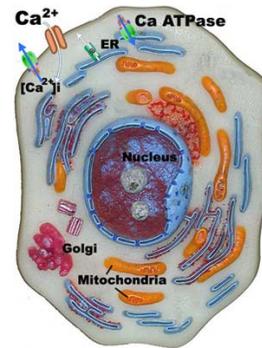


Liquid crystals; biological and artificial membranes

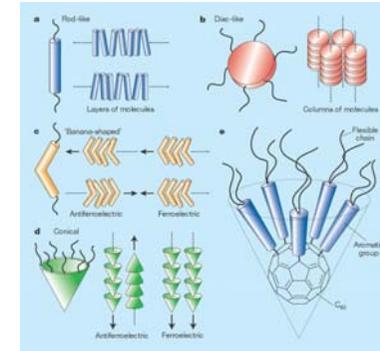
Dr. István Voszka



Liquid crystals: Intermediate state between liquids and crystalline solids – anisotropic liquids. (anisotropy = the physical properties depend on the direction)

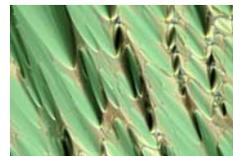
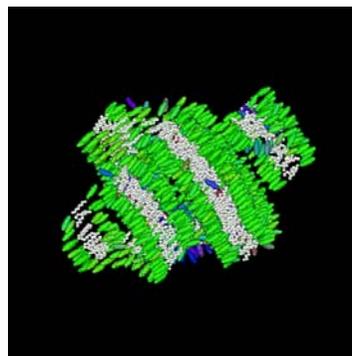
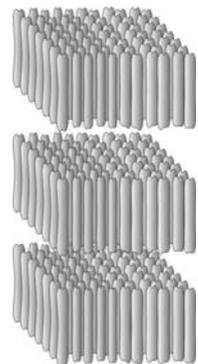
Formed from rod-like, disc-like, thread-like (anisodimensional) molecules. (one dimension of the molecules is much shorter or much longer, than the other two)

Kind of order: - according to the position of mass centres (translational) according to the direction of molecular axis (orientational)

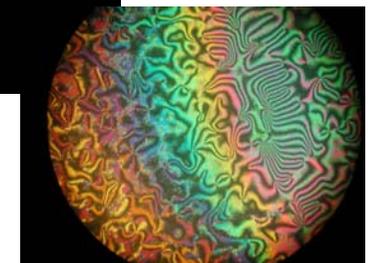
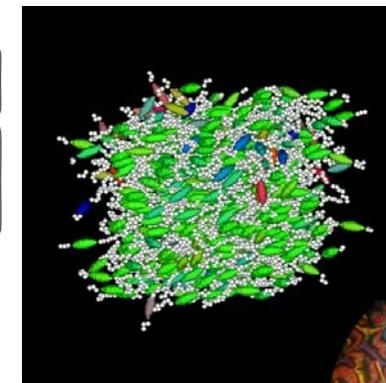
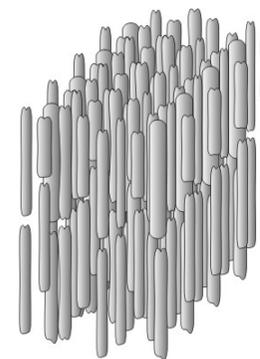


Structural forms:

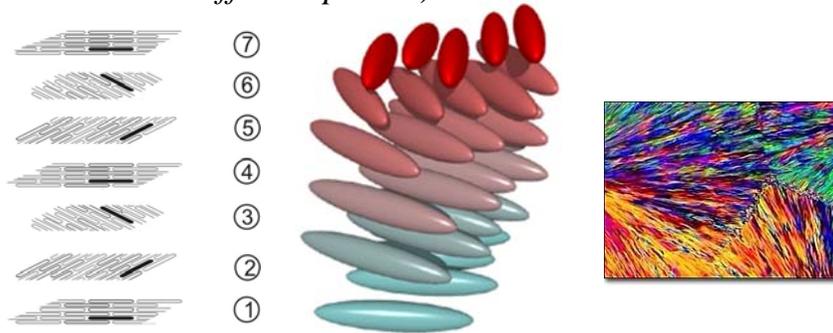
- **smectic** (smegma = soap): translational (*mass centres form planes*) and orientational order (*molecular axes are parallel*)



- **nematic** (nema = thread): orientational order (*molecular axes are parallel*)



- **cholesteric** (twisted nematic): orientational order
(molecular axes are parallel, but their direction is rotated in different planes)



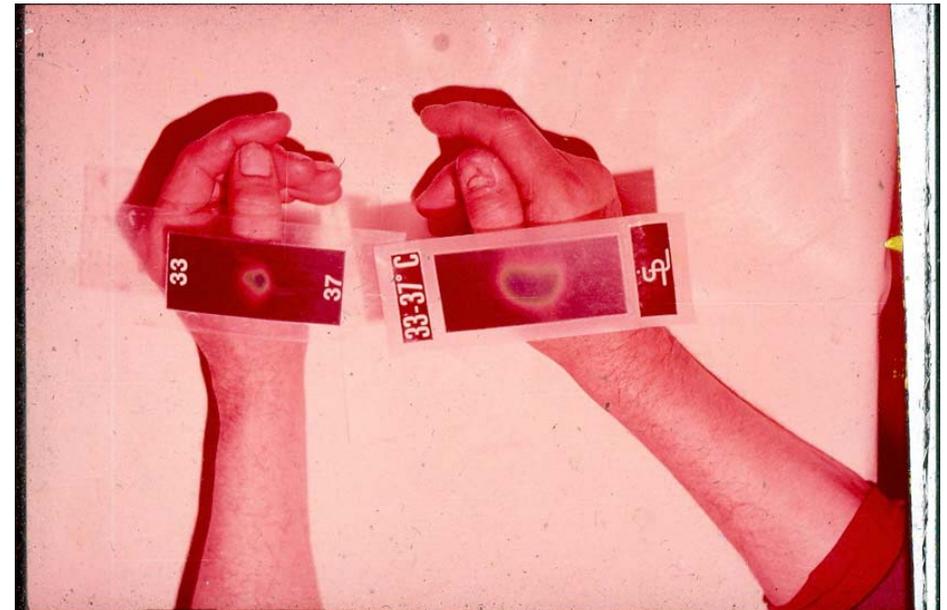
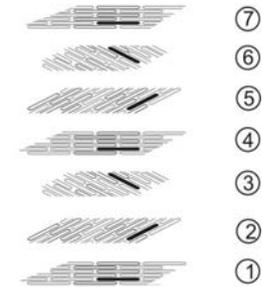
solid → smectic → nematic or cholesteric → liquid

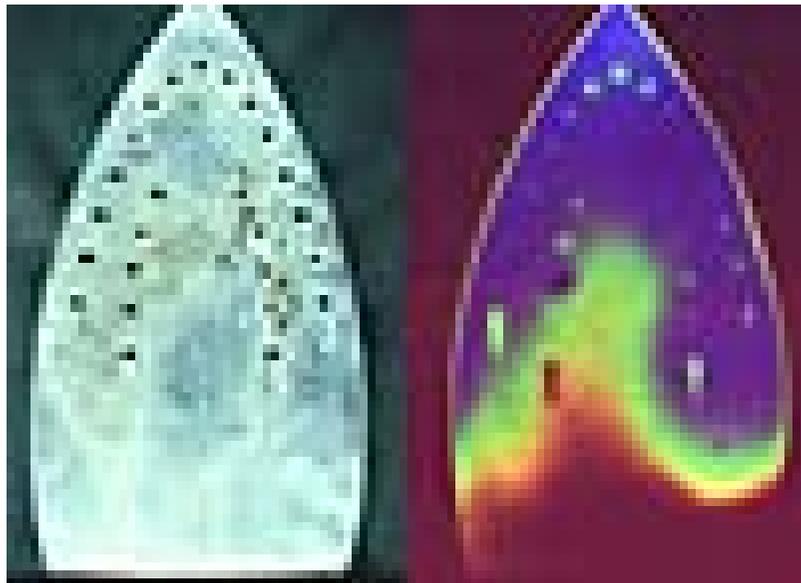
Types

1. **Thermotropic** – the degree of order depends mainly on the temperature

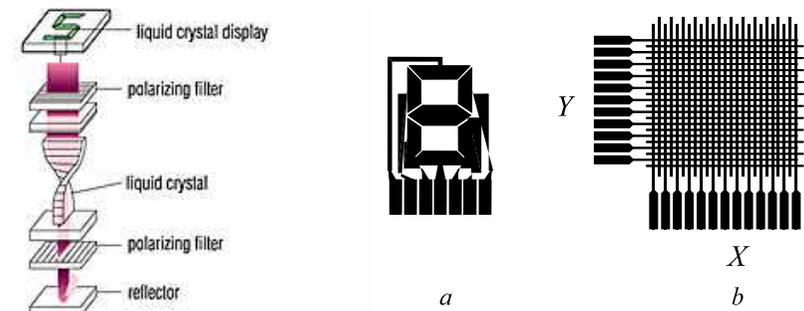
Practical applications

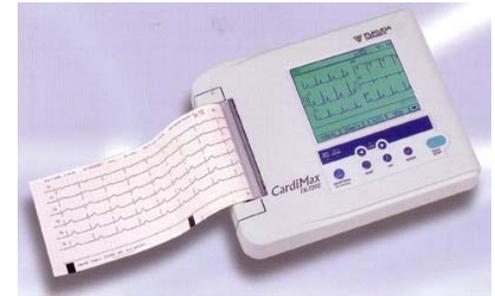
- Based on *thermo-optical phenomenon*: the pitch of cholesteric liquid crystal depends on the temperature → the condition of destructive interference is fulfilled to different wavelengths, when the light is reflected from layers in various distance → different color can be seen ⇒ contact thermography





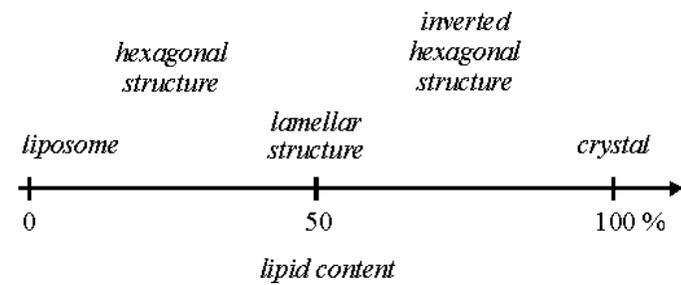
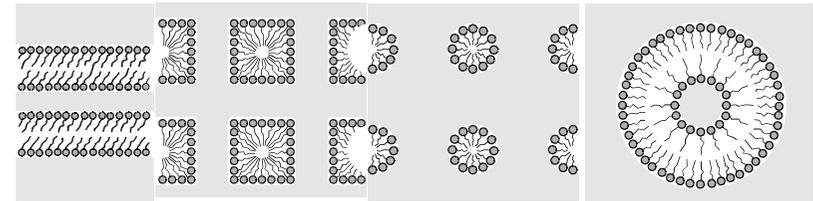
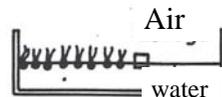
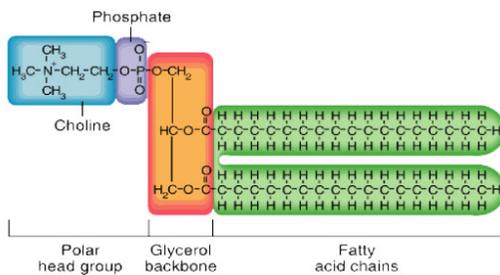
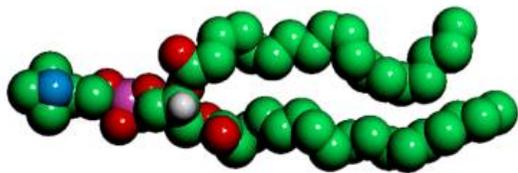
- Based on *electrooptical phenomenon*: the order of molecules having dipole moment in a nematic liquid crystalline system depends on the electric field → reflection of polarized light from a mirror behind the layer is different depending on the electric field ⇒ liquid crystal displays (LCD)



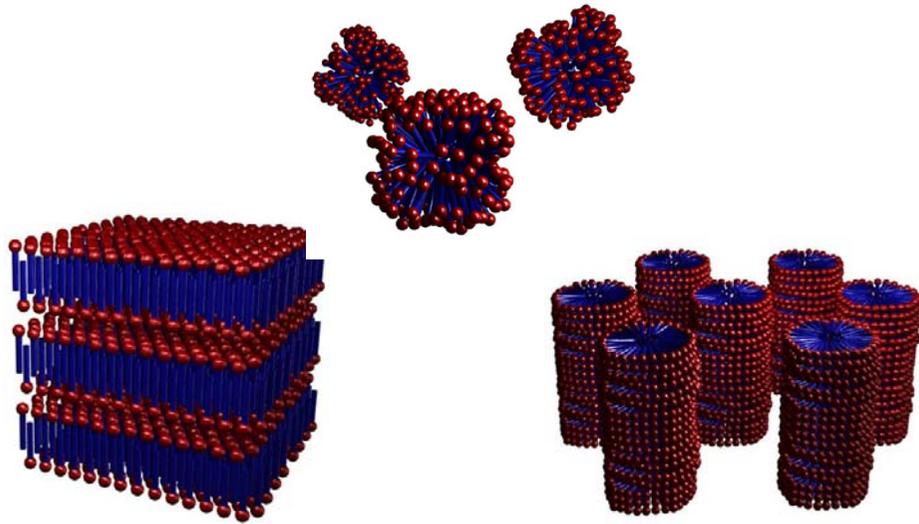


2. **Lyotropic** – the degree of order depends mainly on concentration ratio
 Formed by amphiphilic molecules (e.g. phospholipid) in solvent

↓
 polar (hydrophilic) part
 apolar (hydrophobic) part

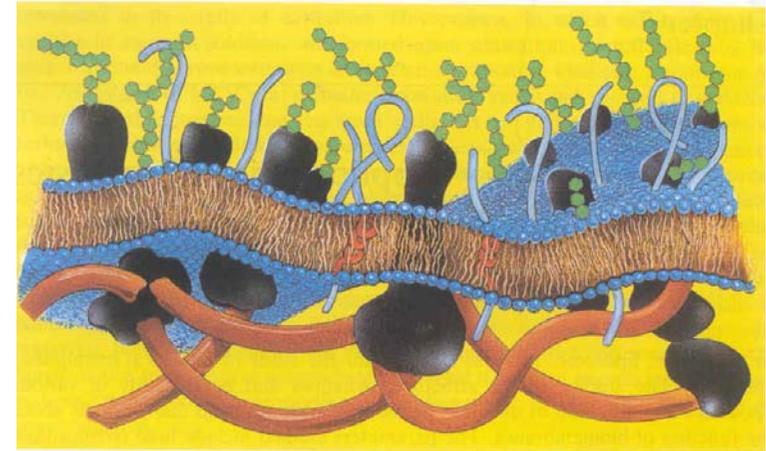


Lyotropic liquid crystalline structures



e.g.: lipid membranes: lipid bilayer containing proteins

- H-bonds, ionic bonds between lipid head groups or lipids and polar amino acids
- van der Waals bonds between fatty acid chains or fatty acid chain and apolar amino acids



Other factors influencing the order:

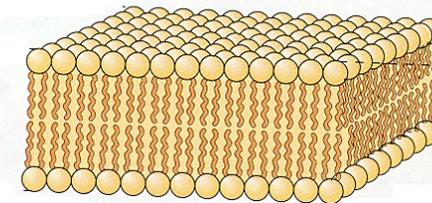
- type of molecule (the ratio of head group and tail diameters)

Lipids	Shape	Organization	Phase
Soaps Detergents Lyso-phospholipids			Isotropic hexagonal I
Phosphatidyl- choline - serine - inositol Sphingomyelin Dicetylphosphate DODAC	Inverted cone $P < \frac{1}{2} - \frac{2}{3}$	Micelles	
Phosphatidyl- ethanolamine Phosphatidic acid Cholesterol Cardiolipin Lipid A			Lamellar (Cubic) Bilayer
Mixtures Lysophosphatidyl- choline and Phosphatidyl- ethanolamine	$P > 1$		Reverse micelles hexagonal II
	$P = 1$		Lamellar

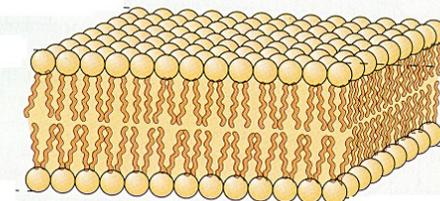
- temperature

gel phase--low temperatures

hydrocarbons are tightly packed

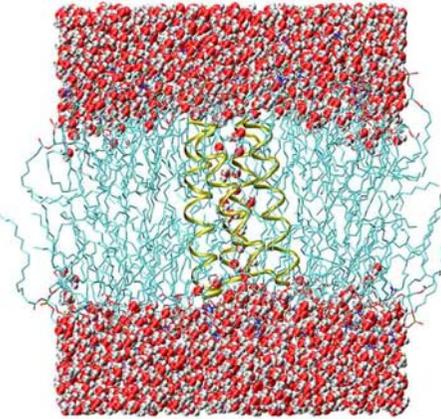
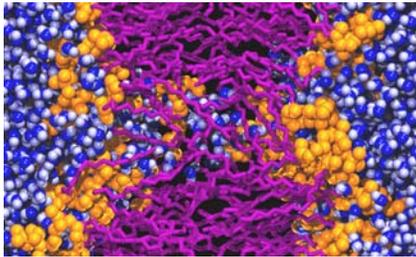
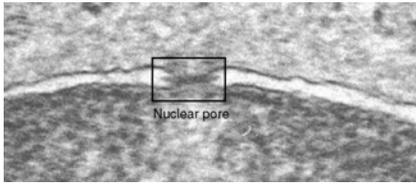


at higher temperatures--moves to fluid phase



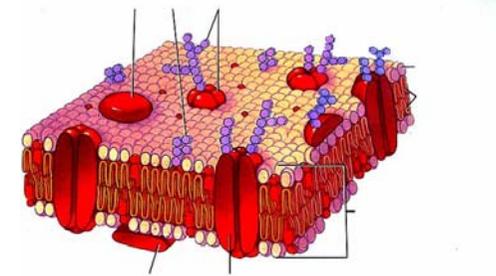
bilayer "melts", movement is allowed

- pressure
- ions in the solution, pH
- “impurities” – their functional role (pores, channels)



The role of biological membranes

- Separation of different fluid compartments
- Selective transport of ions and molecules
- Signal transduction

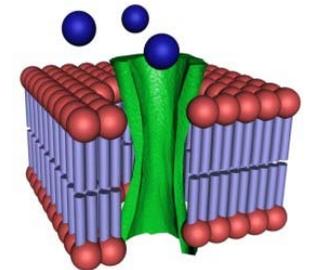
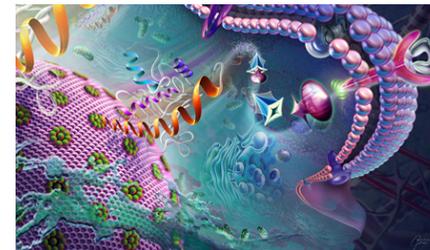


Main components of membranes

- **Lipids** (40-60 %)
 - phospholipids
 - neutral, negatively, positively charged
 - saturated or unsaturated
 - cholesterol
 - other lipids (sphingolipids, glycolipids)
- **Proteins** (30-50 %)
 - integrated (transmembrane) or peripheral

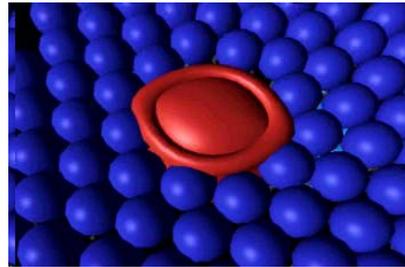
Membrane proteins

They play role mainly in signal transduction across membrane and in transport of ions and molecules



Transport across membrane (1)

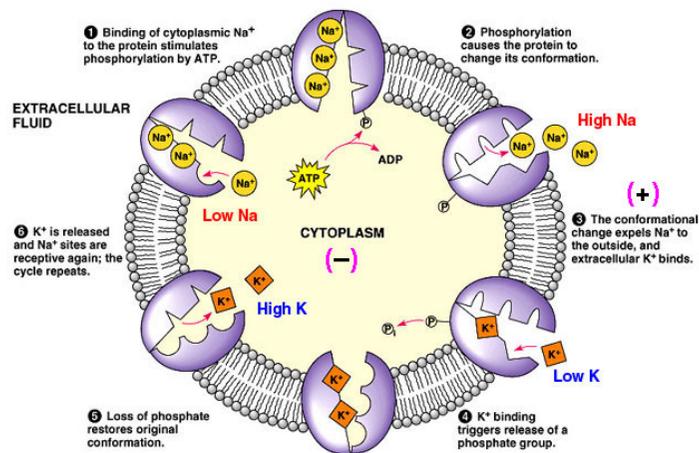
- **Passive** – according to concentration drop (=towards lower concentration) → diffusion, osmosis (water, O₂, CO₂)
- Facilitated diffusion – across channel, according to concentration drop. Opening and closing of the channel is controlled by ligand, voltage or other factors.



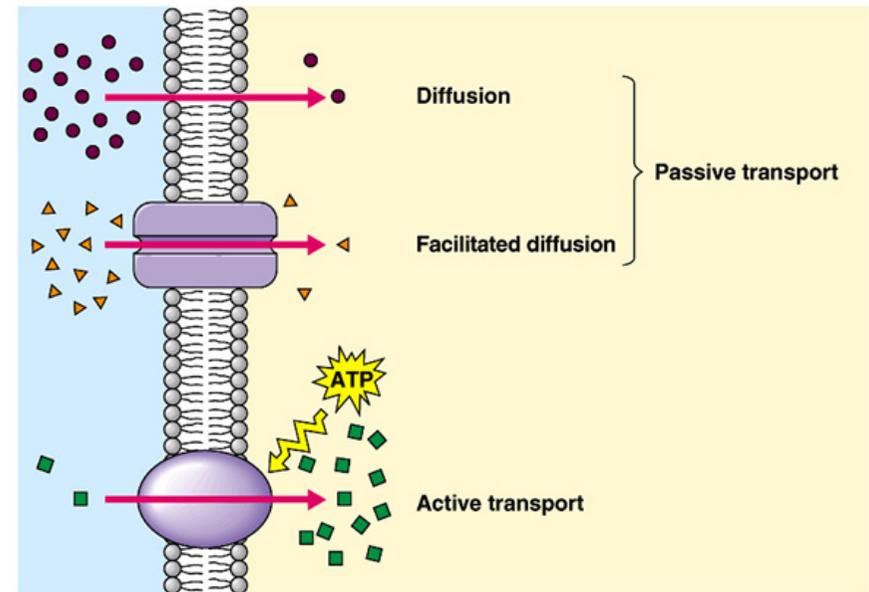
Transport across membrane (2)

- **Active** – against concentration drop
 - The energy requirement is covered usually by ATP (e.g. Na⁺-K⁺-ATP-ase)
- Indirect active transport – a transport process towards concentration drop and another one **against** it are connected.
 - symport – both processes are in the same direction (e.g. Na⁺- **glucose** transport)
 - antiport – the transports are in opposite direction (e.g. H⁺-**Na⁺** transport in plants)

Na⁺-K⁺-ATP-ase



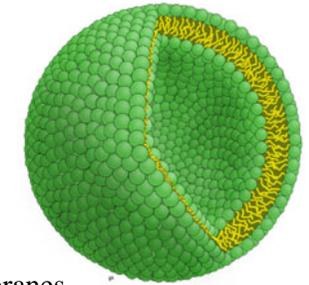
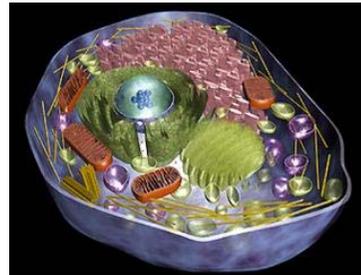
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Cell organelles containing membrane

- Cell membrane
- Nuclear membrane
- Mitochondria
- Endoplasmic reticulum
- Golgi complex
- Lysosome



Artificial membranes

Goals: - research, modelling of biological membranes
 - diagnostics, therapy (targeting of drugs)

Liposomes

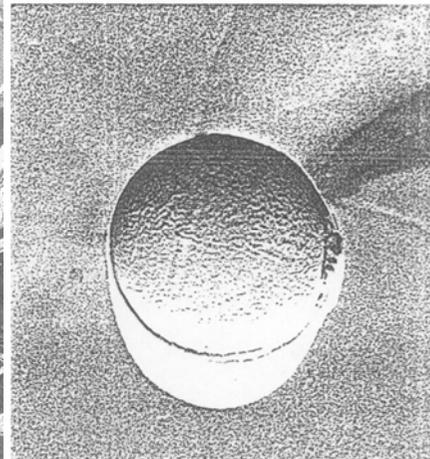
Lipid spheres made of one or more bilayers. Drugs, diagnostics, DNA can be enclosed

Advantages:

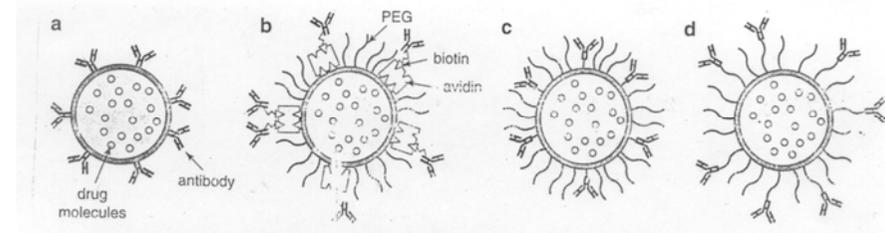
- targeted delivery
- less side effects
- lower dose, effective concentration for longer time

Classification of liposomes

1. – multilamellar (MLV)
 - unilamellar (SUV, LUV)



2. – conventional (C): removed from circulation by macrophages
 - sterically stabilised (stealth – S): hidden from immune system by polymer chains, longer circulation time
 - immunoliposomes: antibodies are attached to the surface → specific antigen – antibody reaction on the surface of target cells



Examples for medical applications of liposomes.

They are used for the encapsulation of

a) diagnostics

- X-ray contrast materials

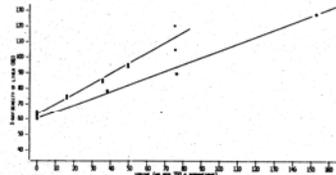
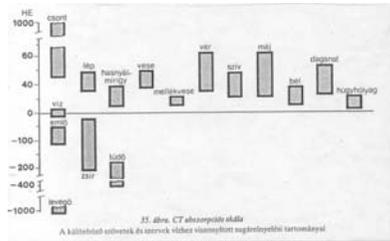


Fig. 4. Correlation between X-ray density of the liver and amount of iodine administered. (The values are average values from 10 different regions of the liver.) Dose: liposome encapsulated Angiografin, lipid mixture: egg-PC:CH₂ = 7:3; rat liver, 60 min after iv. injection, stain: free radiocontrast agent, human liver, 40 sec after iv. injection (Clausen).

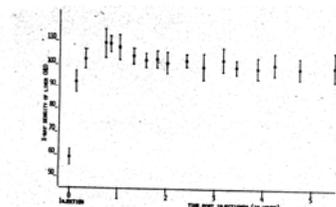


Fig. 5a. Time course of intensified X-ray density of the rat liver after iv. injection of liposome encapsulated Angiografin. (The values are average values from 10 different regions of the rat liver, lipid mixture: egg-PC:CH₂ = 7:3, injection iodine content 90 mg iodine.)

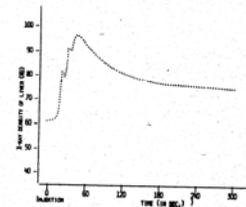


Fig. 5b. Time course of intensified X-ray density of the human liver after iv. injection of free radiocontrast agent (Clausen). (The values are average values from 10 different regions of the human liver.)

- radioisotopes, radiopharmacoons

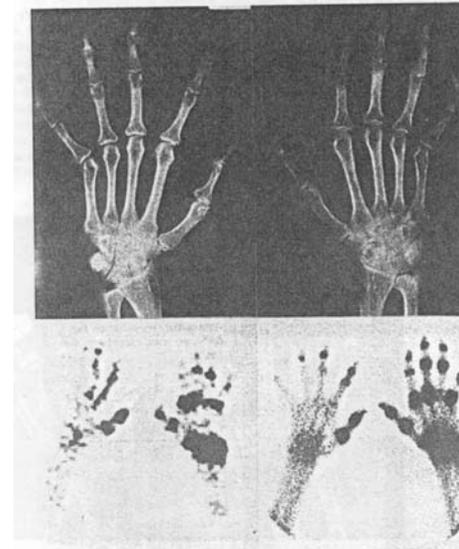


Fig. 2. Radiographs, liposome scan (bottom right) of a patient with active psoriatic arthritis. Note loss of cartilage at wrists and erosions at metacarpophalangeal, proximal interphalangeal, and distal interphalangeal joints. Note also increased activity at these joints, especially the right hand on the bone scan. The liposome scan also shows increased activity, but there is more diffuse activity over the left index finger where clinically there was active tenosynovitis.

Better signal/noise ratio

a) therapeutic drugs (useful in case of severe side effects)

- antibiotics – against bacteria
- against fungi

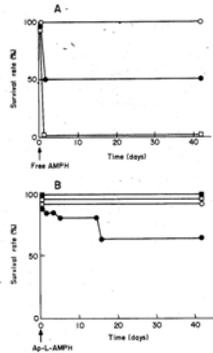
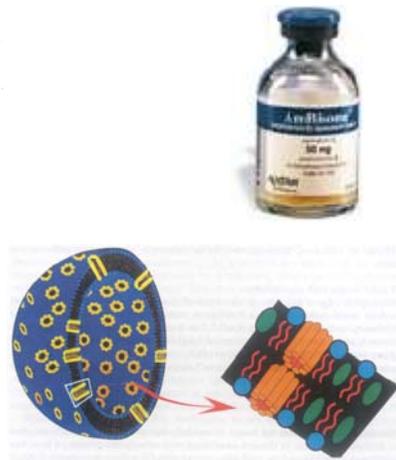
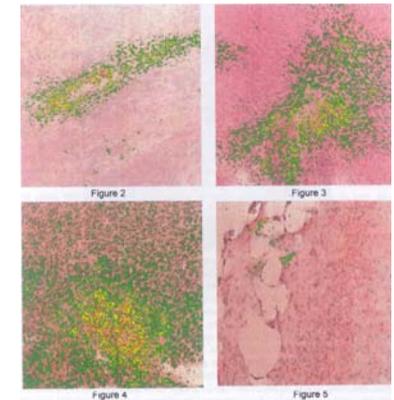
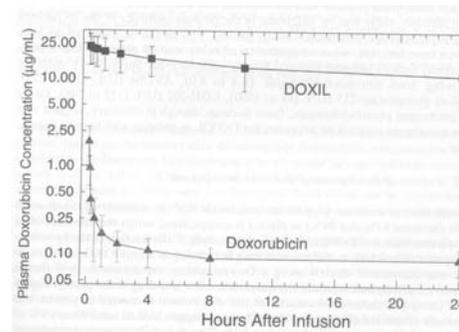


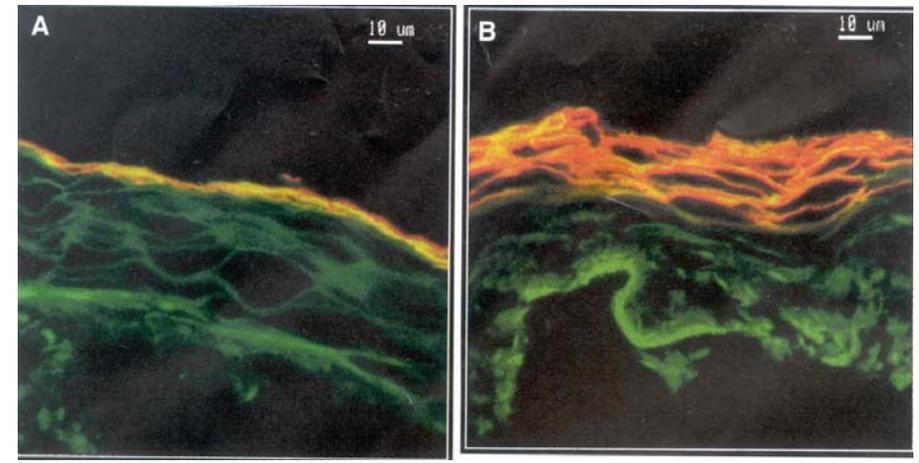
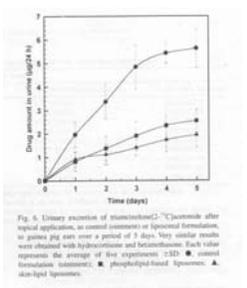
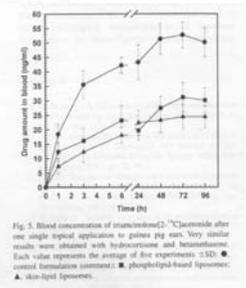
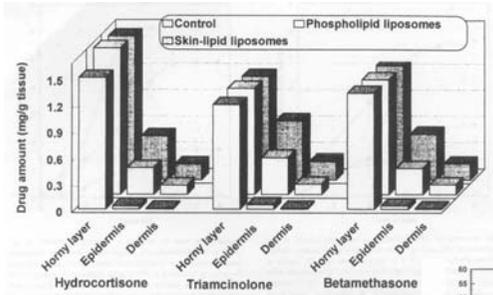
Fig. 2. Toxicity to normal mice. (A) Free amphotericin B. LD₅₀ was 1.2 mg/kg. The maximum dose without acute lethality was 0.8 mg/kg. n=10. Dose of free amphotericin B: 0.8 mg/kg (○—○); 1.2 mg/kg (●—●); 2.0 mg/kg (□—□). (B) Amphotericin-coated liposomal amphotericin B. LD₅₀ was greater than 10 mg/kg. All mice treated at a dose of 5.0 mg/kg were alive. n=10. Dose of amphotericin-coated liposomal amphotericin B: none (●—●); 2.5 mg/kg (□—□); 5.0 mg/kg (○—○); 10.0 mg/kg (●—●).



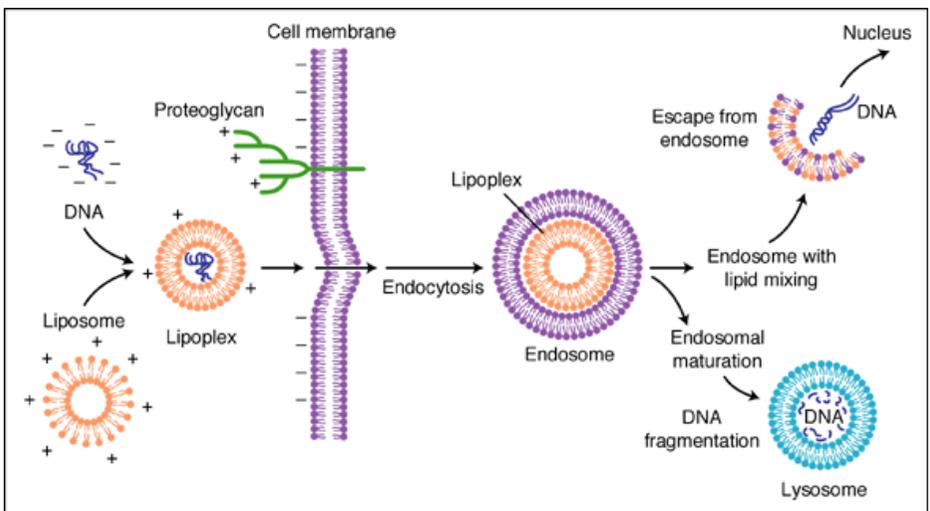
- citostatic (antitumoral) drugs to decrease severe side effects



- drugs for local treatment (e.g. on the skin) to increase the drug penetration into the deeper layers of skin and to avoid the penetration into the systemic circulation



DNA encapsulation (gene transfer)



Lipoplex-mediated transfection and endocytosis
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