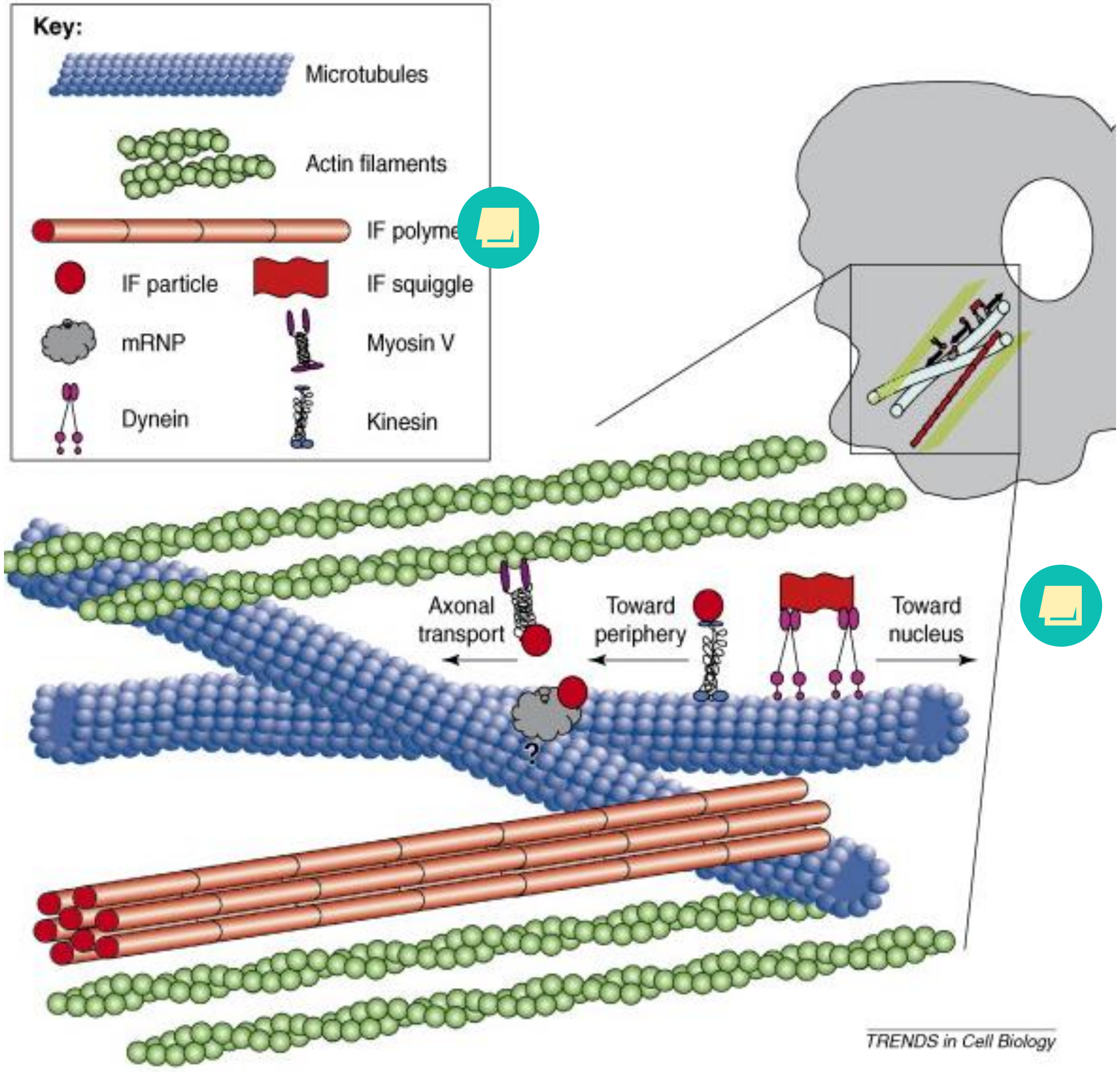
Lecture #5

- Structural proteins in cells
- Globular proteins
- Membrane proteins
- Protein Data Base (PDB)

Fibers inside cells

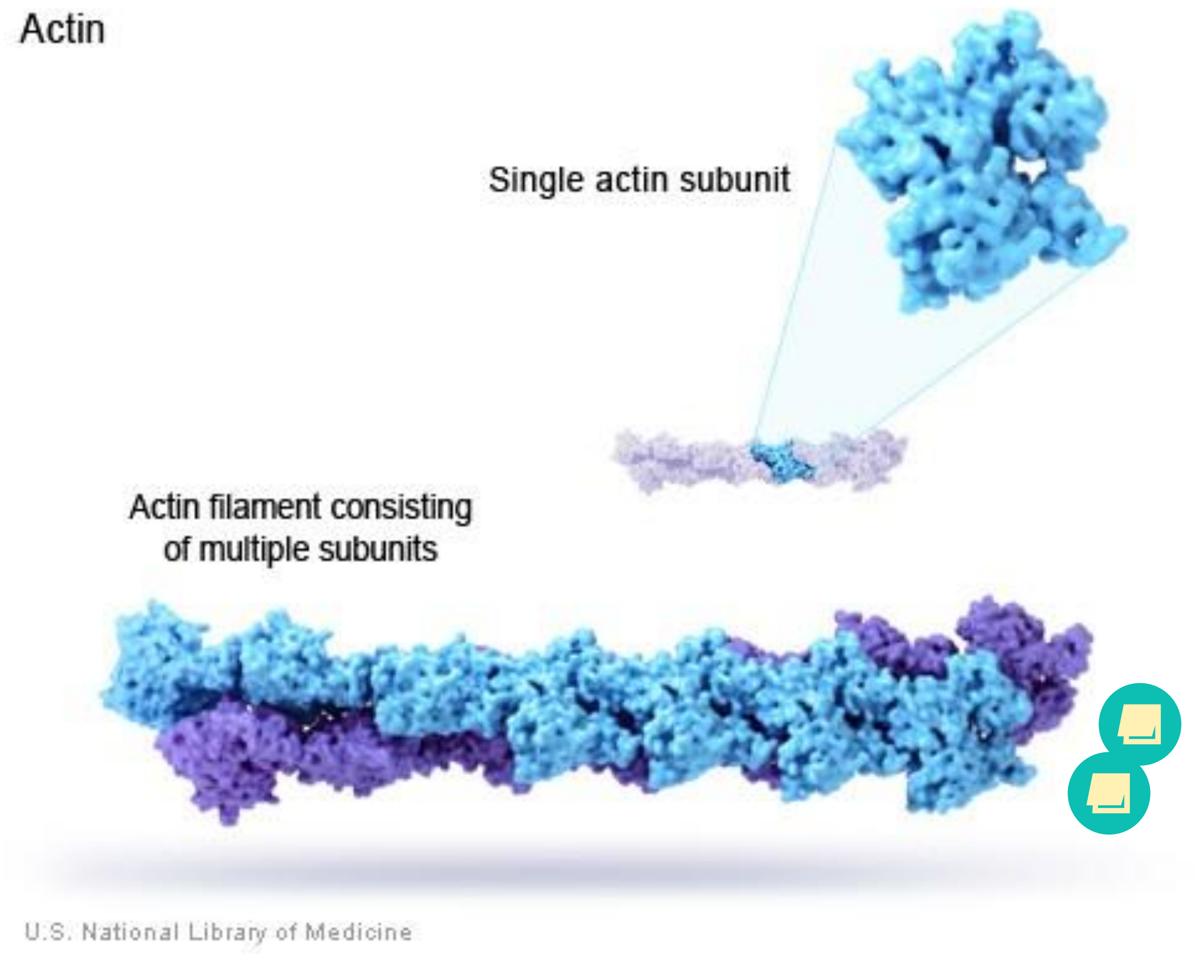
- Make up cytoskeleton inside cell
- Actin
- Microfilaments
- Intermediate filaments
- Cell shape and movement

Cytoskeleton



TRENDS in Cell Biology

Actin filament



U.S. National Library of Medicine

Globular proteins

- Have folded, roughly spherical structures
- Many are enzymes, with active sites that bind substrates and catalyze reactions
- Consist largely of secondary structure elements, including helices, sheets and turns

Globular proteins: myoglobin

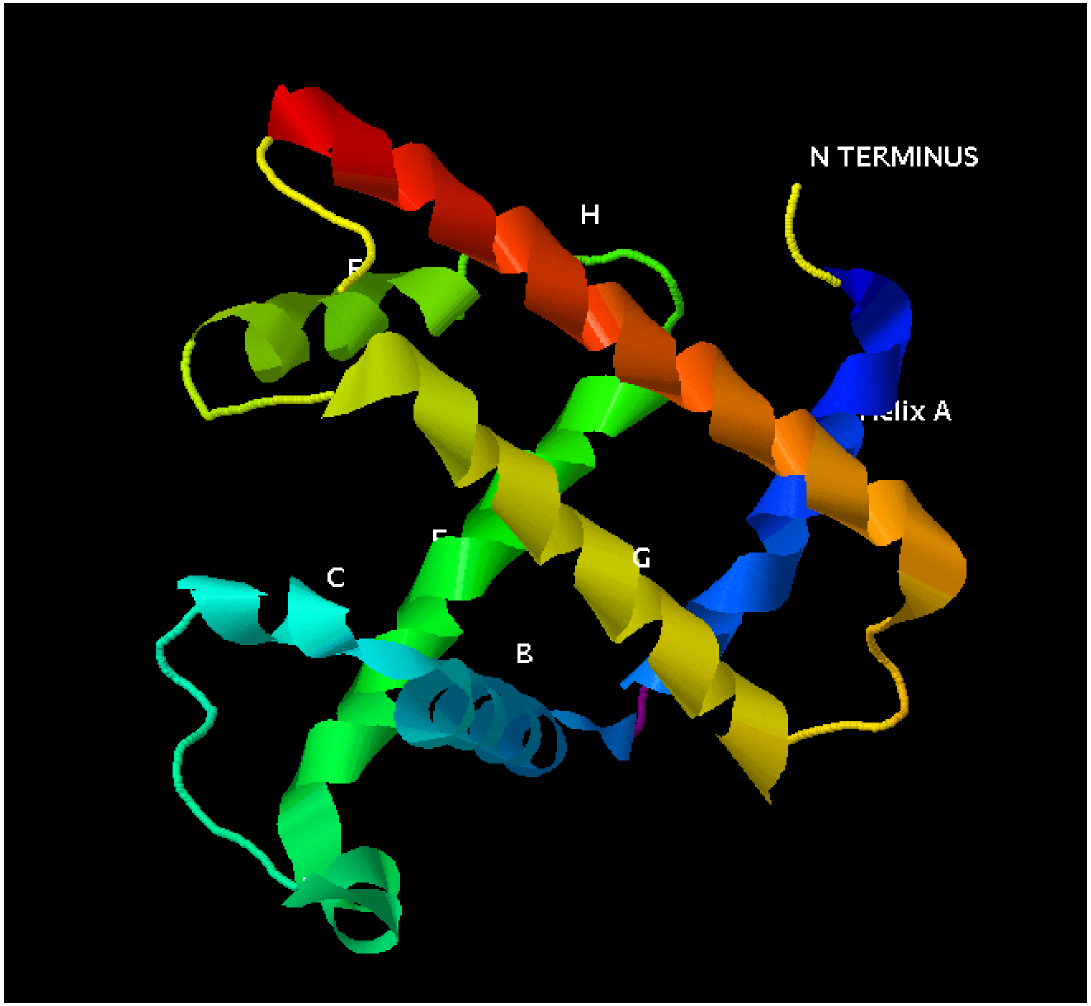
- Richest source: muscles of aquatic vertebrates like whales
- ‘Box’ for a heme group: Fe-heme binds oxygen, protein stores it until required for metabolic oxidation
- Dimensions: 44 x 44 x 25 angstroms
- 1st protein structure determined

Globular proteins: myoglobin

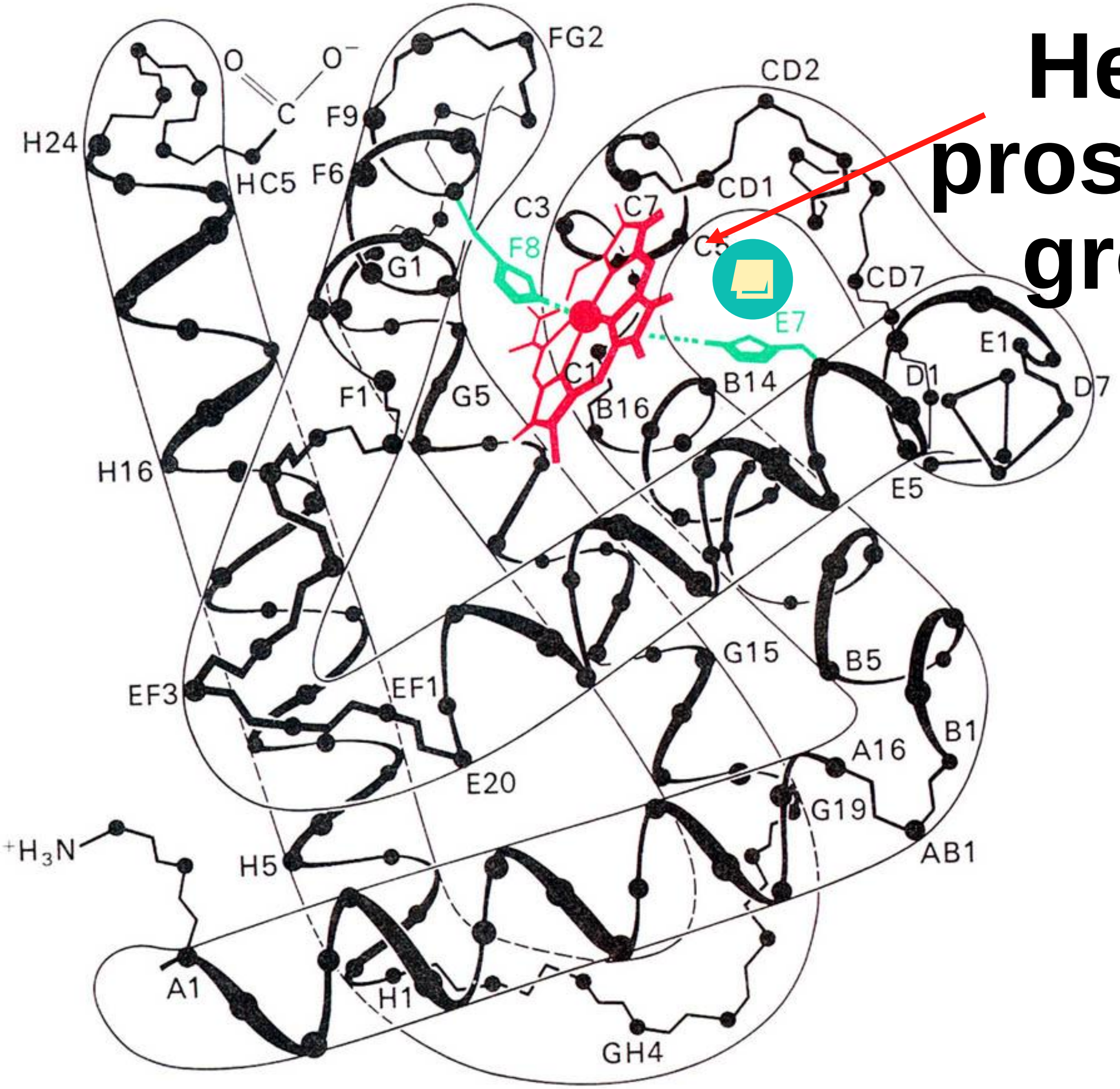
- 153 amino acids; 121/153 in α-helices
- 8 connected helix segments (form heme pocket)
- Helices fold via β-turns; several turns contain Pro residues
- Strongly hydrophobic core

  (V, L, I, M, F)

X-ray structure of myoglobin

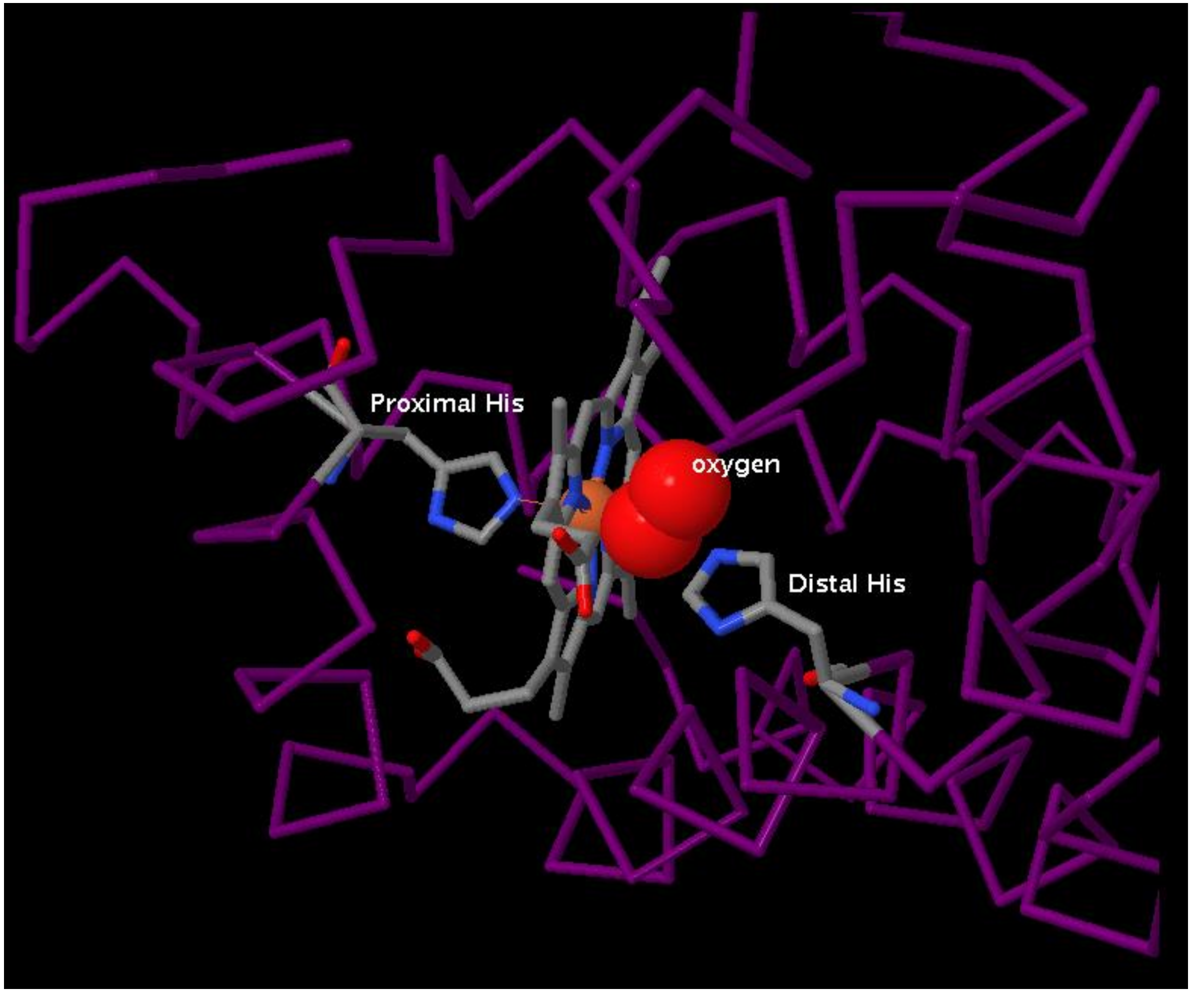


X - ray structure of myoglobin



Heme prosthetic group

Oxygen binding site in myoglobin



Globular proteins: ribonuclease A

- Chain-cutting enzyme, cleaves the polyribonucleotide chains of RNA but not DNA
- Taco-shaped molecule with the active site in a crevice running across the molecule

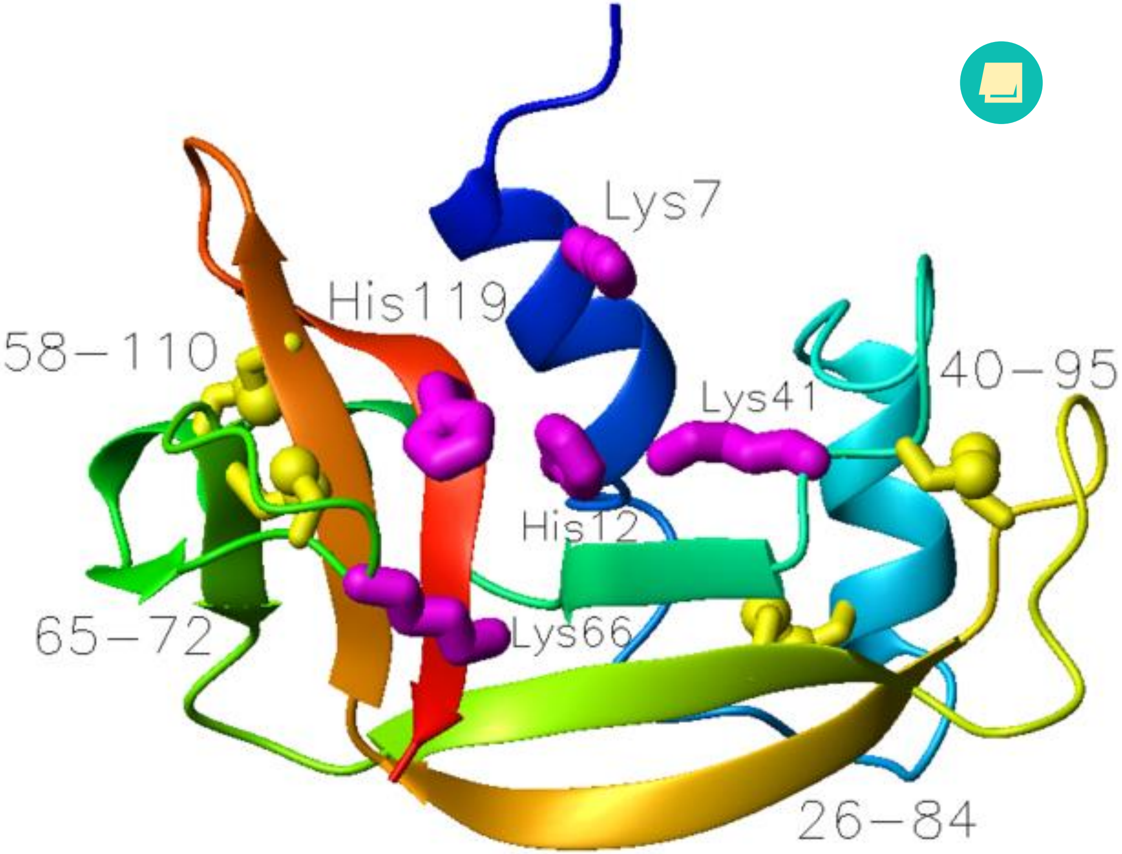
Globular proteins: ribonuclease A

- Secreted by the pancreas
- Has significant segments of β-sheet and α-helix
- Consists of 124 AAs, MW 13,700
- Has four disulfide bond

Globular proteins: ribonuclease A

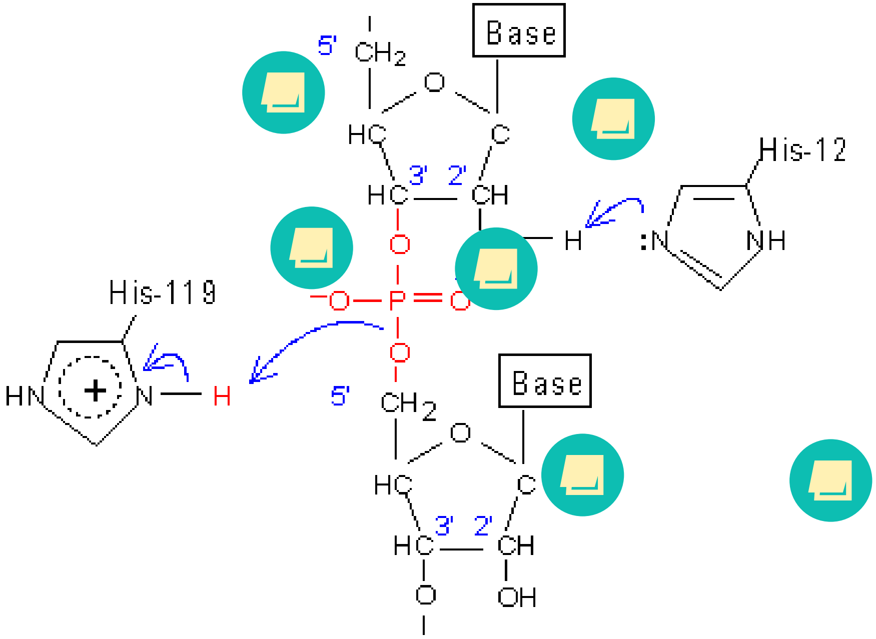
- Active site located by binding an inhibitor, performing X-ray crystallography, and locating the inhibitor in the structure
- Active site residues include: His12, His119, and Lys41

X-ray crystallographic structure of ribonuclease

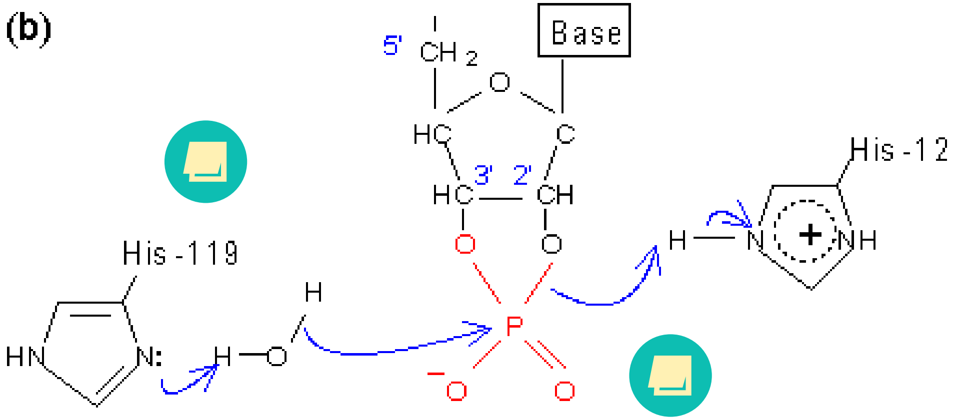


Mechanism of ribonuclease

(a)



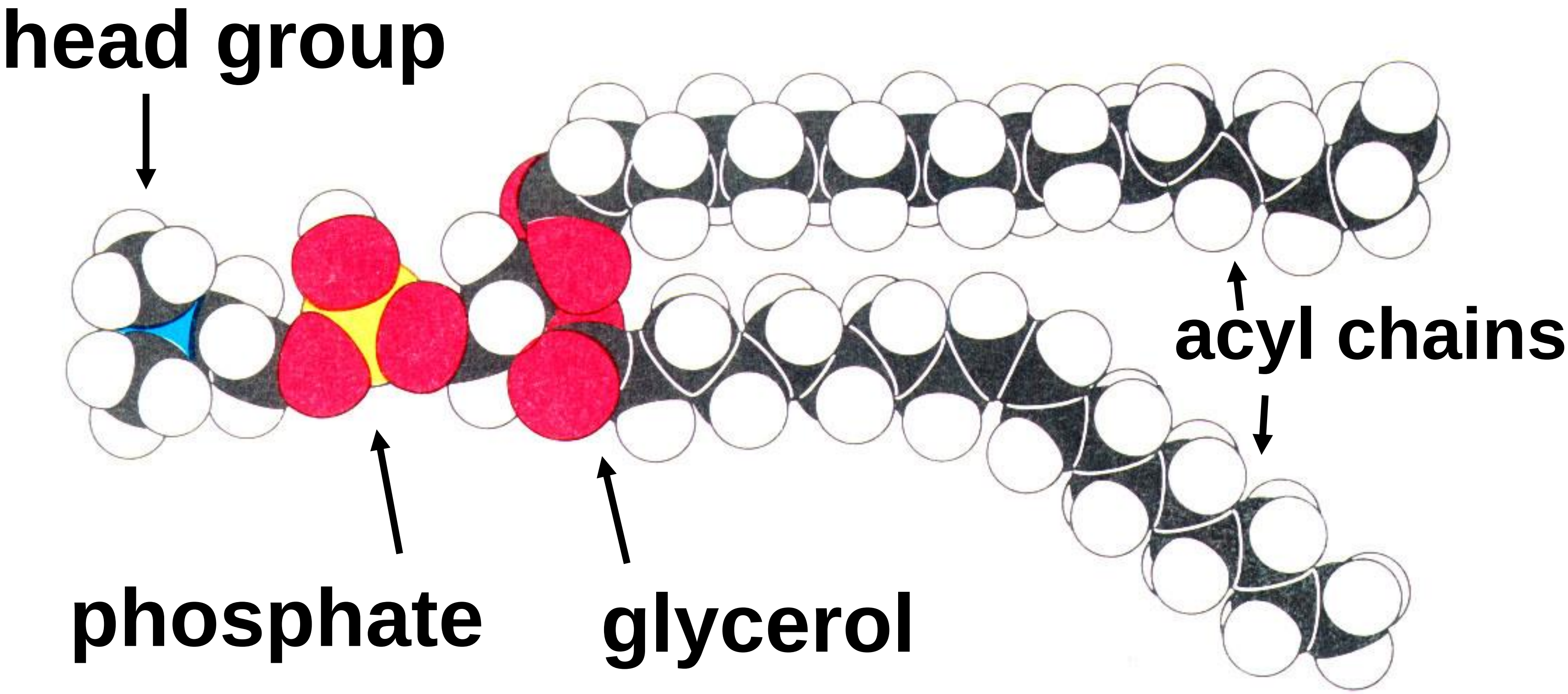
(b)



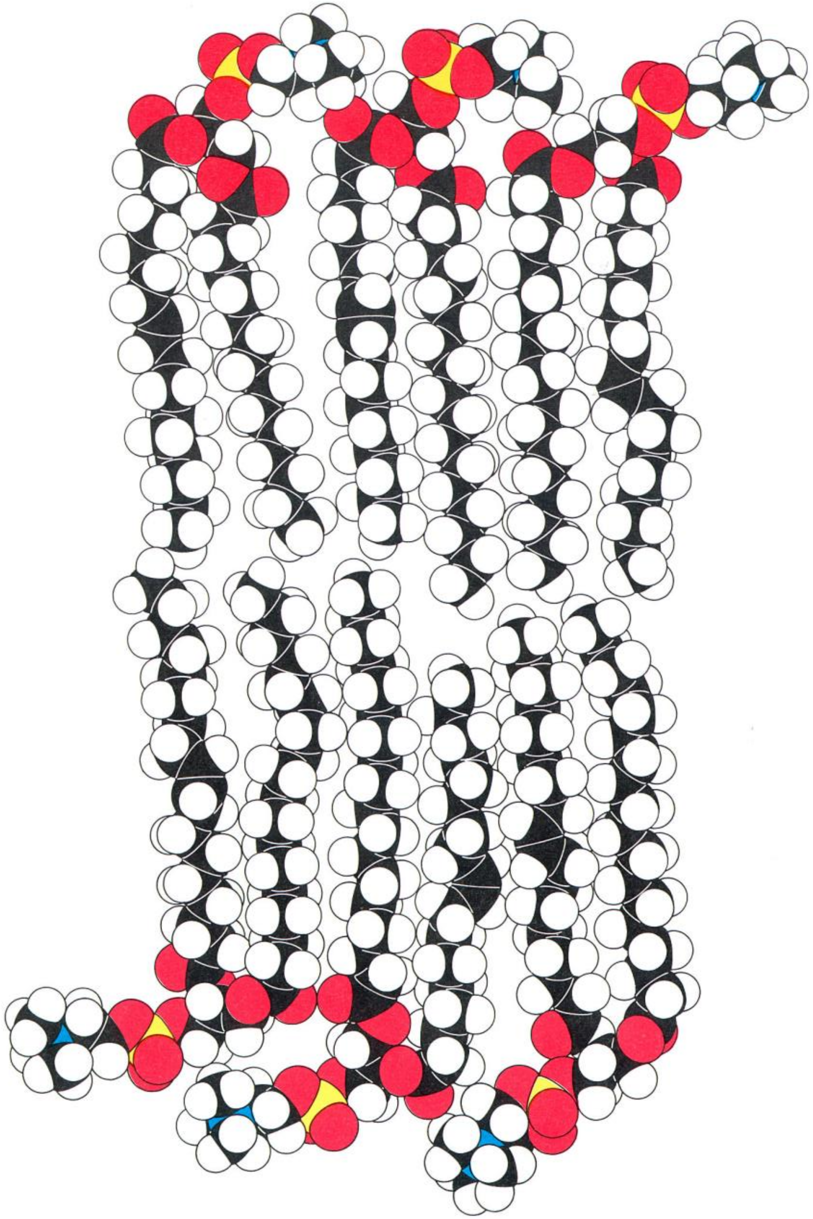
Membrane proteins

- Membrane proteins are responsible for key cellular processes
- Functions include transporters, channels, receptors, enzymes
- Embedded in lipid bilayer

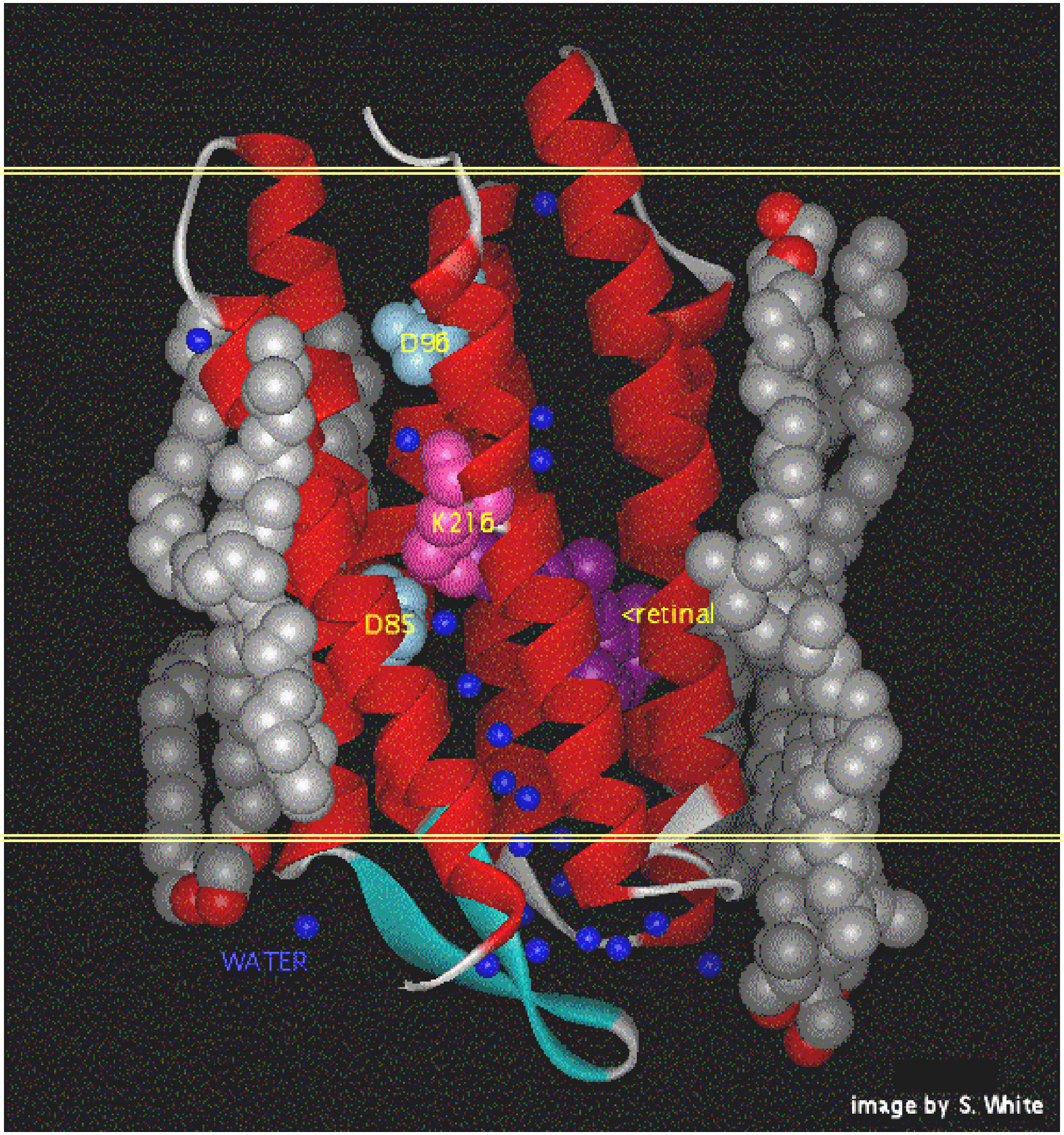
Space-filling model of a phosphatidylcholine molecule



Lipid Bilayer



Structure of a membrane protein: bacteriorhopsin



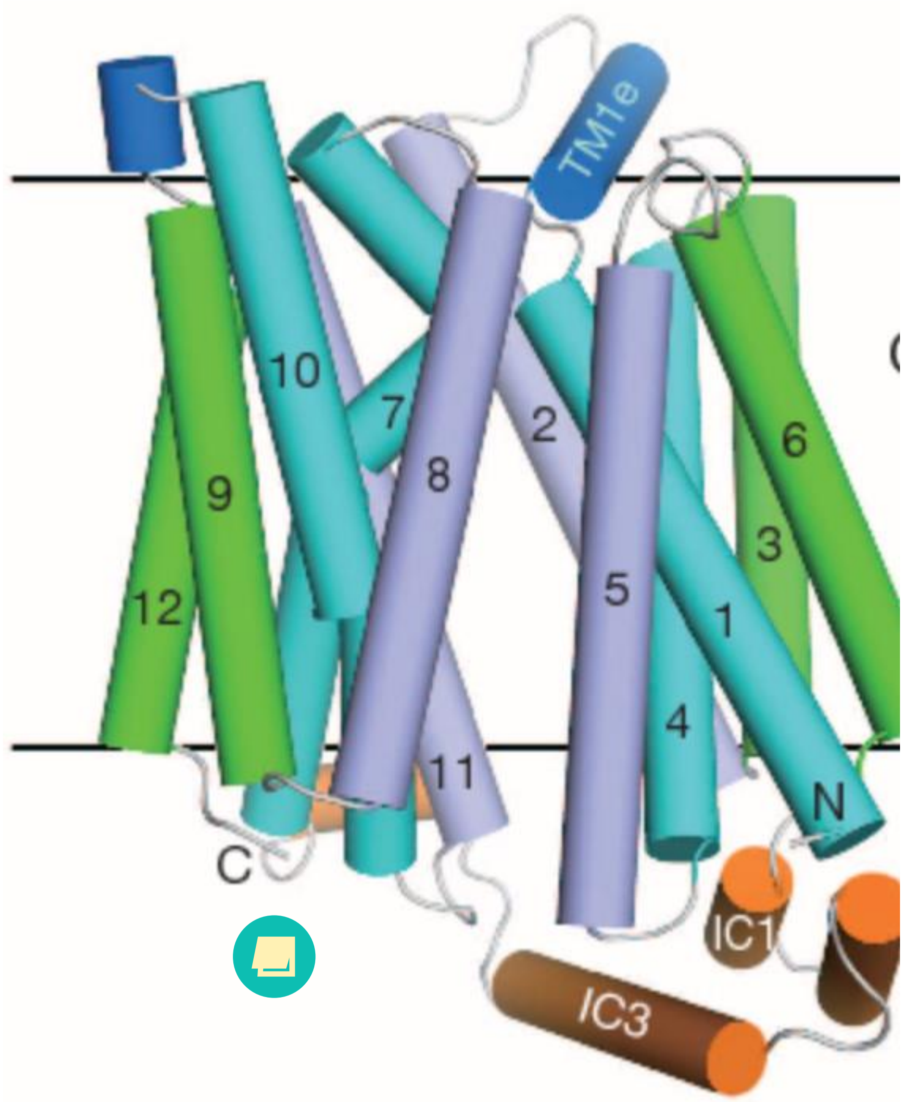
Membrane proteins: transport

- Membrane proteins carry out movement (transport) of substrates in and out of the cell across the plasma membrane
- Transporters, channels and pumps
- Energy (ATP) required for pumps
- Electro-chemical gradient often involved as driving force

Transporters

- Membrane transport proteins use substrate gradient across the membrane
- Substrates move from high to low
- Example: the glucose transporter
- Substrate specificity due to nature of binding site
- Two states: outward and inward-facing

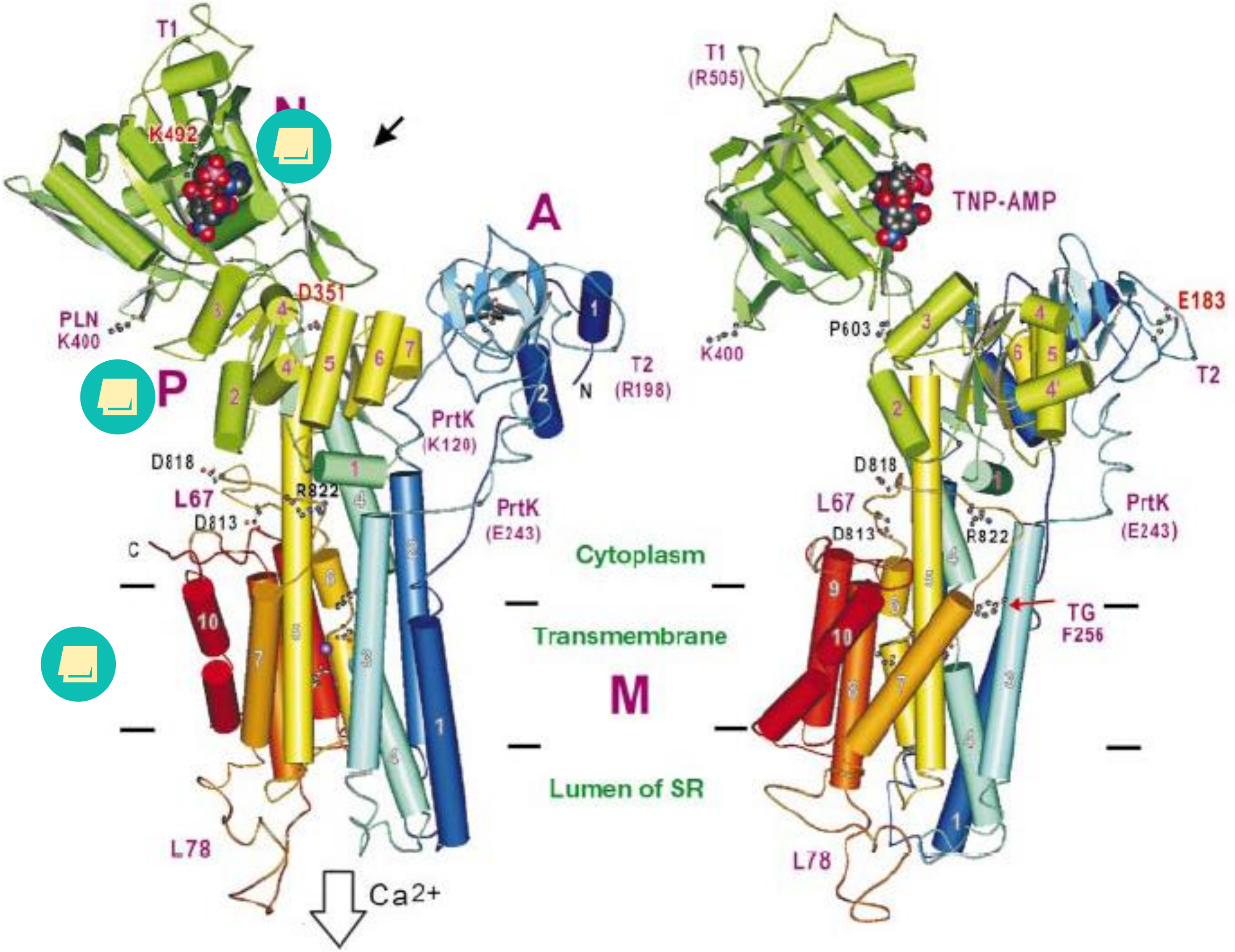
Structure of Glucose Transporter



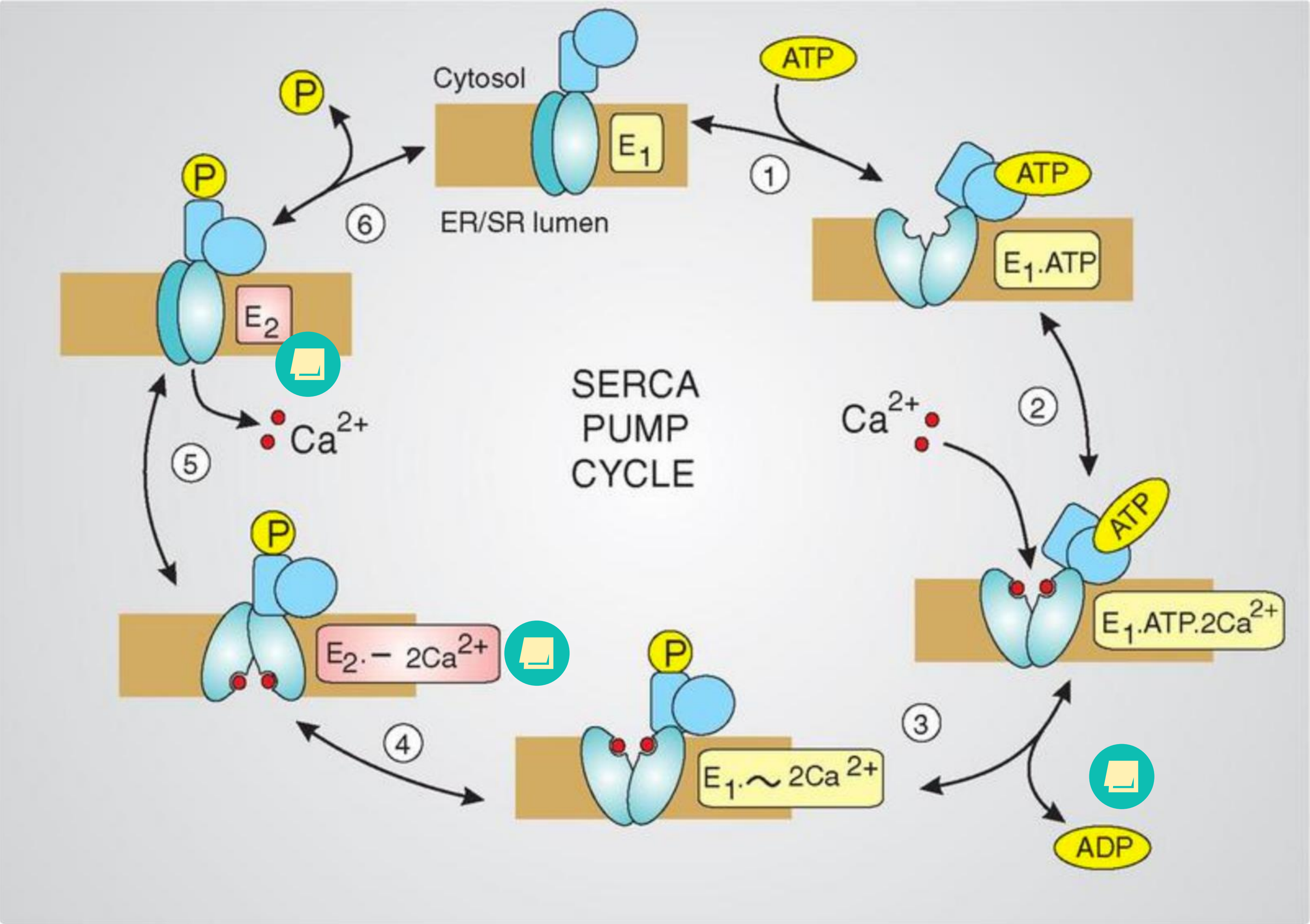
Pumps: ATP required

- Transport is coupled to conformational change in membrane protein
- Example: the sarcoplasmic reticulum Ca^{2+} ATPase system
- ATP is required in a process that pumps Ca^{2+} ions ‘uphill’ against their concentration gradient

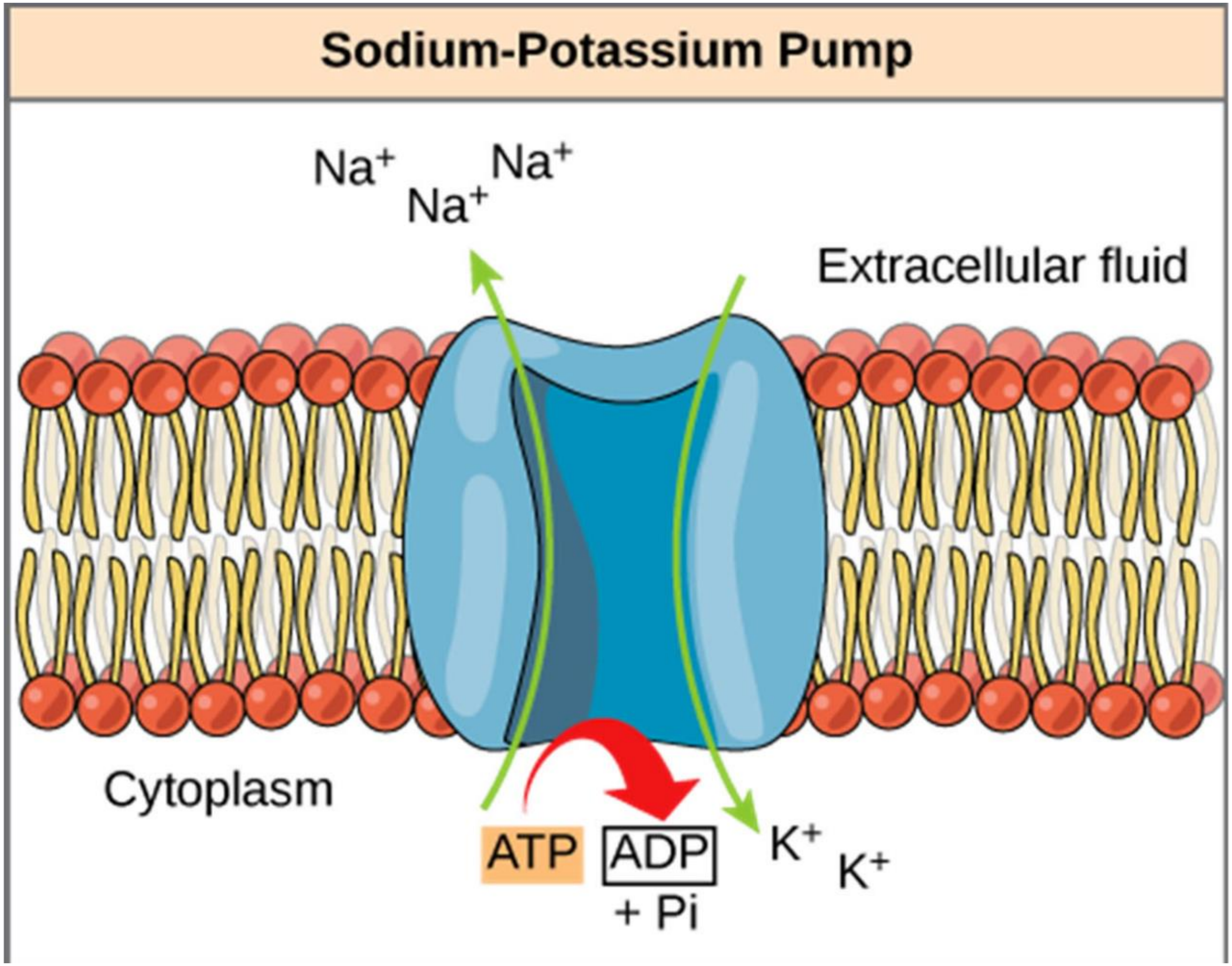
Calcium ATPase pump



Calcium ATPase Cycle



Sodium/Potassium ATPase

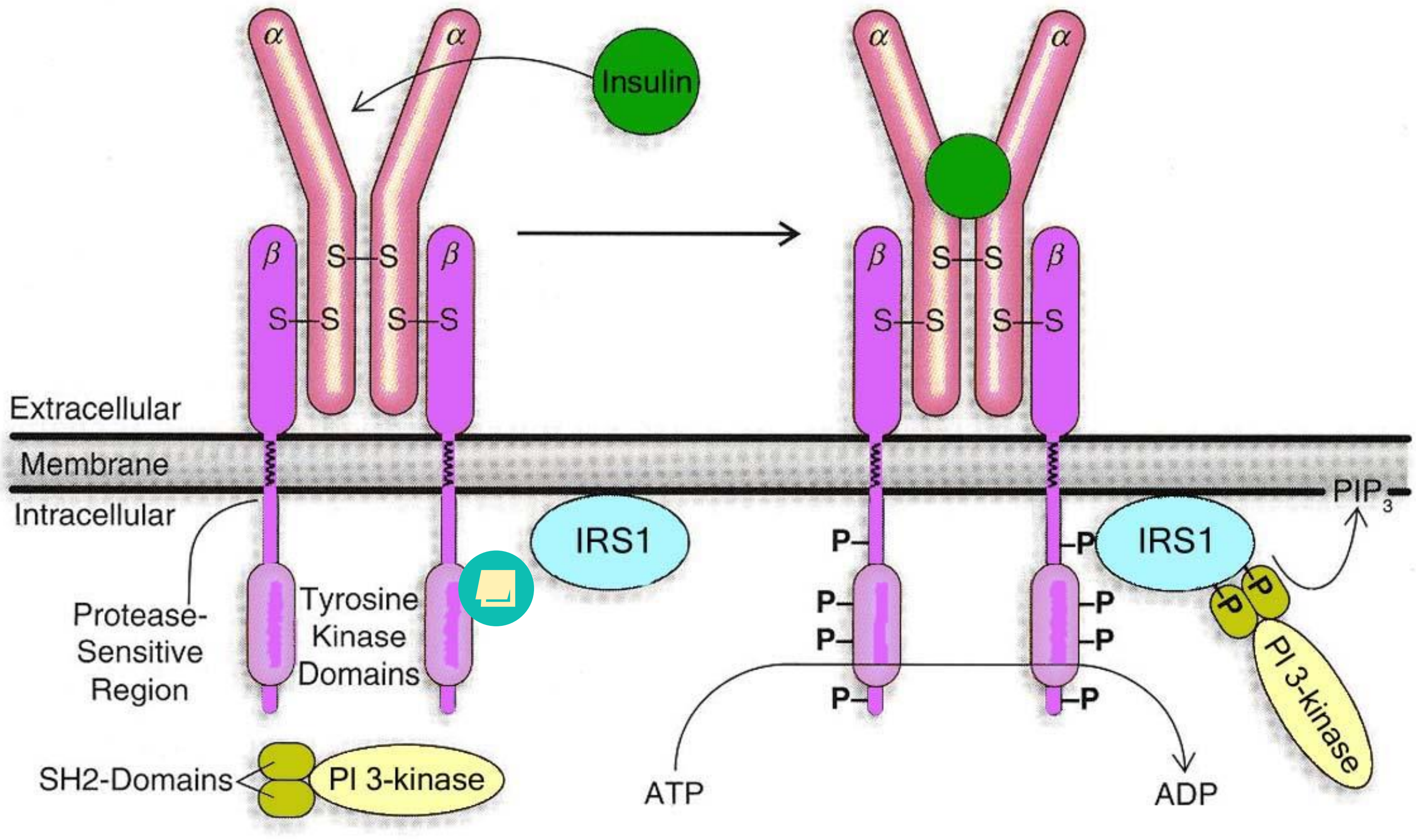


Receptor proteins

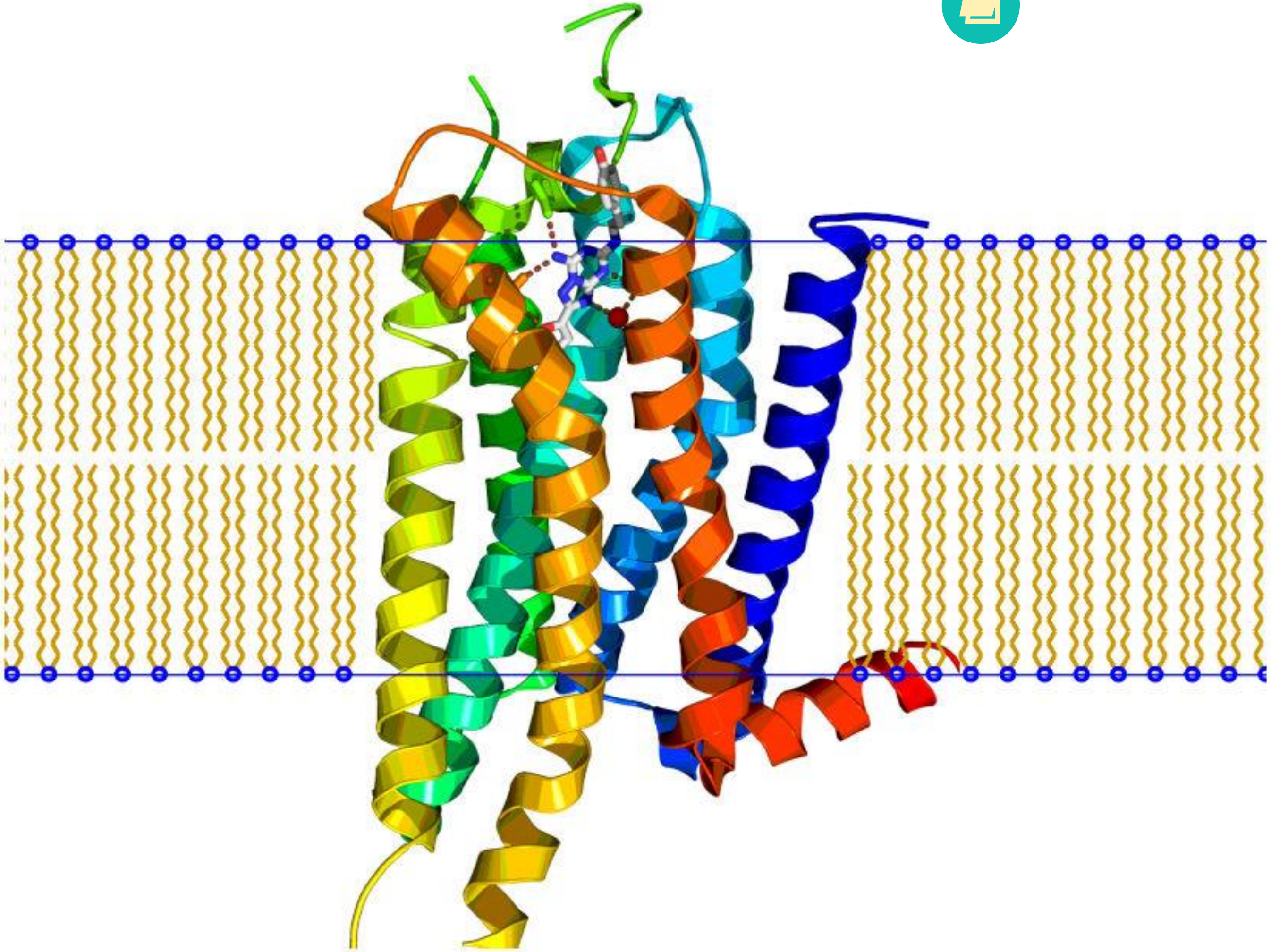
- Receptors transmit signals across membranes (nothing is transported)
- Ligand binding to receptor on the cell surface induces internal signal
- Receptors may be single-spanning (insulin receptor) or multi-spanning (G-protein-coupled receptors)

Insulin receptor signalling

Figure 11.7 Diagrammatic structure of stimulation of the insulin receptor



G-protein coupled receptors (GPCRs)



Protein Data Base (PDB)

- PDB
  - http://www.rcsb.org/pdb/home/home.do
- **PDB-101**
  - http://www.rcsb.org/pdb/101/structural_view_of_biology.do
- **There are over 40,000 protein structures in the PDB**

Ribonuclease A
PDB: 7RSA

PDB

- Use the PDB to find the structure of human insulin:
- https://www.rcsb.org/pdb/home/home.do
- What metal is associated with insulin?

RCSB PDB Mobile App