MSE-238
Structure of Materials

Week 12 – biological materials (and hybrid materials)

Spring 2025

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EPFL

General Outline

- introduction and reminder of atomic bonds, crystals – week 1

Part I: crystallography - weeks 2-6

- packing of spheres, constructing crystal structure week 2
- crystal lattice and symmetry operations week 3
- mathematical description of the lattice, Miller indices week 4
- reciprocal space (&diffraction) week 6
- characterization I: diffraction week 7
- diffraction & recap of crystallography week 8

BREAK 18.4. & 25.4.

Part III: amorphous & hierarchical structures – week 9-13

- glasses
- polymers
- Characterization II: scattering
- biological and hybrid materials week 12 & 13

Recap – week 13

- Q&A session: June 27 between 13-15 room DIA 003

Overview

- biological materials

- structure of some important biological building blocks:
  - nucelic acids (DNA/RNA)
  - proteins
  - polysaccharides
  - lipids
  - amphiphilies
  - biominerals

- hybrid materials/composite materials

- reinforced composites

- functional composites

- biocomposites

- hierachical materials

Additional reading

- "Soft Condensed Matter", Jones, Oxford

- "Introduction to Materials Science" Mercier, Zambelli, Kurz, Elsevier

- "Introduction to soft matter: synthetic and biological self-assembling materials", Hamley, Wiley

Biological Materials: main components of life

- Polymeric molecules:
  - Nucleic acids (DNA, RNA)
  - Proteins
  - Polysaccharide (random sequence)

- Lipids: fats and oils

- Amphiphilic molecules (self-assembly)
  - phospholipids

- Biominerals
  - Calcium phosphate (example: hydroxyapatite in bone)
  - Calcium carbonate (example aragonite and calcite in mollusk shells)
 - Silicates (diatoms)

Nucleic acids

DNA (deoxyribonucleic acid)

- store and transmit information

- genetic code: complementary base pairs with specific hydrogen bonding

- double helix

- robust polymer

- free energy about 3kBT/basepair: melting into single strands at 50-90°C

RNA (ribonucleic acid)

- involved in transcription of information into proteins

- slightly different chemical composition

- single stranded
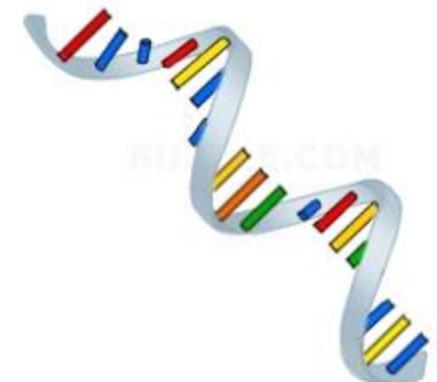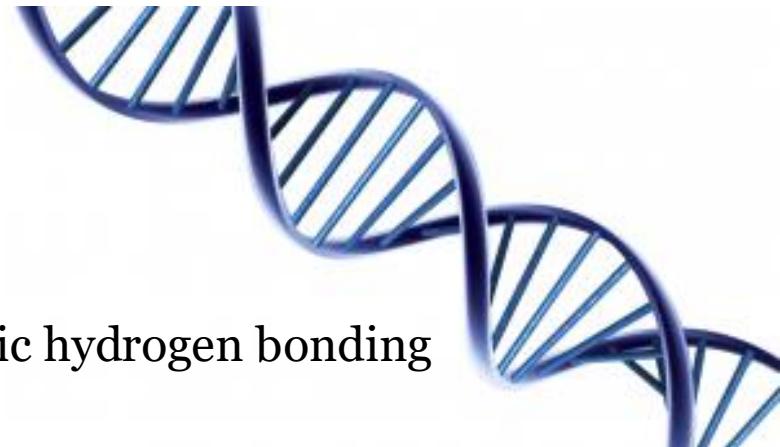
© Buzzle.com

DNA base pairs

DNA backbone: phosphate and deoxyribose
4 different bases:
thymine (T), cystosine (C), adenine (A) and
guanine (G)

specific base pairing
A-T and C-G (hydrogen bonds)

allows to reproduce a copy from a first strand
--> DNA replication
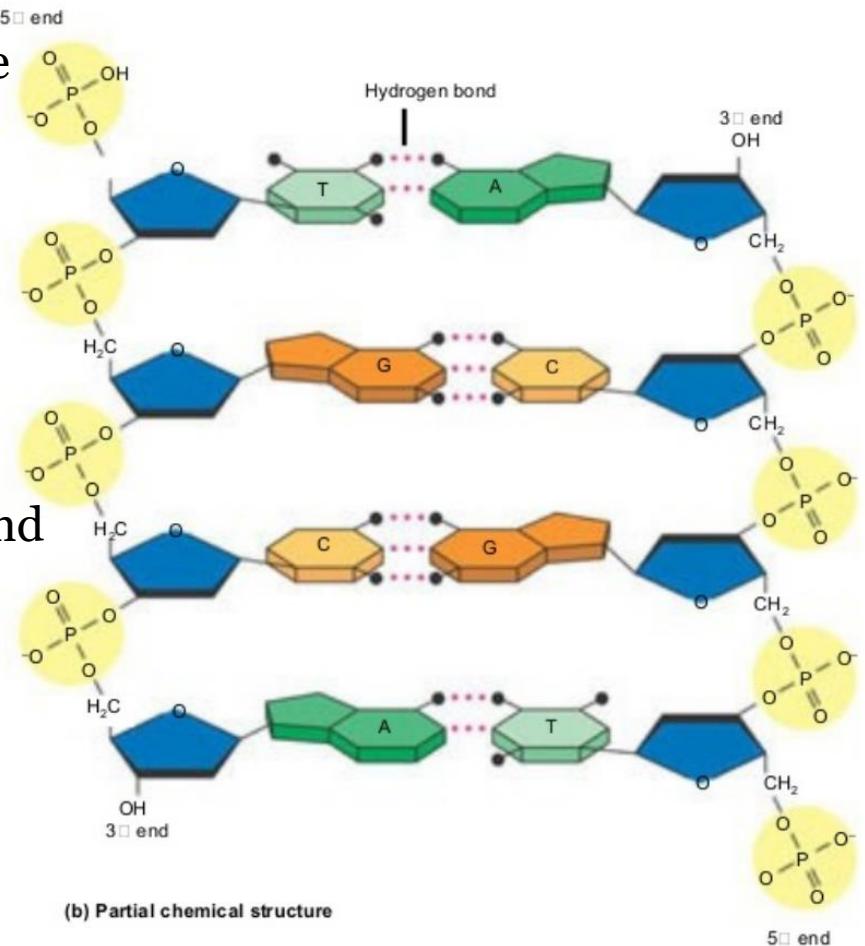

(b) Partial chemical structure

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Chromosome

- double helix: rigid molecule, at length scales smaller than the persistence length l_p = 60 nm the molecule is stiff (compare to *a = 0.34 nm*)

- larger length scales: random walk

- largest human DNA has *280 x 10⁶ monomers units*

- what is the total contour length?

- what is the end-to-end distance?

- worm-like chain model end-to-end distance: $\left[2l_p aN\right]^{1/2}$

Worm-like chains: persistence length

- For stiff polymers an alternate model is used: continuously bending worm-like chains.
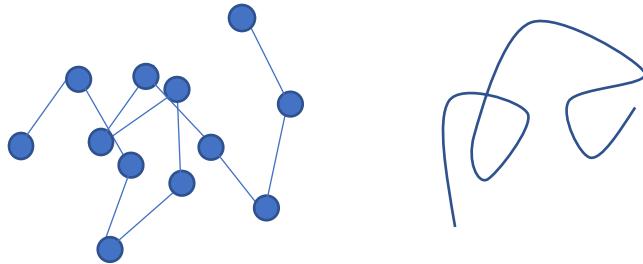
- but also here: there is a loss of correlation of direction over a certain distance, the **persistence length** l_p. Correlation decays exponentially

$$R_{\text{wlc}} = \left[2l_p r_{\text{max}} \left[1 - \frac{l_p}{r_{\text{max}}} \left[1 - \exp\left(-\frac{r_{\text{max}}}{l_p} \right) \right] \right] \right]^{1/2}$$

for $r_{\text{max}} = Na \gg l_p$ the random walk is recovered $R\big|_{r_{\text{max}} \gg l_p} \approx \left[2l_p r_{\text{max}} \right]^{1/2} = \left[2l_p aN \right]^{1/2}$

comparing to the Kuhn length: $R = [abN]^{1/2}$ so $b = 2l_p$

Chromosome

- double helix: rigid molecule, at length scales smaller than the persistence length l_p = 50-60nm the molecule is stiff (compare to $a = 0.34\ nm$)

- larger length scales: random walk

- worm-like chain model end-to-end distance: $\left[2l_p aN\right]^{1/2}$

- largest human DNA has $280\ x\ 10^6$ monomers units

- for the end-to-end distance of the largest human DNA molecule with a total contour length of 95 mm results in about 100 µm: no space in the cell nucelus (around 6µm)!

- complex, hierarchical structure including proteins and supercoiling

- → Chromosome (human cell contains 24)

Chromosome
Nucleosome
DNA double helix
Coils
Supercoils
Histones
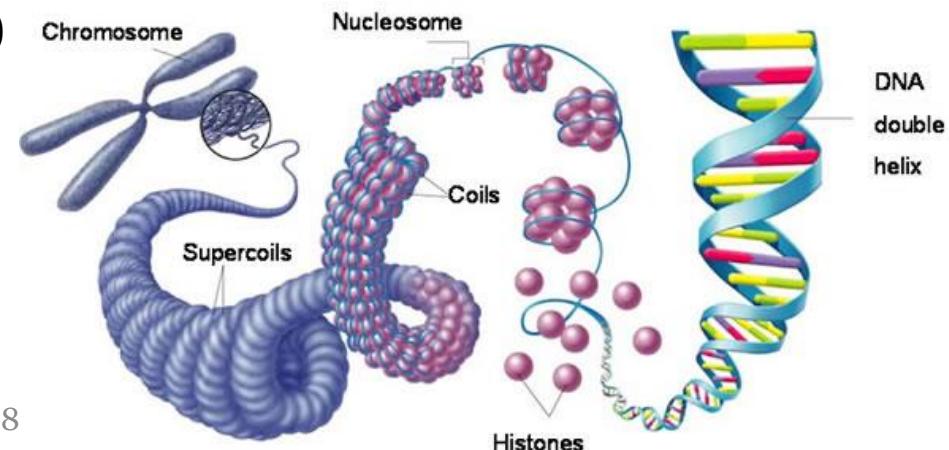
DNA origami

utilizing the possibility to create DNA sequences and their specific hybridization, well defined self-assembly of 2D structures
each oligonucleotide can serve as a 6-nm pixel
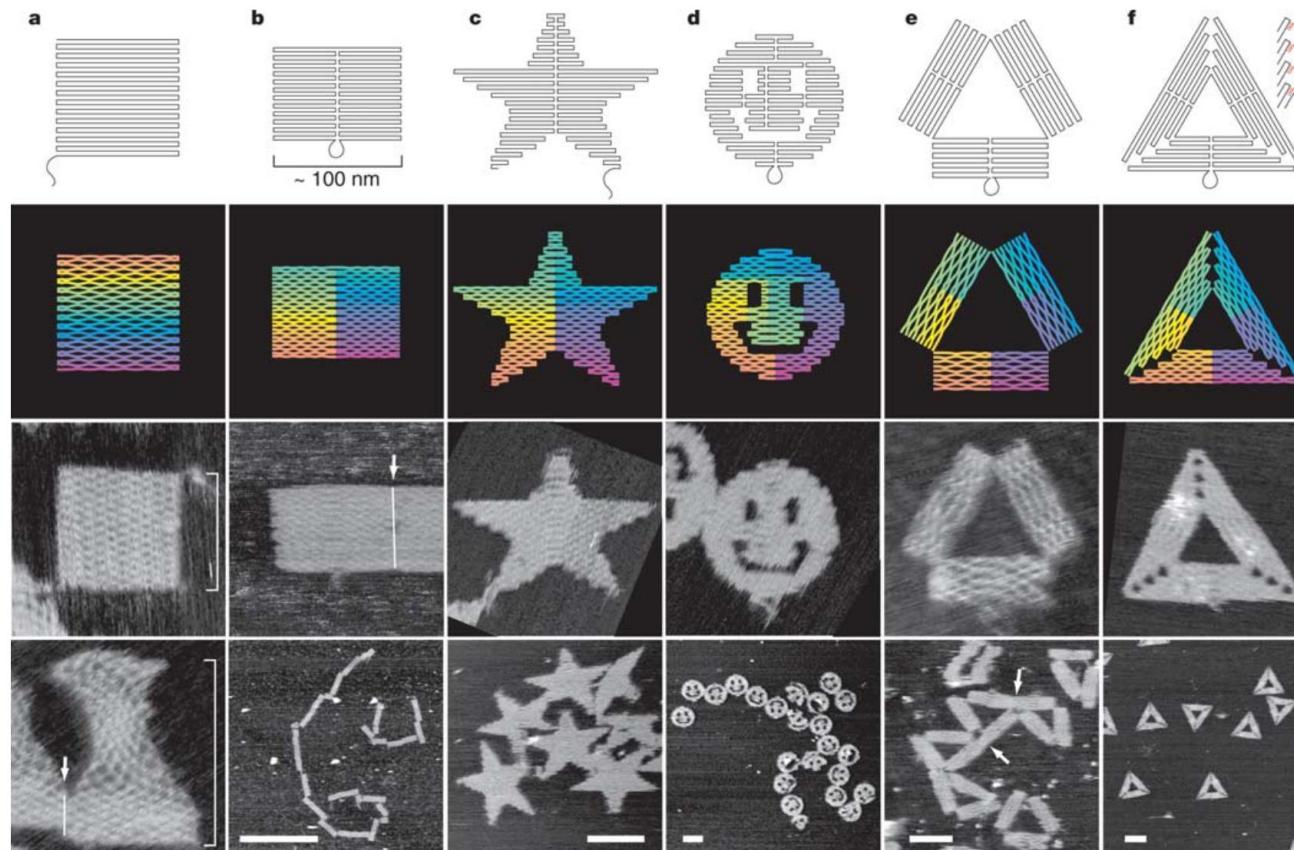
from Gene to Protein

- DNA molecule codes for the amino acid sequence of the protein

- RNA transcription and Protein translation
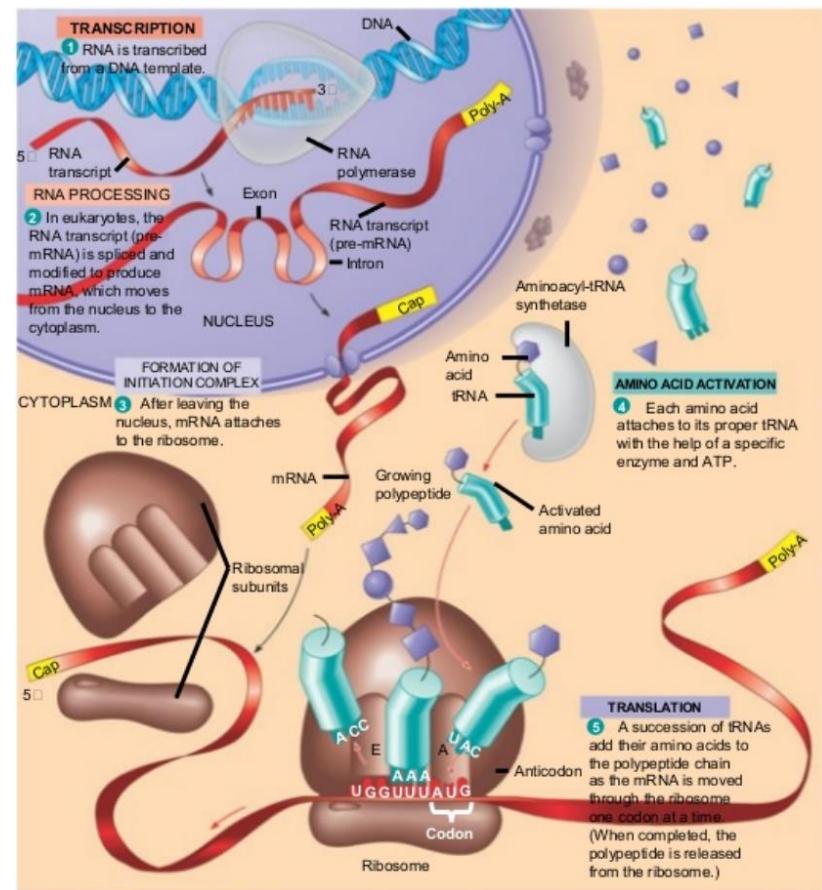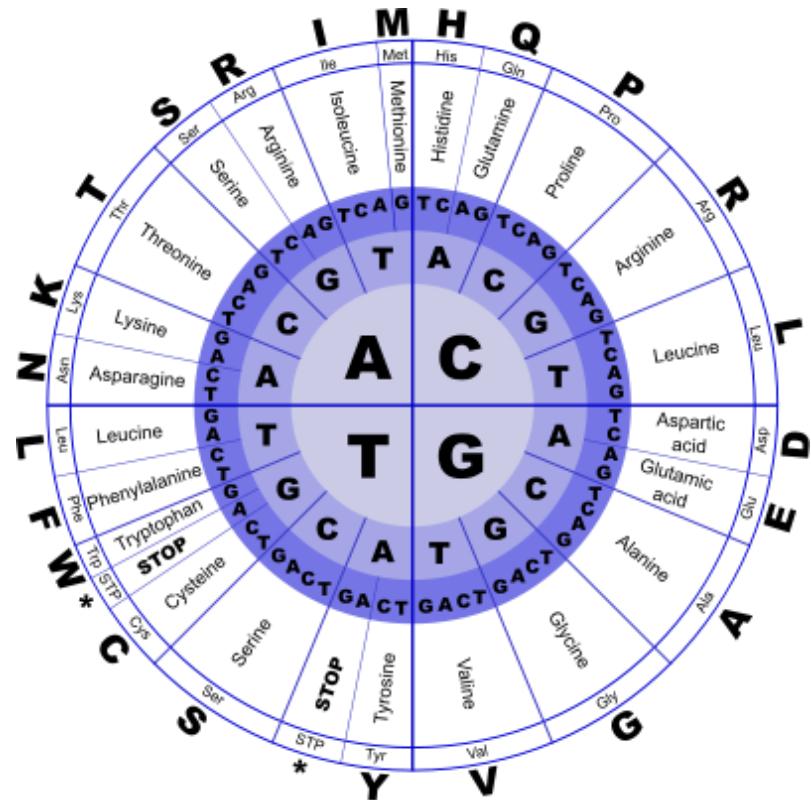
Protein

- Amino acid sequence = primary structure, determined by genetic code

- 22 different proteinogenic amino acids

- all proteinogenic amino acids (except glycine) are **chiral**, only the L-enatiomer exists in biological systems

- there exists three groups of amino acids:
  - hydrophobic (unpolar)
  - hydrophilic uncharged (polar)
  - hydrophilic and charged (acidic or basic)

- hydrophilic and hydrophobic parts in the same molecule → self-assembly to minimize contact between hydrophobic groups and water, maximize contact hydrophilic and water

Protein functions

- Enzymes: biological catalysts

- cell signaling and signal transduction, e.g. insulin

- membrane proteins: regulate transport and sense the environment (receptor)

- adaptive immune system (antibodies)

- transport proteins, e.g. Haemoglobin transporting oxygen

- structural proteins: cytoskeleton, collagen, spider silk

- molecular motors: convert chemical energy to mechanical motion

Proteins: hierarchical structure

function with 3D structure:

protein folding into secondary and tertiary structure

assisted self-assembly (chaperones)

→ don't follow random walk model of polymers

Primary structure
amino acid sequence

Secondary structure
regular sub-structures

alpha helix

beta sheet

Tertiary structure
three-dimensional structure

P13 protein

hemoglobin

Quaternary structure
complex of protein molecules

©LadyofHats/ commons.wikimedia.org
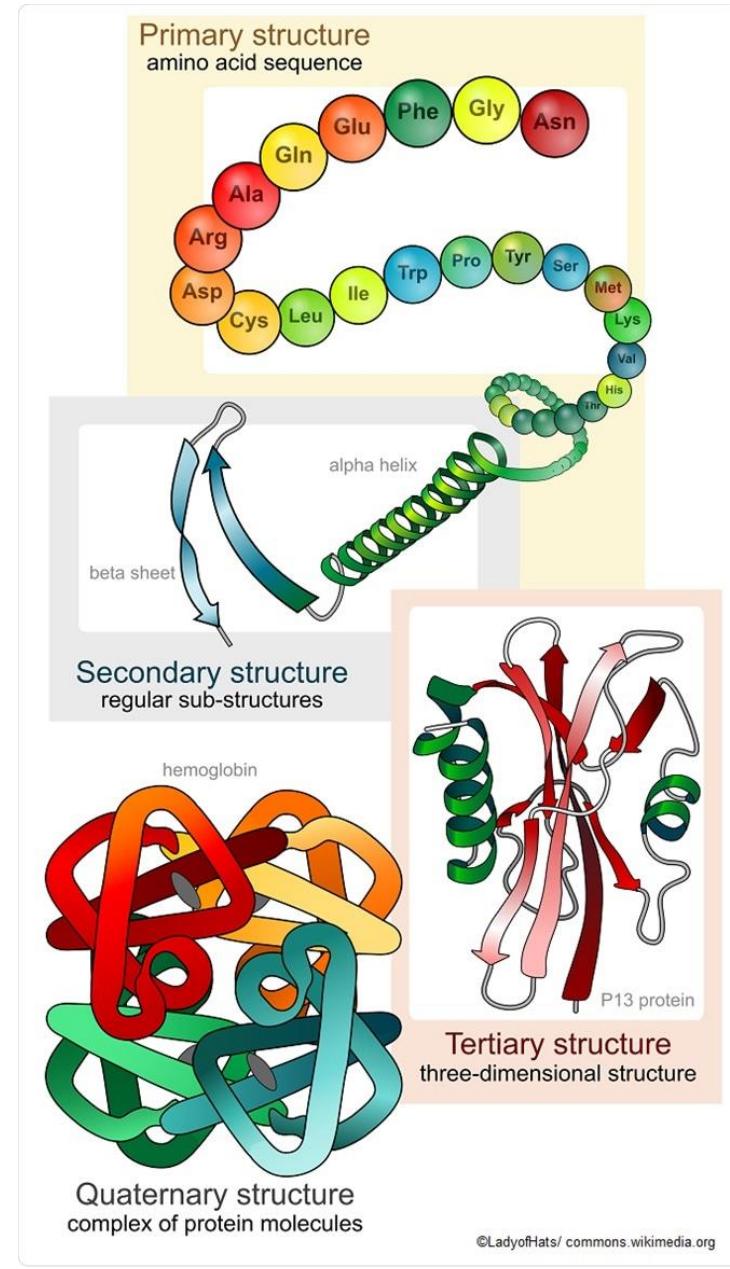
Proteins

- native form: single, well-defined structure, compact

- denaturated form: more open, random conformation, tertiary structure and maybe also secondary structure is destroyed: loss of biochemical activity, can be irreversible

- protein sequences are not random, they have evolved specifically to have the property of one well defined structure

- energy landscape, protein folding towards successively lower energy
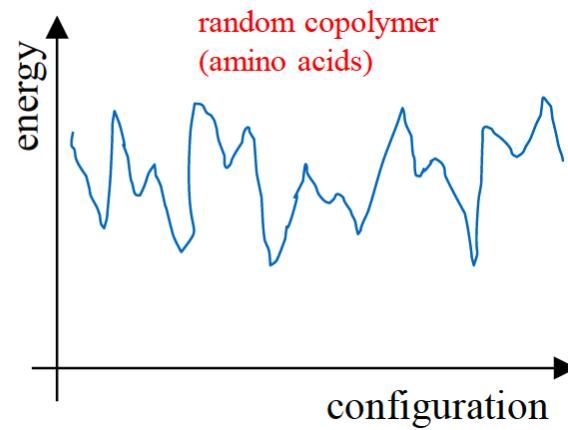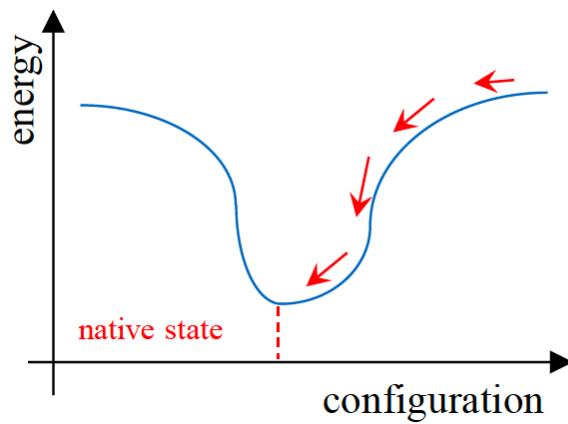
Reminder: protein crystallography

study the three-dimensional structure of biological macromolecules.

Data collection: wave length = 0.097nm, Canadian
Light Source - 1 second per frame,
total of ~360 frames,
step size 0.5 degrees
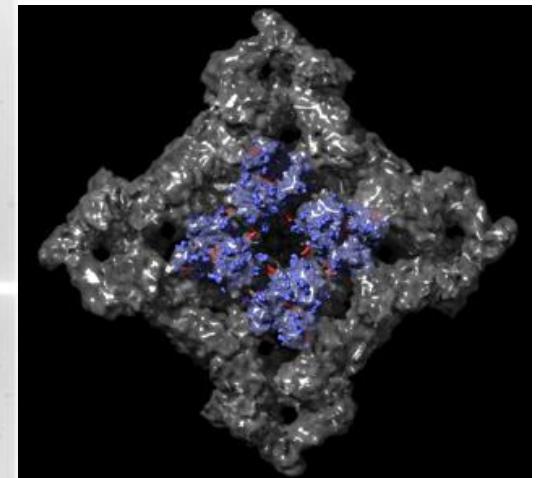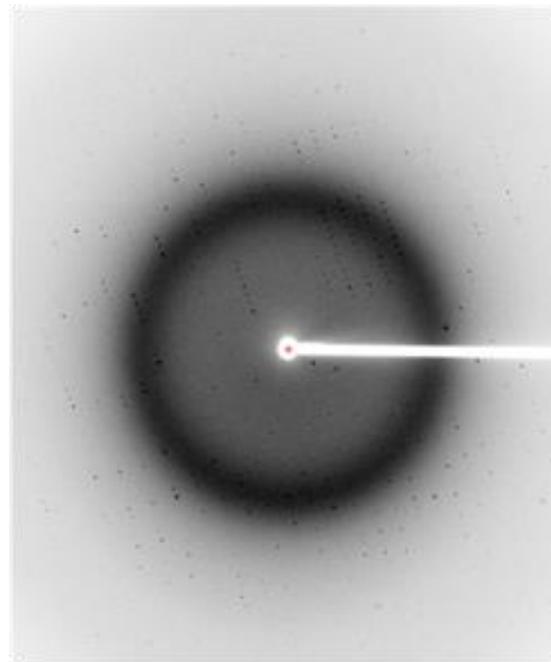
Courtesy: F. Van Petegem, UBC, Canada

For structure determination from single crystal diffraction one needs to retrieve...

in order to solve this problem, the space group will restrict the model **fewer atoms** because symmetry will automatically place equivalent atoms.
→ Refine the structure more efficiently using fewer parameters.

to reach higher resolution in the structure determination one needs....

Protein Crystallography

Reminder:

14 Bravais lattices

32 point groups

230 space groups

230

The Space Group List Project

by Frank Hoffmann

Point Symmetry operations in 3D

- **Rotation axis**
  1-fold (no symmetry)
  2-fold (180° rotation)
  3-fold (120° rotation)
  4-fold (90° rotation)
  6-fold (60° rotation)

→ in 2D rotation axis perpendicular to the plane
→ in 3D there can be several axes in idfferent directions
  (but always through the center of the object)

- **Reflection or mirror plane**

- **the inversion center and the roto-inversion axis**
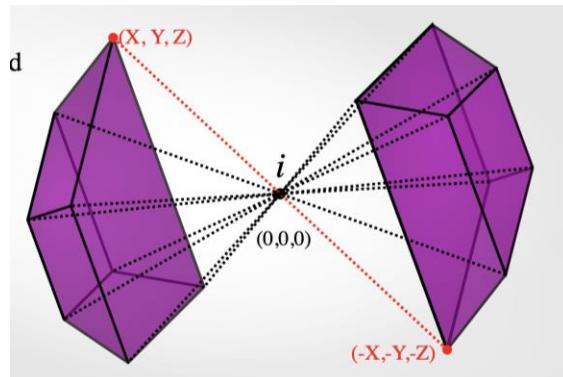
every point pulled through center of inversion *I*

rotation and inversion combined → roto-inversion
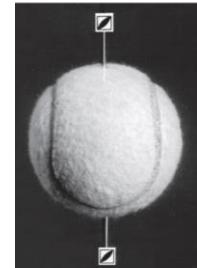
Protein Crystallography

Reminder:

14 Bravais lattices

32 point groups

230 space groups

- proteins are chiral, chiral molecules cannot exist in crystals with symmetry operations that invert handedness, such as:

- Mirror planes (m)

- Inversion centers (i)

- Rotoinversion axes (like $\bar{3}, \bar{4}, \bar{6}$)

- 65 chiral space groups, called "Sohnke space groups" are **non-centrosymmetric** and lack **mirror** or **inversion** symmetry.

Protein crystallography

- from the 65 possible space groups for proteins, only 50% of them have been observed for proteins.

- one particular space group (P2₁2₁2₁ (No. 19) makes up more then 30% of all known protein crystals

- Orthorhombic and monoclinic crystal systems dominate

- symmetric proteins, often as quaternary structure crystallize on the other hand more often in space groups which can accommodate for that symmetry, often in the tetragonal or trigonal structure with helical screw symmetries

Tobacco mosaic virus, with the RNA genome in red.
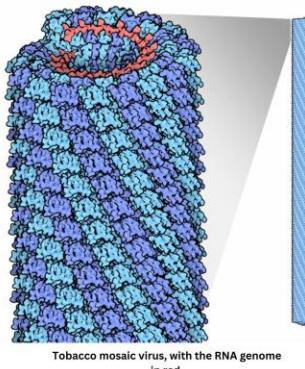
Wukovitz & Yeates *Nature structural biology* 1995 *2,12*

Spider Silk
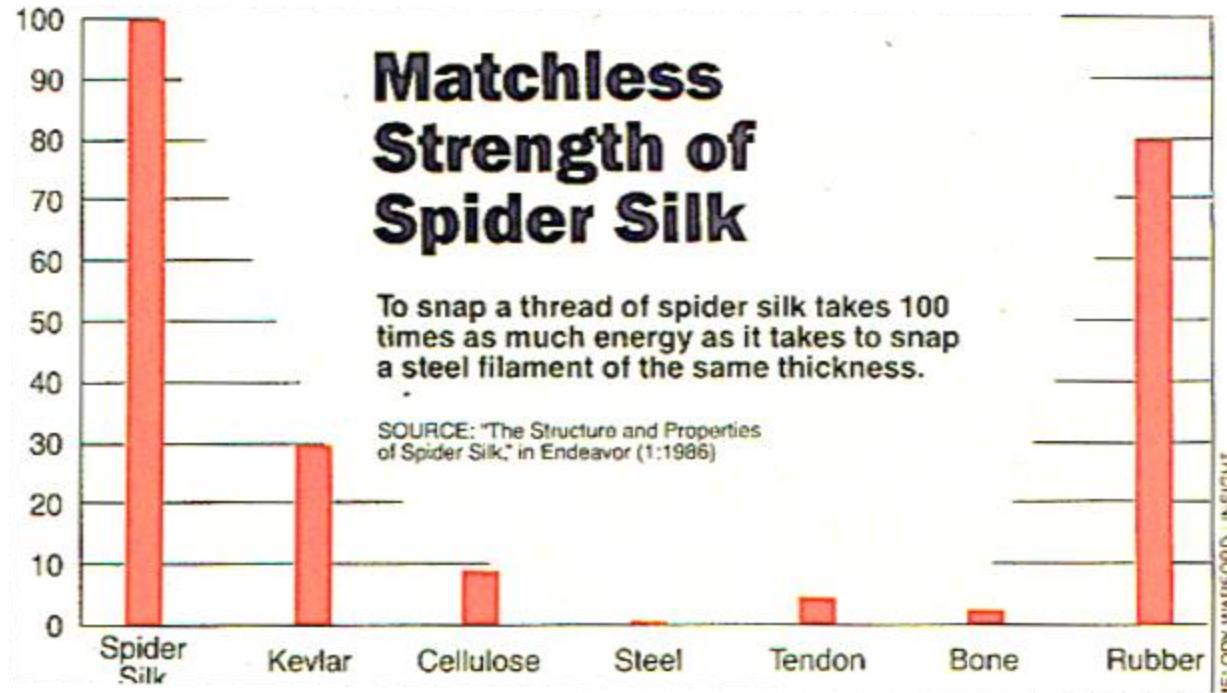
A cable made of spider silk which is no thicker than 5 cm diameter could support an aeroplane

Spider silk

silk protein in solution

4nm

4nm

conformational change through processing

Oxford Silk Group

β-sheets
Amide I
Amide II

Shear starts

Δ Absorbance

Wavenumbers (cm⁻¹)

Time (seconds)

Spider Silk

Fiber   Nano-fibril   Nano β-crystallite
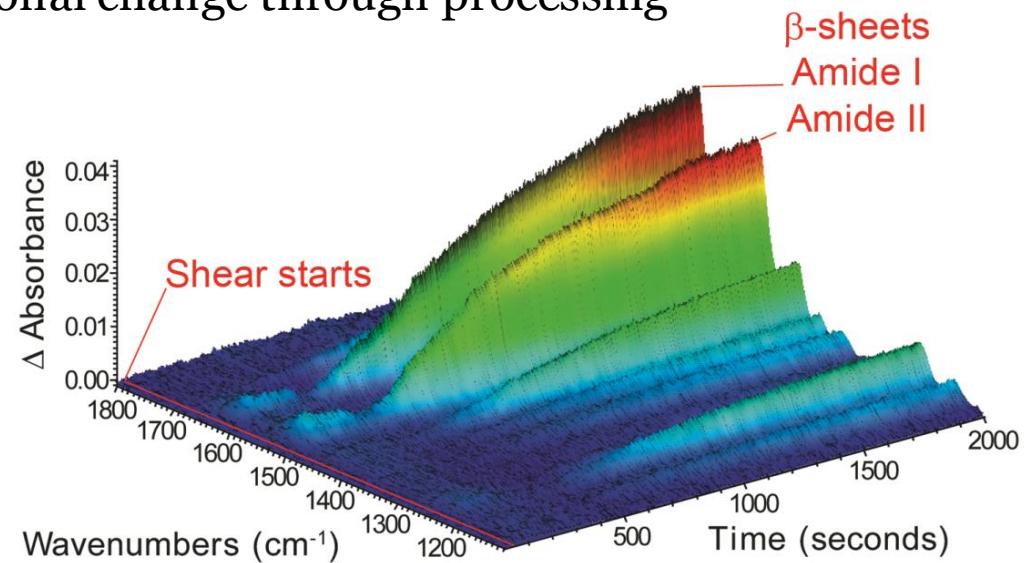
Xu et al. SoftMatter, **10**, 2116 (2014)

7 different types of spider silk
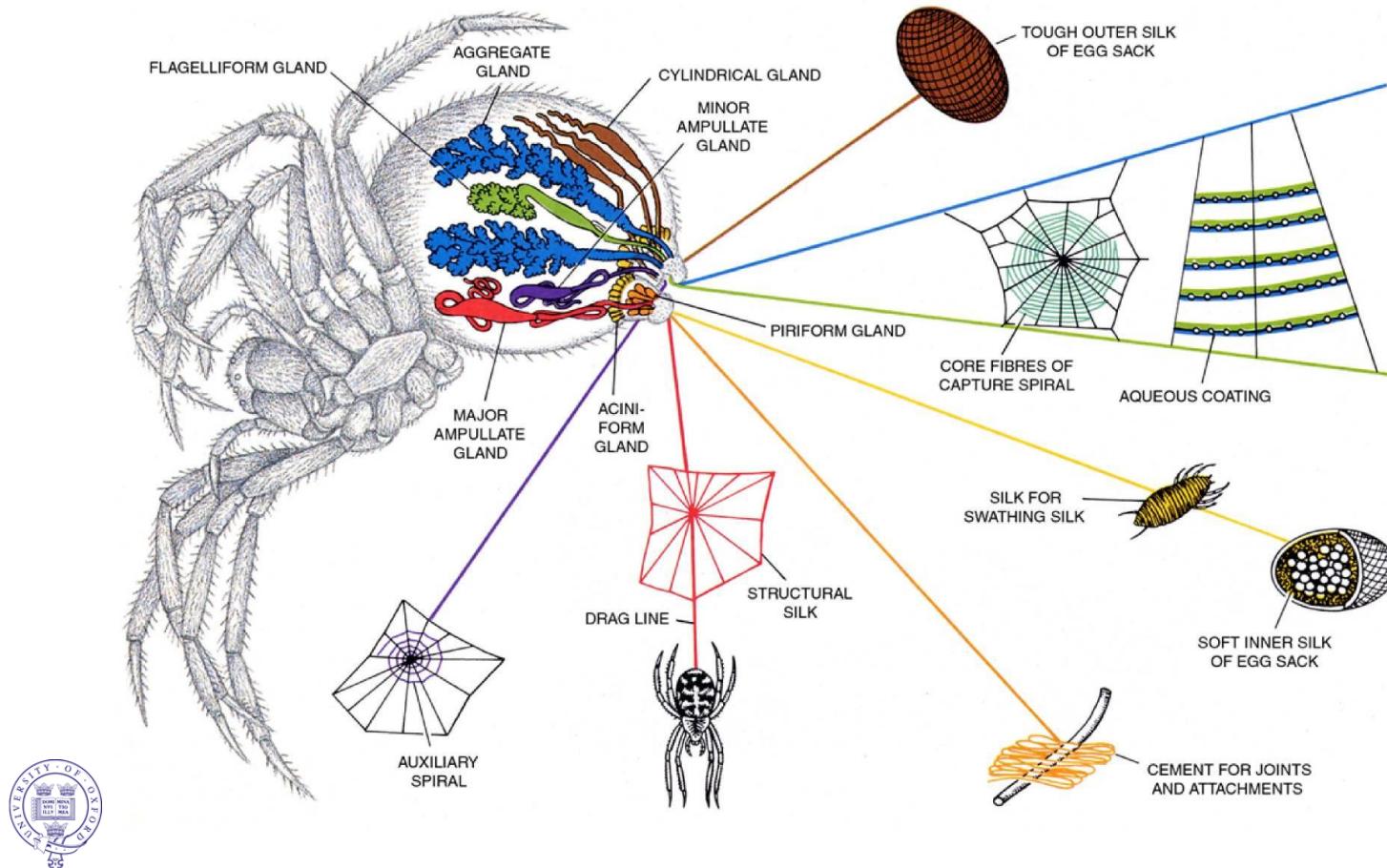
Oxford Silk Group
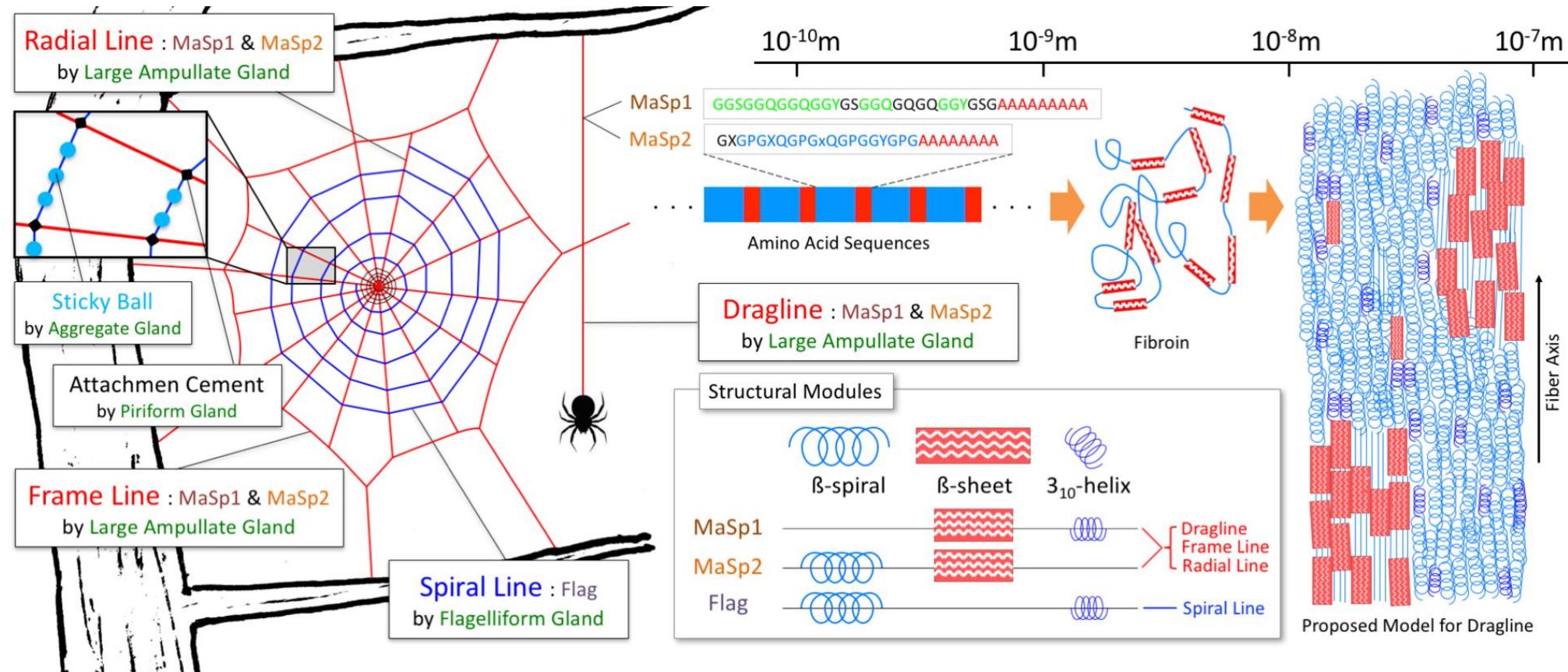
Spider silk

Zhao, Yet al. Appl. Phys. B (2017) 123: 188.

Spider silk...
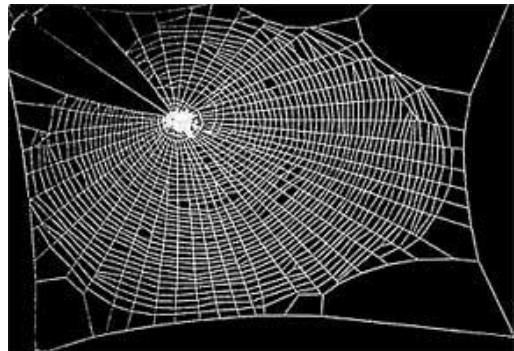
Normal
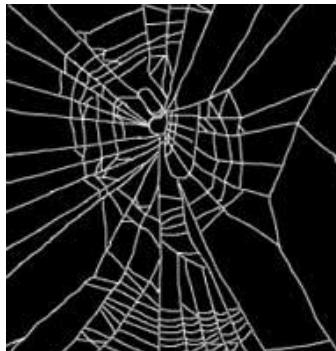
Benzedrine (Speed)
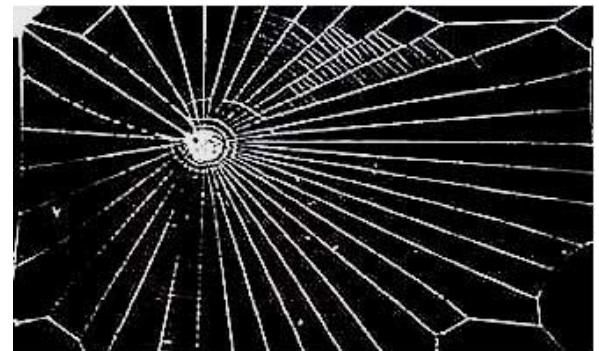
LSD
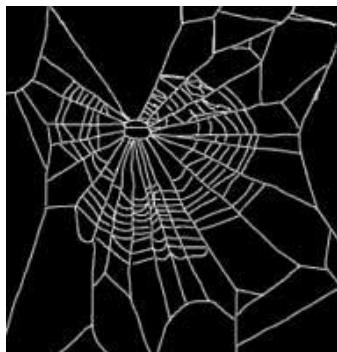
Marijuana
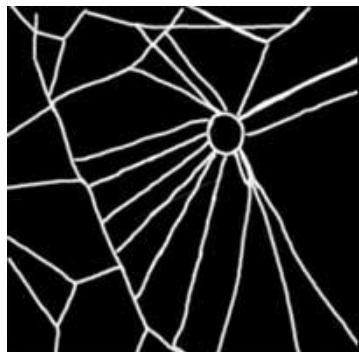
Sleeping pills

Caffeine
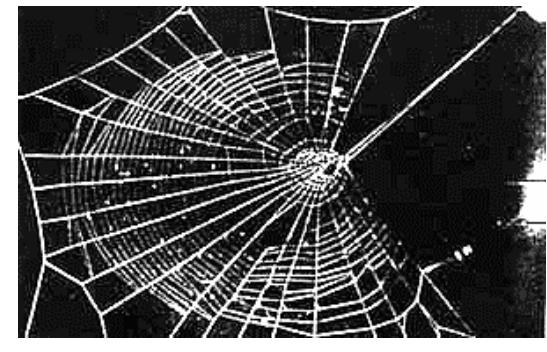
Mescaline/Peyote

Oxford Silk Group

Polysaccharides

- carbohydrates, general formula $C_x(H_2O)_y$, monomers: various sugars
- no defined sequence and architecture (side-chains)
- store energy: starch (amylose and amylopectin), glycogen
- structural polymer: cellulose, chitin
- amylose, amylopectin, glycogen and cellulose same chemical composition
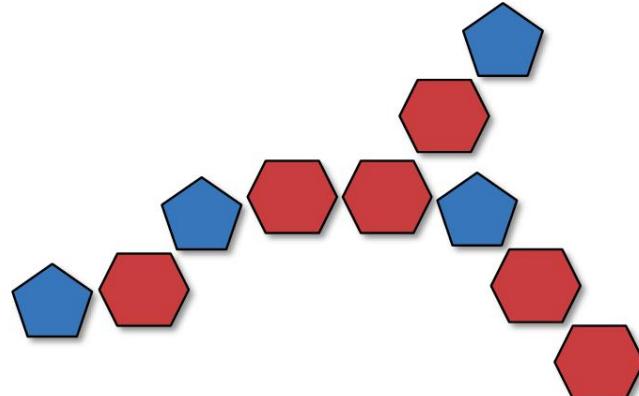
# Cellulose: X-ray diffraction

cellulose fiber

Powder diffraction pattern

Cellulose I

c

b

a

c

b

a

Crystalline cellulose fibers
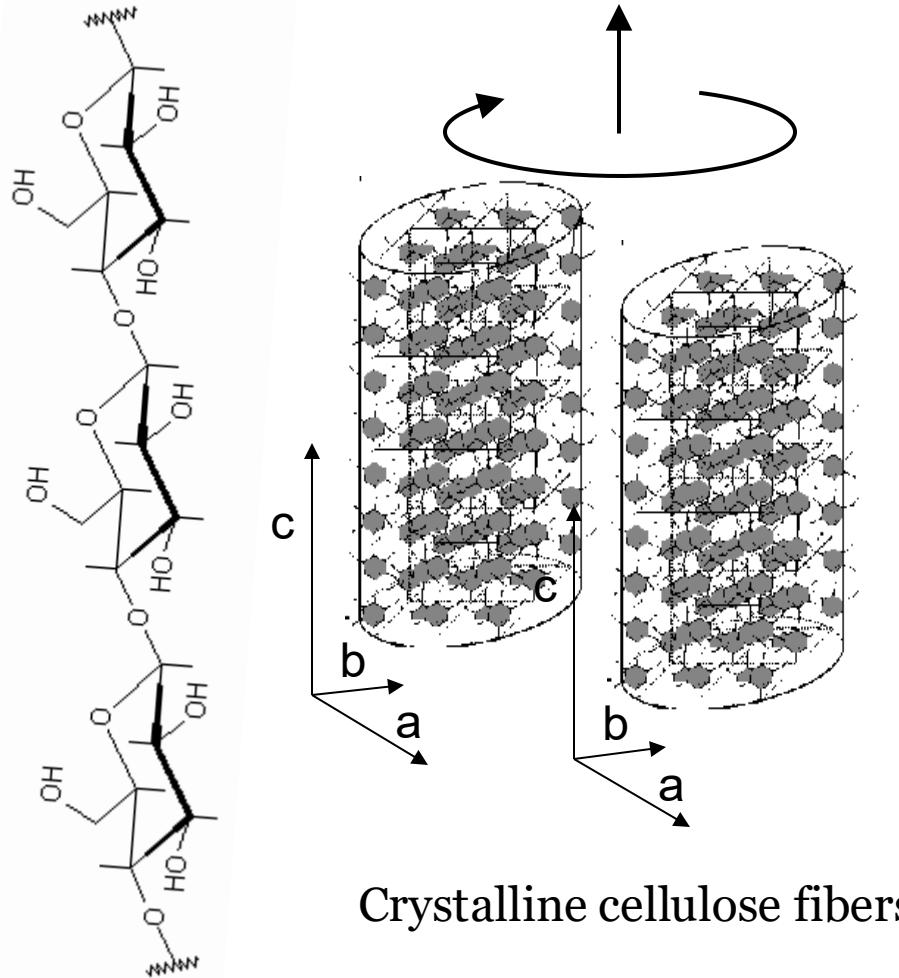
Cellulose molecule
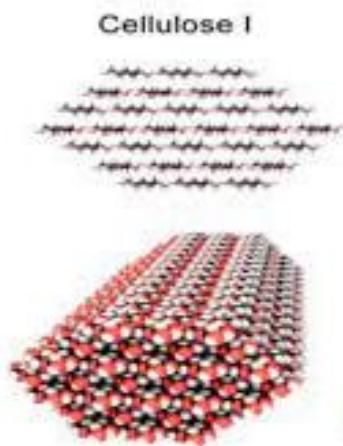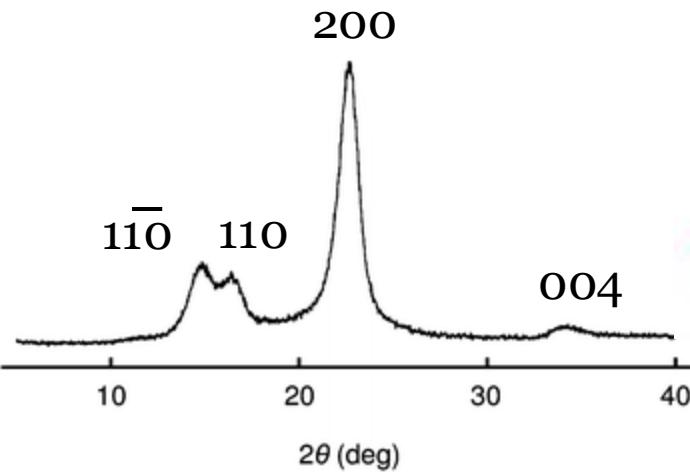
2D diffraction pattern

004

$1\bar{1}0$

110

200

012
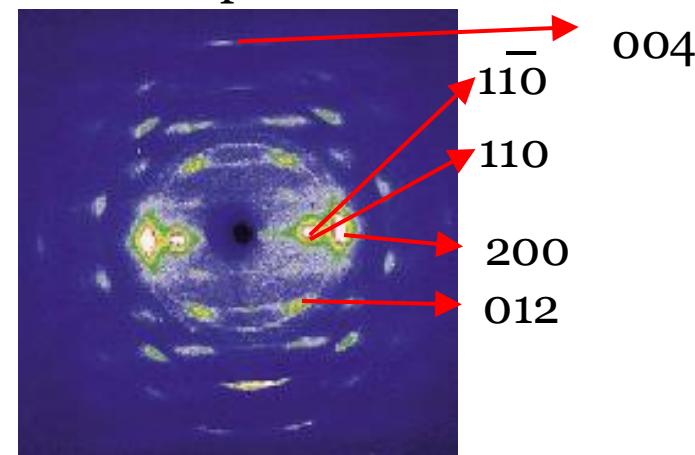
Copolymer

Polysaccharides can form copolymers together with proteins

→ glycoproteins or peptidoglycans

Glycosylation: attachment of sugars to existing proteins

One example is mucin contained in mucus: the slimy surface of exposed tissue like nose, lung, stomach

prevents particles and infectious microorganisms from reaching the cell
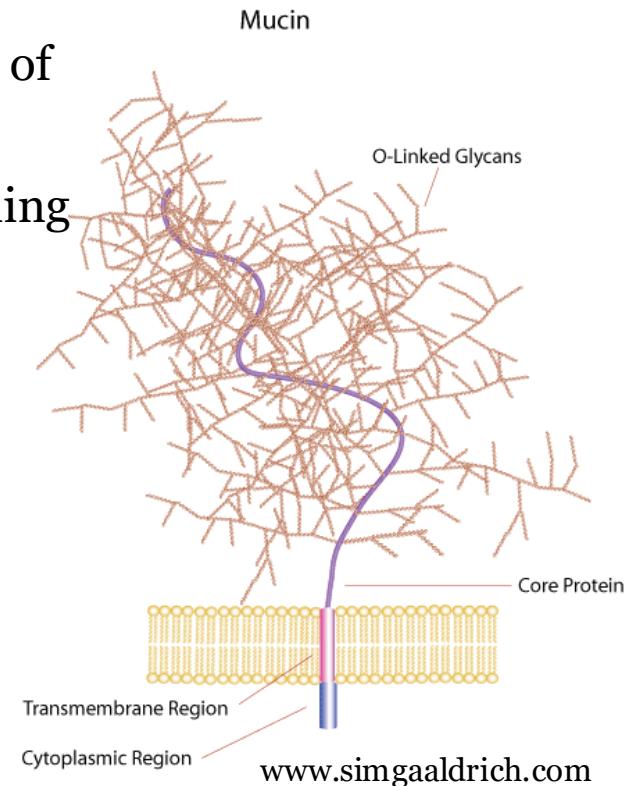
Mucin

O-Linked Glycans

Core Protein

Transmembrane Region

Cytoplasmic Region

www.simgaaldrich.com

Biological Materials: main components of life

- Polymeric molecules:
    - Nucleic acids (DNA, RNA)
    - Proteins
    - Polysaccharide (random sequence)

- **Lipids: fats and oils**

- Amphiphilic molecules (self-assembly)
    - phospholipids

- Biominerals
    - Calcium phosphate (example: hydroxyapatite in bone)
    - Calcium carbonate (example aragonite and calcite in mollusk shells)
   - Silicates (diatoms)

Lipids

- hydrophobic or amphiphilic molecules
- biological functions:
  - storing energy
  - structural components of cell membranes
  - signaling
  - vitamins

- eight categories
  - fatty acids
  - **glycerolipids**
  - **glycerophospholipids**
  - spingolipids
  - saccarolipids
  - polyketides
  - sterol lipids (e.g. cholesterol, steroids)
  - prenol lipids (fat soluble vitamins)

Cholesterol

A free fatty acid

A triglyceride

A phospholipid
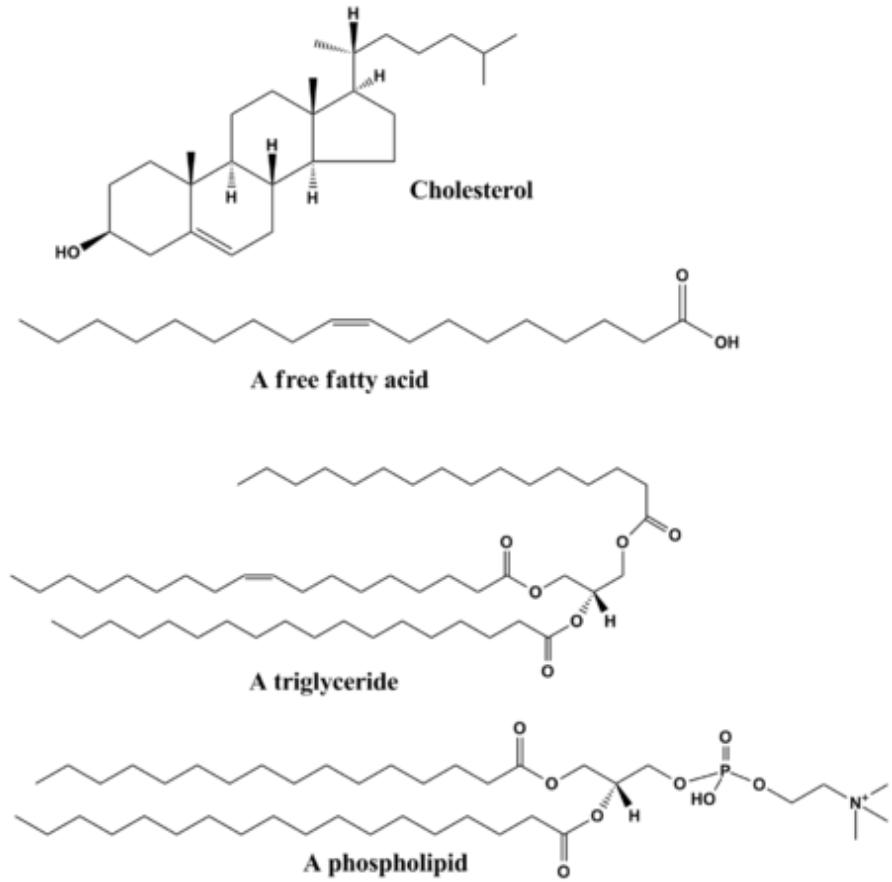
Triglyceride

- energy storage: main constituents of body fat and vegetable fat/oil
- in food: fat dissolves most aroma compounds
- saturated and unsaturated
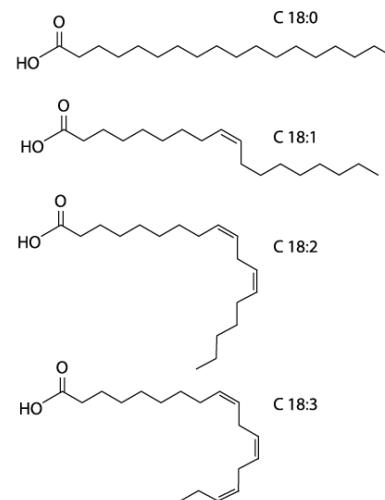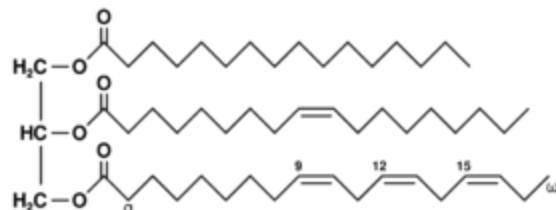
Chocolate

- cacao butter, main component POS and many other triglycerides

- polymorphism: 6 different crystalline forms: γ, α, III, β_{IV}, β_V, β_{VI}

- β_V: desired form due to melting behaviour gloss, texture and breaking behaviour BUT: is not the thermodynamically most stable form
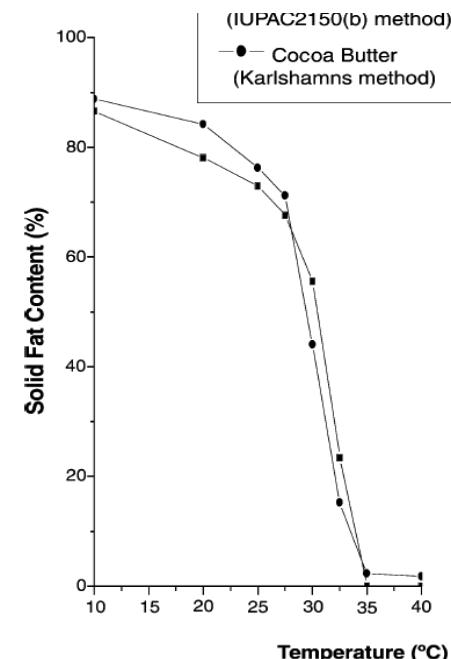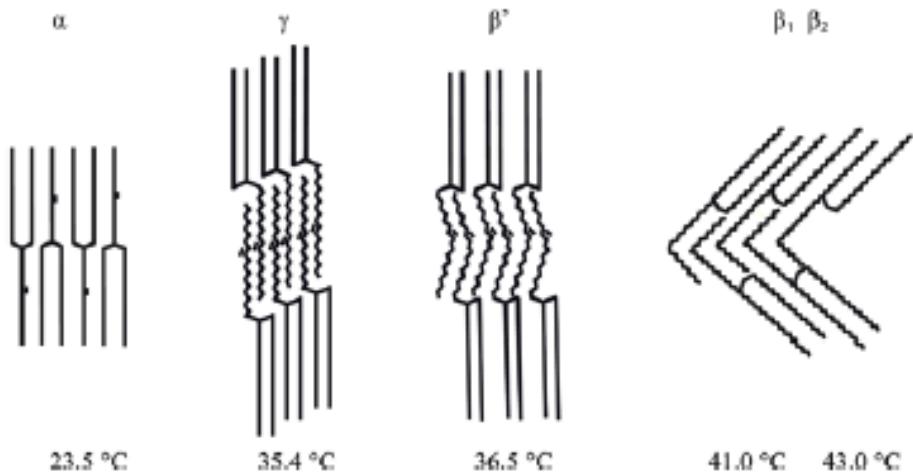
α   γ   β'   β₁ β₂

23.5 °C   35.4 °C   36.5 °C   41.0 °C   43.0 °C

(IUPAC2150(b) method)
— Cocoa Butter (Karlshamns method)

Solid Fat Content (%)

Temperature (°C)

# Biological Materials: main components of life

- Polymeric molecules:
  - Nucleic acids (DNA, RNA)
  - Proteins
  - Polysaccharide (random sequence)

- Lipids: fats and oils

- **Amphiphilic molecules (self-assembly)**
  - **phospholipids**

- Biominerals
  - Calcium phosphate (example: hydroxyapatite in bone)
  - Calcium carbonate (example aragonite and calcite in mollusk shells)
  - Silicates (diatoms)

Amphiphilic molecules

Amphiphiles: contain hydrophobic group and hydrophilic group

Surfactant: surface active molecule, often used for man-made amphiphiles
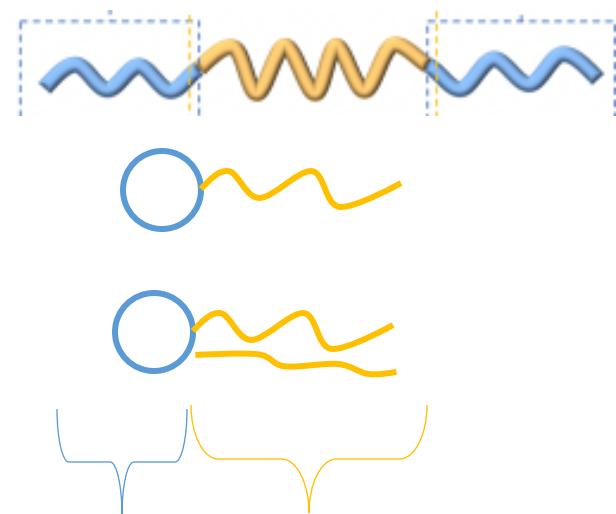
hydrophilic   hydrophopic

Aggregates of amphiphiles

The aggregates formed is determined by the <u>geometry</u> of the amphiphile, maximizing the contact of the hydrophilic head with water while minimizing its contact with the hydrophobic tail

Radius $r \leq l_c$ critical chain length

v chain volume

a_o optimal headgroup area

sphere   cylinder   bilayer
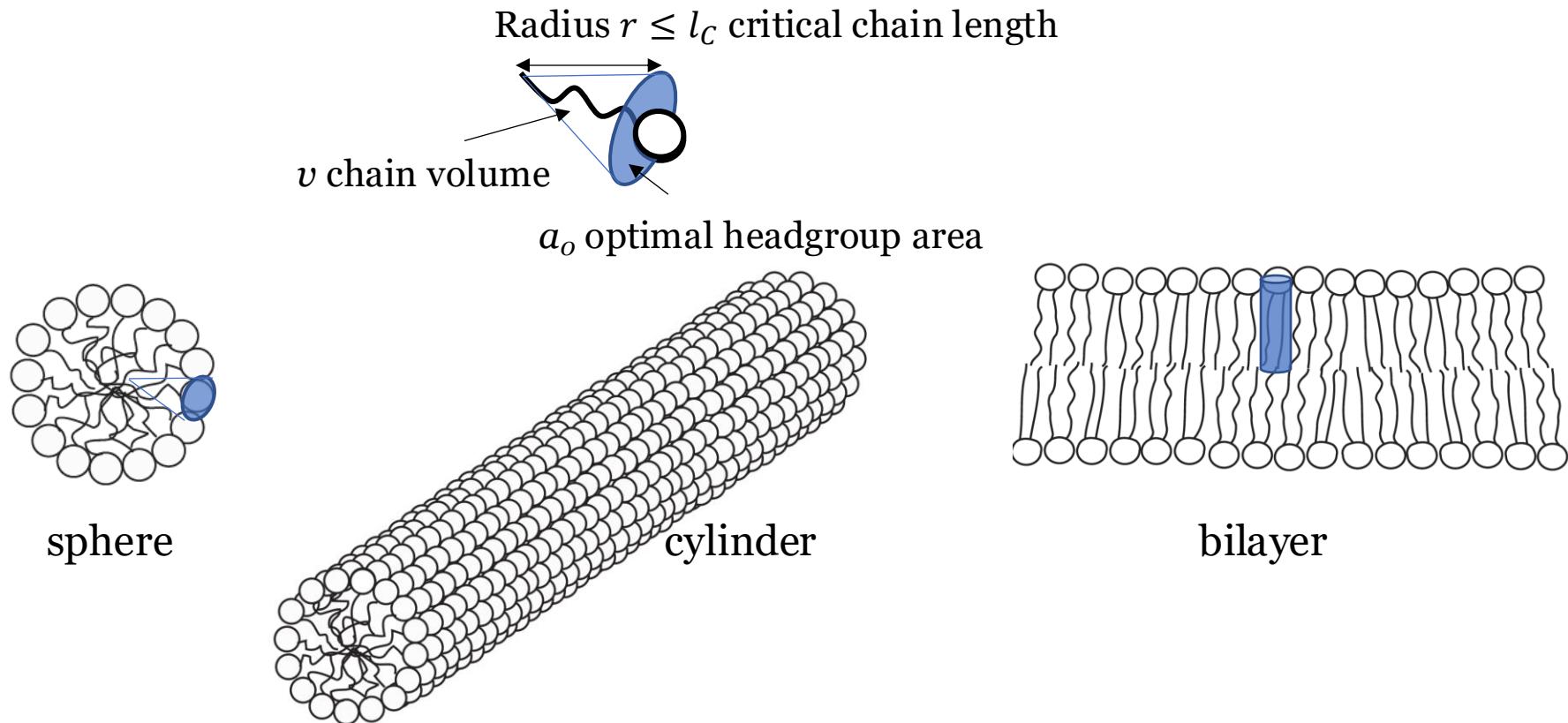
Packing parameter

Packing parameter $\quad \dfrac{v}{a_0 l_c}$

Radius $r \leq l_c$ critical chain length

v chain volume

a_o optimal headgroup area

For micelle:
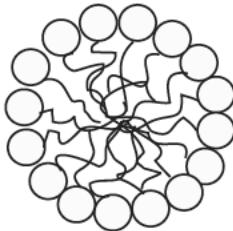
$V = \dfrac{4\pi r^3}{3} = Nv$

$A = 4\pi r^2 = Na_0$

$r = \dfrac{3v}{a_0}$

$\dfrac{v}{a_0 l_c} < \dfrac{1}{3}$

For a bilayer: $\quad \dfrac{v}{a_0 l_c} \approx 1$

For a cylinder:
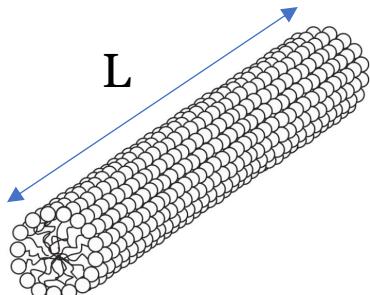
$V = \pi r^2 L = Nv$

$A = 2\pi r L = Na_0$

$r = \dfrac{2v}{a_0}$

$\dfrac{v}{a_0 l_c} < \dfrac{1}{2}$

L
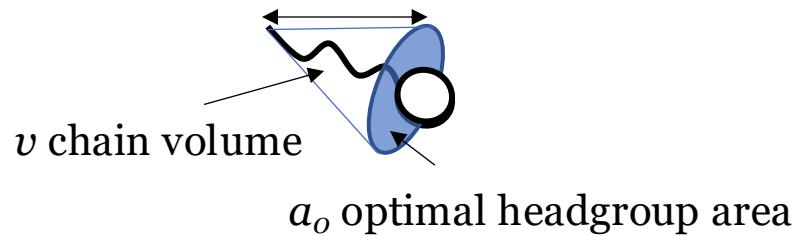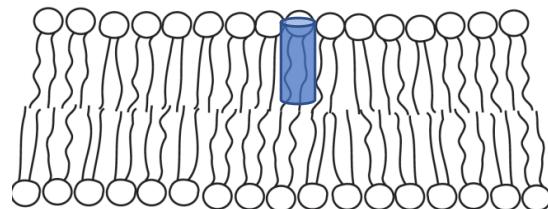
For inverted structures: $\dfrac{v}{a_0 l_c} > 1$

Biological amphiphiles

Phospholipids
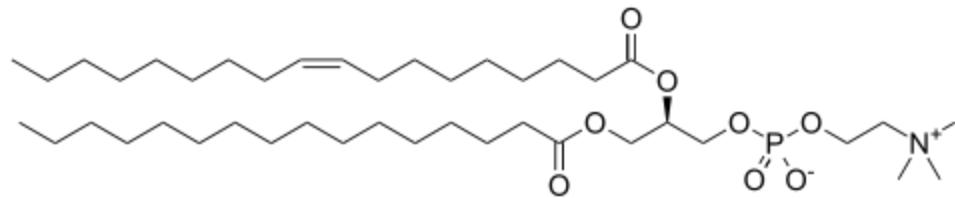
1-palmitoyl-2-oleyl-*sn*-glycero-3-phosphatidylcholine POPC

- large hydrocarbon volume compared to headgroup: bilayer assembly

Radius $r \leq l_c$ critical chain length

v chain volume

$$\frac{v}{a_0 l_c} \approx 1$$

a_o optimal headgroup area
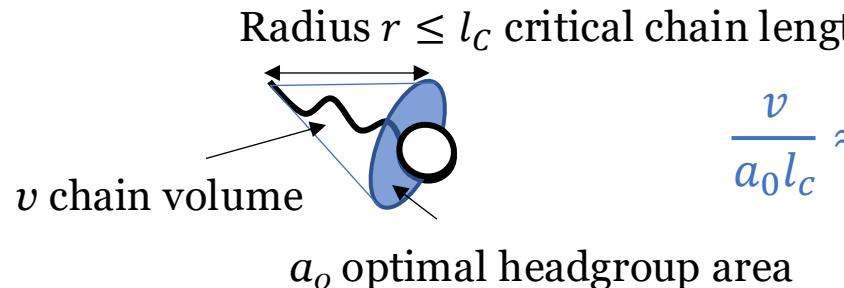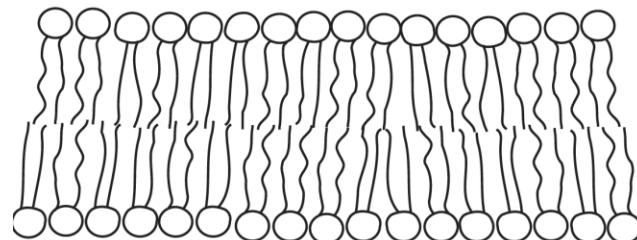
- two chains: very insoluble, stable as membrane
- quite big headgroup: low probability for flipflop: different sides of membranes

Membrane properties

- bilayer provides barrier for ions, charged, polar and large molecules: allows compartmentalization into different environments

- cell membrane: complex mixture, raft formation, cholesterol alter stiffness and permeability, membrane proteins, asymmetric, outside polysaccharides, inside link to cytoskeleton
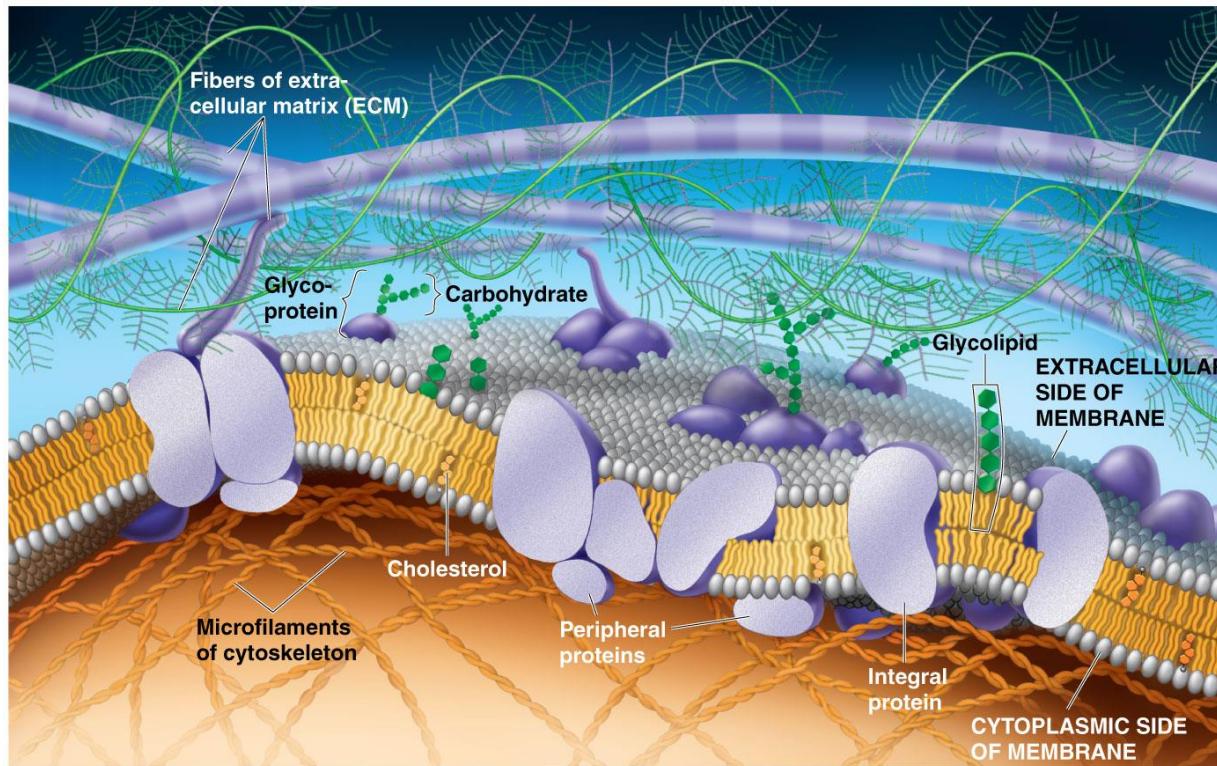
Vesicle

A self-closed bilayer is called a vesicle

In human body for cell-cell communication

Encapsulation of objects, drug delivery

Model of cells and cell membranes

Minireactor in chemistry



200 nm
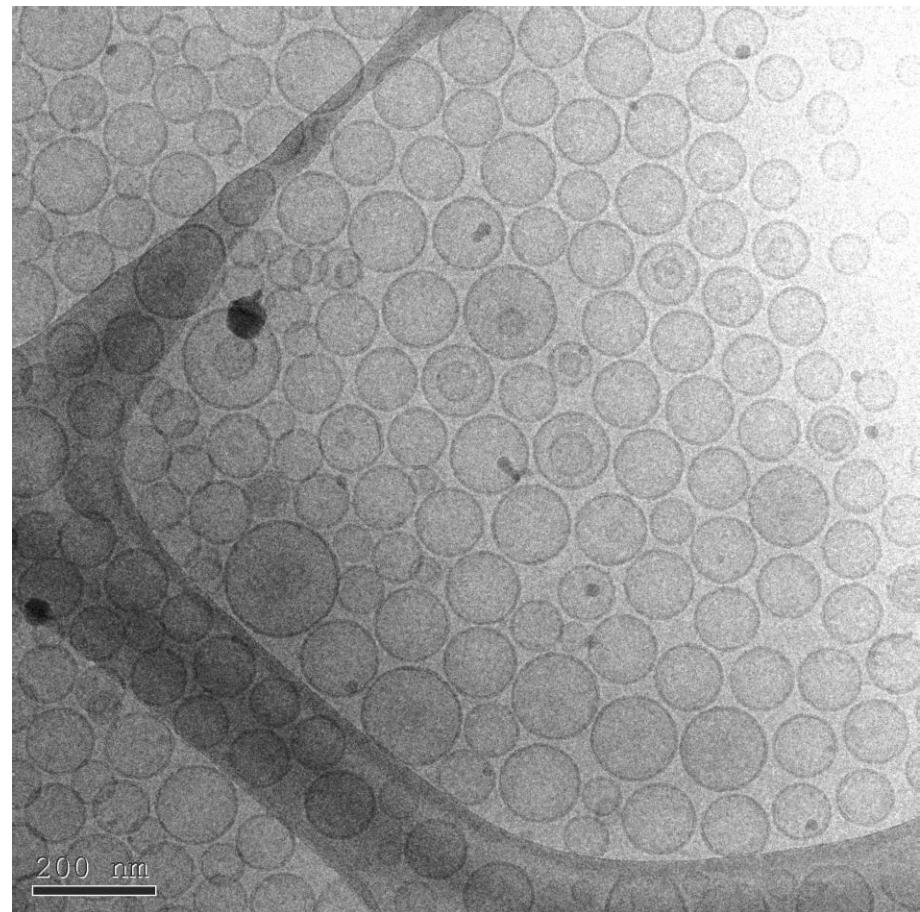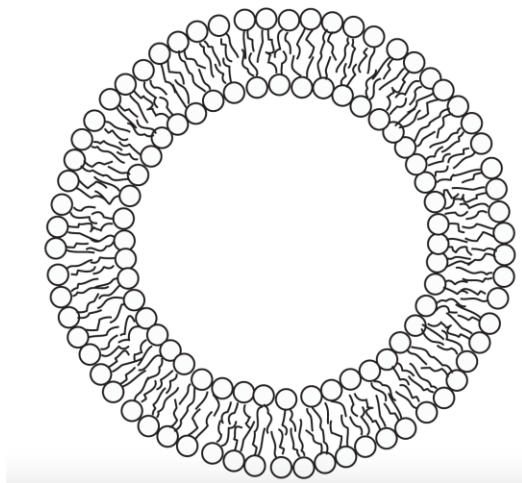
Hagfish defending mechanism

Great Barrier Island, NEW ZEALAND   Depth: 681m

Hagfish slime

Lukas Böni, Simon Kuster ETH Zurich

composition of hagfish slime

swell & rupture

Vesicles → **Mucin**

Exudate + *water* + *flow* → **Slime**

Skeins unravel → **Threads**

15 µm

150 µm

30 µm

+ water + flow
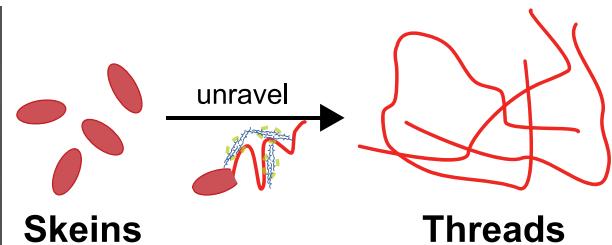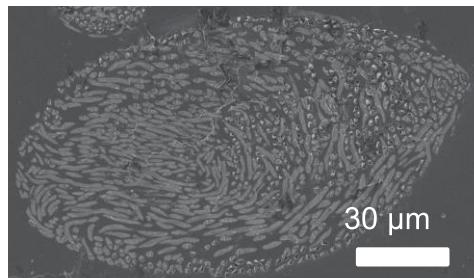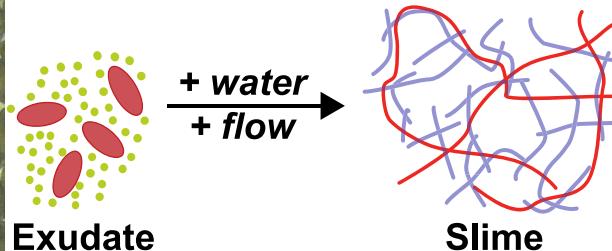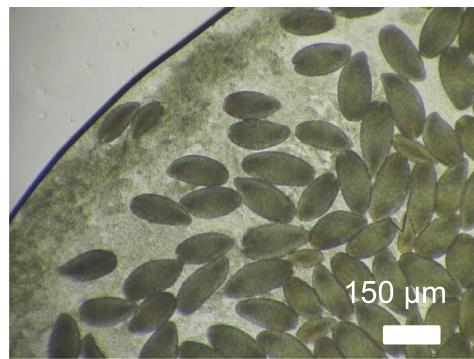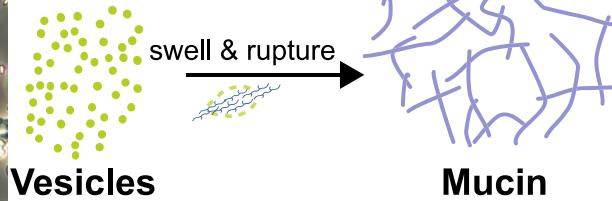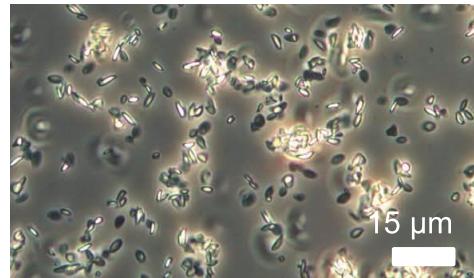
Lukas Böni, Simon Kuster ETH Zurich
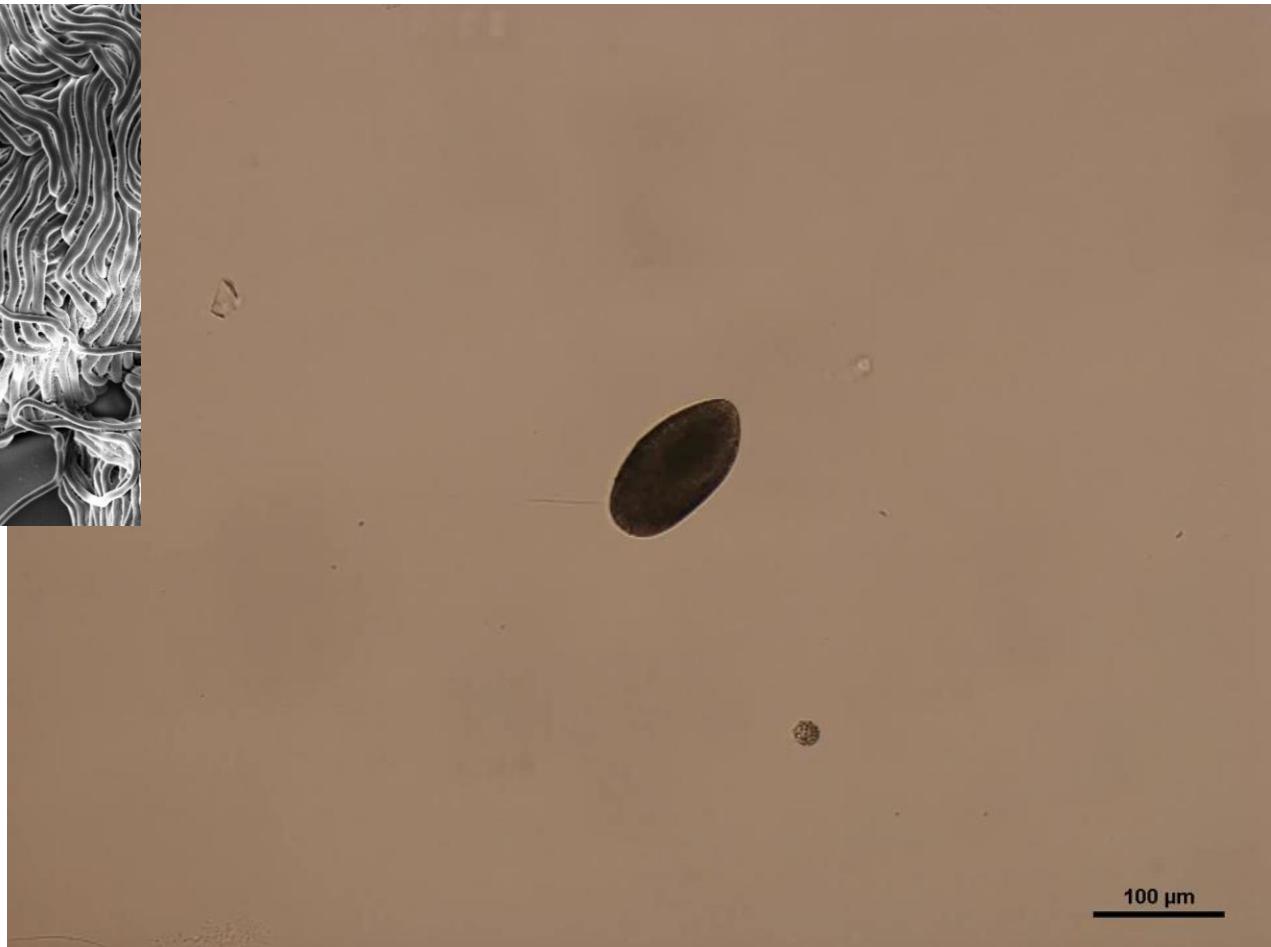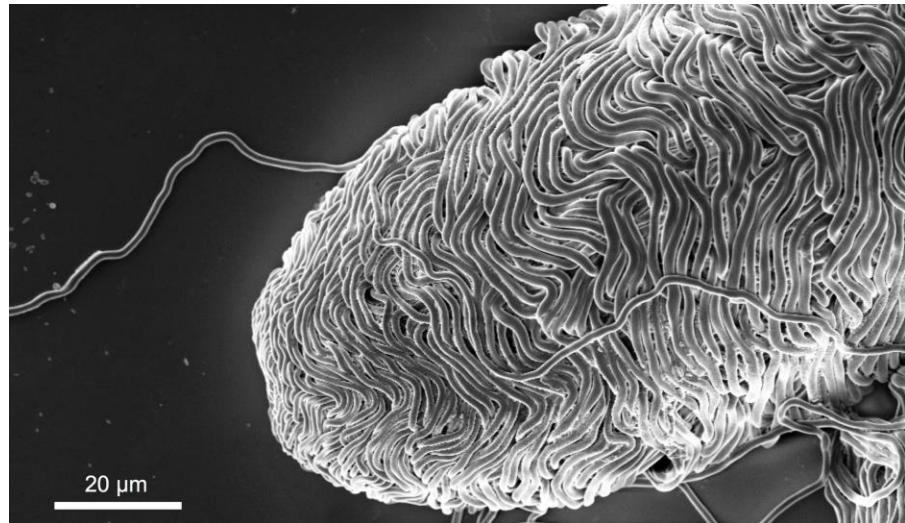
Lukas Böni, Simon Kuster ETH Zurich
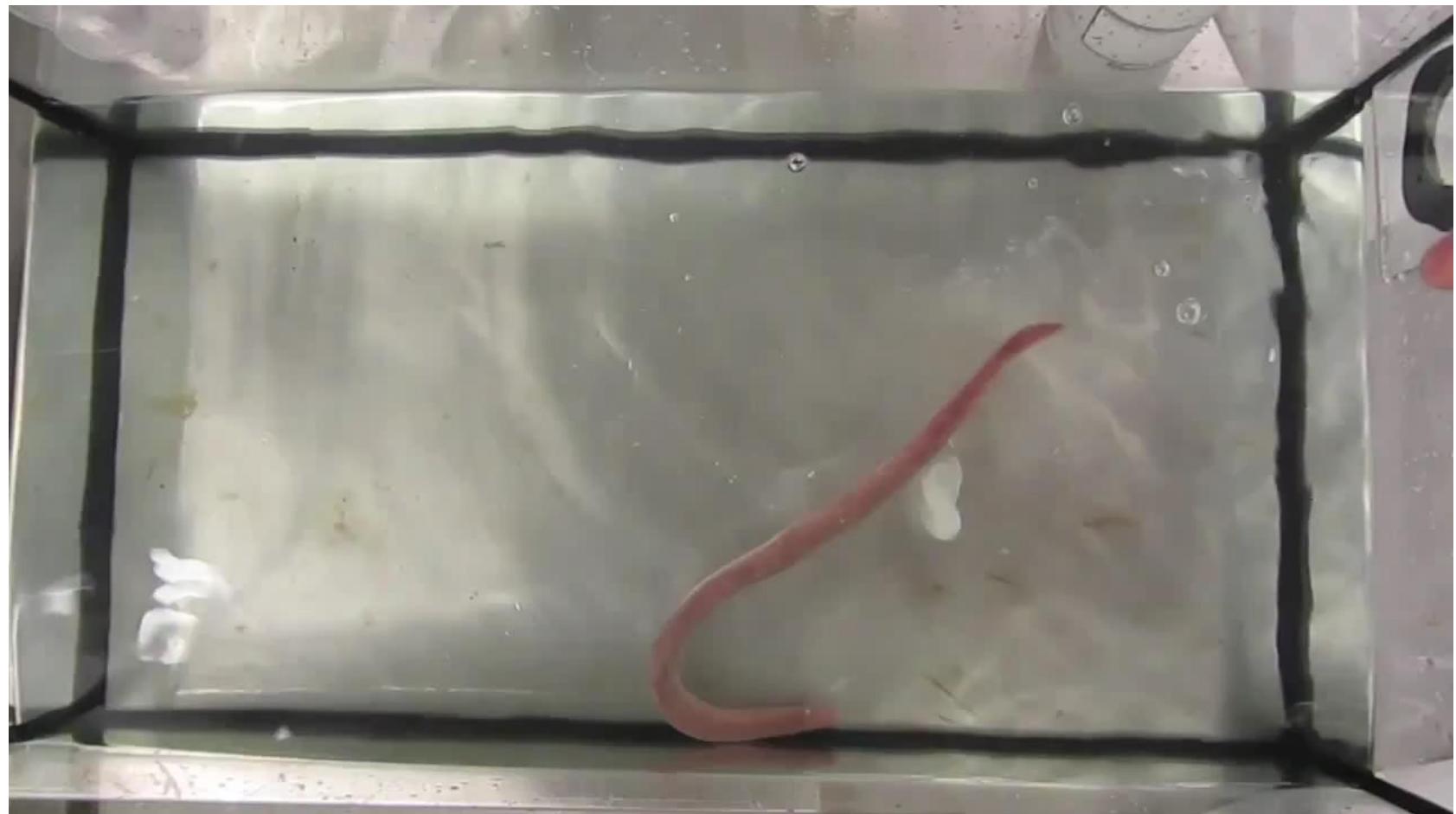
Scientific Reports **6**, 30371 (2016)

# Biological Materials: main components of life

- Polymeric molecules:
    - Nucleic acids (DNA, RNA)
    - Proteins
    - Polysaccharide (random sequence)

- Lipids: fats and oils

- Amphiphilic molecules (self-assembly)
    - phospholipids

- **Biominerals**
    - **Calcium phosphate** (example: hydroxyapatite in bone)
    - **Calcium carbonate** (example aragonite and calcite in mollusk shells)
    - **Silicates** (diatoms)

# Biomineral: example calcium carbonate

The crystalline structure of Calcium carbonate: Polymorph
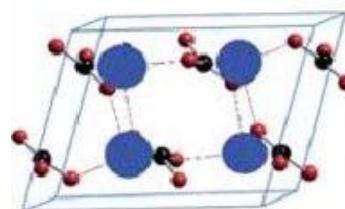

trigonal — Calcite
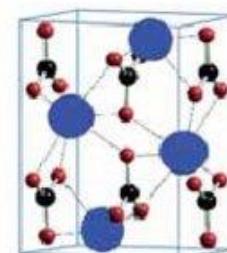
orthorombic — Aragonite

hexagonal — Vaterite
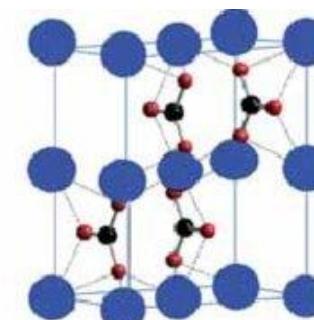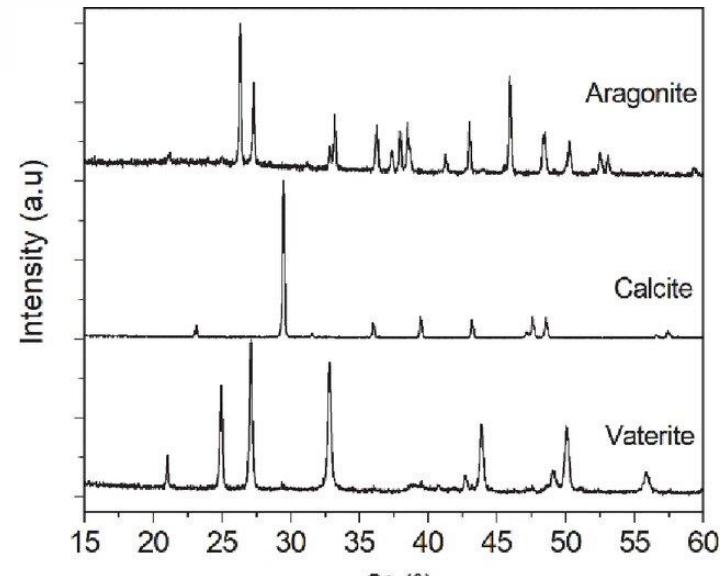
CO_3^{2-} Ca^{2+}

Biomineral: example calcium carbonate

The crystalline structure of Calcium carbonate: Polymorph
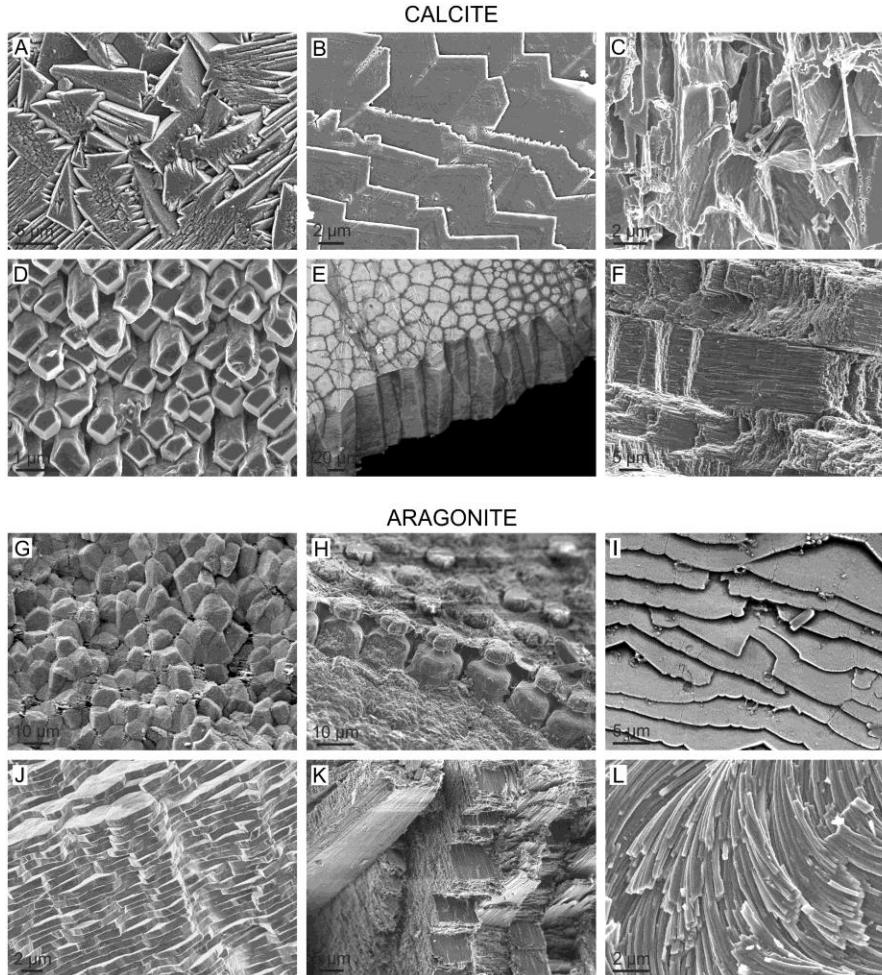
and different microstructure for the same crystal structure

Checa A.G. "Physical and Biological Determinants of the Fabriation of Molluscan Shell Microstructure", Front. Mar. Scie, 2018, 5

Example: Mollusk shell

The crystalline structure of Calcium carbonate: Polymorph

prismatic layer: mainly calcite

nacre layer: mainly aragonite
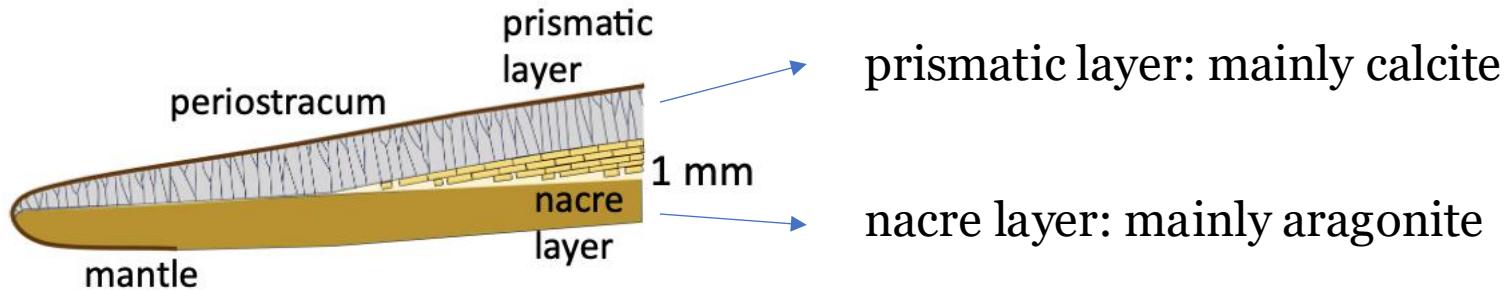
composite material of crystalline component (95-99%) and an organic fraction (0.1-5%)

Chen, Y., et al. (2021). Advances in mechanics of hierarchical composite materials. *Composites Science and Technology*, *214*, 108970.

Summary biological materials

- biological materials

- structure of some important biological building blocks:
    - nucleic acids (DNA/RNA), specific base pairing for replication and encoding of protein structure, chromosome and random walk
    - proteins, hierarchical structure, specific 3D structure for function (not random walk!), chiral space groups
    - polysaccharides: carbohydrates, energy & strutcture
    - lipids
    - amphiphilies, aggregates formed depend on the molecular packing parameter
    - biominerals, crystal structure polymorph and strictly controlled in biological crystallization