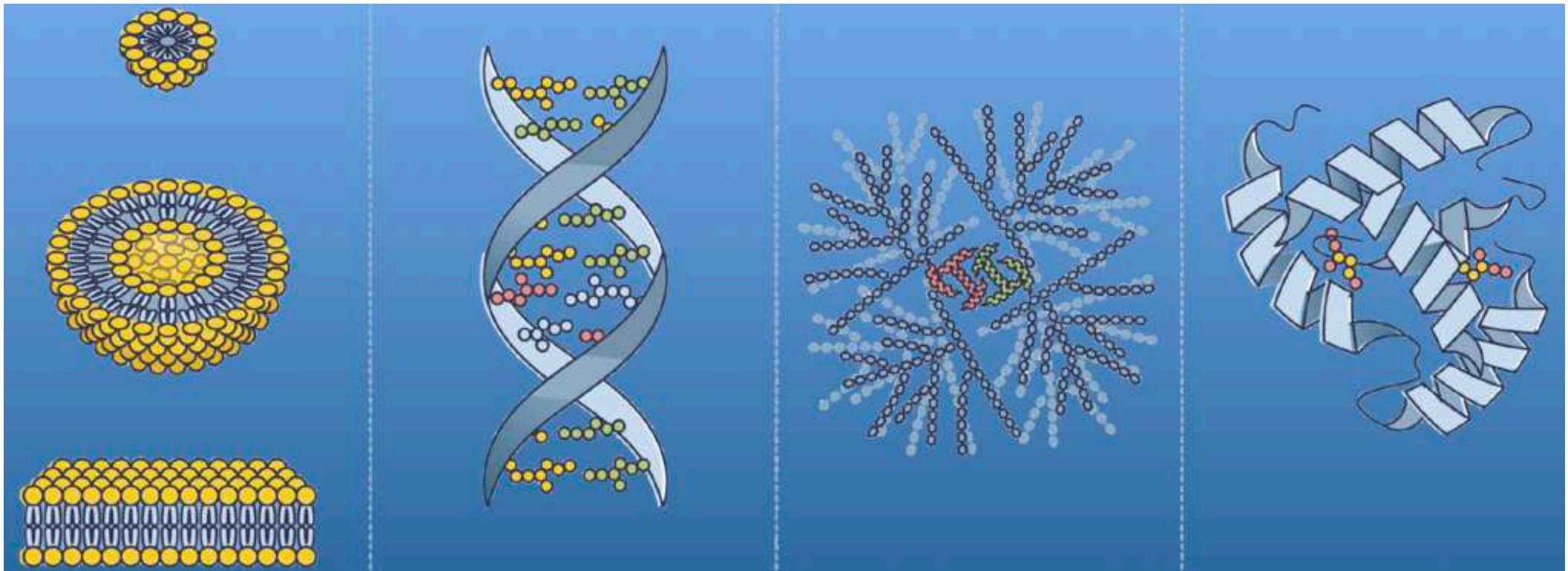


The molecular logic of life

Small molecules (building blocks) common to all organisms are ordered into unique macromolecules or polymers (biomolecules)



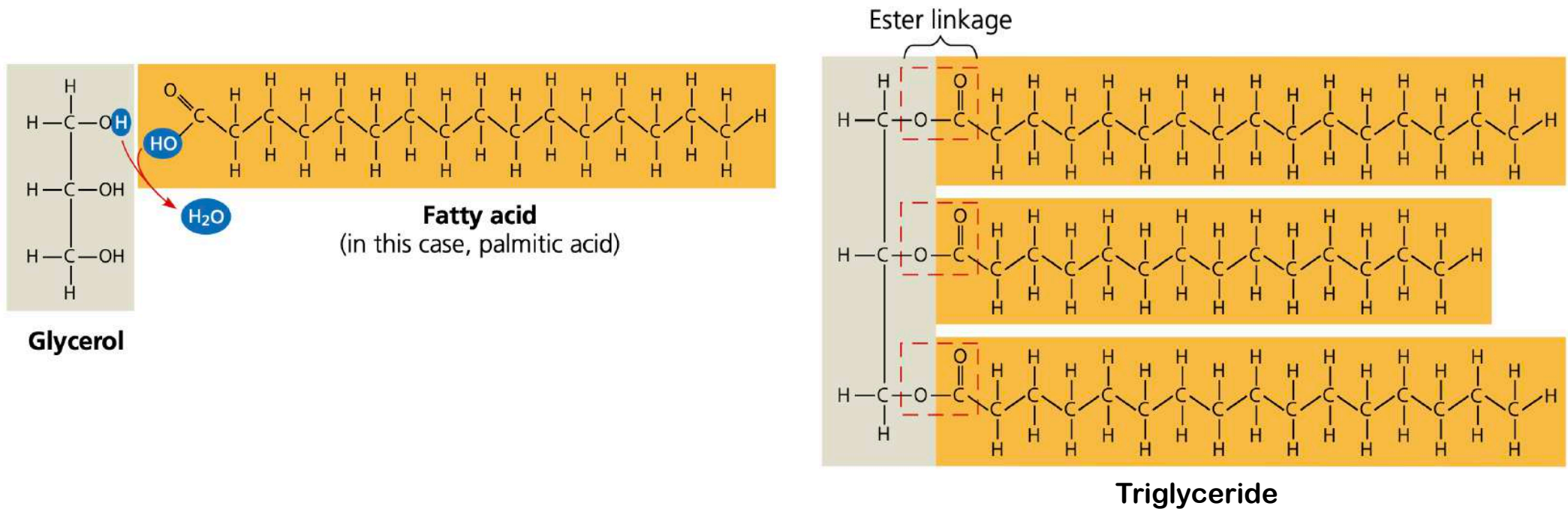
Lipids
(Fat)

Nucleic Acids
(DNA or RNA)

Carbohydrates
(Sugars, Starches
and Fibers)

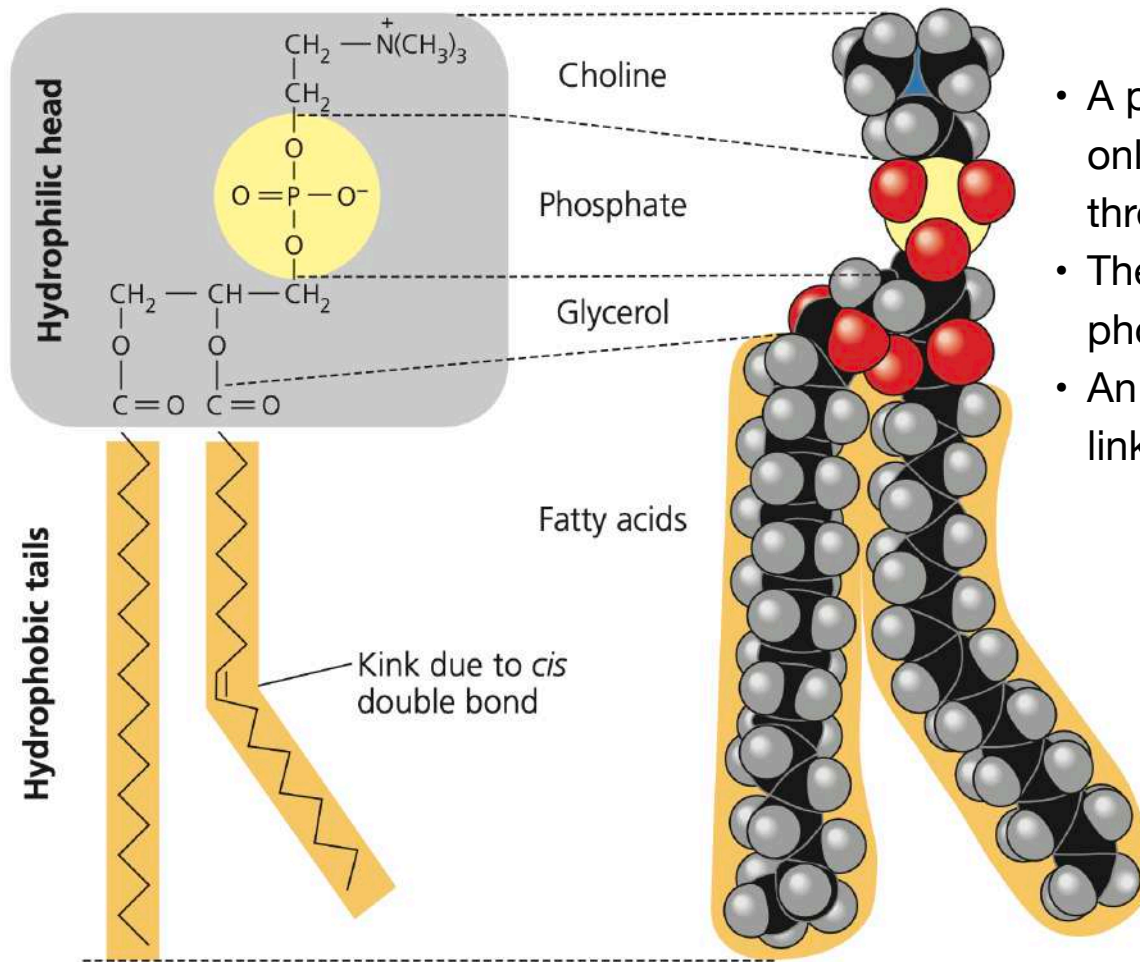
Proteins

Lipids (fats)



- Not true polymers
- Large biomolecules assembled from two kinds of smaller molecules: glycerol and fatty acids
- Instead of glycerol, lipids can also have Sphingosine = sphingolipids
- One lipid molecule is three fatty acid molecules joined to glycerol by an ester linkage = Triacylglycerol or Triglyceride

Phospholipids

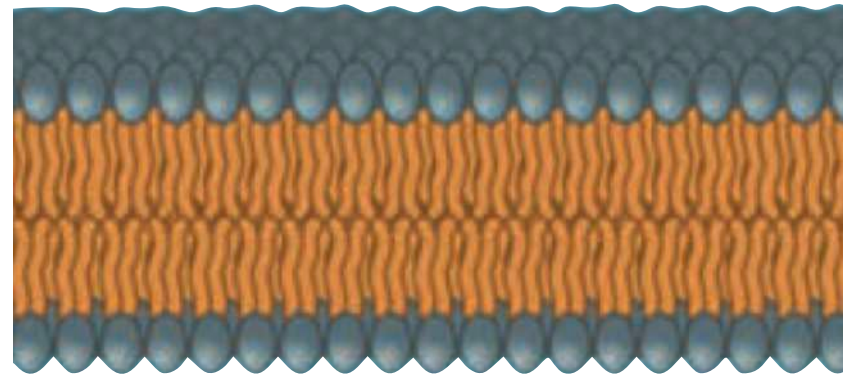
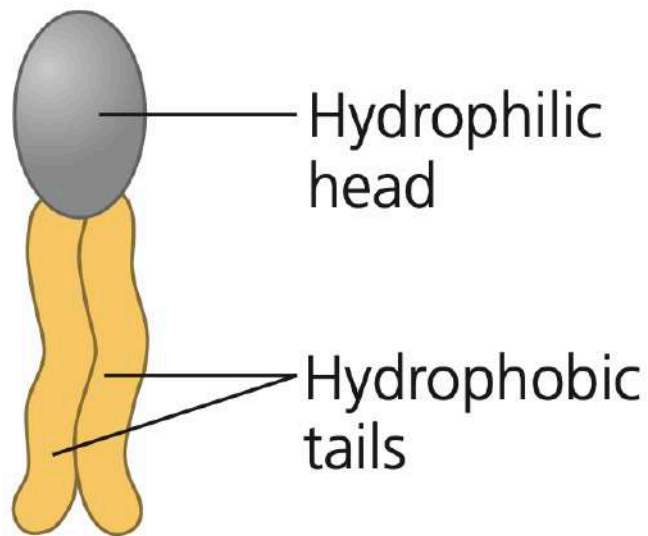


- A phospholipid is similar to a fat molecule but has only two fatty acids attached to glycerol instead of three
- The third hydroxyl group of glycerol is joined to a phosphate group
- An additional small charged or polar molecule is also linked to the phosphate group - e.g. choline

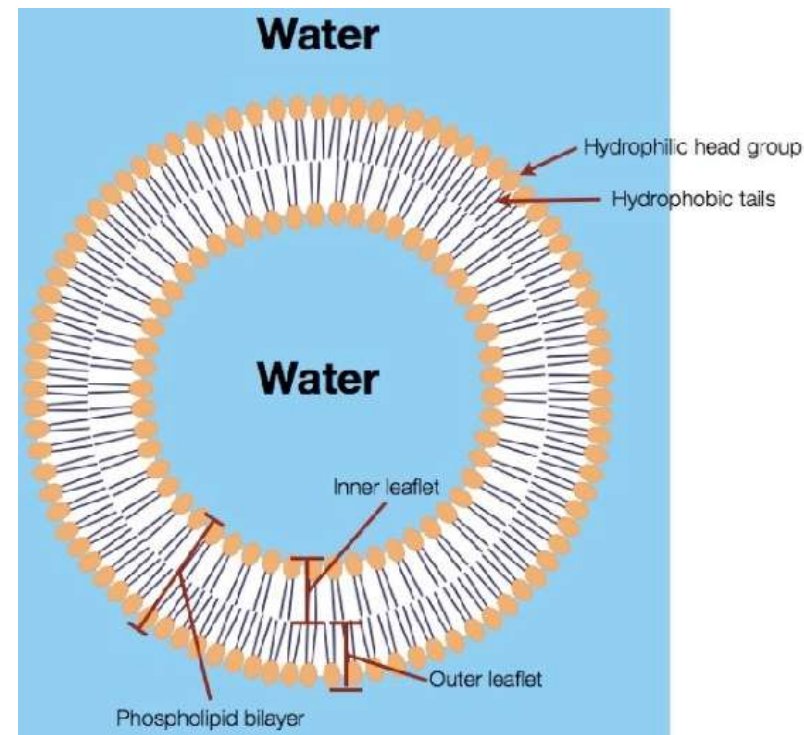
Phospholipids have a phosphate “head” and a lipid “tail”

- The “head” is hydrophilic and “tail” is hydrophobic
- Due to this property, when phospholipids are added to water, they self assemble into biomolecules

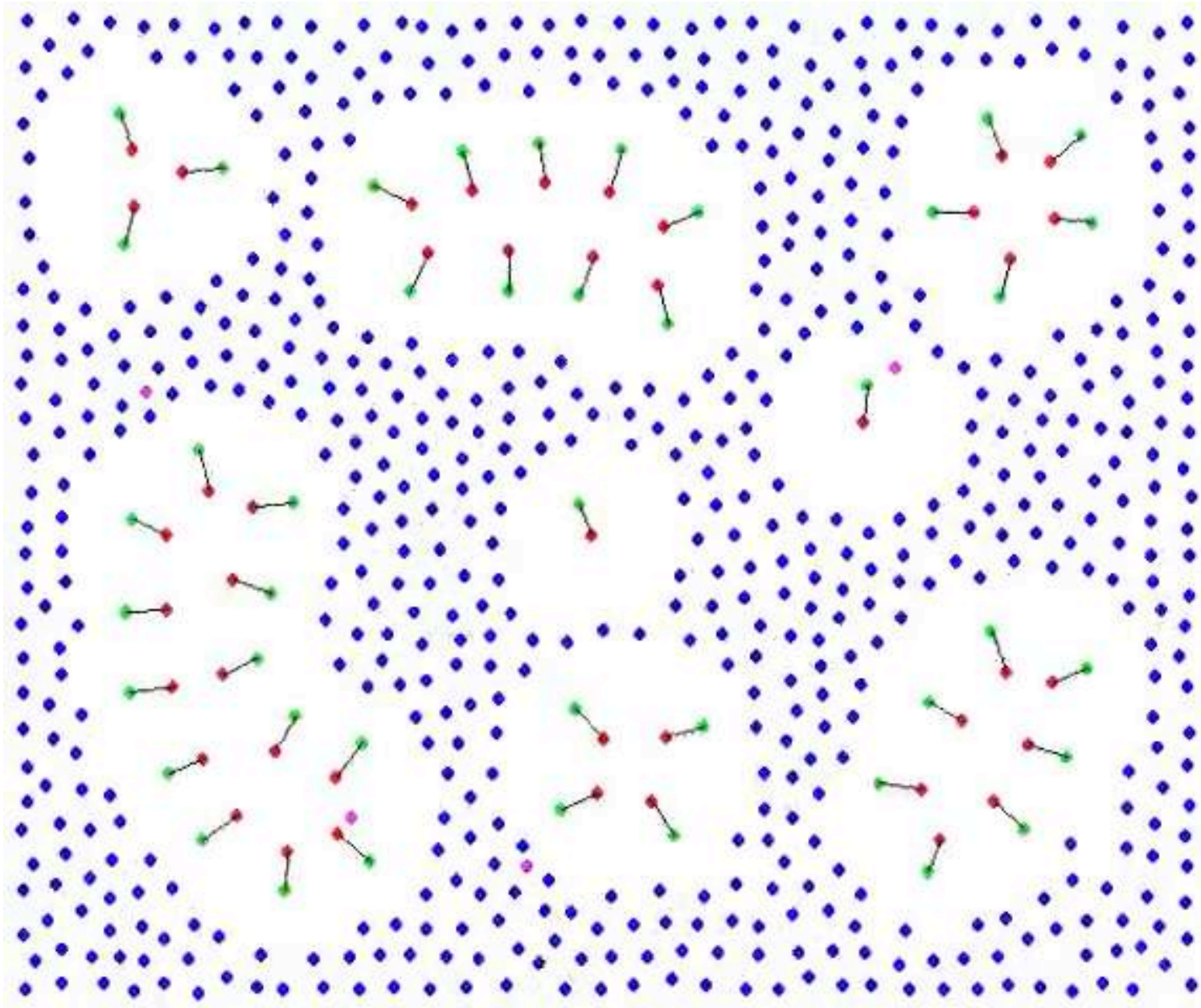
What will phospholipid self-assembly in water look like?



These self-assembled structures are known as lipid bilayers
They are the “envelope” for enclosures known as “cells”

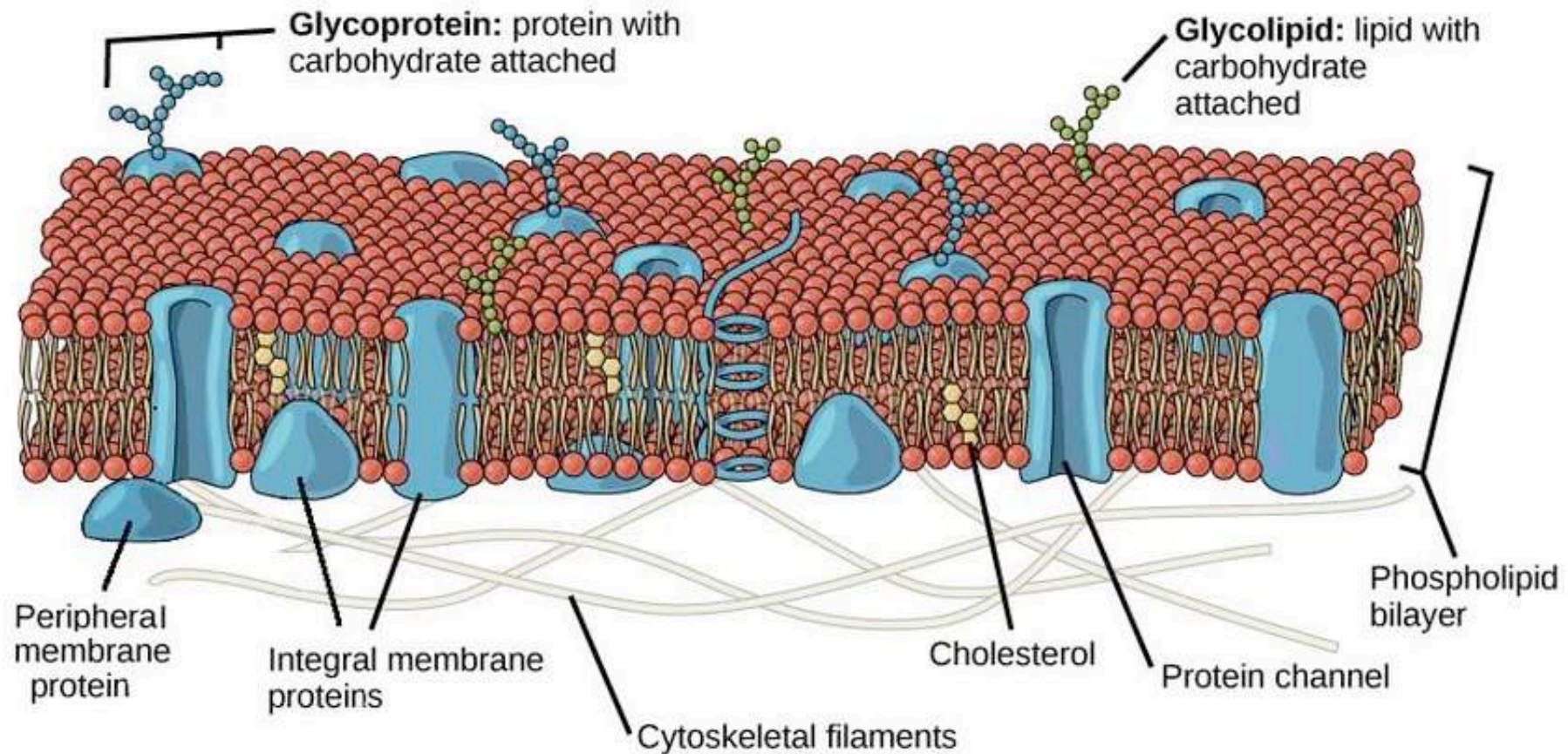


A 2D model of lipid bilayers self-assembling in water



Code for the animation: <https://www.openprocessing.org/sketch...>

The fluid mosaic model of the cell membrane



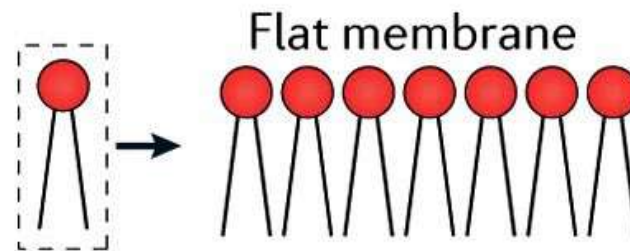
- Singer-Nicolson Fluid Mosaic model for cell membranes proposed in 1972
- Cell membrane is discontinuous - biomolecules interspersed with lipids, embedded and spanning the bilayer
- It is a barrier with variable mechanical properties - depends on composition of the phospholipids, types of proteins, etc
- Phospholipids can “flip” across the bilayer

size balance between the head group and hydrophobic tails of lipids affect membrane spontaneous curvature

Lipid species and spontaneous membrane curvature

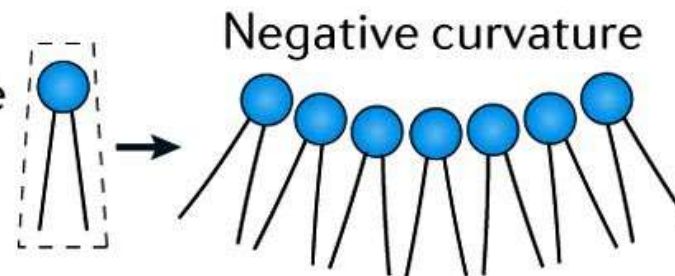
Cylindrical

- Phosphatidylcholine
- Phosphatidylserine



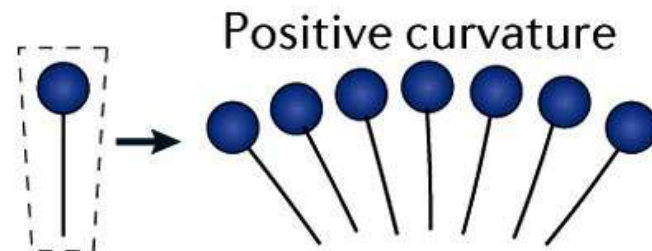
Conical

- Phosphatidylethanolamine
- Phosphatidic acid

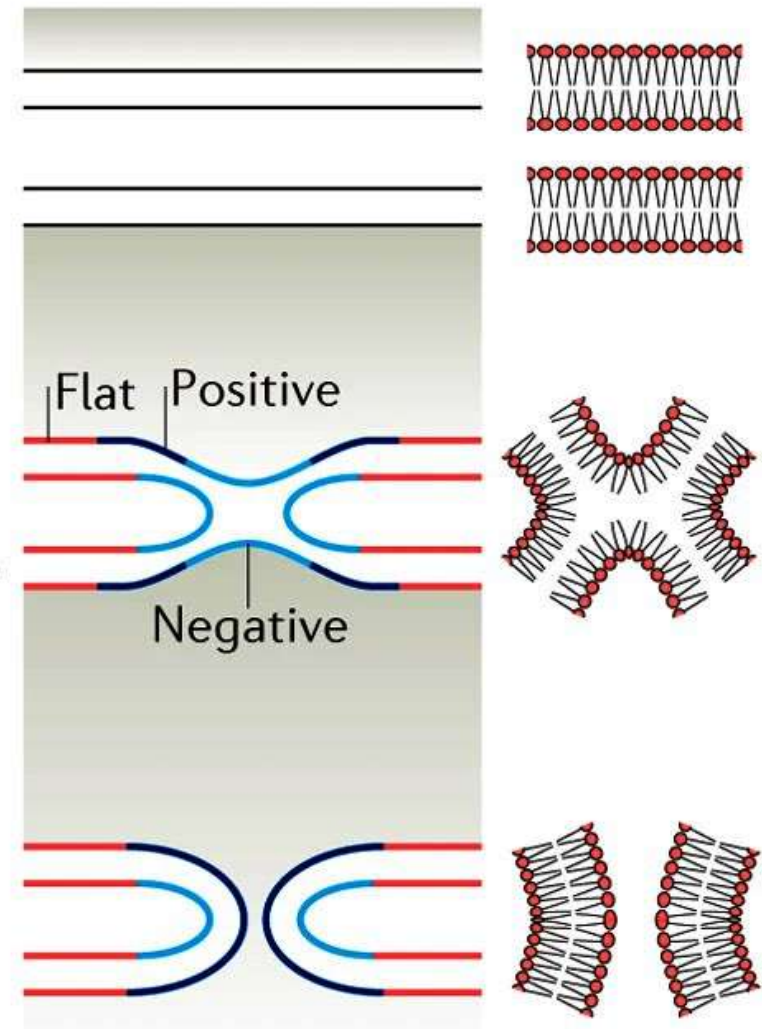


Inverted-conical

- Lyso-GPLs
- Phosphoinositides



Membrane curvature and fission

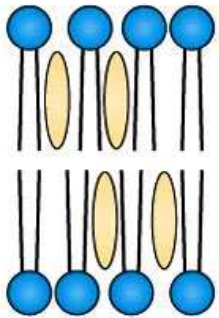


Type of lipids in the cell membrane affect membrane contours and mechanical properties

b Fluidity and/or phase behaviour

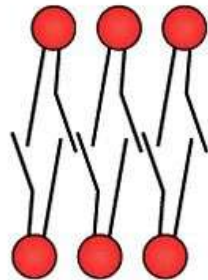
Model membranes

Liquid-ordered

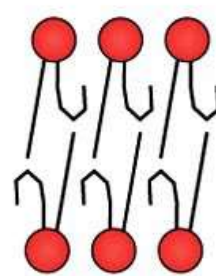


- Saturated lipids
- Cholesterol

Liquid-disordered



Mono-unsaturated lipids



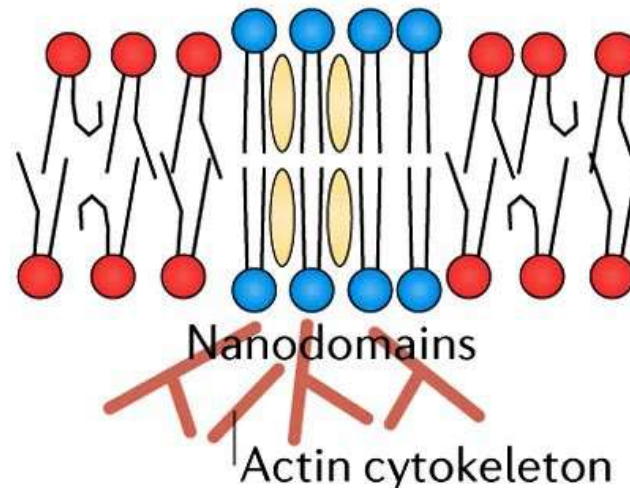
Poly-unsaturated lipids

- Unsaturated lipid tails increases membrane fluidity.
- Extent of unsaturation of lipids in the membrane might affect its organization.
- Saturated lipids and cholesterol generate liquid-ordered phases, and unsaturated lipids generate liquid-disordered phases

Cells

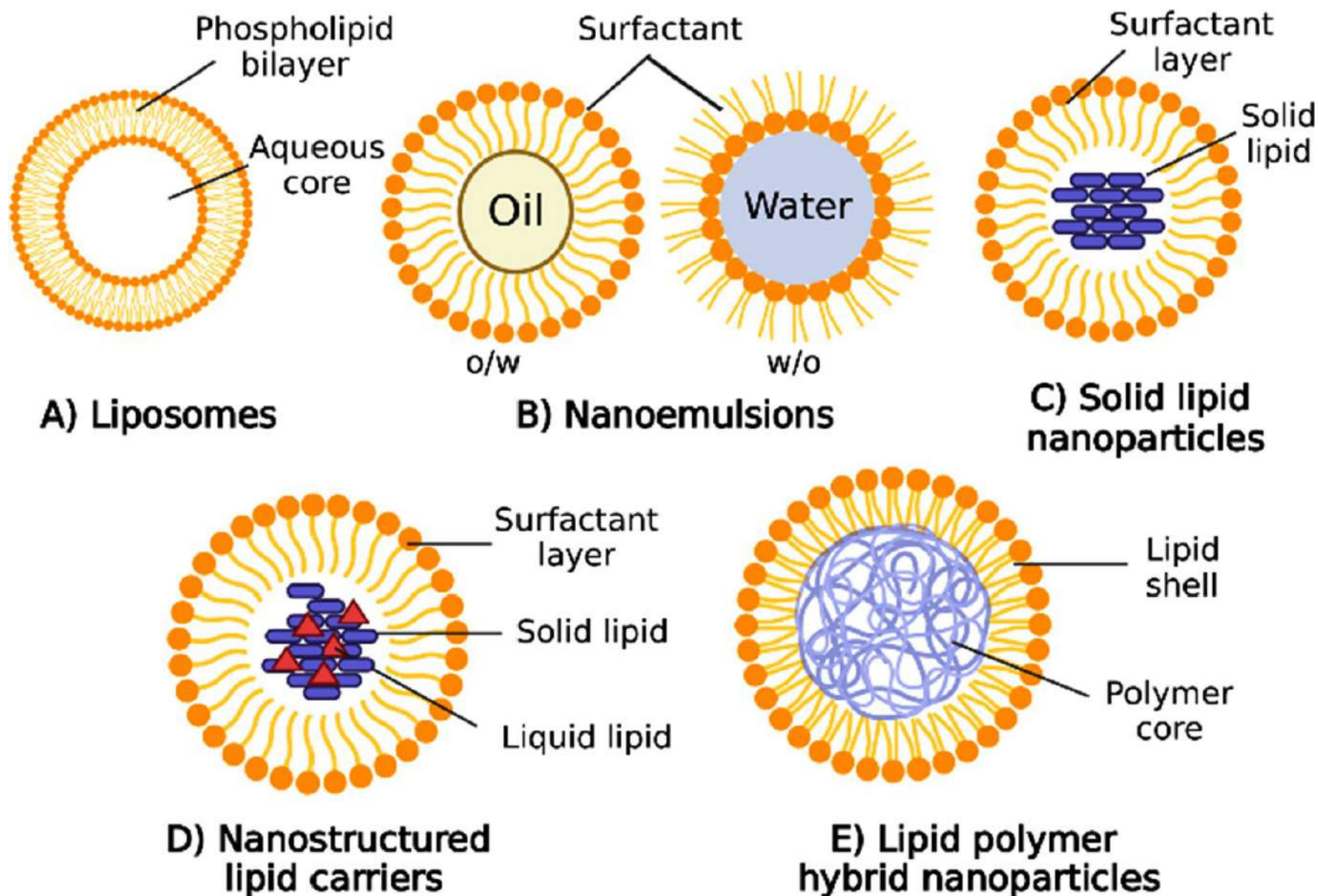
Lateral heterogeneity

- Initiated by proteins and stabilized by lipids
- Driven by lipid immiscibility and phase separation?



Lateral heterogeneities in membrane fluidity generating distinct nanodomains - special areas where different types of activity can occur

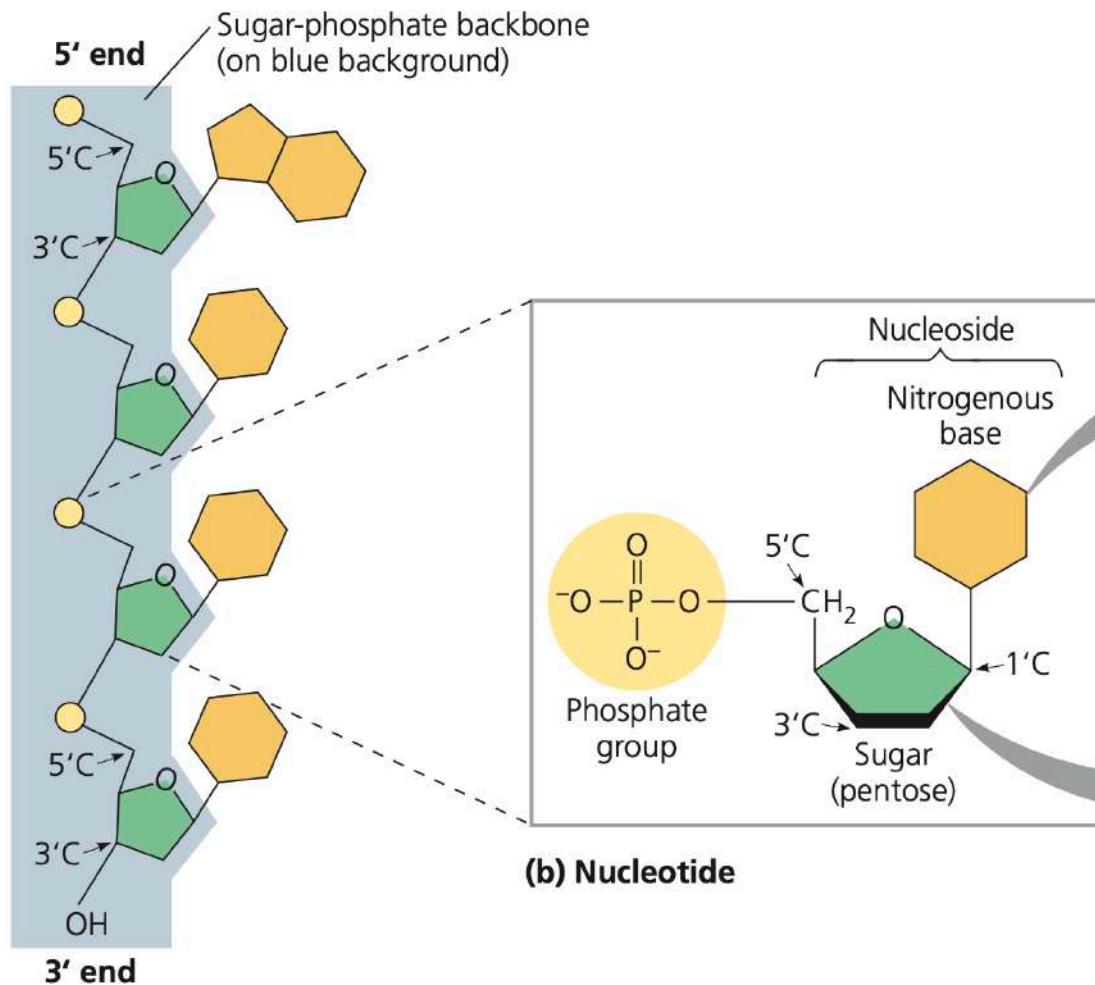
Lipids for drug delivery - Lipid Nano Particles



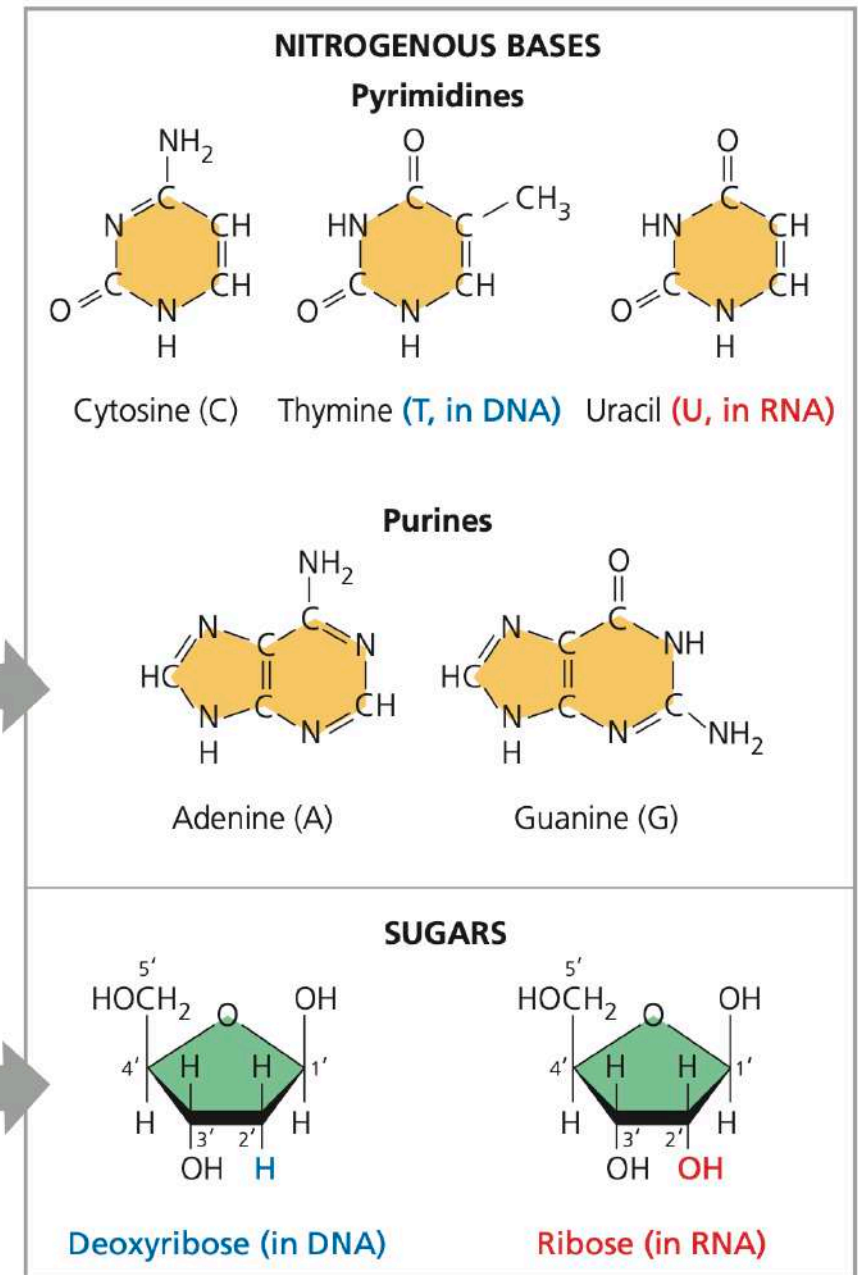
Used for targeted and contained drug delivery

Nucleic Acids (DNA and RNA)

- Nucleic acids are polymers of polynucleotides
- monomer is a nucleotide
- Nucleotide has 3 parts: a five-carbon sugar (a pentose), a nitrogen-containing (nitrogenous) base, and one or more phosphate groups



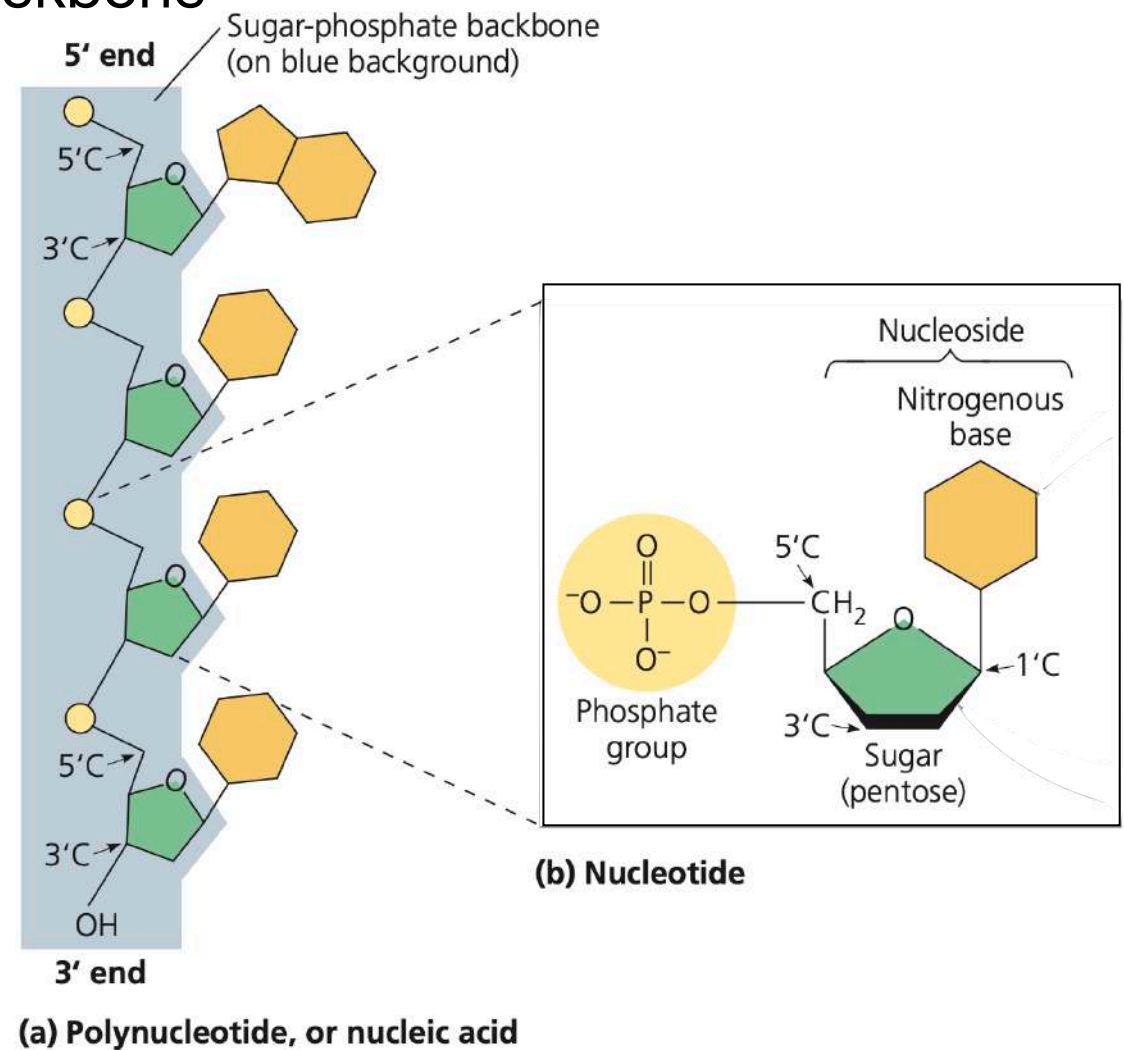
(a) Polynucleotide, or nucleic acid



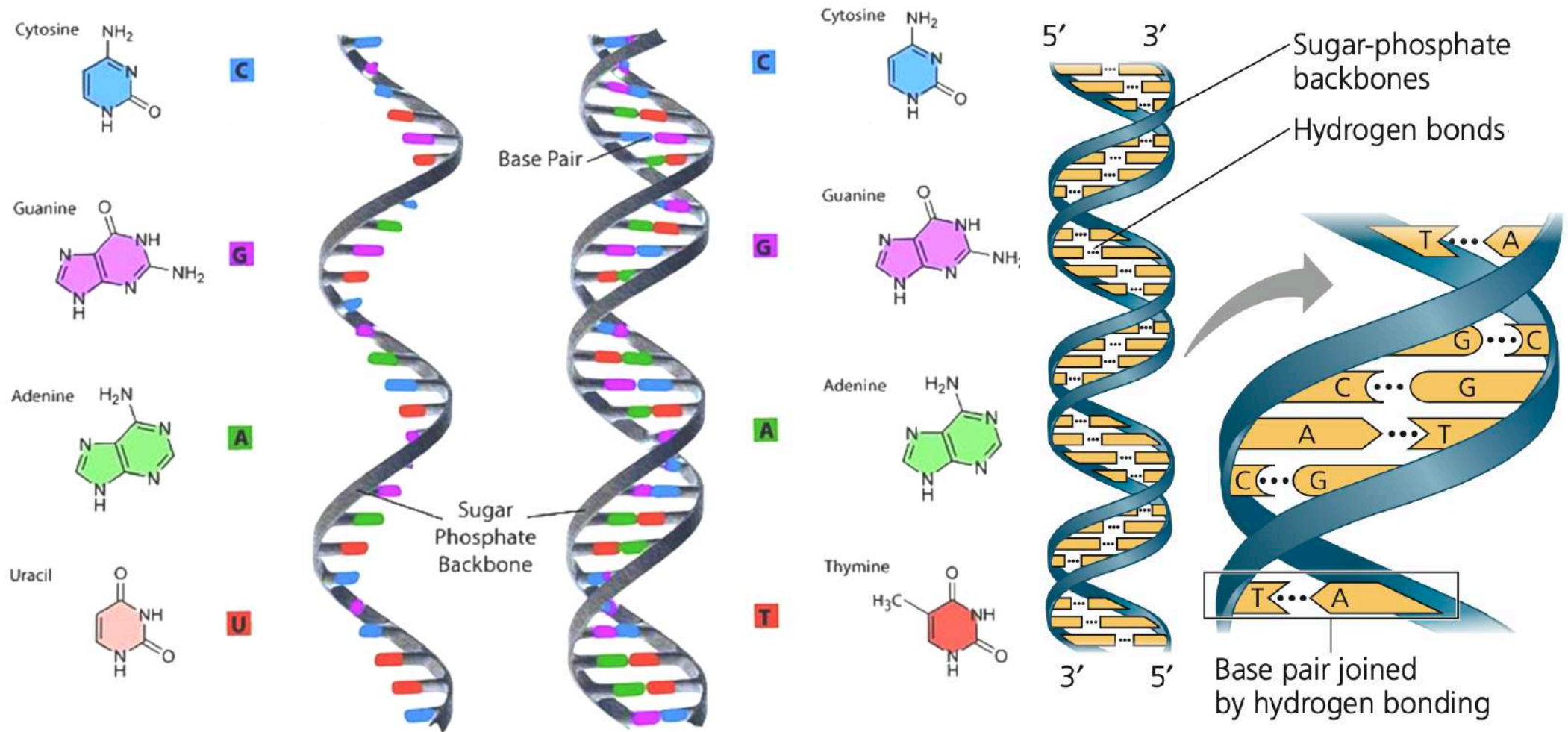
(c) Nucleoside components

- Nucleotides are joined by a phosphodiester linkage = a phosphate group linking sugars of two nucleotides.
- This bonding results in a repeating pattern of sugar-phosphate units called the sugar-phosphate backbone

- The two free ends of the polynucleotide are distinct - one end has a phosphate attached to a 5' carbon, and the other end has a hydroxyl group on a 3' carbon
- These are known as the 5' end and the 3' end, respectively, giving the polynucleotide a built-in directionality along its sugar-phosphate backbone, from 5' to 3'

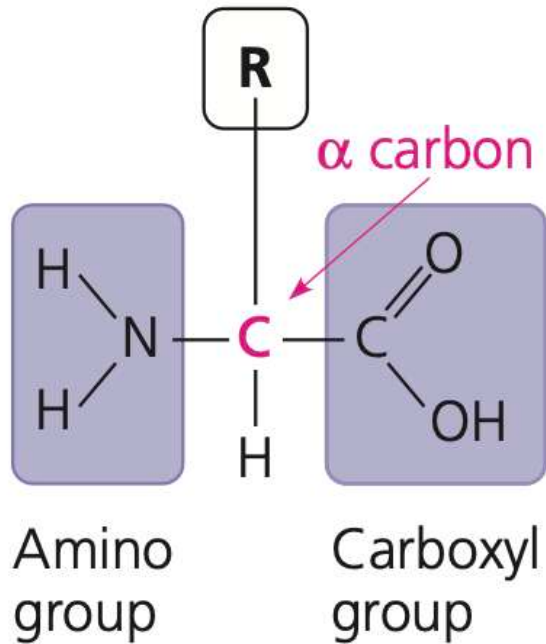


Deoxyribonucleic acid and Ribonucleic acid

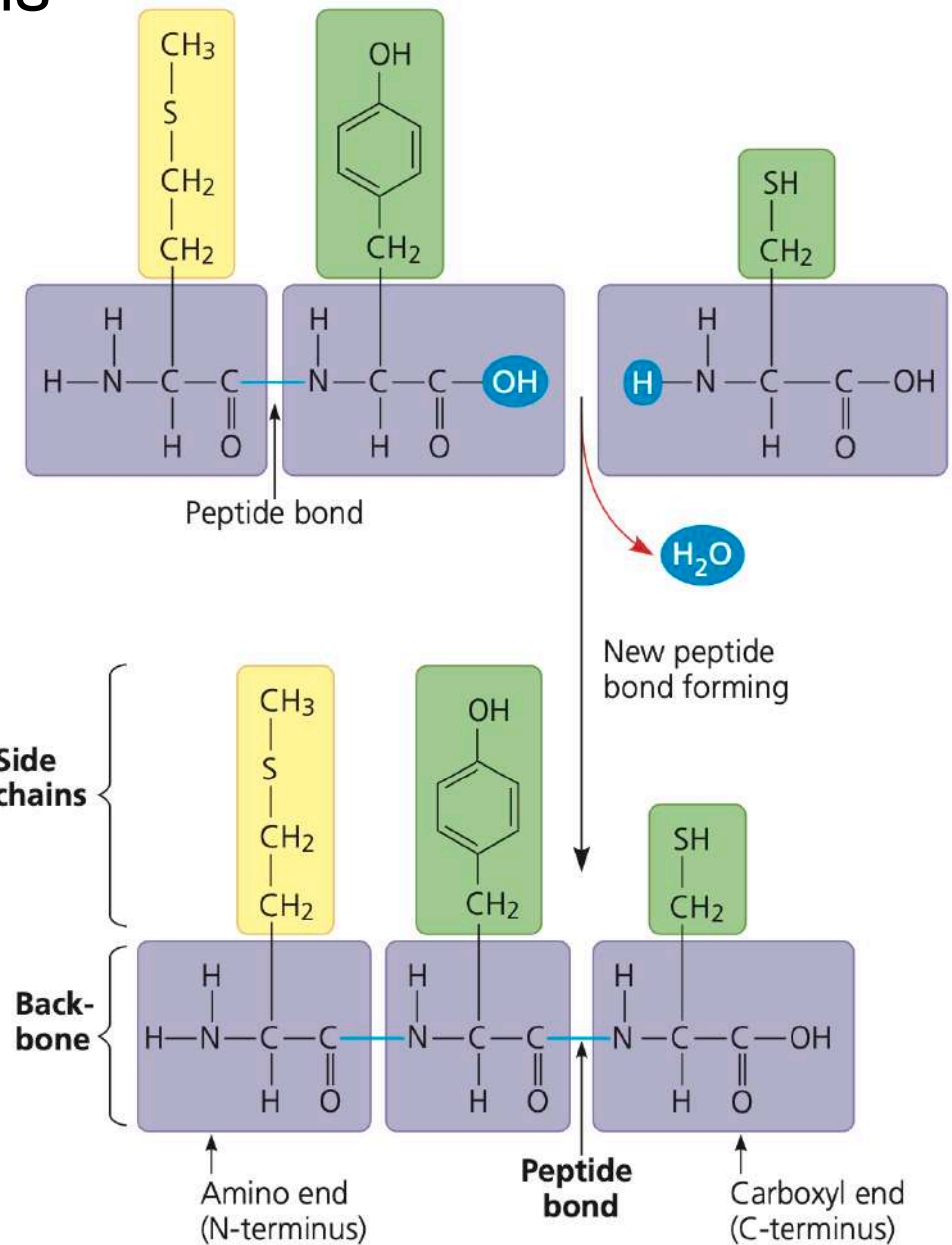


- Base complementarity between A-T/U and G-C
- If you know one, you can predict the other half of a pair of nucleotides
- If you know information in one strand - you can predict the information in the other
- If you know the information in DNA - you can predict the information in the RNA
- If you know the information in RNA - you can predict the information in the DNA

Side chain (R group)

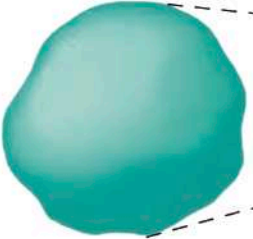
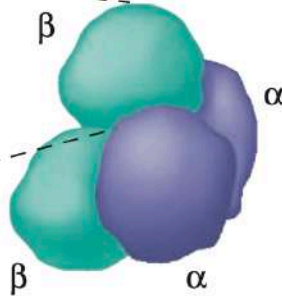
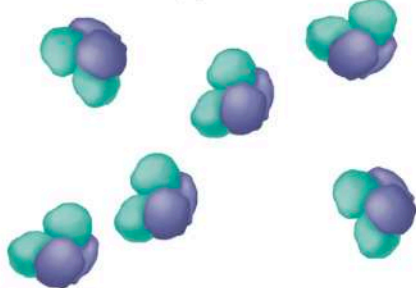

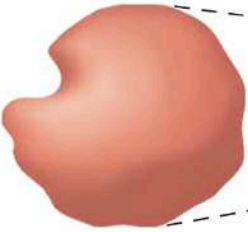
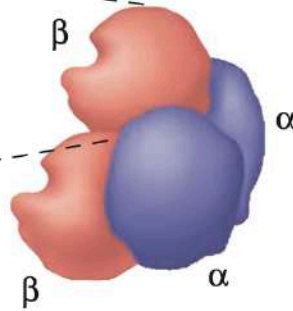
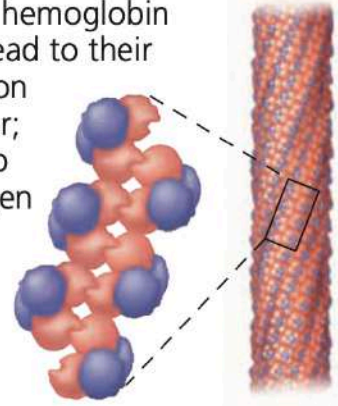



Proteins



- An amino acid is an organic molecule with both an amino group and a carboxyl group
- The R group, also called the side chain, differs with each amino acid
- Amino acids are joined by a covalent (called a peptide bond) to form polymers known as proteins

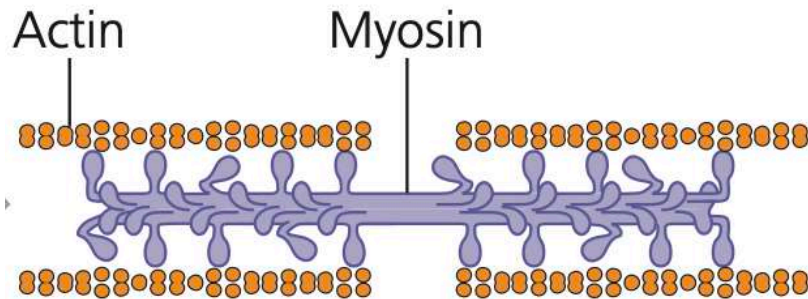
Protein sequence, structure and function

	Primary Structure	Secondary and Tertiary Structures	Quaternary Structure	Function	Red Blood Cell Shape
Normal hemoglobin	1 Val 2 His 3 Leu 4 Thr 5 Pro 6 Glu 7 Glu	Normal β subunit 	Normal hemoglobin 	Normal hemoglobin proteins do not associate with one another; each carries oxygen. 	Normal red blood cells are full of individual hemoglobin proteins.  5 μ m
Sickle-cell hemoglobin	1 Val 2 His 3 Leu 4 Thr 5 Pro 6 Val 7 Glu	Sickle-cell β subunit 	Sickle-cell hemoglobin 	Hydrophobic interactions between sickle-cell hemoglobin proteins lead to their aggregation into a fiber; capacity to carry oxygen is greatly reduced. 	Fibers of abnormal hemoglobin deform red blood cell into sickle shape.  5 μ m

- Protein sequence is the primary structure
- The protein adopts secondary, tertiary and quaternary structures based on interactions amongst amino acids and cellular environment
- Protein structure is important for function

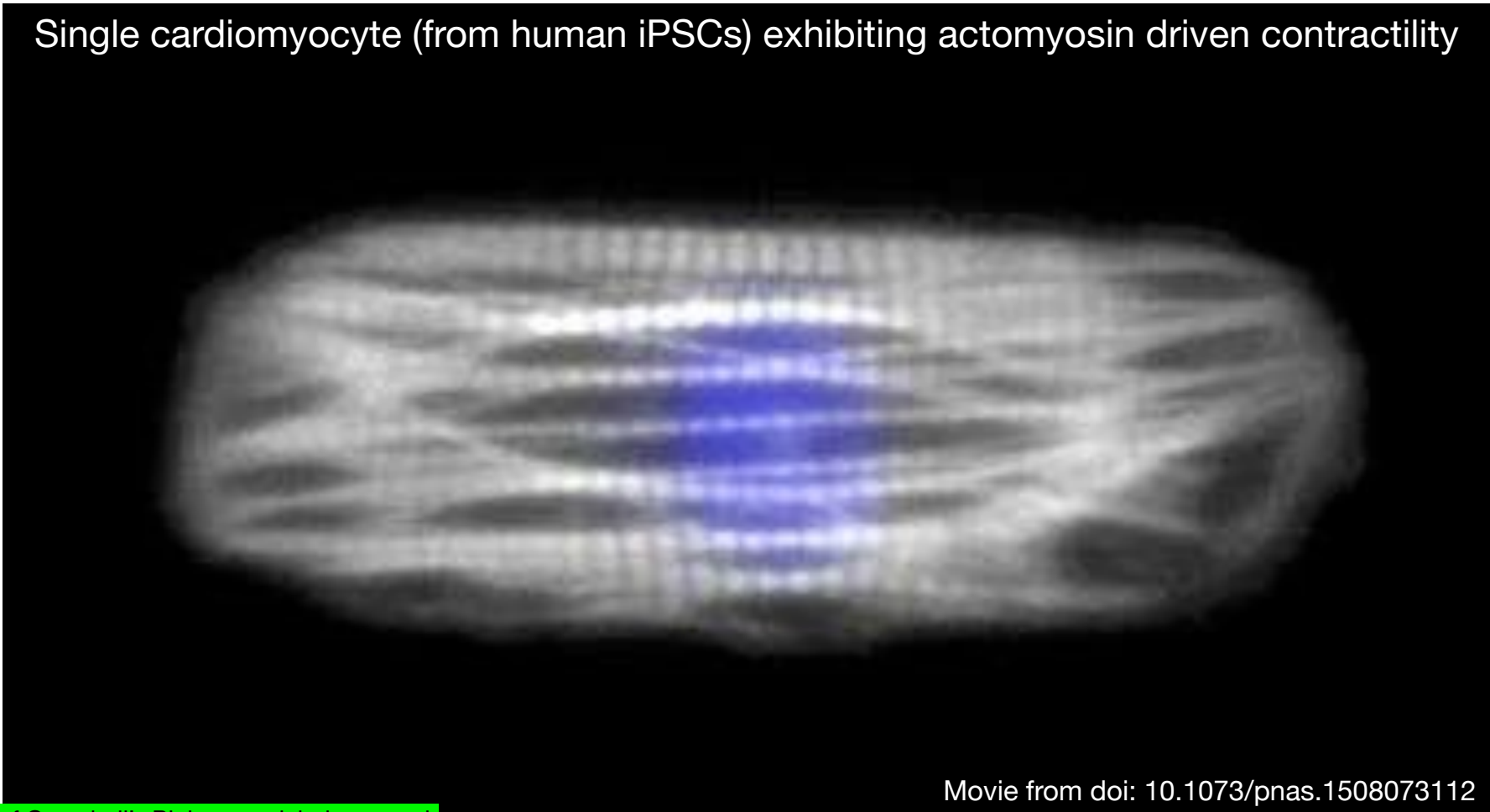
Protein function example: movement

Visible at the **level of entire cell** or at sub-microscopic levels inside cells



Cardiac muscle cell contraction: result of interactions between two proteins - actin and myosin inside cardiomyocytes of the heart

Single cardiomyocyte (from human iPSCs) exhibiting actomyosin driven contractility



Movie from doi: 10.1073/pnas.1508073112

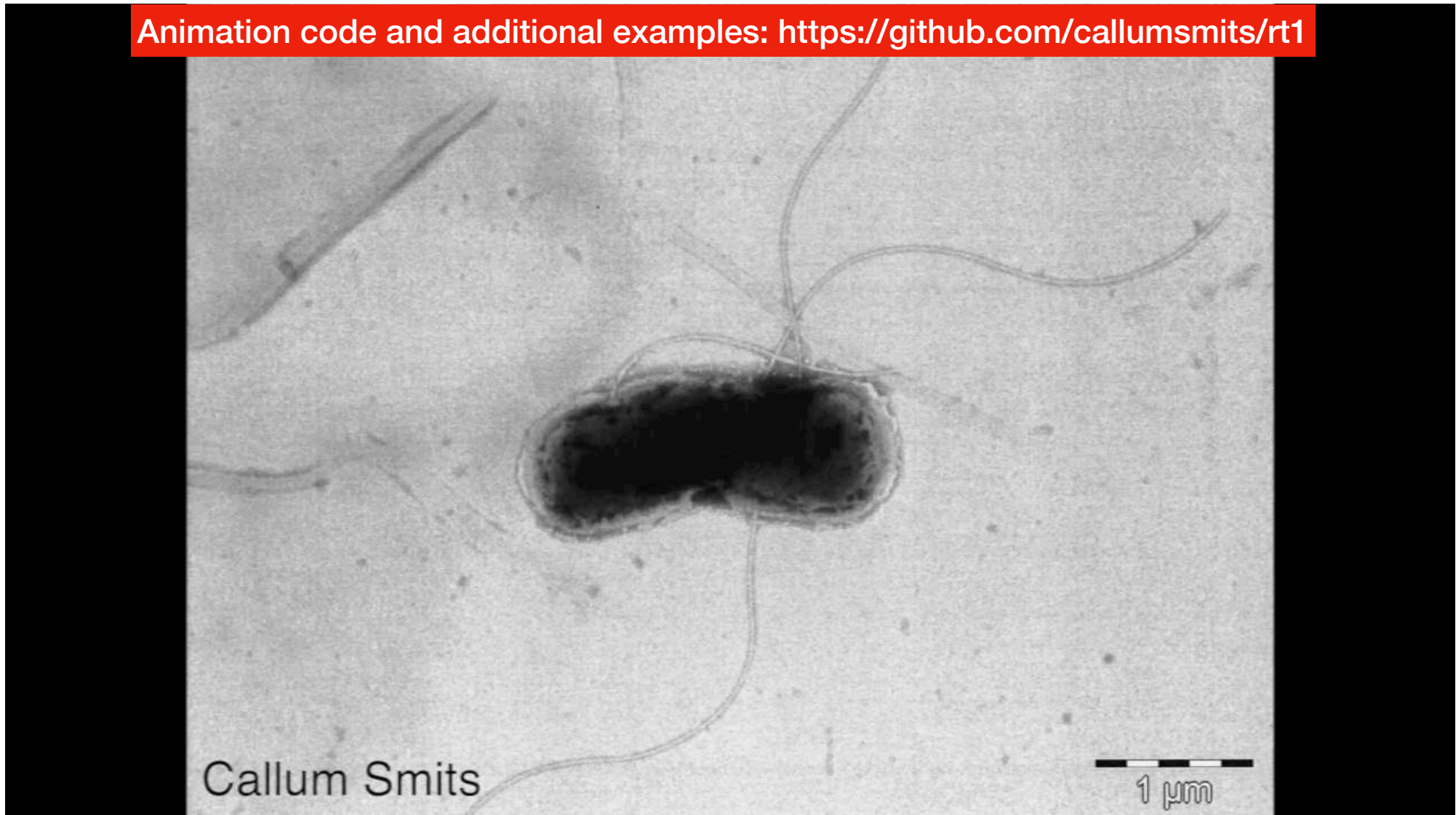
Protein function example: movement

Visible at the **level of entire cell** or at sub-microscopic levels inside cells

Some bacteria have “flagella” which help in their movement

Flagella is an organelle made of multiple proteins

Animation code and additional examples: <https://github.com/callumsmits/rt1>



Protein function example: movement

Visible at the level of entire cell or at **sub-microscopic levels inside cells**

- Cells have “roads” - microtubules and actin on which “motors” - kinesin, dynein, myosin “walk”
- This system is responsible for all transport inside cells

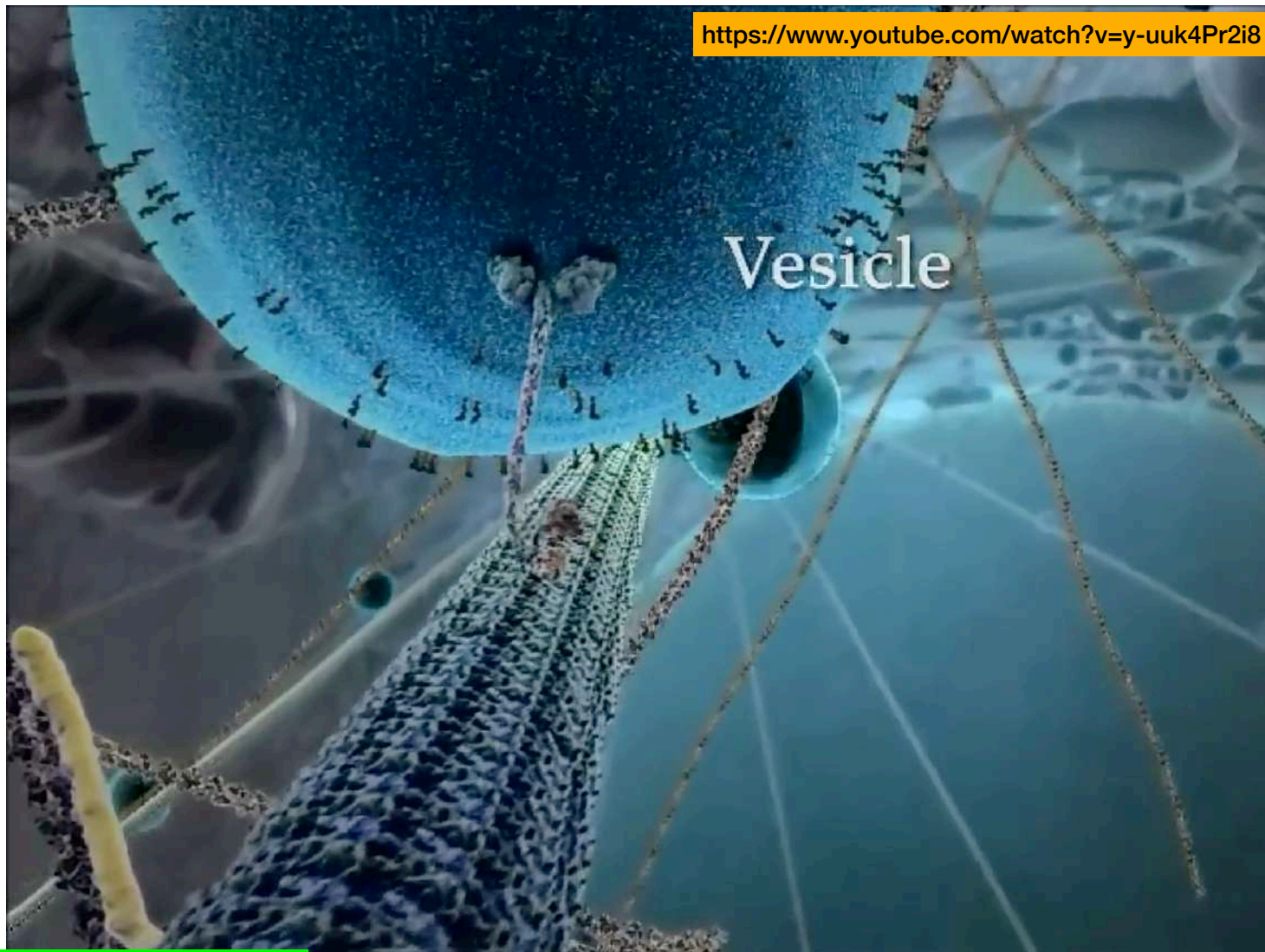


Figure 5.13 of Campbell's Biology: a global approach

Protein structure

Primary structure

–Ala–Glu–Val–Thr–Asp–Pro–Gly–

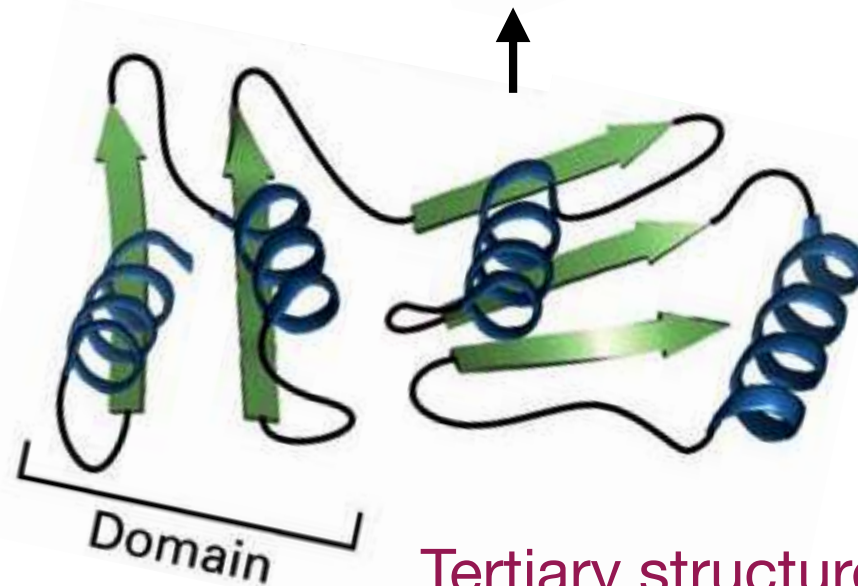
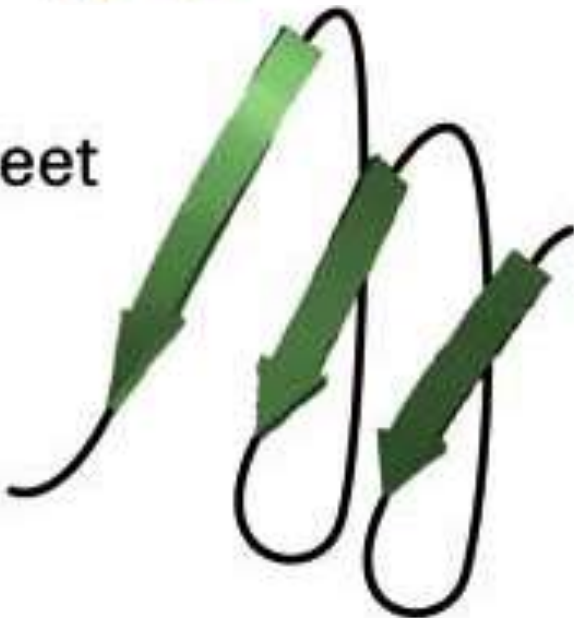


Secondary structures (examples)

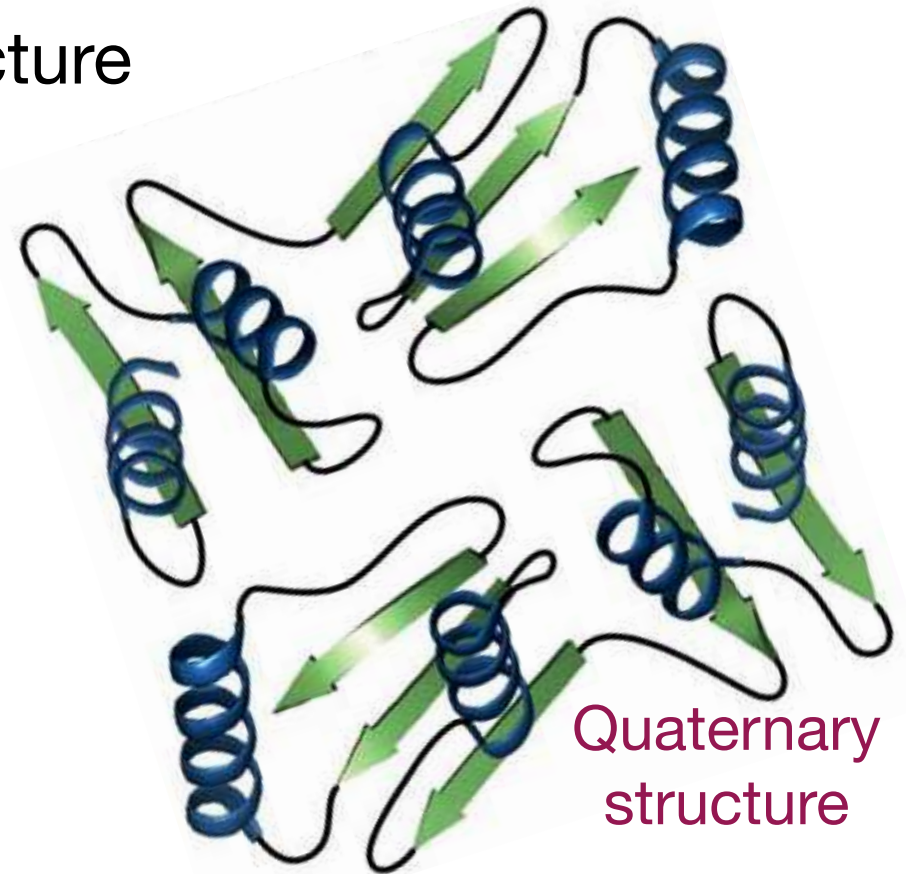
α helix



β sheet



Tertiary structure

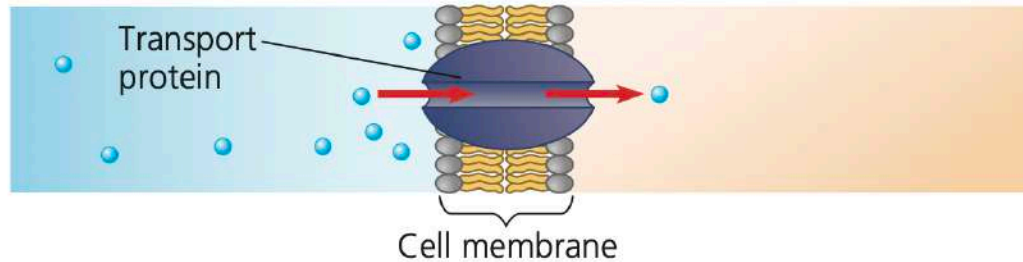


Quaternary
structure

Transport proteins

Function: Transport of substances

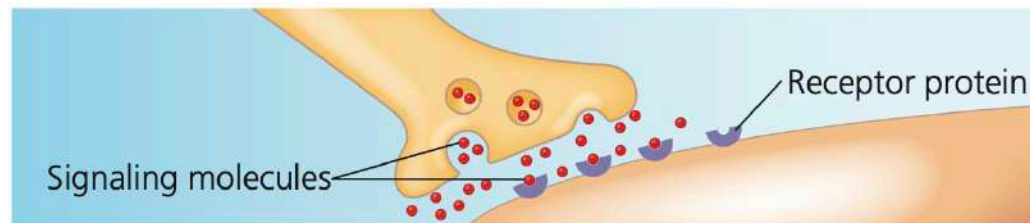
Examples: Hemoglobin, the iron-containing protein of vertebrate blood, transports oxygen from the lungs to other parts of the body. Other proteins transport molecules across membranes, as shown here.



Receptor proteins

Function: Response of cell to chemical stimuli

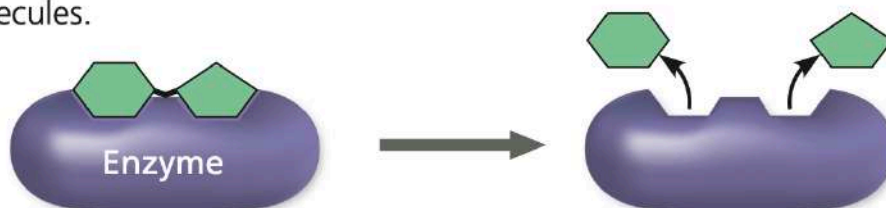
Example: Receptors built into the membrane of a nerve cell detect signaling molecules released by other nerve cells.



Enzymatic proteins

Function: Selective acceleration of chemical reactions

Example: Digestive enzymes catalyze the hydrolysis of bonds in food molecules.

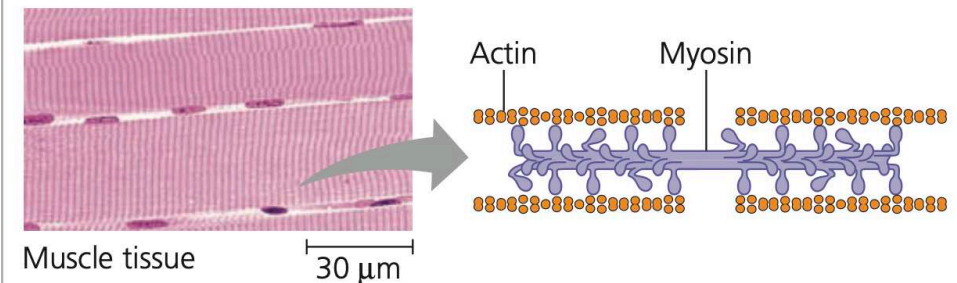


Examples of function of proteins

Contractile and motor proteins

Function: Movement

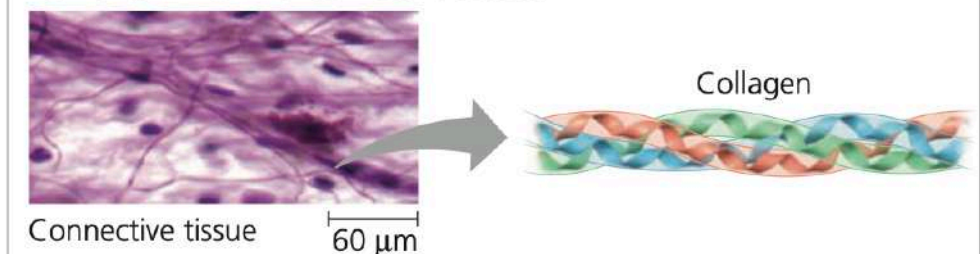
Examples: Motor proteins are responsible for the undulations of cilia and flagella. Actin and myosin proteins are responsible for the contraction of muscles.



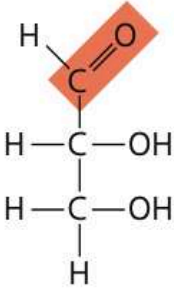
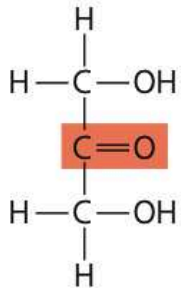
Structural proteins

Function: Support

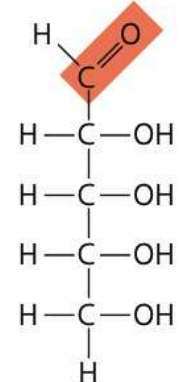
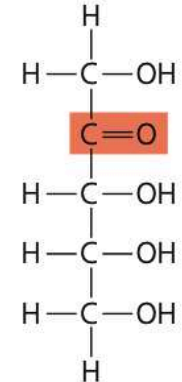
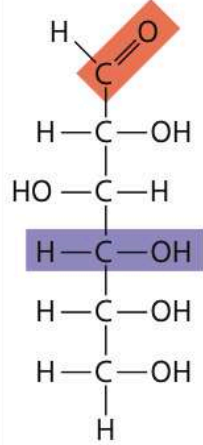
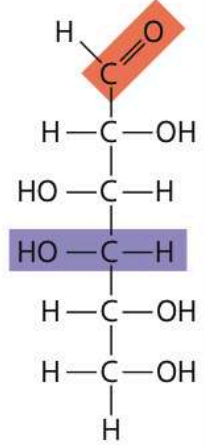
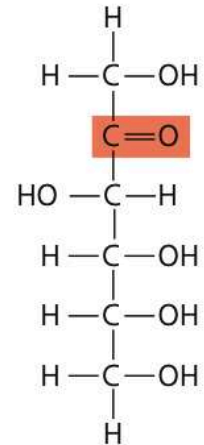
Examples: Keratin is the protein of hair, horns, feathers, and other skin appendages. Insects and spiders use silk fibers to make their cocoons and webs, respectively. Collagen and elastin proteins provide a fibrous framework in animal connective tissues.



Carbohydrates

Aldoses (Aldehyde Sugars) Carbonyl group at end of carbon skeleton	Ketoses (Ketone Sugars) Carbonyl group within carbon skeleton
Trioses: 3-carbon sugars ($C_3H_6O_3$)	
 <p>Glyceraldehyde An initial breakdown product of glucose</p>	 <p>Dihydroxyacetone An initial breakdown product of glucose</p>

- Carbohydrates include sugars
- polymers of sugars - polysaccharides
- Usually reserves of energy in cells
- Can also provide structural support - e.g. cellulose in plant cells
- In aqueous solutions, most pentose and hexose sugars form rings

Pentoses: 5-carbon sugars ($C_5H_{10}O_5$)		
 <p>Ribose A component of RNA</p>	 <p>Ribulose An intermediate in photosynthesis</p>	
Hexoses: 6-carbon sugars ($C_6H_{12}O_6$)		
 <p>Glucose Energy sources for organisms</p>	 <p>Galactose Energy sources for organisms</p>	 <p>Fructose An energy source for organisms</p>

Polysaccharides in plants and animals

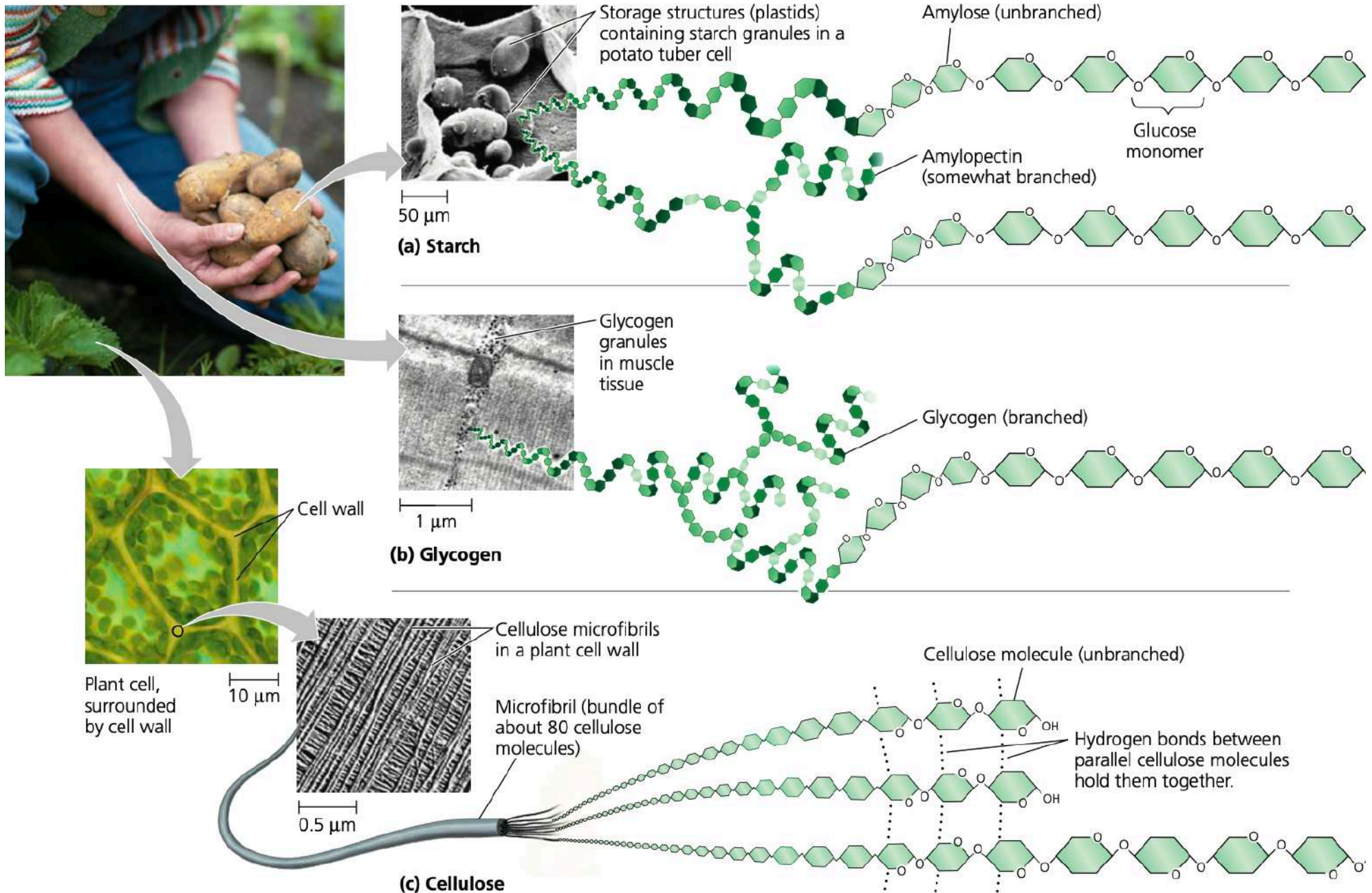
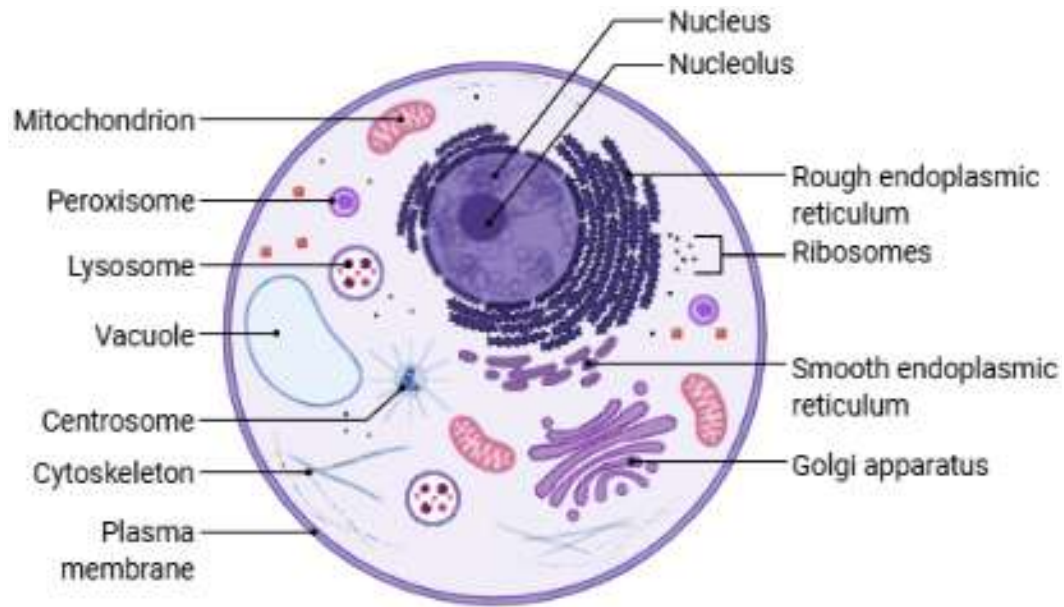


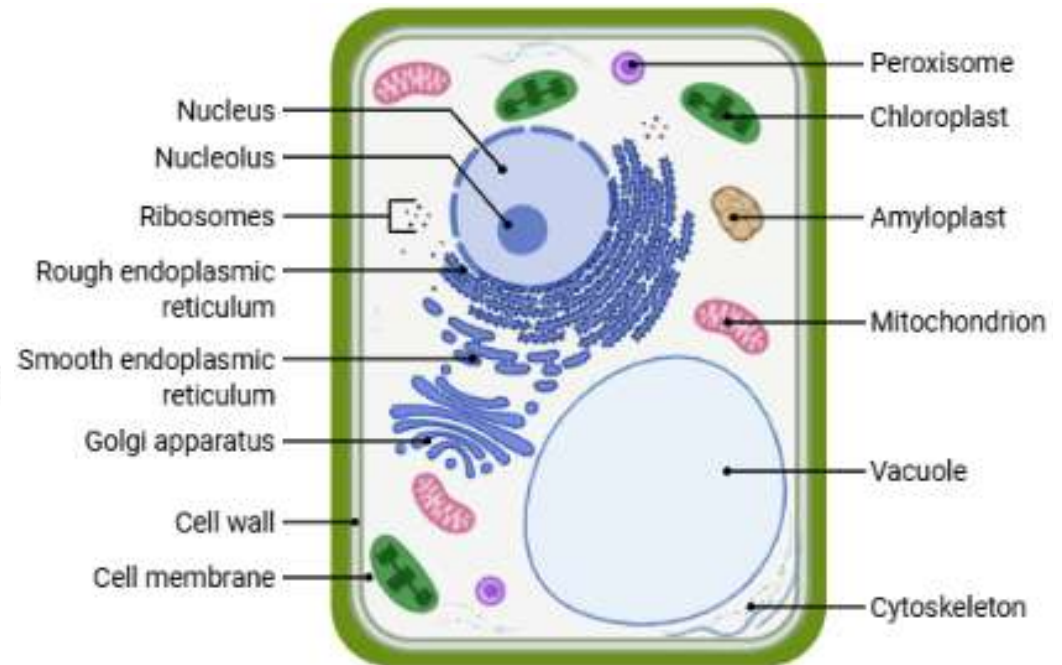
Figure 5.6 of Campbell's Biology: a global approach

Eukaryotic cells

Animal cell



Plant cell



Compartments → “rooms” in which different activities can occur

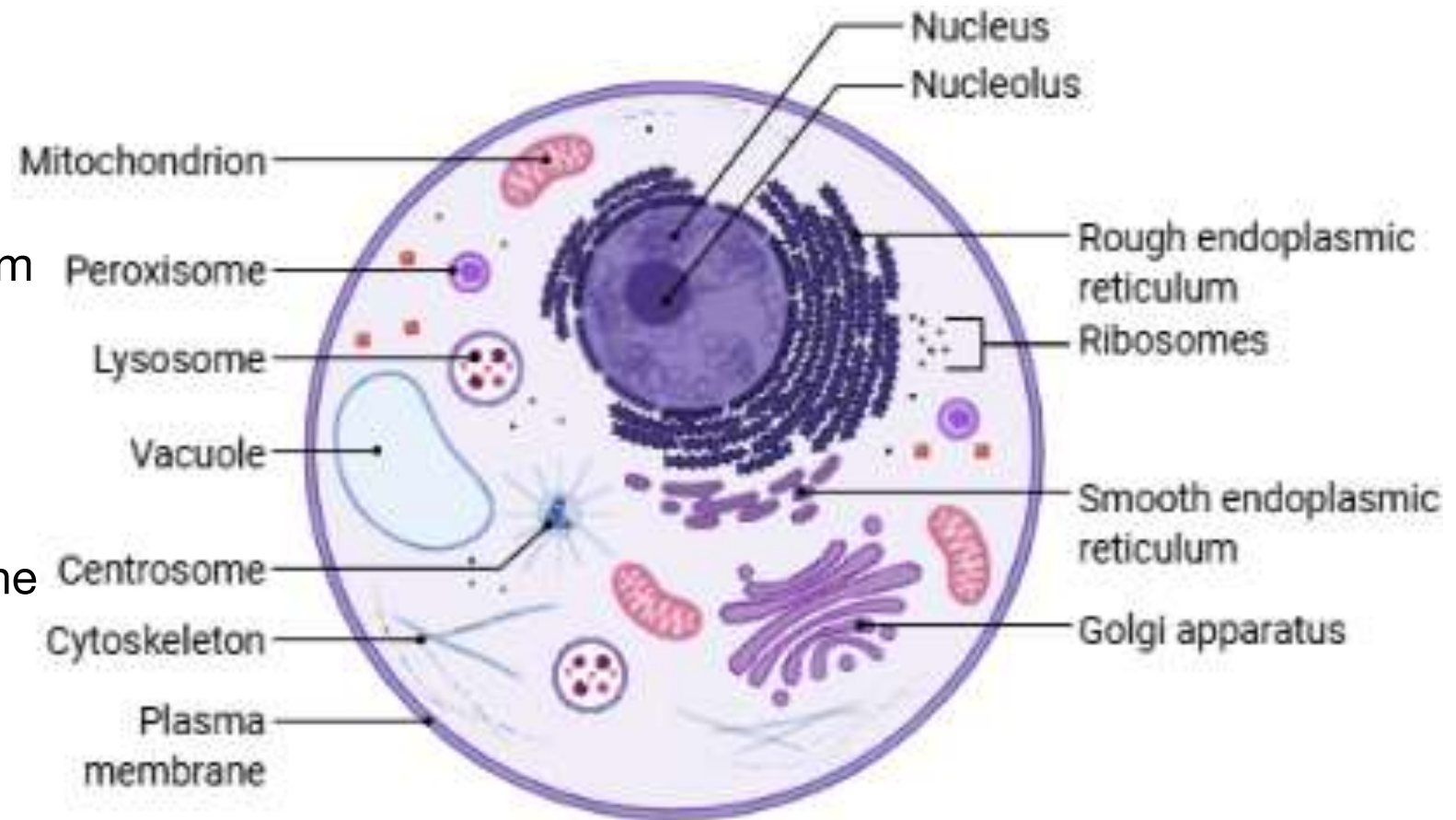
Organized → “layout” decides the optimal sequence in which activities can occur

Eukaryotic cells and apartments



Endomembrane system in cells

- Nuclear envelope
- Endoplasmic reticulum
- Golgi apparatus
- Lysosomes
- Vesicles
- Vacuoles
- The plasma membrane



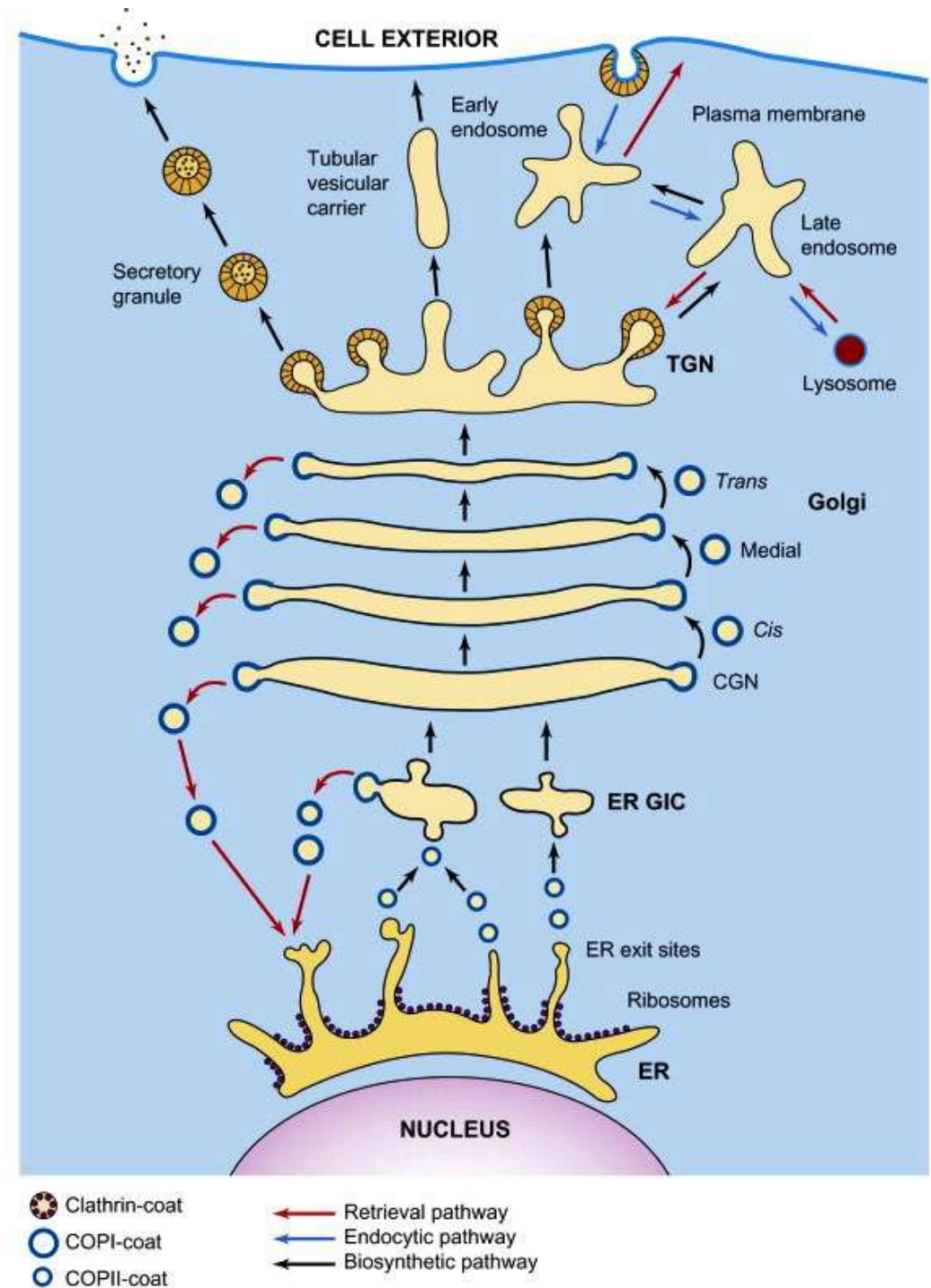
- Membranes of this system are related either through direct physical continuity or by the transfer of membrane segments as tiny vesicles (sacs made of membrane)
- Allows exchange of materials between compartments
- Allows stuff to get in and get out of cells
- Exists in prokaryotes, animal and plant cells

Entry and Exit routes in cells

ER-Golgi secretory pathway

Allows cells to send out information
Allows cells to receive information

Also makes cells
vulnerable to hijacks



Hijacking a cell

- Need a “key” to get in
- “Hitch a ride” with something that normally gets inside cells
- When inside:
 - “Blend in” with the background
 - “Hide” from detection systems
 - “Masquerade” as something already present in cells
- When the time is right “reveal and fight” or “escape” from the cell

