



INTERNATIONAL COLLEGE
OF PHARMACEUTICAL
INNOVATION

国际创新药学院

Interfacial Phenomena II

Course	BSc(Pharm) & BSc (ATT)
Year	2024-2025 II
Module	Medicines Pharmaceutics 2
Lecturer	Dr. Congcong Xu

LEARNING OUTCOMES

- | |
|--|
| 1. Describe the adsorption processes that occur at liquid interfaces |
| 2. Distinguish between soluble monolayers and insoluble monolayers |
| 3. Appreciate the rich history of physical pharmacy |
| 4. Explain the physical behavior of surfactants in disperse systems |
| 5. Outline why micellisation is important from a physiological perspective |



RECOMMENDED READING



Chapter 19 Interfacial Phenomena

Paul M. Bummer, PhD and Yvonne Perrie, PhD

MARTIN'S

PHYSICAL PHARMACY AND
PHARMACEUTICAL SCIENCES

15 INTERFACIAL PHENOMENA

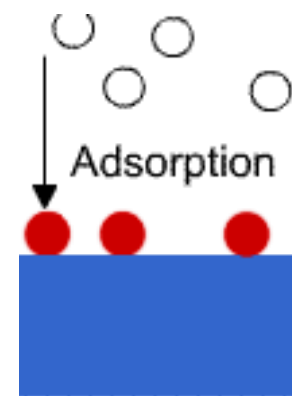
thePoint For additional ancillary materials related to this chapter,
please visit [thePoint](#).



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ADSORPTION

- Certain molecules and ions, when dispersed in the liquid, move of their own accord 自发地 to the interface. Their concentration at the interface then exceeds their concentration in the bulk of the liquid. The surface free energy and the surface tension of the system are automatically reduced. Such a phenomenon, **where the added molecules are partitioned in favour of the interface**, is termed *adsorption*, or, more correctly, positive adsorption. Other materials (e.g., inorganic electrolytes) are partitioned in favour of the bulk, leading to negative adsorption and a corresponding increase in surface free energy and surface tension.



- *Adsorption should not be confused with absorption.* Absorption sees the penetration of substance into a phase (e.g. The taking up of water by a sponge is absorption). Adsorption is solely a surface effect (e.g. alkaloid 生物碱 molecules on the surface of clay 黏土 is adsorption)

ADSORPTION

Positive adsorption

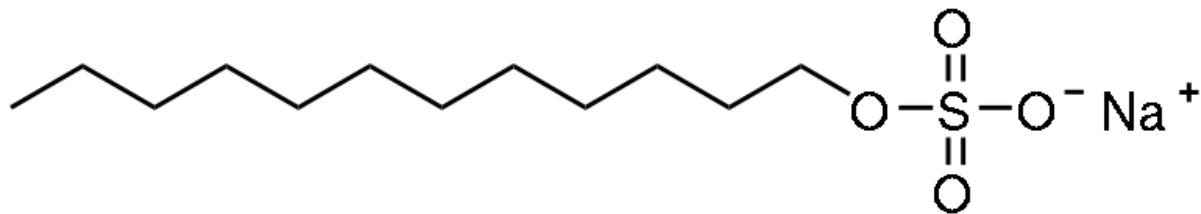
- Lowers surface tension
- Lowers interfacial energy
- Examples: surfactants

Negative adsorption

- Increases surface tension
- Increases interfacial energy
- Examples: high concentrations of solutes (e.g. 6 M NaCl increases surface tension from 72 to 78)



SURFACTANTS

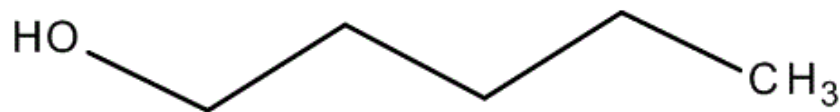


- **SURFACTANTS**: Molecules and ions that are adsorbed at interfaces are termed *surface-active agents* or *surfactants*. An alternative term is **amphiphile** 两亲分子, which suggests that the molecule or ion has a certain affinity for both polar and nonpolar solvents.
- Depending on the number and nature of the polar and nonpolar groups present, the amphiphile may be predominantly **hydrophilic** (water-loving), **lipophilic** (oil-loving), or reasonably well balanced between these two extremes
- For the amphiphile to concentrate at the surface it must have correct **hydrophilic/lipophilic balance** (HLB system)
- In a liquid system results in a **reduction in surface tension** owing to these molecules or ions being adsorbed as a monolayer

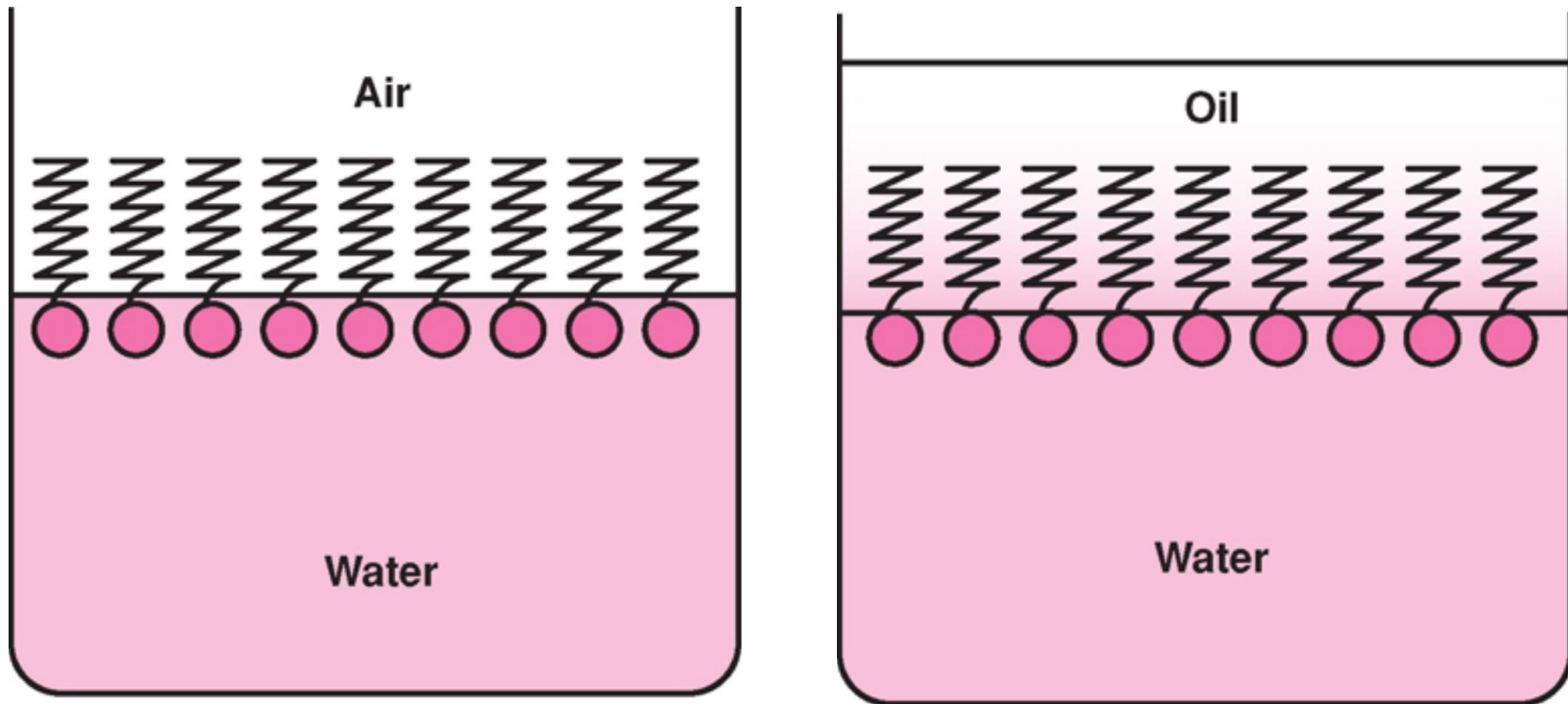


SURFACE ACTIVITY & SURFACE ACTIVE AGENTS

- Strong adsorption of surfactants in the form of an orientated monomolecular film is termed **surface activity**. Surface active agents are molecules that preferentially adsorb at interfaces.
- It is the amphiphilic nature of surface-active agents that causes them to be absorbed at interfaces, whether these are liquid–gas or liquid–liquid interfaces.
- In an aqueous dispersion of amyl alcohol 戊醇(below), the polar alcoholic group is able to associate with the water molecules. The nonpolar portion is rejected, however, because the adhesive forces it can develop with water are small in comparison to the cohesive forces between adjacent water molecules. As a result, the amphiphile is adsorbed at the interface.



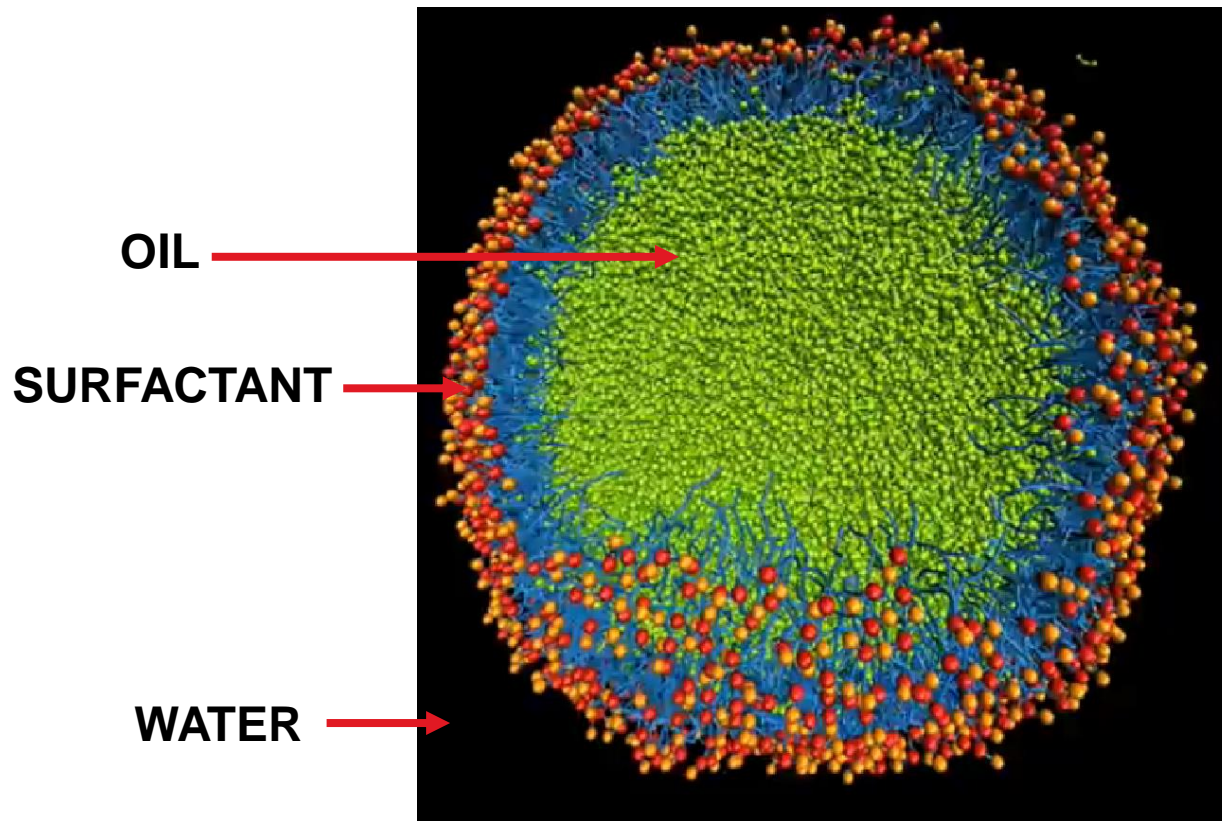
ADSORPTION AND ORIENTATION AT INTERFACES



Adsorption of fatty acid molecules at a water–air interface and a water–oil interface

At the air–water interface, the lipophilic chains are directed upward into the air; at the oil–water interface, they are associated with the oil phase. For the amphiphile to be concentrated at the interface, it must be balanced with the proper amount of water- and oil-soluble groups. If the molecule is too hydrophilic, it remains within the body of the aqueous phase and exerts no effect at the interface. Likewise, if it is too lipophilic, it dissolves completely in the oil phase and little appears at the interface.

SURFACTANT ADSORPTION IN EMULSION STABILISATION (MONOMOLECULAR FILM)



O/W EMULSION



IMPORTANT PARAMETERS RELATED TO ADSORPTION AT LIQUID SURFACES

- It will become apparent in the following slides that three interrelated parameters are important in studying liquid interfaces:

- (a) Surface Tension (γ)** *is the reversible work needed per unit area to form a surface.*
- (b) Surface Excess 表面过剩, (Γ)** (the amount of amphiphile per unit area of surface in excess of that in the bulk of the liquid)
- (c) Concentration (C)** (of amphiphile in the bulk of the liquid)



TYPES OF MONOLAYER AT LIQUID SURFACES

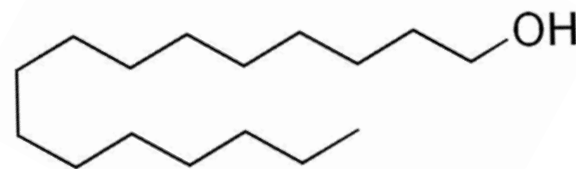
Two arbitrary classes:

INSOLUBLE MONOLAYERS

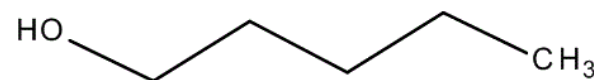
SOLUBLE MONOLAYERS

The distinction is made on the basis of the solubility of the adsorbate in the liquid sub-phase.

Cetyl alcohol 十六烷醇



Amyl alcohol 戊醇



INSOLUBLE MONOLAYERS

- **Insoluble monolayers**: Are monomolecular films formed at the boundary between phases. In the case of Liquid-Vapour Interface, the adsorbate (surfactant) is not soluble in the sub-layer liquid and so 100% of the surfactant seeks out the interface and there is no equilibrium between surfactant present in the bulk of the phase and the surface.

EXAMPLES

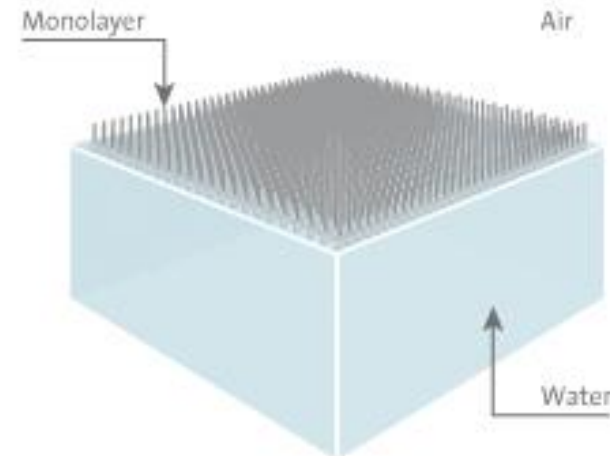
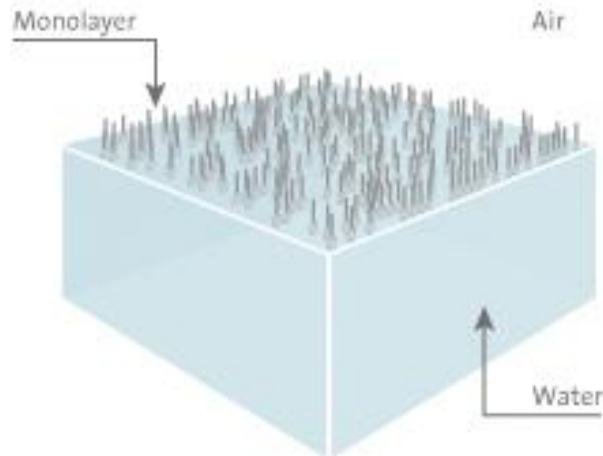
- Oleic acid 油酸
- Cetyl alcohol 十六醇



Irving Langmuir
(Nobel Prize 1932)

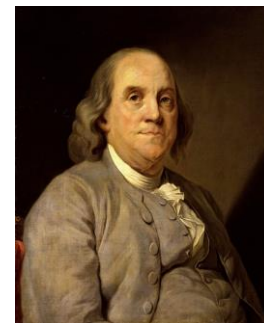


Katharine
Blodgett



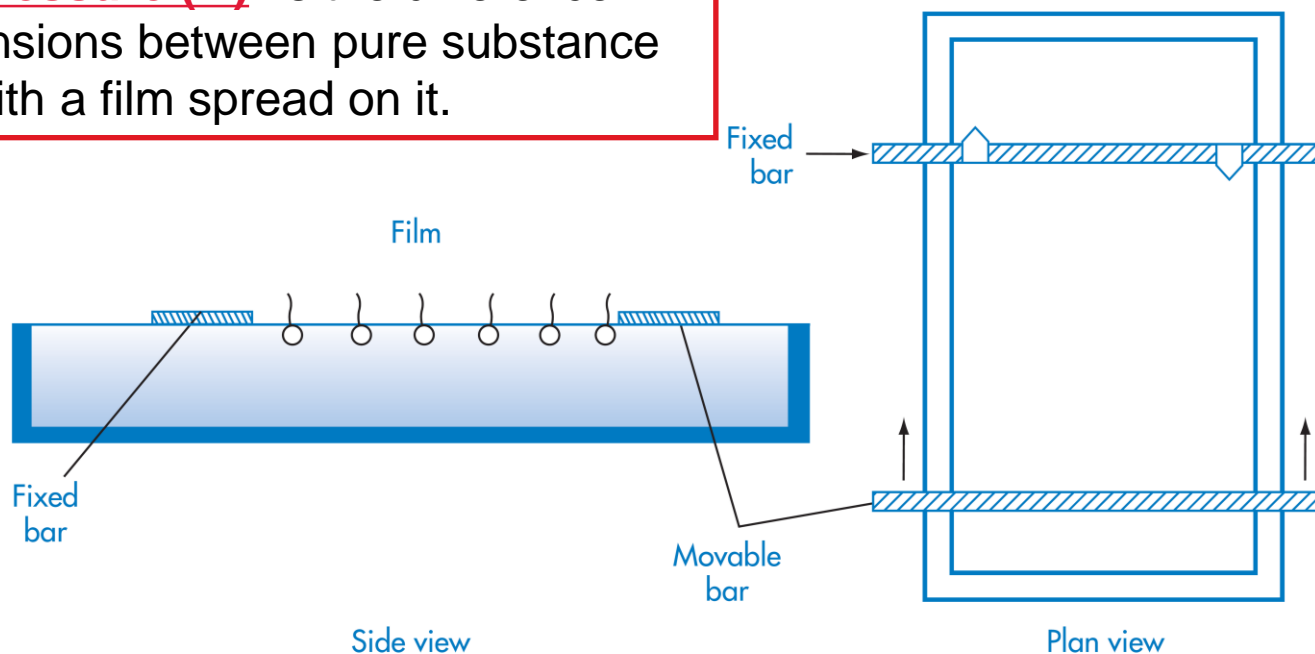
THE HISTORY OF MONOMOLECULAR FILMS

Insoluble monolayers have a fascinating history that goes back to before the American Revolution 美国独立战争. During a voyage to England in 1757, **Benjamin Franklin** observed, as had seamen for centuries before him, that when cooking grease was thrown from the ship's galley onto the water, the waves were calmed by the film that formed on the surface of the sea. In 1765, Franklin followed up this observation with an experiment on a half-acre pond in England and found that the application of 1 teaspoonful of oil was just sufficient to cover the pond and calm the waves. In 1899, Lord Rayleigh showed that when small amounts of certain slightly soluble oils were placed on a clean surface of water contained in a trough 槽, they spread to form a layer one molecule thick (monomolecular layer). Prior to Rayleigh's work, a woman named **Agnes Pockels**, from Lower Saxony, Germany, who had no formal scientific training, developed a "film balance" for studying insoluble monolayers. She carried out a series of experiments, which she summarized in a letter to Lord Rayleigh in January 1881. In fact, she invented the film balance in 1883, more than 30 years before Langmuir, whose name is normally associated with this type of apparatus.



SURFACE PRESSURE & LANGMUIR TROUGH

Surface pressure (π): is the difference in surface tensions between pure substance and that with a film spread on it.



$$\pi = \gamma_0 - \gamma_m$$

Surface pressure is an expansion pressure that opposes contraction of the water surface. This is achieved by insertion into the interface where they reduce resistance of water to expansion.

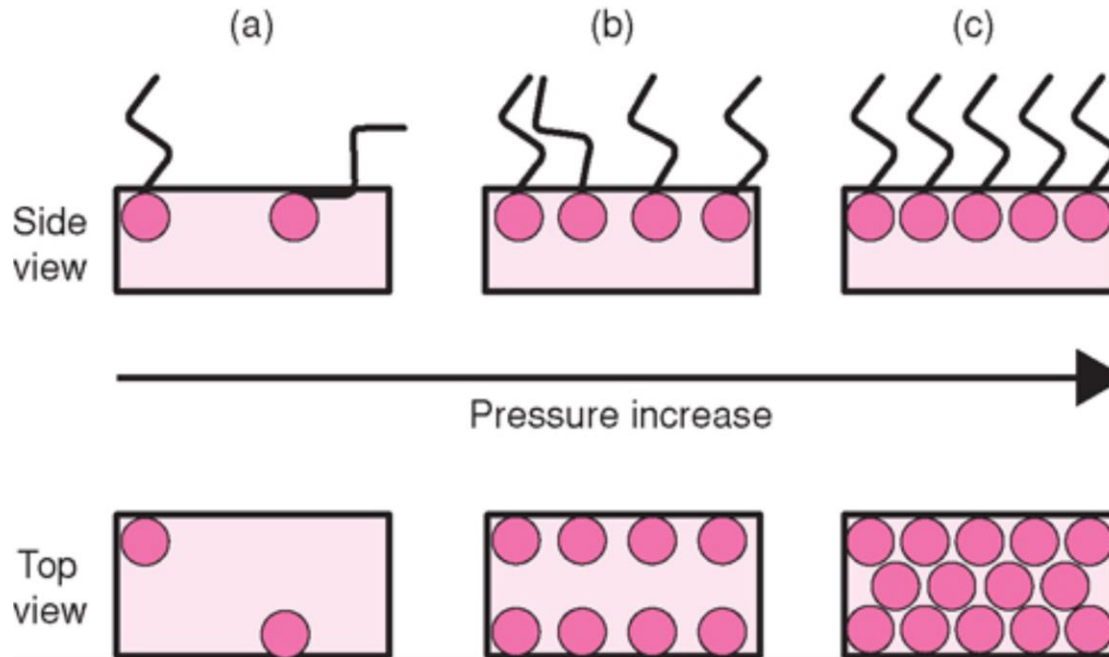
π = surface pressure

γ_0 = surface tension of “clean” liquid (without monolayer)

γ_m = surface tension of liquid covered with a monolayer



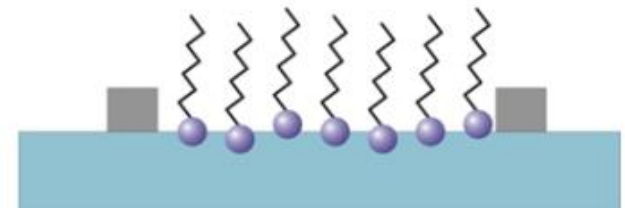
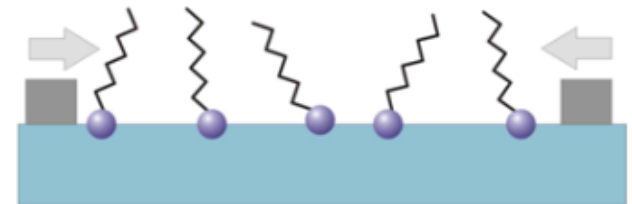
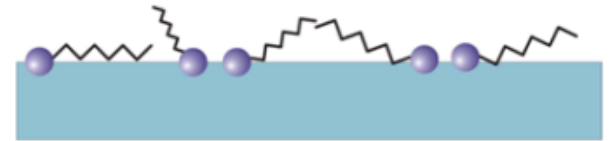
MONOLAYER STATES



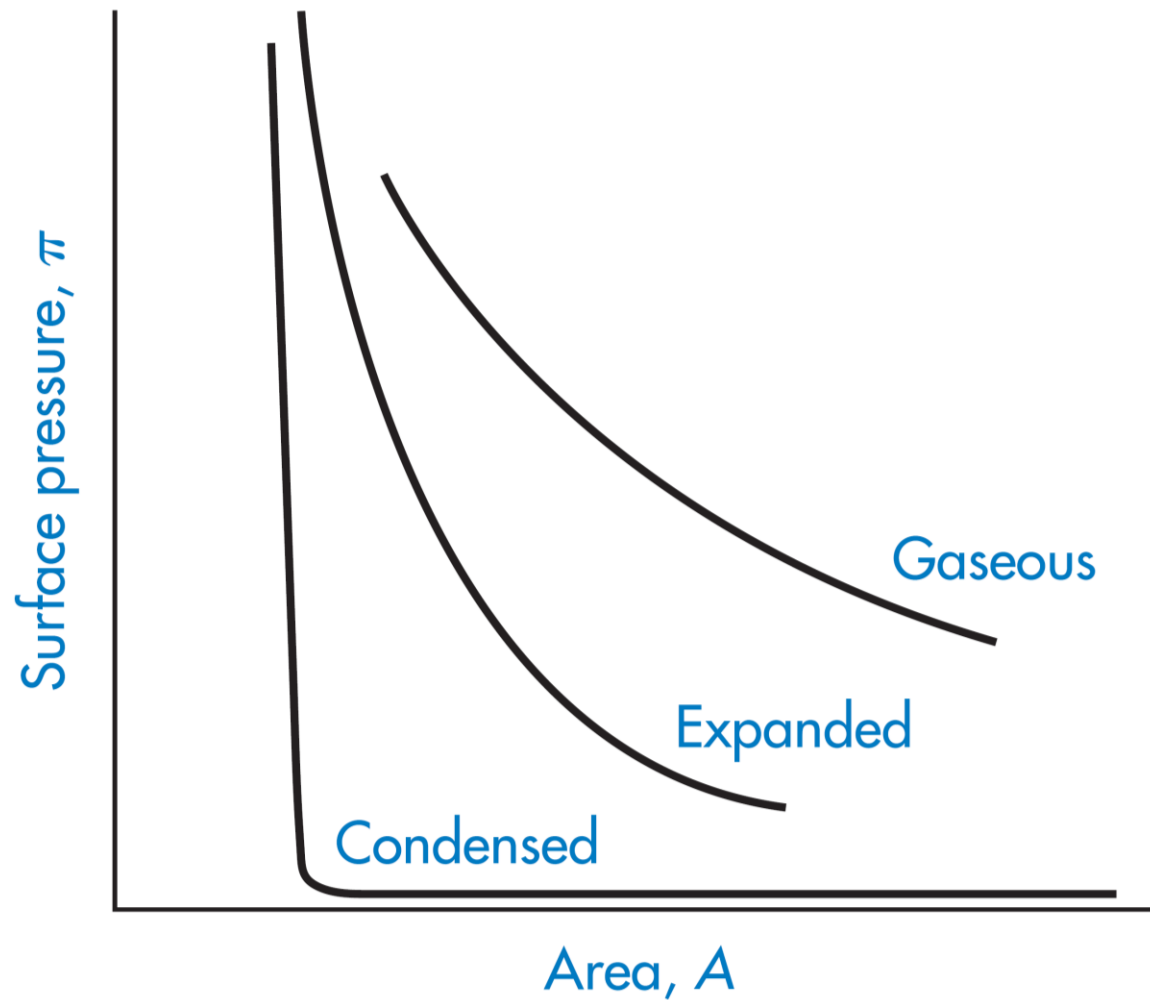
Insoluble monolayer films exhibit characteristics that can be equated to those of the solid, liquid, and gaseous states of matter. (a) **Gaseous film**. Molecules are apart and have significant surface mobility. The molecules essentially act independently. (b) **Expanded/Liquid film**. Monolayer is coherent and relatively densely packed but is still compressible. (c) **Condensed film**. Monolayer is coherent, rigid, essentially incompressible, and densely packed, with high surface viscosity. The molecules have little mobility and are oriented perpendicular to the surface.

MONOLAYER STATES

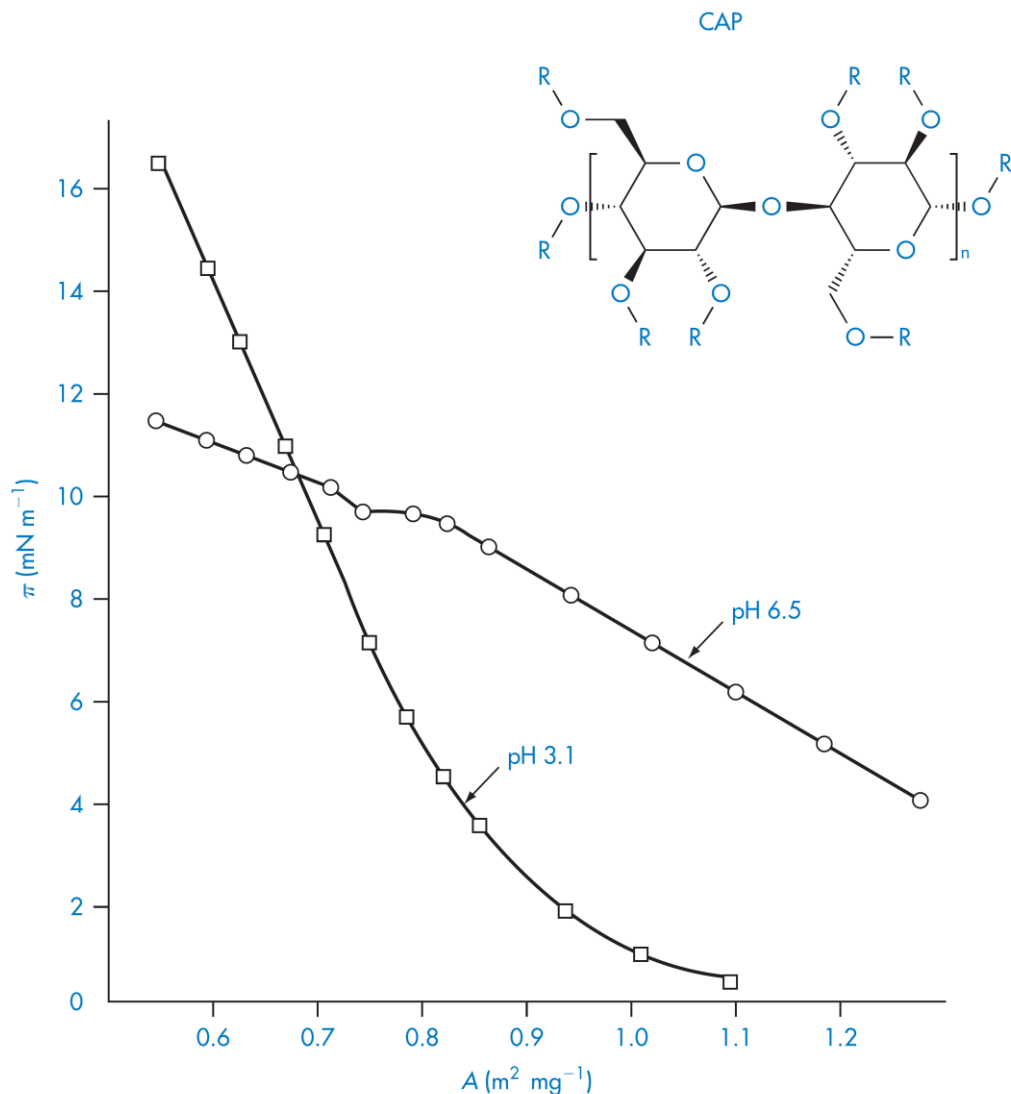
- *Gaseous state:* These films represent the opposite extreme in behaviour to the condensed film. They resemble the gaseous state of three-dimensional matter in that the molecules move around in the film, remaining a sufficiently large distance apart so as to exert very little force on each other. Upon compression, there is a gradual change in the surface pressure.
- *Expanded state:* Various named liquid-expanded, expanded or liquid, these monolayers represent intermediate states between gaseous and condensed films. The π - A plots are quite steeply curved and extrapolation to a limiting surface area yields a value which is usually several times greater than the cross-sectional area from molecular models. Films of this type tend to be formed by molecules in which close packing into condensed films
- *Condensed state:* The film pressure remains very low at high film areas and rises abruptly when the molecules become tightly packed on compression.



MONOLAYER STATES



MONOLAYERS AND FILM COATING STUDIES



- **Cellulose acetate phthalate (CAP)**邻苯二甲酸乙纤维素
- **CAP formed more condensed film at pH=3**
- **CAP suitable for enteric coating 肠溶包衣**

pH 3.1（酸性环境）：CAP在此条件下不溶解。其分子中的邻苯二甲酸基团在低pH环境中保持质子化状态，导致聚合物链间疏水作用增强，形成稳定的保护层。

pH 6.5（中性至弱碱性环境）：当pH接近或超过CAP的临界溶解pH（约5.5–6.0）时，邻苯二甲酸基团去质子化，亲水性增加，聚合物链溶胀并溶解，释放包衣内的药物。



SOLUBLE MONOLAYERS

- Soluble (or Gibbs) monolayer: Is a monolayer formed by a molecule that is soluble in one of the phases separated by the interface.

Gibbs Adsorption Isotherm (non-dissociating compounds, dilute solutions)

Describes equilibrium between surfactant molecules at surface or interface and those in the bulk (desorption isotherm)

$$\Gamma = -\frac{c_2}{RT} \left(\frac{d\gamma}{dc_2} \right)$$

*First described
quantitatively by
Gibbs (1876)*

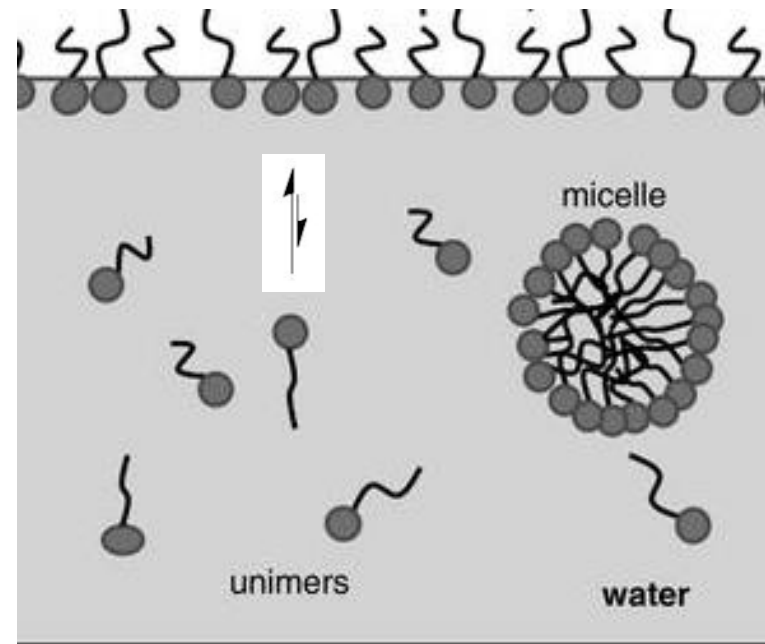
Γ is the surface excess

c bulk concentration,

R is the gas constant

T is the absolute temperature

$d\gamma/dc$ change in surface tension with change in bulk conc of substance.



PROPERTIES OF SURFACTANTS

TRAUBE'S RULE



Isidor Traube

“For a particular homologous series of surfactants in dilute aqueous solution the molar concentration necessary to produce an equal lowering of surface tension decreases by a factor of three for each additional CH_2 group”

特劳贝规则 (Traube's rule) 有机物溶液表面张力随浓度变化的经验规则。对同系有机物的水溶液来说, 每增加一个 CH_2 基团, 达到某一定表面张力的溶液浓度约为原来的 $1/3$ 。

Surfactant A

Polar group- $(\text{CH}_2)_{15}$
 γ lowering: 15mNm^{-1}
Necessary $[\text{A}] = 0.1\%$

Surfactant B

Polar group- $(\text{CH}_2)_{16}$
 γ lowering: 15mNm^{-1}
Necessary $[\text{B}] = (0.1\%)/3$

Surfactant C

Polar group- $(\text{CH}_2)_{17}$
 γ lowering: 15mNm^{-1}
Necessary $[\text{C}] = (0.1\%)/9$

A, B and C have the same polar group

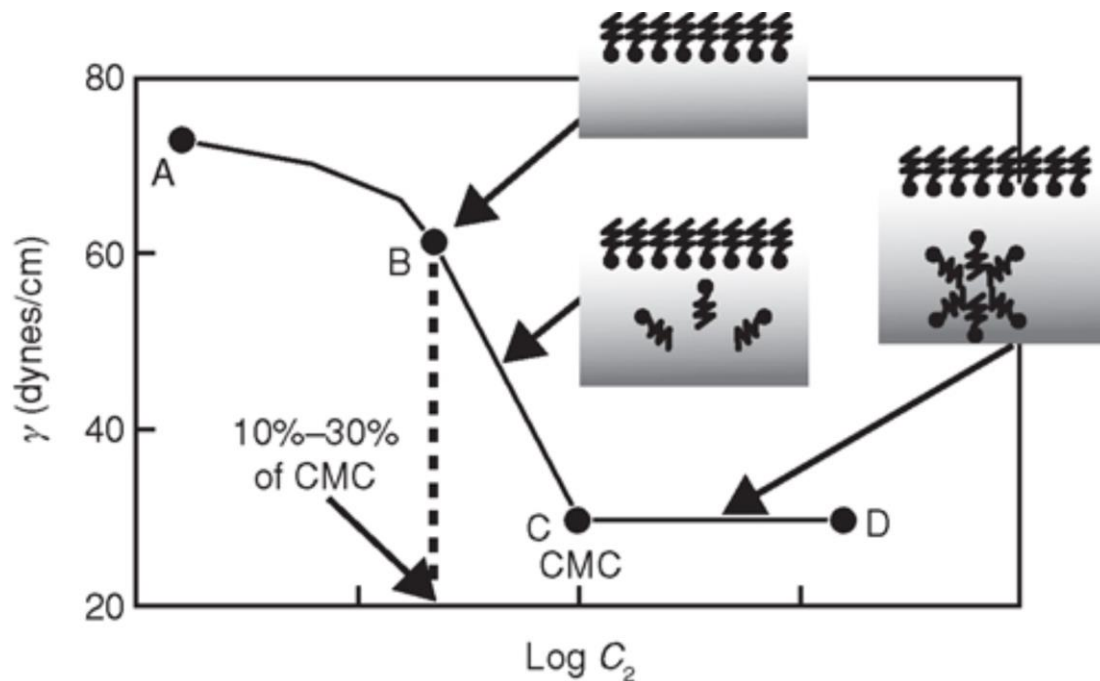


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PROPERTIES OF SURFACTANTS

Critical micelle concentration (临界胶束浓度)

The initial curved segment A–B is followed by a linear segment, B–C, along which there is a sharp decrease in surface tension as $\log c_2$ increases. The point C corresponds to the critical micelle concentration (CMC), the concentration at which micelles form in the solution. Beyond the CMC, the line becomes horizontal because further additions of surfactant are no longer being accompanied by a decrease in surface tension.



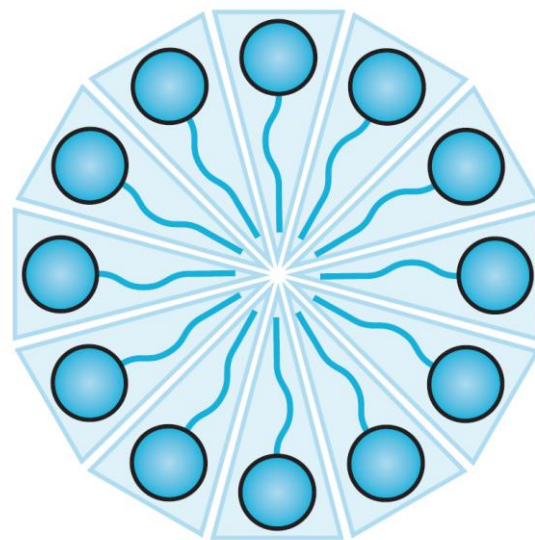
ASSOCIATION COLLOIDS

Decrease in the surface tension of water when a strait-chain amphiphile
(CMC = critical micelle concentration)

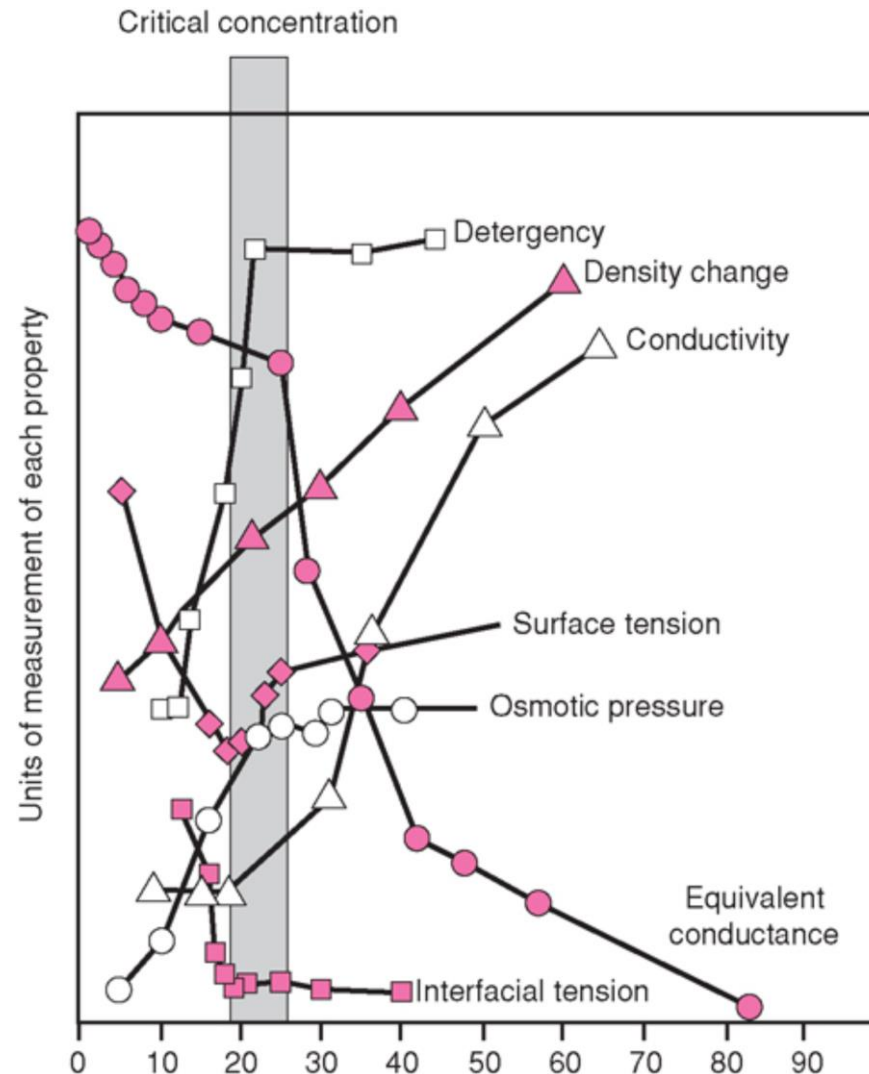


MICELLISATION 胶粒形成

- One all surfaces and interfaces are saturated the lyophobic moiety of the surfactant requires an alternative means of shielding from a solvent so monomers self associate into micelles.
- **Two primary factors contribute to micellisation**
 1. The intermolecular attractions between the hydrocarbon chains in the interior of the micelle (a small effect).
 2. Micellisation allows strong water-water interactions which would otherwise be prevented if the surfactant was in solution as single molecules wedged between the solvent water molecules. This is often referred to as the hydrophobic effect and gives a very large contribution to micellisation.



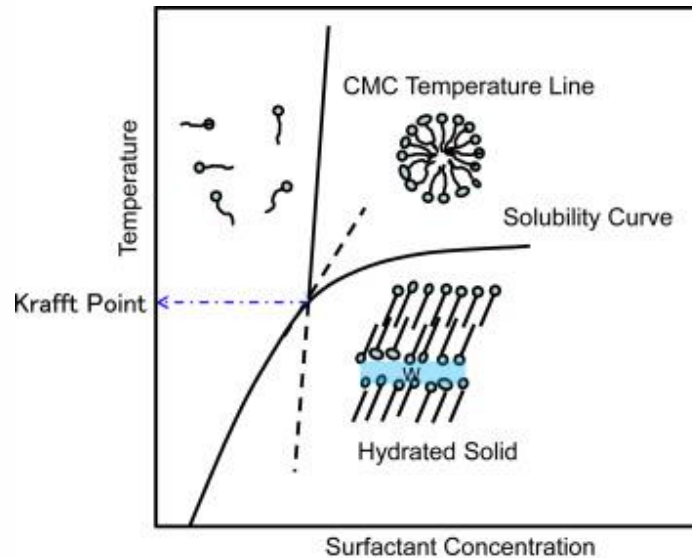
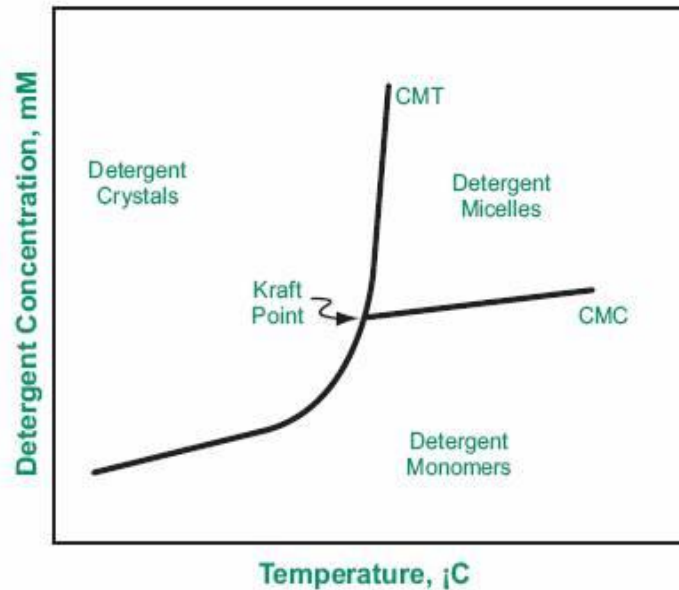
PROPERTIES OF SURFACE-ACTIVE AGENTS SHOWING CHANGES THAT OCCUR SHARPLY AT THE CMC



MICELLAR BEHAVIOUR: KRAFFT POINT

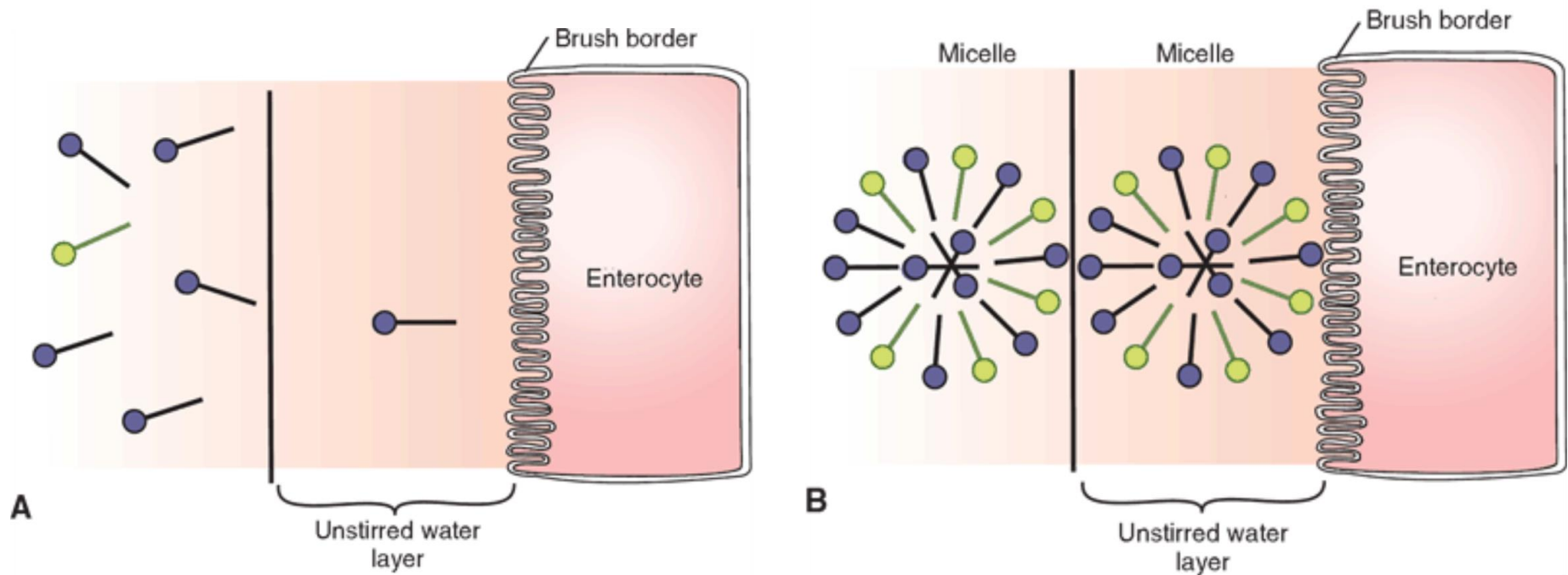
Kraft Point 克拉夫特点: The temperature (more precisely, narrow temperature range) above which the solubility of a surfactant rises sharply.

CMT = Critical Micelle temperature 临界胶束温度,
A minimum temperature at which micelles form



When the surfactant solution is lower than its Kraft point and higher than the CMC, it forms a bilayer structure hydrated solid, and if it is higher than its Kraft point and higher than the CMC, it forms micelles.

MICELLISATION IN THE HUMAN BODY



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