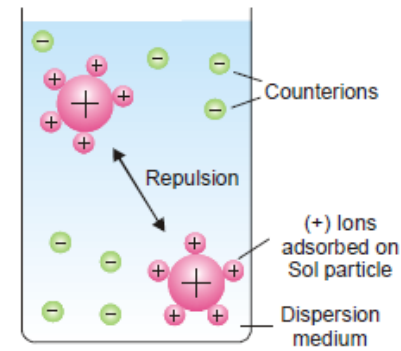
**Emulsions may be unstable, their stability must be ensured in an appropriate way.**

Coalescence (aggregation of particles or droplets)

Stabilization of the suspension by addition of surfactant (reduction of surface tension)



# Phase interface liquid-liquid



## Stabilization of emulsions:

### 1. Electrical double-layer

Repulsive forces between charged droplets prevent coalescence (in diluted emulsions).

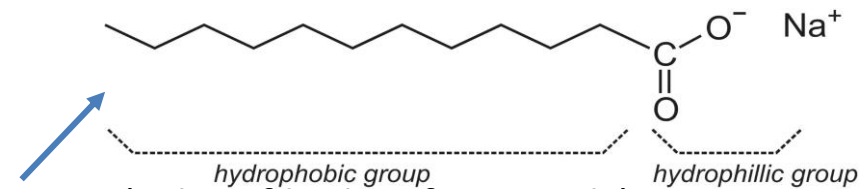
### 2. Surfactants (emulsifiers)

**Types:** a) associative (micellar) colloids – soaps (salts of higher fatty acids)

b) macromolecular colloids – hydrophilic (gelatin, dextrans)

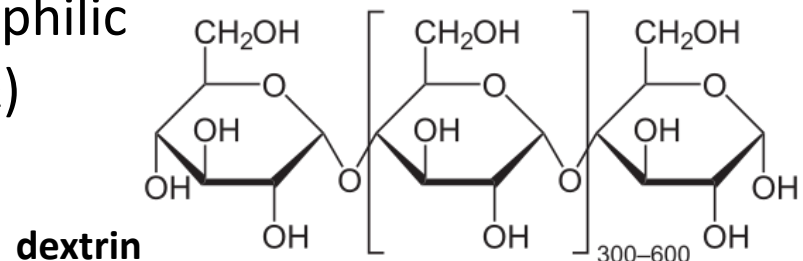
– hydrophobic (rubber, cellulose trinitrate)

c) powders (colloidal  $\text{SiO}_2$ , aluminosilicates)



**Another division** a) ionic surfactants: anionic, cationic, ampholytic

b) non-ionic surfactants: no charge, solubility is due to the presence of hydrophilic groups (eg. -OH, -NH<sub>2</sub>)



# Phase interface liquid-liquid

## The emulsifying effect

Balanced polar and non-polar part of the molecule (determined by the length of the hydrocarbon chains and by affinity of polar groups to water).

**HLB** (hydrophilic-lipophilic balance) - characterizes the relationship between hydrophilic and lipophilic parts.

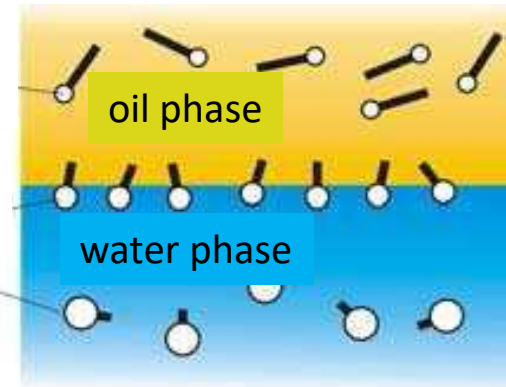
↓HLB = **hydrophobic surfactants**,  
**well stabilized emulsion W / O**

↑HLB = **hydrophilic surfactants**,  
**well stabilized emulsion O / W**

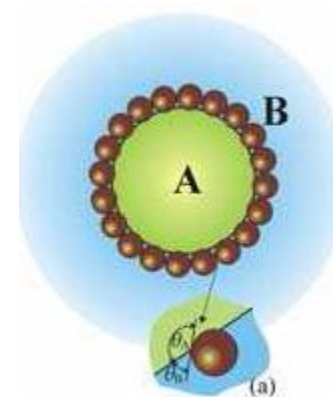
non-polar part  
predominant

balanced polar and  
non-polar parts

polar part  
predominant



**Powder emulsifiers** - partially wetted by both phases; particle size is important (large particles sediment, small particles leave the interface due to thermal motion).



# Phase interface solid-liquid

## Suspension

At least two phases, an internal (dispersed) phase is solid; outer dispersed phase is liquid.

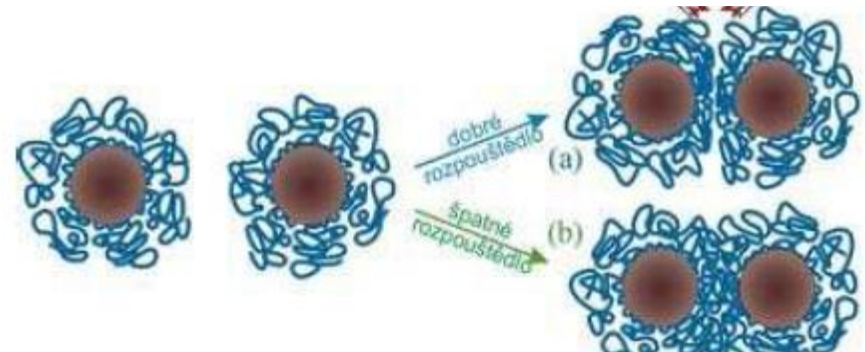
### Stabilization of suspension:

1. **Aggregation** (colloidal dispersion 1-1000 nm)

a) **Electrostatic stabilization** – repulsion of particles with the same charge.

b) **Steric stabilization** – addition of a substance which is adsorbed on the particle surface, but also is soluble in the dispersion medium (surfactants, macromolecules).

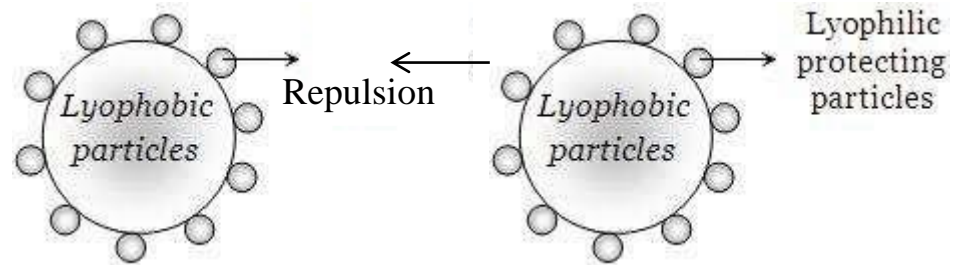
good affinity of the added substance to the solvent - stabilization



bad affinity of the added substance to the solvent - aggregation

# Phase interface solid-liquid

c) **Electrosteric stabilization** – addition of **lyophilic colloid** (stable colloid solution) to **lyophobic colloid** (unstable colloid solution), at least one is electrically charged.



d) **Stabilization by solid particles**

2. **Sedimentation** (coarse dispersion > 1 μm)

a) **Sedimentation rate** (Stokes equation):

$$v = \frac{2 r^2 (\rho_1 - \rho_2) g}{9 \eta}$$

r..... radius of particle

$\rho_1, \rho_2$ ... density of inner and outer phase

$\eta$ ..... viscosity of outer phase

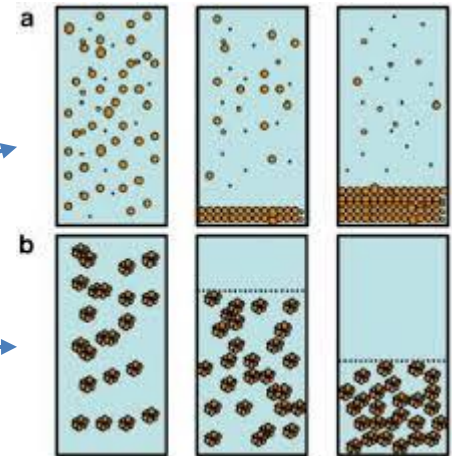
g..... gravitational acceleration



# Phase interface solid-liquid-gas

b) **Surface wettability** – influences redispersion of sediment by shaking and aggregate state of suspended drug:

- **non-flocculated** suspension
- **flocculated** suspension
- **flotated** suspension



Suspension	Wettability	Sediment shakeability	Pharmaceutical applicability
non-flocculated	perfect	not easy (caking)	mainly parenteral application
flocculated	good	not problematic	most of the medicinal suspension
flotated	bad	-	no

## Influence of wettability

- Addition of a surfactant (steric stabilization).
- Addition of electrolyte increases flocculation of suspensions (suppression of electrostatic stabilization).

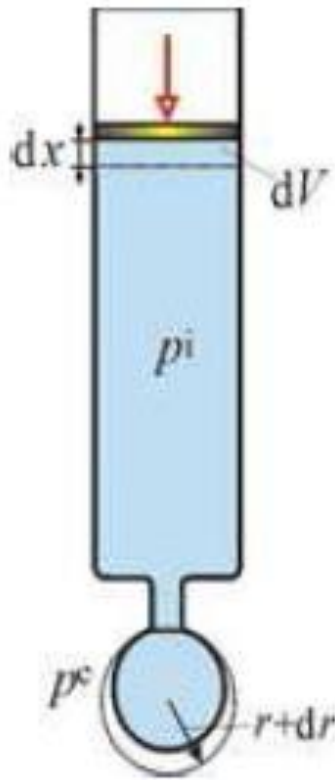
# The equilibrium in systems with phase interface

In each system, spontaneous actions take place to establish equilibrium. The sum of the energies of all phase interfaces in the system is reduced by:

- **Reducing the surface** (curvature) of the phase interfaces
- **Changing of phase interfaces** to different phase interfaces which are energetically more advantageous (wetting, spreading)
- **Adsorption**, i.e. a change in composition on the interface, which leads to the reduction of the interfacial energy

# Reducing the energy of the system by minimization of the area of the phase interface

Curvature of the phase interface (e.g. liquid droplets, bubbles, etc.) affects the properties of the system.



$$p^i \cdot dV = p^e \cdot dV + \gamma \cdot dS$$

$$p^i - p^e = \gamma \cdot dS / dV = \gamma \cdot (1/R_1 + 1/R_2)$$

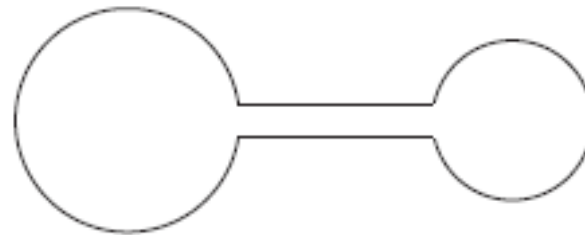
$$\gamma = dW / dS$$

R – radius of curvature

## Laplace equation

spherical drop or bubble ( $R_1 = R_2 = r$ ):  $p^i - p^e = 2\gamma / r$

$$p^i = p^e + 2\gamma / r$$



$\gamma_1$	=	$\gamma_2$
$r_1$	>	$r_2$
$P_1$	<	$P_2$

**Biophysics: effect of surface tension on inflation and deflation of lung alveoli.**

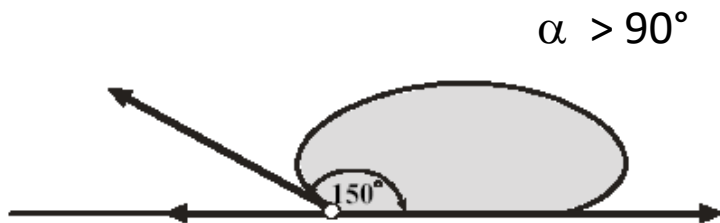


# Reducing the energy of the system by changing of the phase interface

## Interfaces solid-liquid (wetting)

If the surface tension of the solid is greater than the sum of the surface tension of the liquid and the **interfacial tension** of the solid-liquid, liquid wets the solid surface:  $\sigma_s > \sigma_l + \sigma_{sl}$

If it is true  $\sigma_s < \sigma_l + \sigma_{sl}$ , the drop of liquid takes on a solid surface the equilibrium shape, characterized by the **wetting angle**  $\alpha$ .



$\alpha = 180^\circ$

$\alpha > 90^\circ$

$\alpha < 90^\circ$

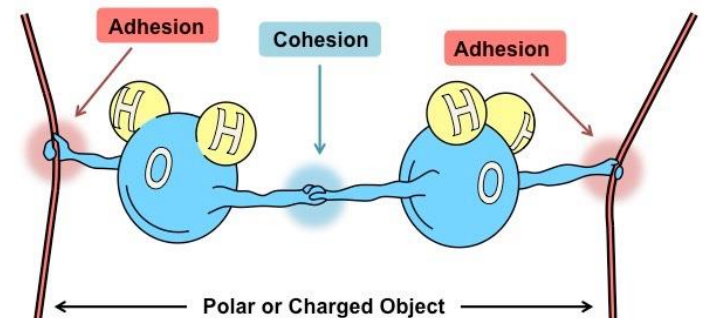
$\alpha = 0^\circ$

perfect non-wetting

poor wetting

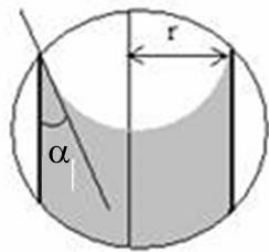
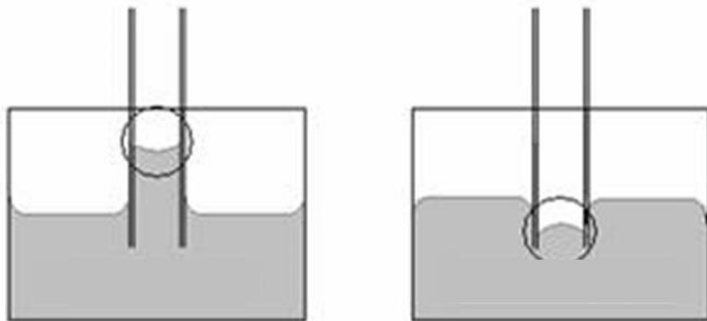
good wetting

perfect wetting

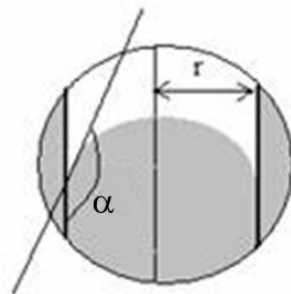


# Interfaces solid-liquid (wetting – capillary actions)

An important case of the equilibrium at the solid-liquid interface is the behavior in thin tubes (capillaries), in which the level of liquid is set higher (**capillary elevation**) or lower (**capillary depression**) than the surrounding liquid level .



concave meniscus



convex meniscus

During capillary elevation, the liquid rises to a level at which the surface and the gravitational force of the liquid will be in equilibrium

$$h = (2 \cdot \sigma \cdot \cos \alpha) / (\rho \cdot r \cdot g)$$

$r$  – capillary radius

$g$  – gravitational acceleration

$\rho$  – density of the liquid

Used for the determination of surface tension of liquids (glass capillaries almost perfectly wetted,  $\cos \alpha = 1$ ).

**Biophysics: capillary action allows the water to rise into the upper parts of plants .**

### Sample problem

The trunk and leaves of a tree can be considered a system of capillaries. **Calculate the capillaries diameter**, if a 41 m tall tree does not dry out. Assume that the water perfectly wets the walls of the capillaries; the surface tension of the water is  $70 \text{ mN m}^{-1}$  and its density is  $1 \text{ g cm}^{-3}$ .

$$h = (2 \cdot \sigma \cdot \cos \alpha) / (\rho \cdot r \cdot g)$$

$$r = (2 \cdot \sigma \cdot \cos \alpha) / (\rho \cdot h \cdot g)$$

$$r = 2 \cdot 0.070 / 1000 \cdot 41 \cdot 9.81$$

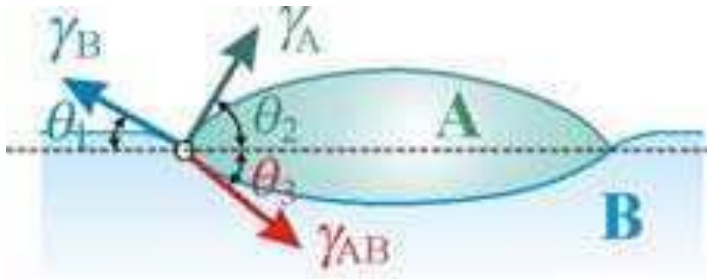
$$r = 3.48 \cdot 10^{-7} \text{ m}$$

$$d = 0.7 \text{ } \mu\text{m}$$



# Interfaces liquid-liquid

The behavior of drop of liquid on the surface of another liquid (immiscible) is similar to the behavior of a drop of liquid on the solid surface.



$$\gamma_B > \gamma_A + \gamma_{AB}$$
$$\gamma_B < \gamma_A + \gamma_{AB}$$

drop spreads out  
drop takes equilibrium shape

## Cohesive and adhesive forces

**Cohesion** - forces between the liquid (A-A). Work of cohesion  $W_c = 2 \gamma_A$

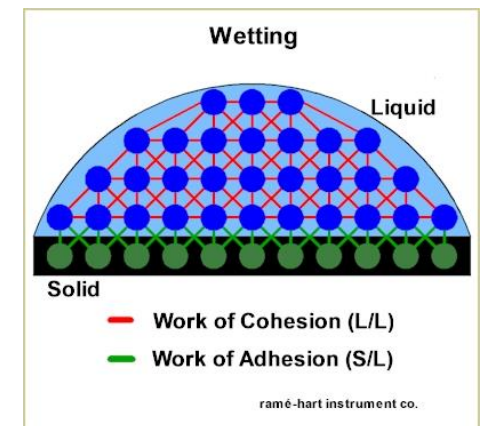
**Adhesion** - forces between the molecules of the two phases (A-B).

Work of Adhesion  $W_a = \gamma_A + \gamma_B - \gamma_{AB}$

Liquid A is spread

(or solid surface is wetted) when:

$W_a > W_c$



# Reducing the energy of the system by adsorption on the phase interface

For multi-component systems, energy is also reduced by changing concentration on the phase interface - **adsorption**. Adsorption typically means **positive adsorption**, in which the concentration of a particular component in the phase interface is higher than in the condensed phases.

## Adsorption versus Absorption



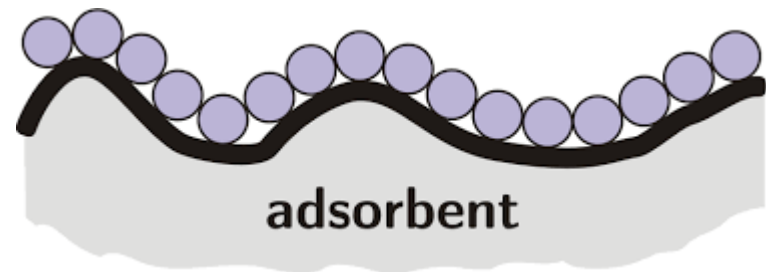
Adsorption on a movable (gas-liquid or liquid-liquid) and solid phase interface (gas-solid or liquid-solid).

# Reducing the energy of the system by adsorption at the phase interface

Adsorption is a spontaneous process, in which, as with any spontaneous process, Gibbs energy decreases.

The gas molecules can only carry two-dimensional motion on the surface of the adsorbent and therefore lose one translational degree of freedom during adsorption -> decrease in entropy occurs. This implies that the heat of adsorption is negative ( $\Delta_{\text{ads}}H = \Delta_{\text{ads}}G + T \cdot \Delta_{\text{ads}}S$ ).

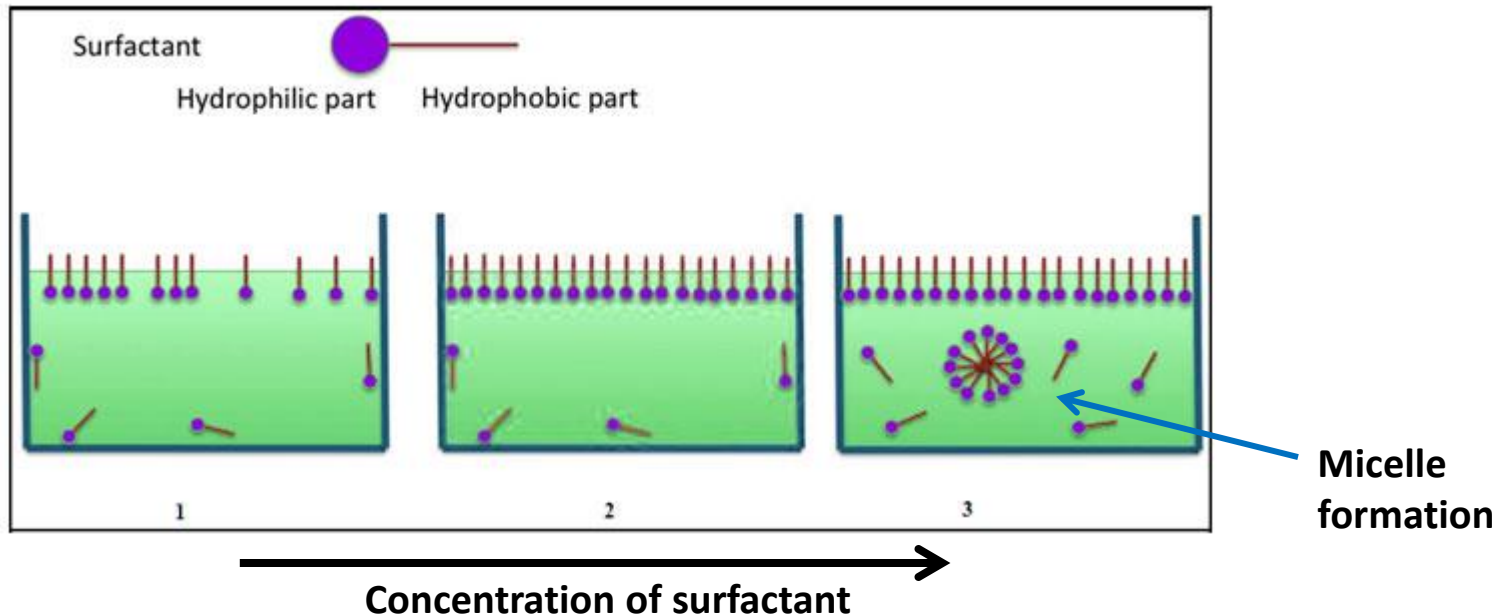
Adsorption is always an exothermic process and the adsorbed amount (at constant pressure) decreases with increasing temperature.



# Interfaces liquid-gas

The concentration of the solute is higher in the surface layer than inside the solution - **adsorption at the liquid surface**.

**Model of saturated monolayer:** The molecules of the solute are closely arranged so that their hydrated polar groups are oriented into the aqueous phase and the hydrocarbon chains are directed outside the aqueous phase.



# Interfaces solid-gas and solid-liquid

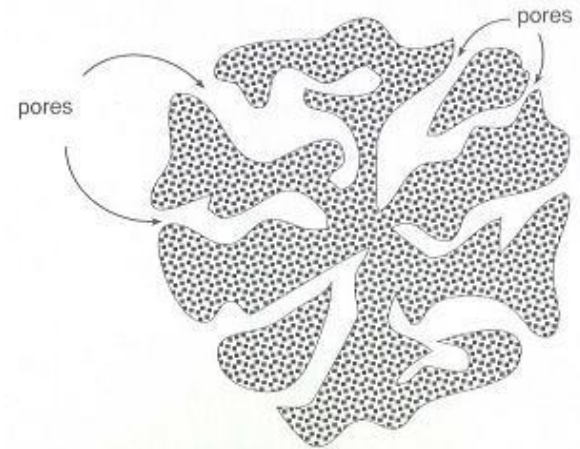
**The surfaces of solids:** unlike liquid, the surface of solids is rough both in microscale and macroscale. **The surface of solids is not homogeneous** and the force acting in the plane of the surface differs in different locations, and is also different in different directions.

**Surface and structure of the pores affects properties of the porous material** (adsorption strength, permeability, reactivity).

**Specific surface** - surface area per unit of mass ( $\text{m}^2/\text{g}$ ).

**The outer surface** - geometric surface of particle (the visible part of the surface).

**The inner surface** - surface of the pores and cracks that permeate the particle.





# Interfaces solid-gas and solid-liquid

**Adsorbent** - solid particles with a large adsorption capacity (i.e. large specific surface).

## Physical adsorption

Molecules are bound to a solid surface by **physical forces** (van der Waals) that act between all particle types. Physical adsorption **is not specific** and is being on the whole surface of the solid.

## Chemisorption

The molecules are bonded to the surface molecules of the adsorbent by **chemical bond formation**; chemisorption is **very specific** - the bond can occur only between certain molecules.

# Adsorption on the interface solid - gas

When the solid is in contact with the gas, the gas molecules are always trapped on solid surface - adsorption (increasing the concentration of molecules of a substance on the phase interface).

**The properties that affect the adsorption of gases on solids:**

1. **Specific surface**
2. **Type of gas**
3. **The heat of adsorption** - the energy released when gas is adsorbed on a solid surface. Exothermic process. Physical adsorption - the released heat is low (about  $5 \text{ kcal mol}^{-1}$ ), chemisorption - the formation of chemical bonds, the released heat is high (about  $20\text{-}100 \text{ kcal mol}^{-1}$ ).
4. **Effect of temperature** - physical adsorption decreases with increasing temperature (Le Chatelier's principle), chemisorption can increase with temperature (activation energy).

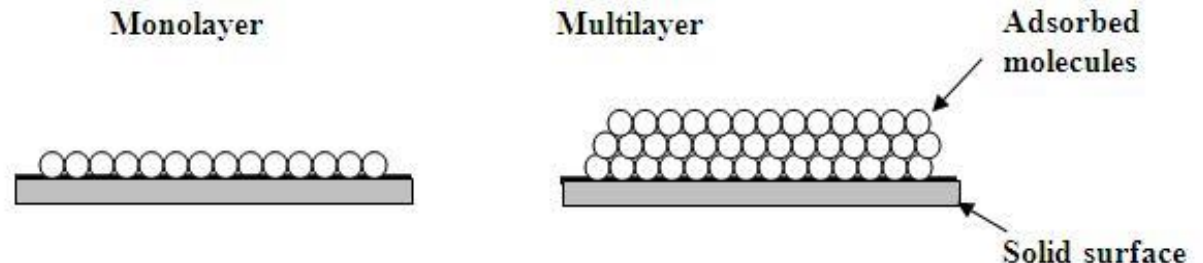
# Adsorption on the interface solid - gas

The properties that affect the adsorption of gases on solids:

5. **Reversibility** - physical adsorption is reversible (adsorption / desorption), chemisorption is irreversible.

6. **Influence of pressure** – increasing pressure leads to a higher physical adsorption; reducing pressure leads to desorption. Chemisorption - the effect of pressure is negligible.

7. **The thickness of the adsorbed layer** - physical adsorption may lead to multilayer adsorption, chemisorption is monolayer (additional layers may be bound by physical forces).



# Kinetics of adsorption

During adsorption the following steps occurring:

1. diffusion to the outer surface of the adsorbent
2. diffusion in pores to the inner surface of the adsorbent
3. adsorption

The slowest process determines the kinetics of adsorption.

Physical adsorption – diffusion in pores is the slowest process in porous adsorbents.

Chemisorption – chemical reaction is the slowest process.

$$k = A \cdot \exp(-E_a/RT)$$

**Arrhenius equation**

k - adsorption rate constant

$E_a$  - activation energy of adsorption

A - frequency factor of adsorption

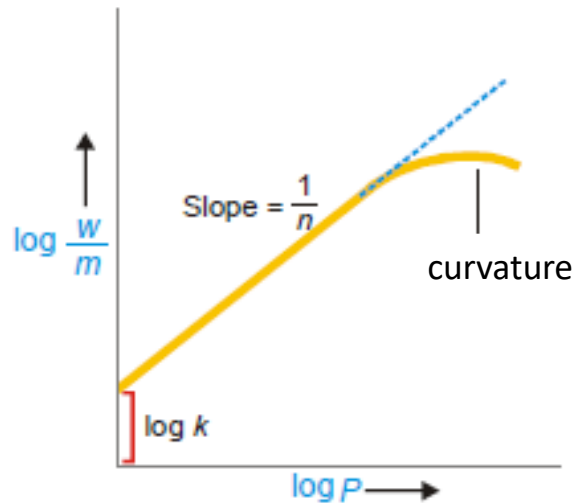
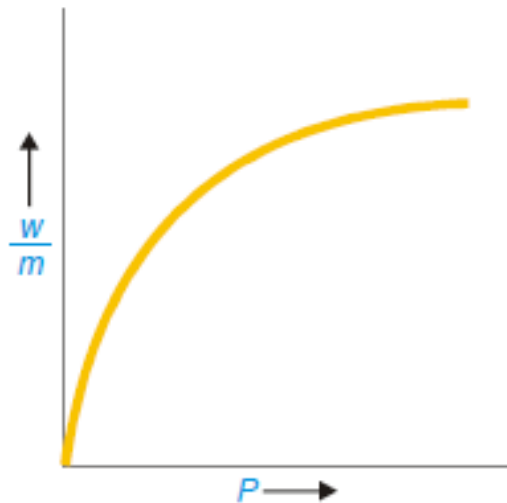
# Freundlich isotherm

dependence of adsorbed amount ( $w/m$ ) at equilibrium pressure  $p$  at a constant temperature:

$$w/m = k \cdot p^{1/n} \quad k, n \text{ are constants}$$

linear equation :

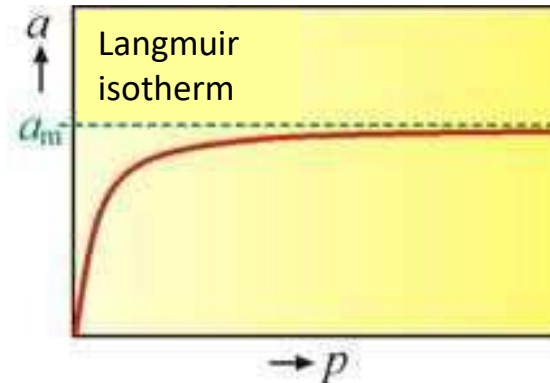
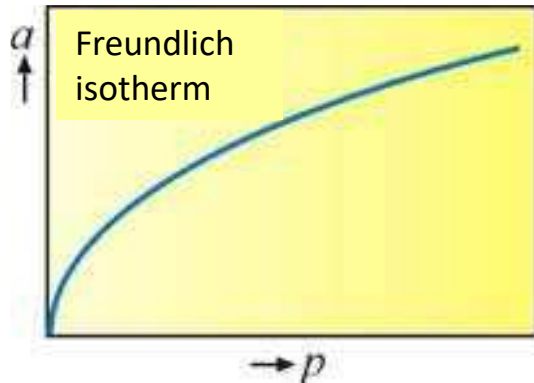
$$\log w/m = \log k + 1/n \log p$$



Limitation: **valid at low pressures**, at higher pressures deviations from linearity.

# Langmuir isotherm

Adsorption at higher equilibrium pressures (concentrations) describes better Langmuir isotherm.



$$a = a_m \cdot (k \cdot p) / (1 + k \cdot p)$$

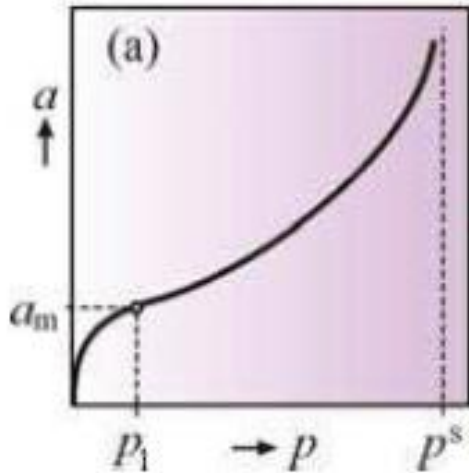
$k$  – adsorption coefficient (it depends on temperature, adsorbent and the adsorbed gas);  $a_m$  – maximum adsorption capacity

linear equation: 
$$\frac{1}{a} = \frac{1}{a_m \cdot k} \cdot \frac{1}{p} + \frac{1}{a_m}$$

Limitation: **Langmuir equation is suitable for monolayer adsorption.**

# BET isotherm

Description of adsorption on planar surfaces (multiple adsorption layers.)



$$a = a_m \cdot \frac{C \cdot p_{\text{rel}}}{(1 - p_{\text{rel}})} \cdot \left( \frac{1 - (x+1) \cdot p_{\text{rel}}^x + x \cdot p_{\text{rel}}^{x+1}}{1 + (C-1) \cdot p_{\text{rel}} - C \cdot p_{\text{rel}}^{x+1}} \right)$$

$a$  – adsorbed amount

$a_m$  – maximum adsorption capacity (at full coverage of the surface by molecular monolayer)

$C$  – constant (depending on the adsorption and condensation heat)

$p_{\text{rel}}$  – the ratio of the equilibrium pressure to the saturated vapor pressure of the adsorbate

$x$  – number of layers ( $x \rightarrow 1$  : Langmuir isotherm)

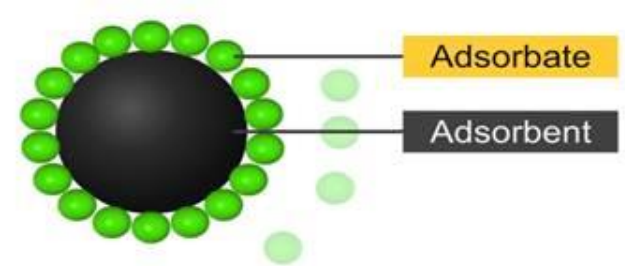
Application of adsorption isotherms: **determination of specific surface of adsorbents**

# Adsorption on the interface solid - liquid

**Adsorption from solutions** – is manifested by the change in the composition of the solution.

**S/L adsorption follows the same principles as adsorption of gases on solids:**

1. Certain adsorbents adsorb some solute effectively than other
2. Increase in temperature decreases the rate of adsorption (exothermic process)
3. Increase of the specific surface increases the adsorption
4. During the adsorption is established equilibrium between adsorbed amount and concentration of the adsorbate in solution

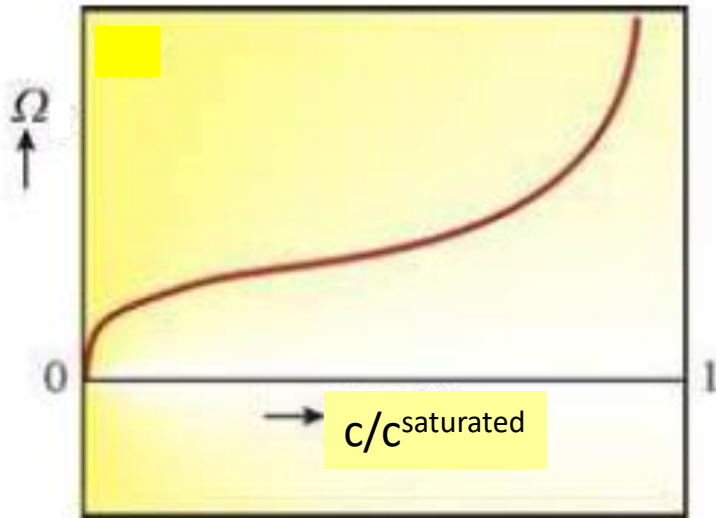




# Molecular adsorption

Whole molecules are adsorbed (or both types of ions in the same extent). Molecular adsorption usually involves physical force – physical adsorption.

## Adsorption isotherms



total adsorption:

$$\Omega = V_0 \cdot (c_0 - c) \quad [\text{mol}]$$

$V_0$  – the initial volume of the solution per 1 g of adsorbent

$c_0$  – concentration of the substance in the solution before adsorption

$c$  – concentration of the substance in the solution after adsorption

$c/c^{\text{saturated}}$  – the relative concentration (ratio of equilibrium concentration to the concentration of a saturated solution)

The theoretical expression is more complex than for gases:

- Freundlich type equation
- Langmuir type equation

# Molecular adsorption

**The relationship between the properties of the system and adsorptivity:**

1. **Polarity**: Polar substances are well adsorbed on polar adsorbents from nonpolar solutions and vice versa.
2. **Solubility**: Solute is adsorbed the more, the less it is soluble in a given solvent.

**Pharmaceutical and industrial applications:**

1. **Adsorption chromatography** (polar solid phase e.g. silica gel; eluent nonpolar e.g. hexane, benzene)
2. **Adsorption of toxic substances and impurities** (medicine, ecology)
3. **Drug carriers** (used e.g. for poorly soluble drugs)
4. **Drying process** (desiccants)
5. **Heterogeneous catalysis** (reactive molecules adsorbed on the surface of the catalyst)

# Ion exchange adsorption

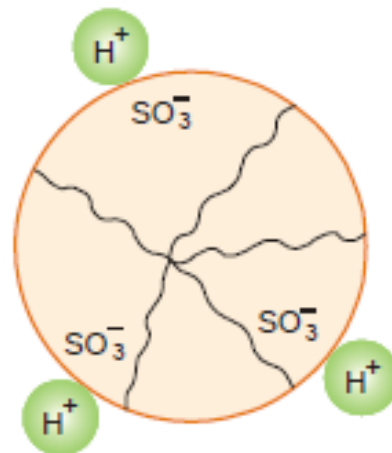
Preferably is adsorbed one of the ions from electrolyte .

The adsorbent replaces the ions adsorbed by the solution with other ions which release it into the solution.

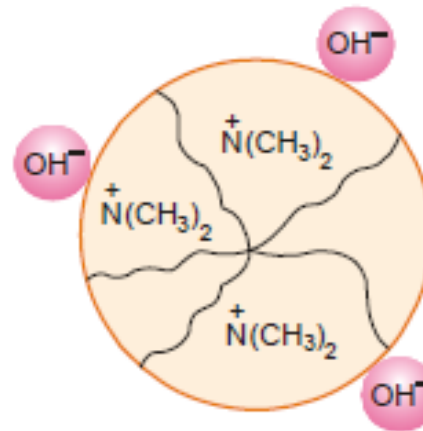
The **cation exchanger** – Polymers containing acidic functional groups.



The **anion exchanger** – polymers containing basic functional groups.



Cation exchange resin

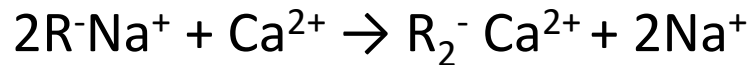


Anion exchange resin

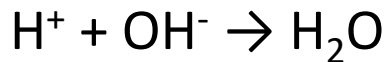
# Ion exchange adsorption

## Applications:

1. **Water softening** (removal of  $\text{Ca}^{2+}$  and  $\text{Mg}^{2+}$ ) – industry (preventing the formation of limescale)



2. **Production of deionized water** – industry, pharmacy  
- use of cation exchangers and anion exchangers



3. **Drugs based on ion exchange**

Cation exchangers: adjusting the electrolyte balance in the body (edema treatment).

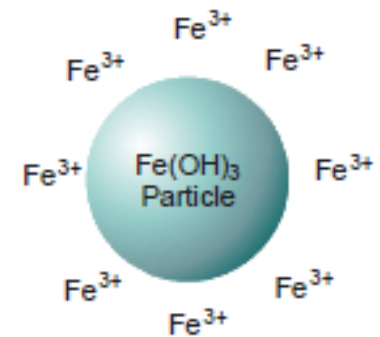
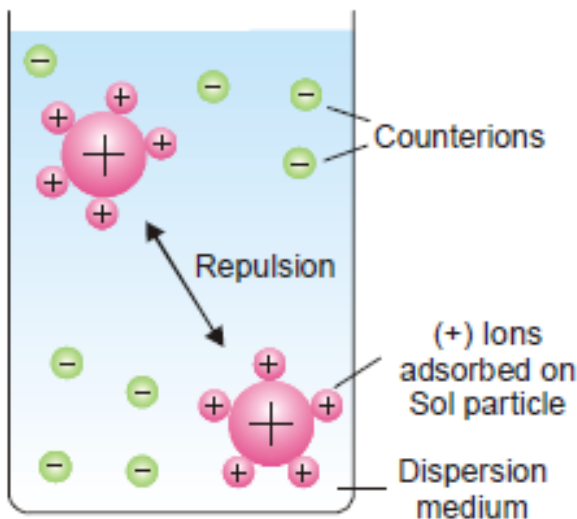
Cation and anion exchangers: treatment of intoxication.

Nicorette - ion-exchange resin to control the rate of release of nicotine

# Electrical properties of the interface

The generation of electrical charge at the phase interfaces of heterogeneous systems (**colloids**) affects their stability. Some mechanisms of formation of electrical charge:

1. dissociation of functional groups in surface layers
2. preferential dissolution of one of the ions in the crystal lattice
3. adsorption one type of ions



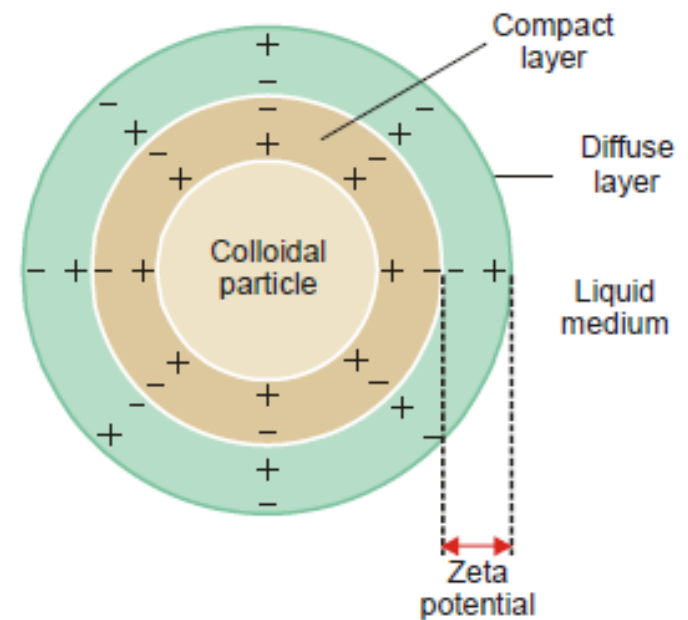
Mutual repulsion between similarly charged particles prevents the formation of aggregates – **important for the stability of colloidal systems.**

# Electrical double layer

## Stern model

The outer layer is bonded to the inner mainly by **adsorptive forces**. The rest of charge of the inner layer is neutralized by ions, which are bound by **electrostatic forces** (form a diffusion layer).

When particle is moving relative to the liquid, the inner layer and the part of outer layer which is bonded by adsorptive forces are moved together with particle. The rest of diffuse double layer is moved with the liquid. There is a difference in potential between the compact layer and the bulk of solution across the diffuse layer - **zeta potential**.



# Electrical double layer

## Zeta potential

- Size of zeta potential indicating the potential **stability** of the colloidal system.
- If all particles in the suspension have a large negative or positive zeta potential, then they will tend to repel each other (don't aggregated). The boundary between stable and unstable suspensions is generally taken at either +30 mV or -30 mV.
- The sign of the zeta potential is strongly influenced by the addition of electrolyte.
- Zeta potential is strongly affected by **pH** (affecting dissociation).

