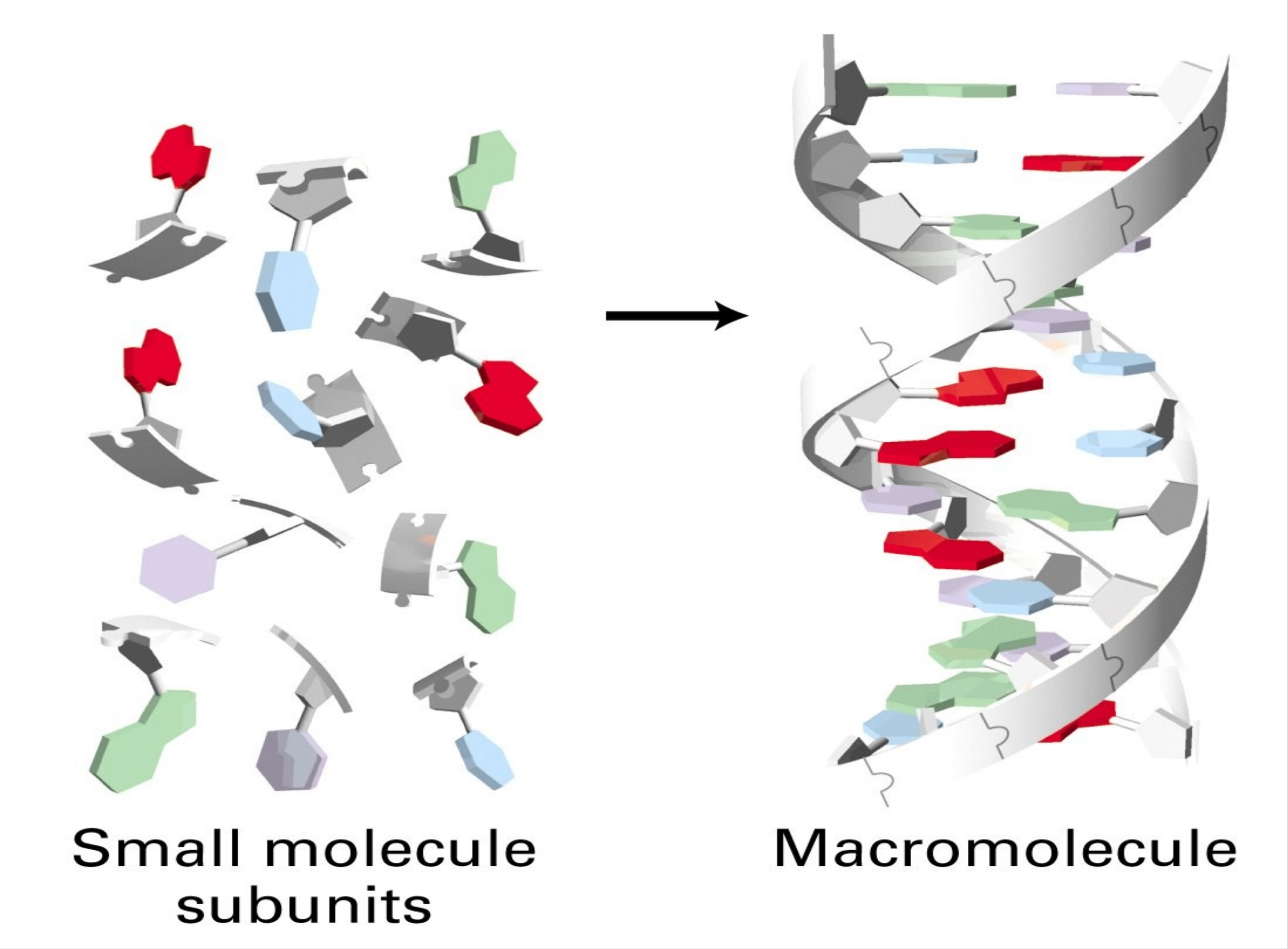
Biology from an EE perspective
Lecture 5

Look at Proteins
Structure
Function
(Essentially via cartoons to see the structure-function links)

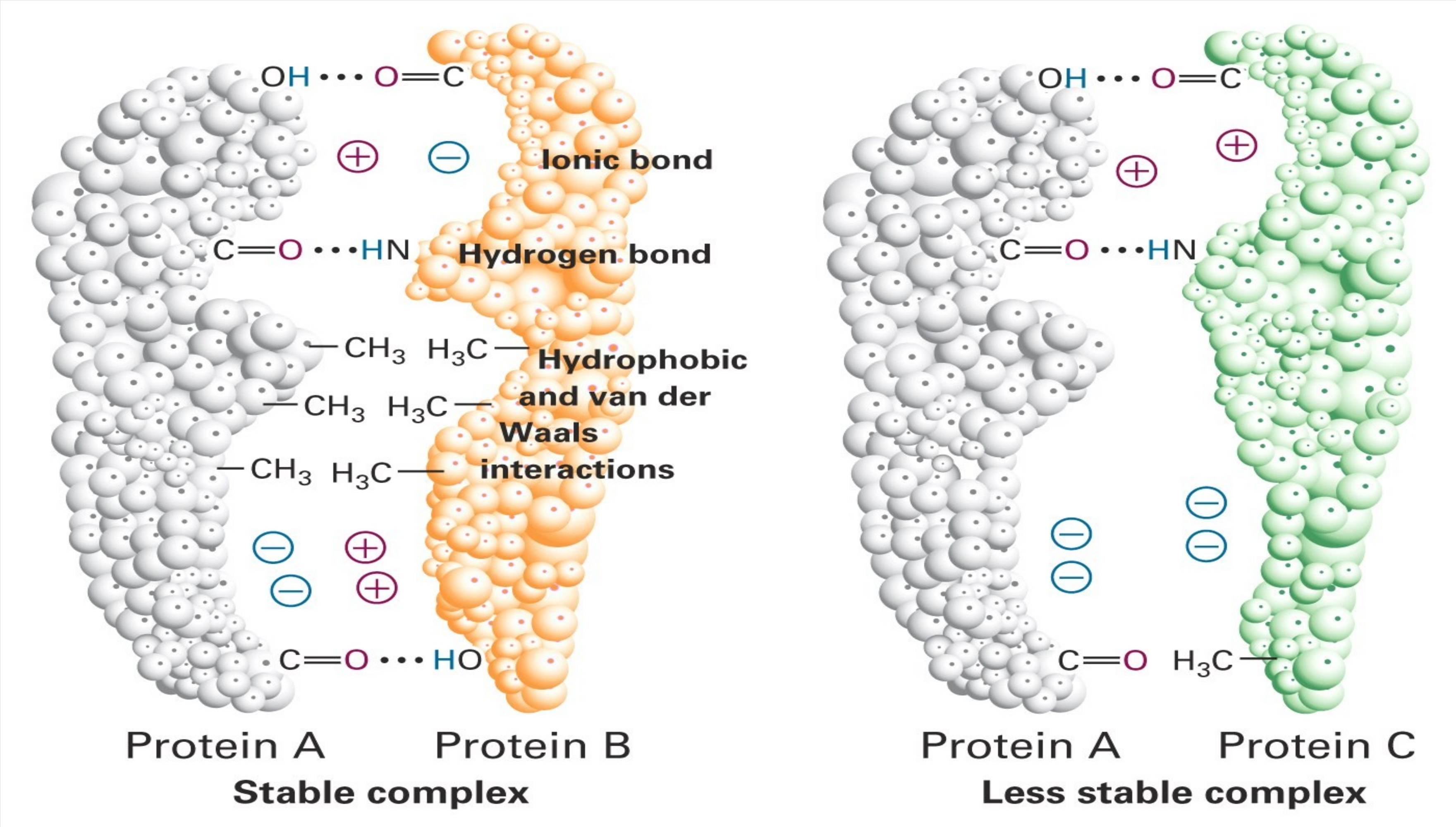
Rakesh K Lal

Organisms synthesize building blocks that can self-assemble or can be catalyzed to self assemble

Something like “legos” at the molecular level!

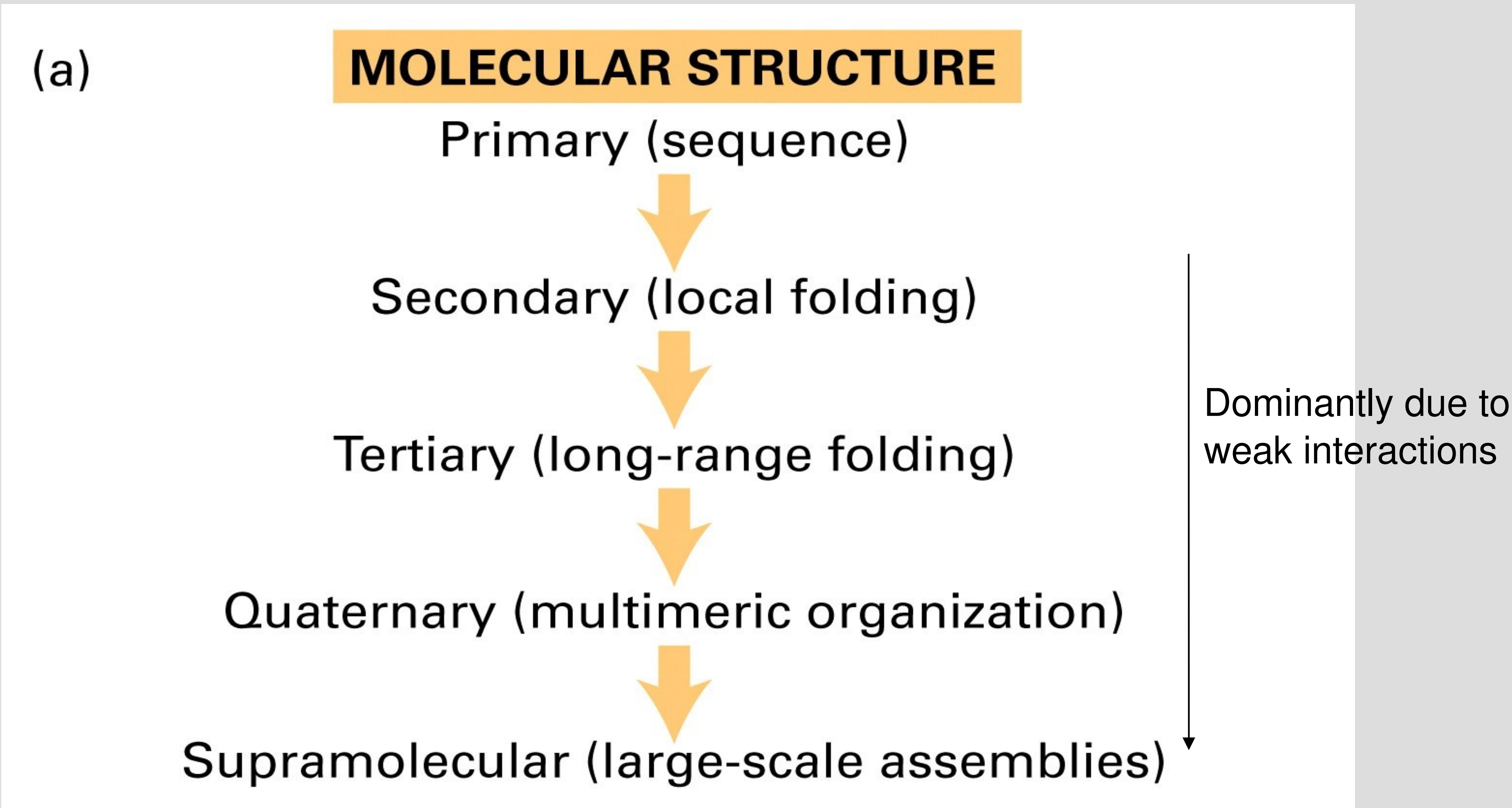


The weaker interactions very important for biomolecules and processes

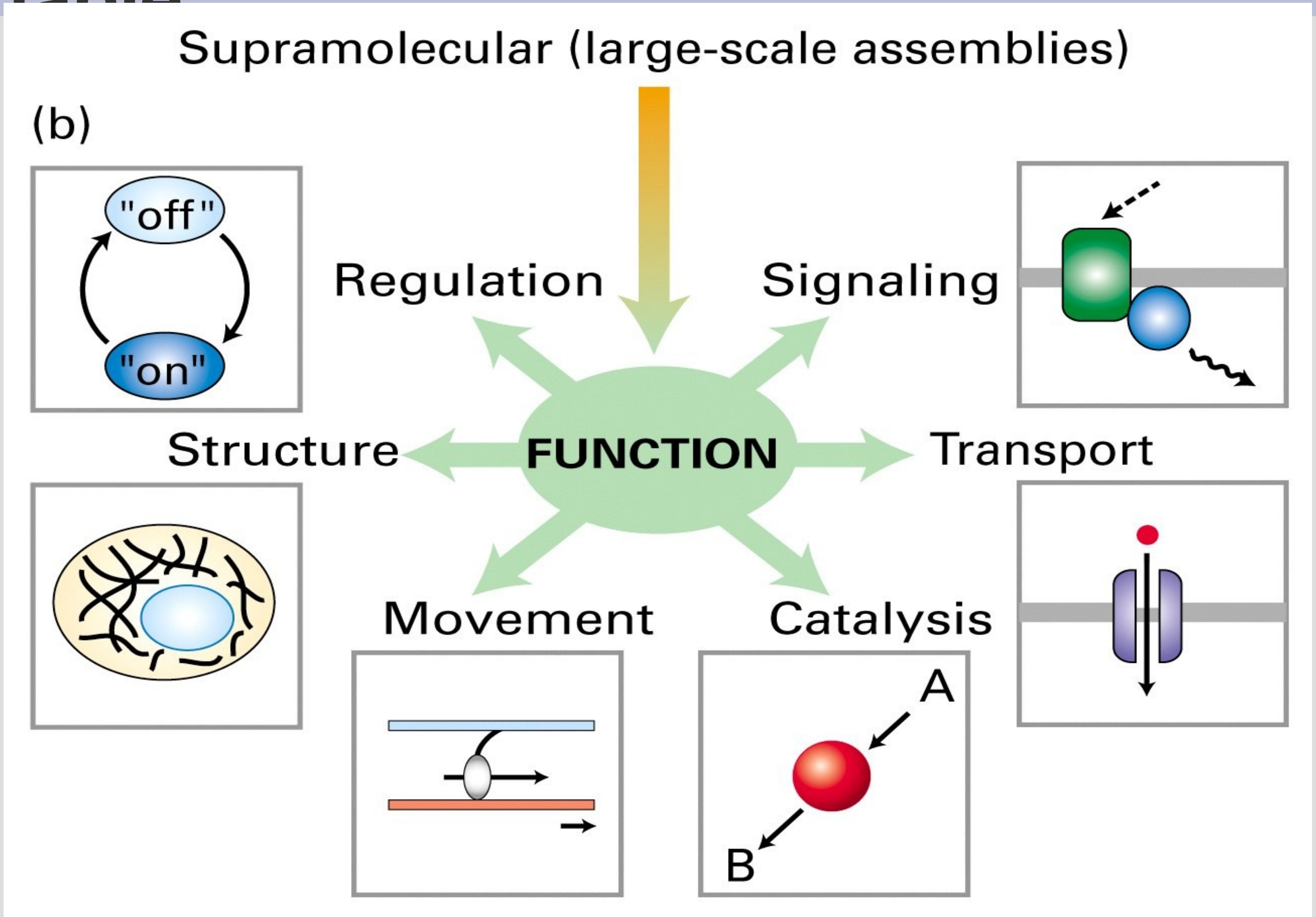


Why weak interactions important?

Consider proteins: Weak interactions give proteins the shapes needed for their function



What do these molecules & supramolecular assemblies of proteins enable



Peptides and proteins -1

- Proteins built of monomers called amino acids that have amine and carboxyl functional groups plus a side chain "R" and have a general formula: $NH_2CHRCOOH$

  ^ α-carbon
- α-carbon is the carbon atom to which the amine and carboxyl groups are attached
- The side chain R could just be H in glycine or could be a heterocyclic group in tryptophan
- Amino acids used to synthesize proteins or other molecules or used as an energy source

Peptides and proteins -2

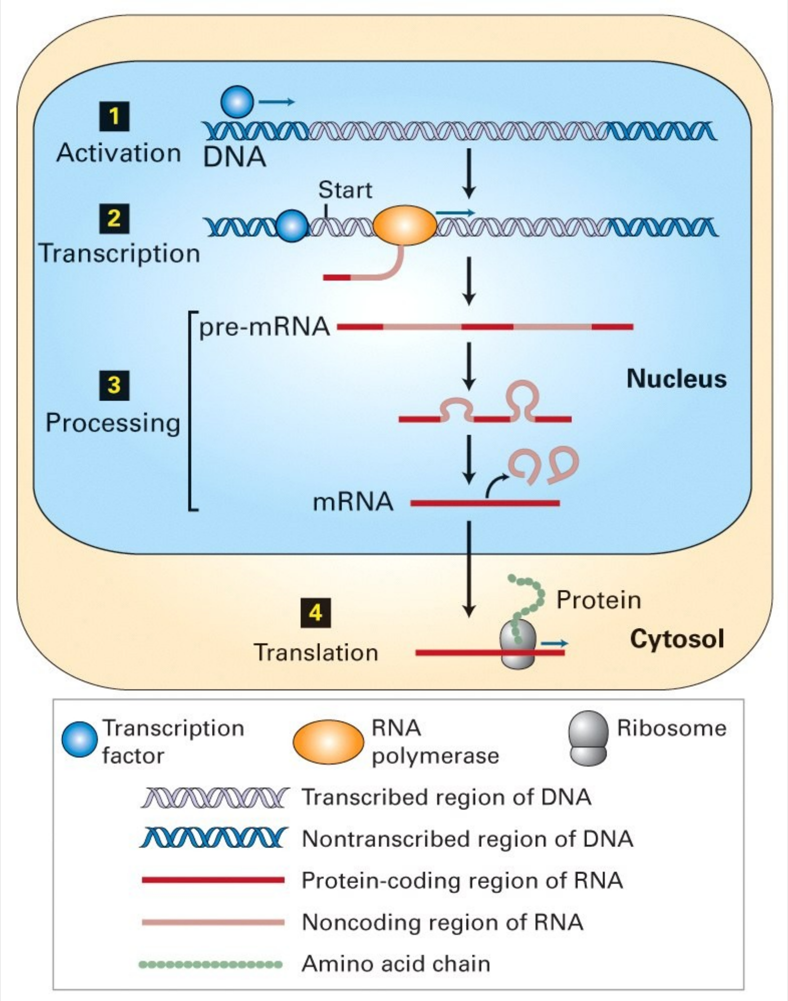
- Oligomers and short chains are called peptites (<50 monomers); longer chains are called proteins
  - Non-protein amino acids & peptides serve as signaling molecules or are used in the synthesis of other molecules such as
- Proteins serve as structural molecules, enzymes (catalyst) and antibodies

Peptides & proteins -3

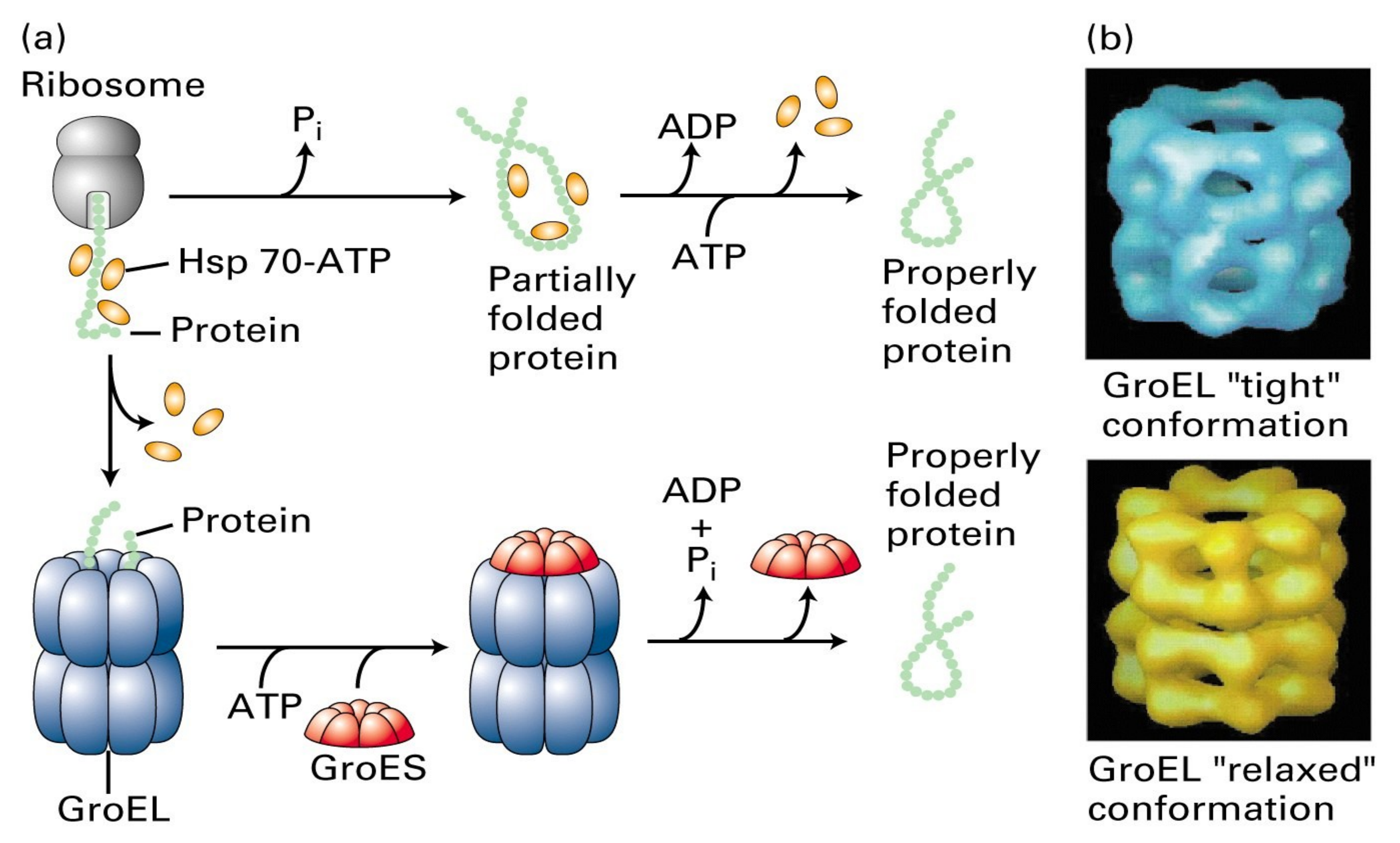
- The sequence of amino acids in a protein is coded in the genome and when the protein has to be synthesized an mRNA template is used for the synthesis (see gist of processes for genetic expression of proteins in the next slide)
- Twenty amino acids have codes in the genetic code, but some times other amino acids (a few hundred are known in nature) are necessary for protein function & these are inserted by post translational modifications
- After a protein is synthesized, various classes of molecules (proteins again) help them fold to the right conformation

Gene expression

- Proteins synthesized when required
- Specific genes activated & pre-mRNA transcribed
- mRNA spliced from pre-mRNA
- mRNA diffuses out of the nucleus to the cytosol to ribosomes that polymerize proteins using the mRNA as template for the amino acid sequence



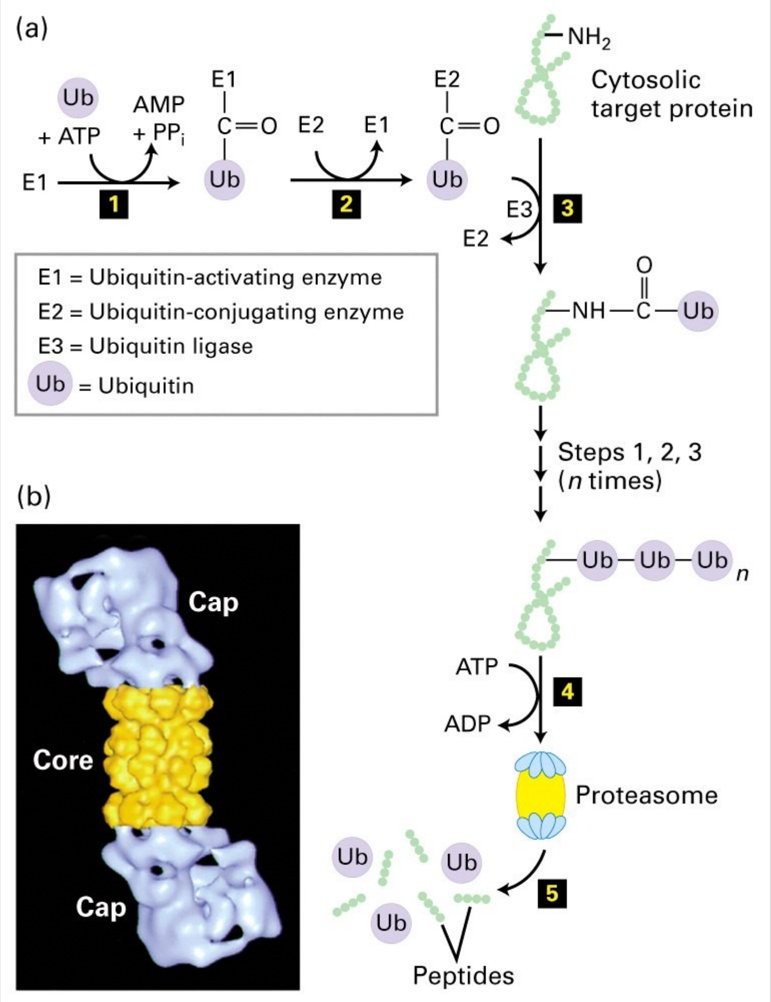
Protein folding – aided by a class of proteins called chaperones



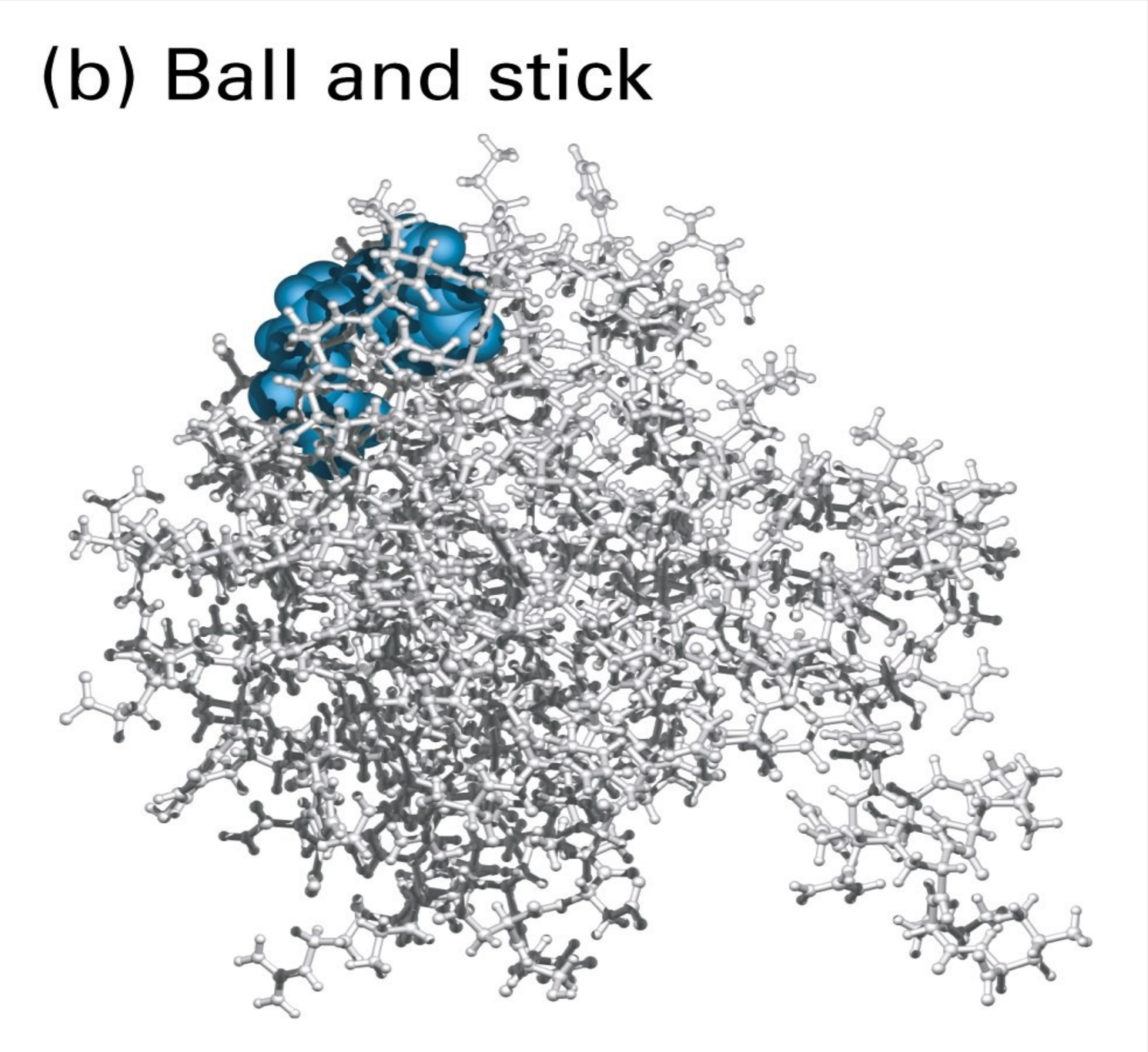
More on protein folding

Proteins that are damaged or do not fold correctly are:

- tagged with ubiquitins,
- bound to proteosomes
- degraded to polypeptides by proteolysis
- polypeptites further hydrolyzed to amino acids for new protein synthesis

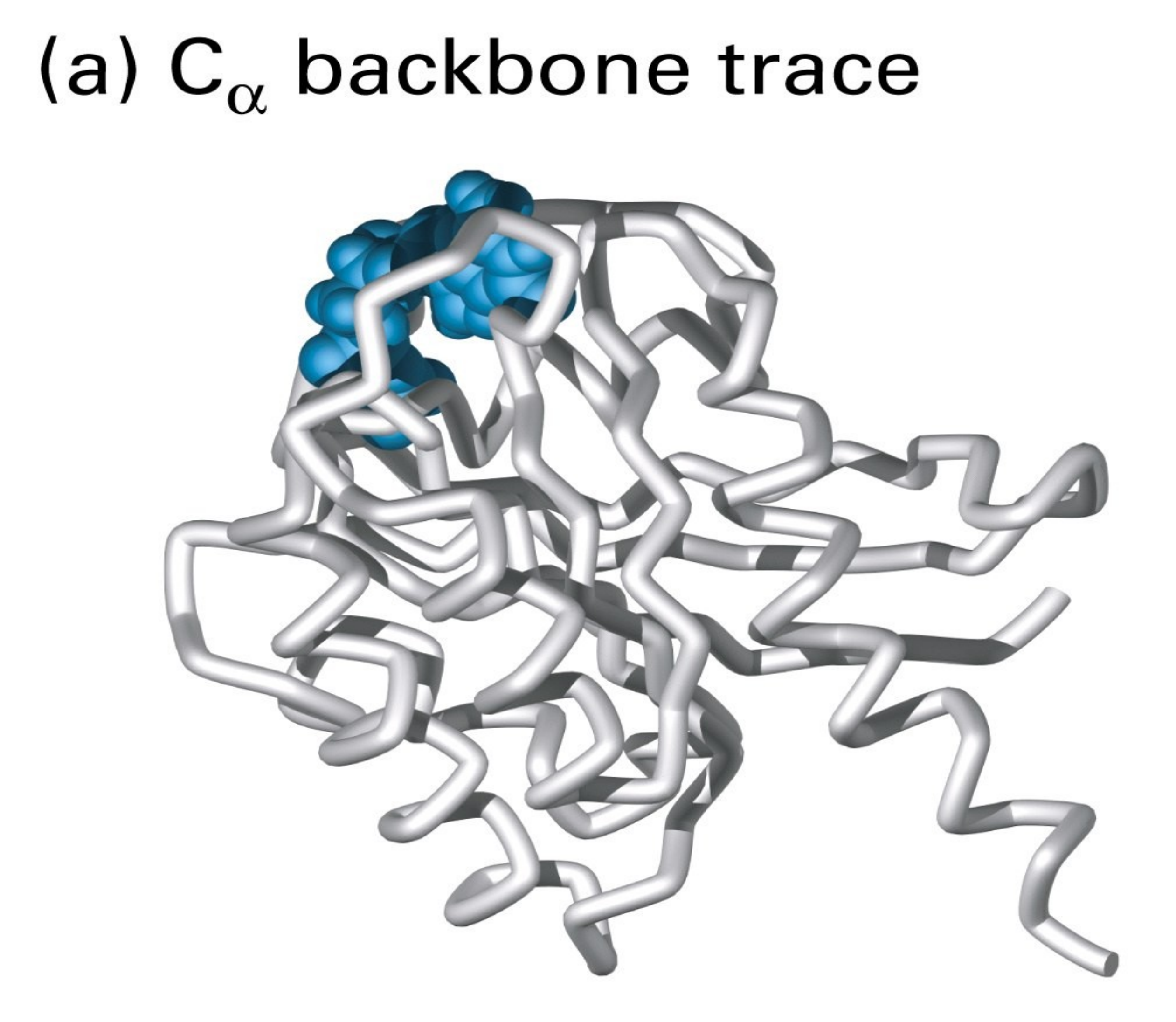


Cartoon: Ball & stick model (too much info)



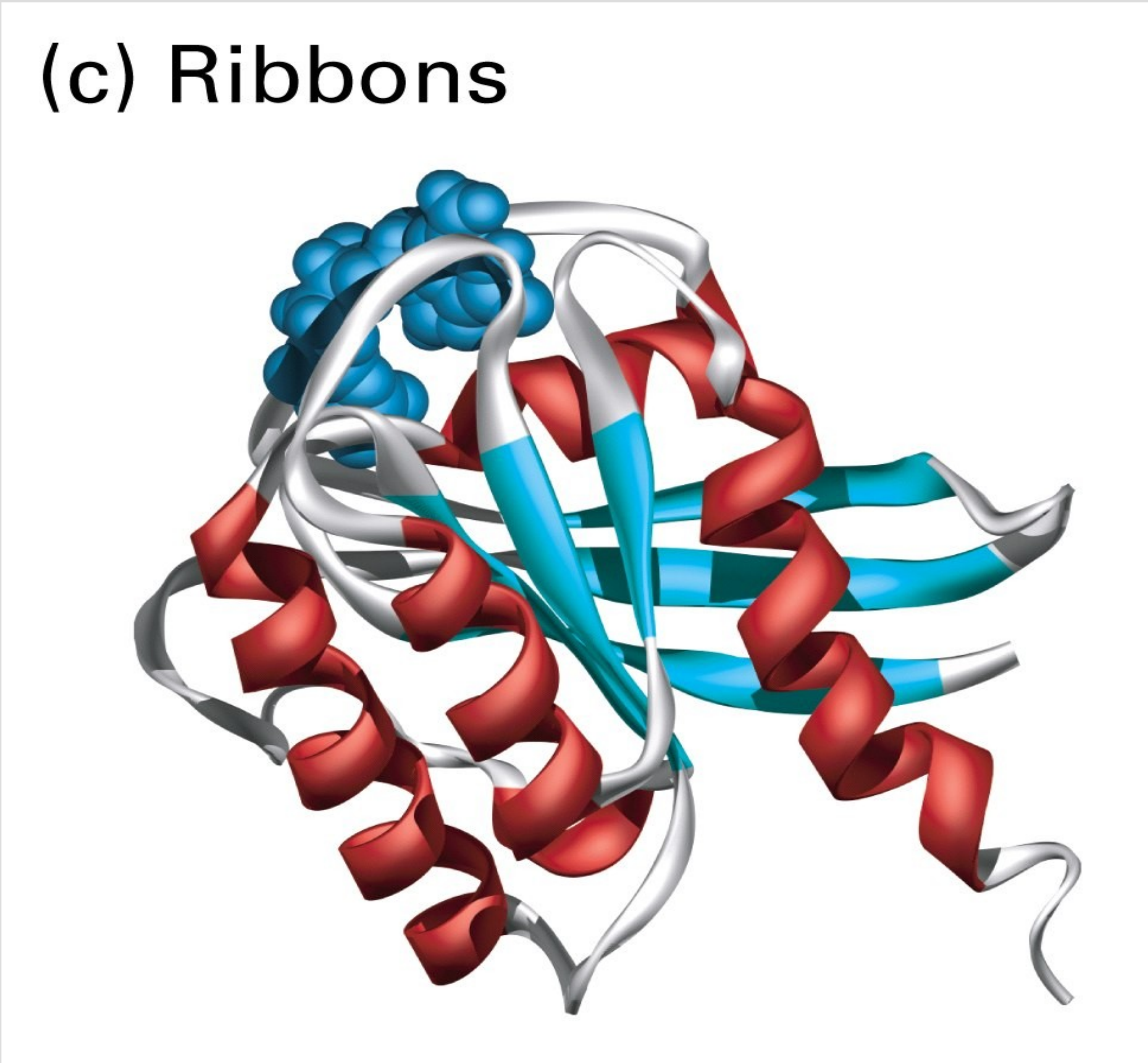
Cartoon: C_α backbone trace

Gives 3D structure to identify regions of interest



Cartoon: Ribbons

More information on properties of different regions



Residue code

Red – acidic

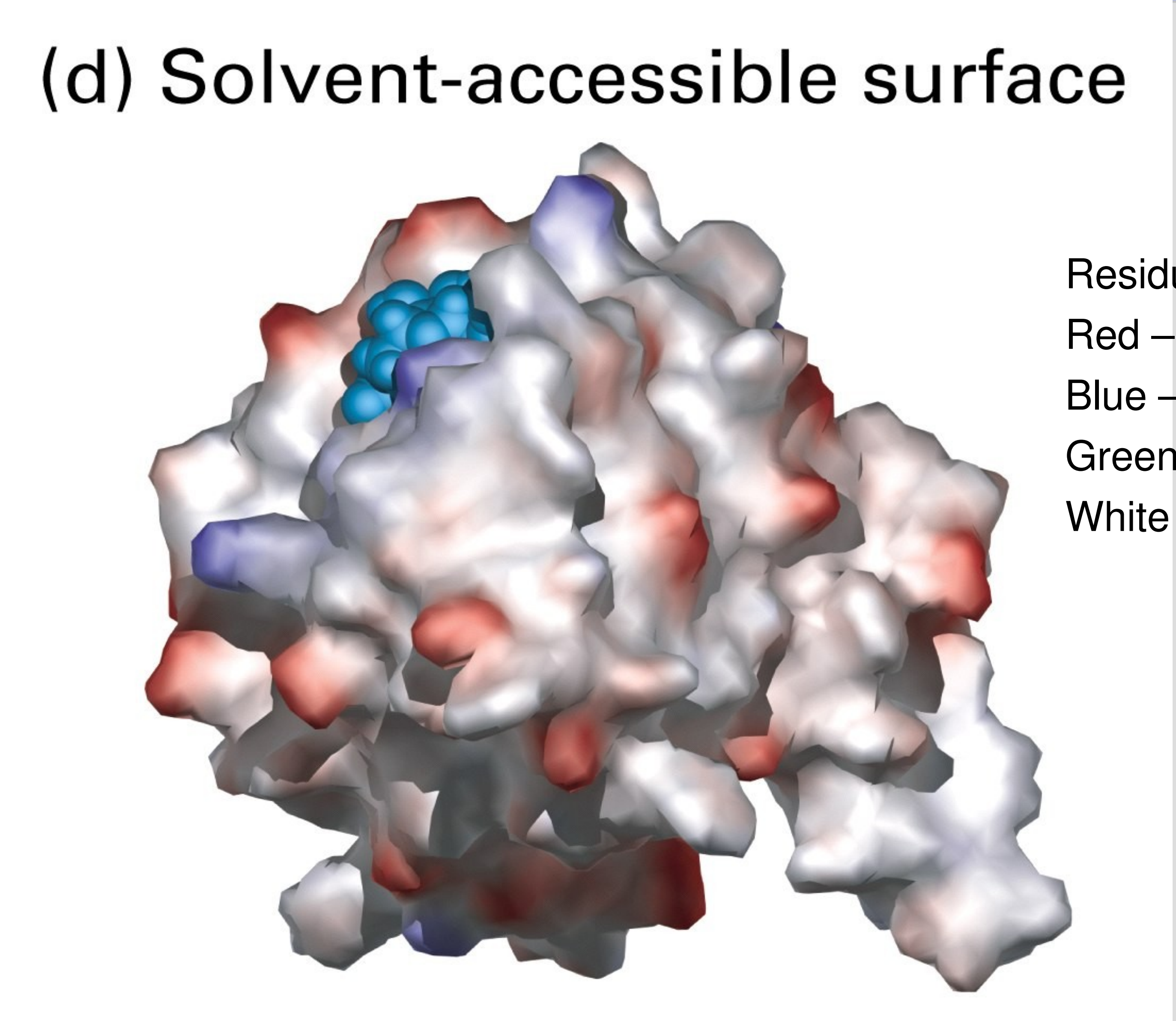
Blue – basic

Green – polar

White – non-polar

Cartoon: Solvent accessible surfaces

Additional info on hydrophilic-hydrophobic interactions, etc



Residue code

Red – acidic

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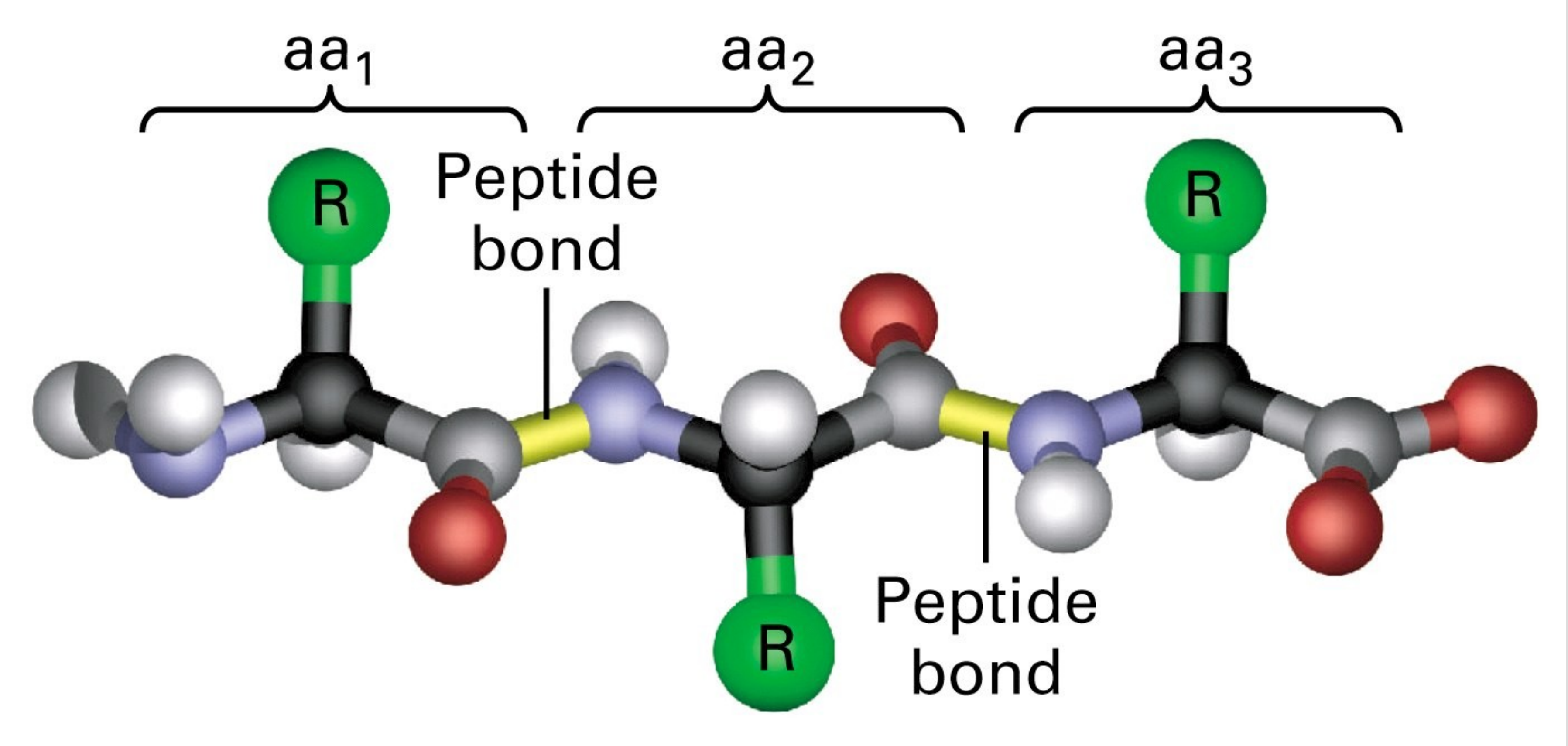
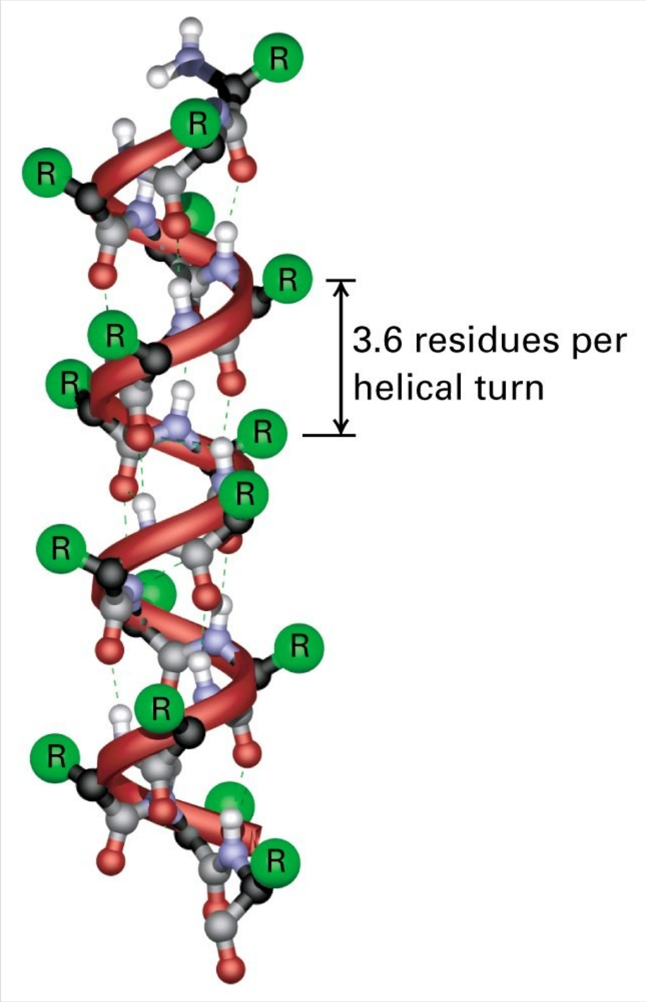
Peptide bond & primary structure



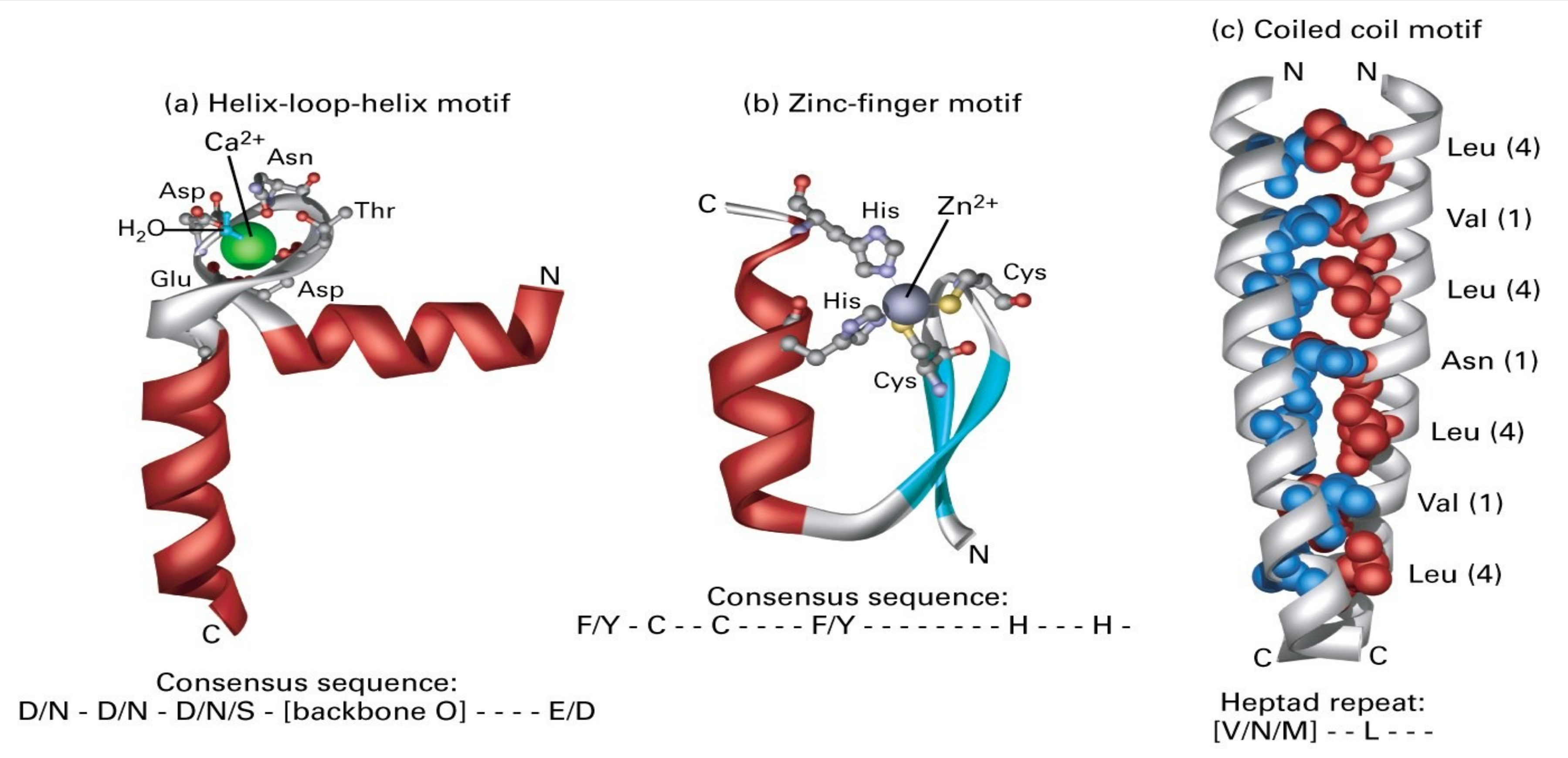
Protein folding: secondary structure

Local folding stabilized by hydrogen bonds

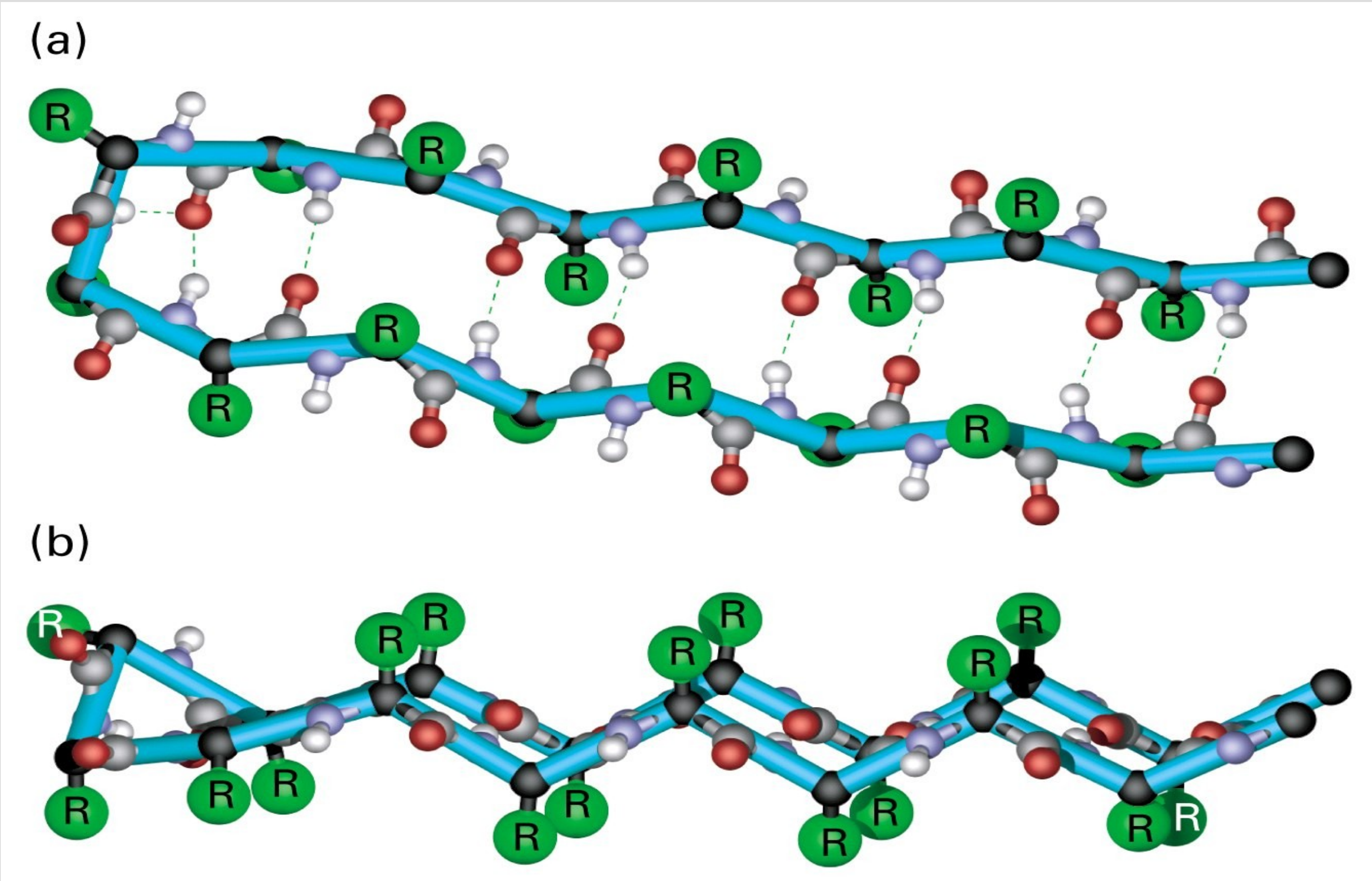
- α-helix a tightly packed right handed helical structure with the N-H group of an amino acid forming an hydrogen bond with the C O group four residue earlier
- Coiled coil and other motifs with α-helices
- α-helix part of many proteins that control gene expression since they bind to DNA – the diameter of the α-helix same as the width of the major grove
- α-helix also parts of structural proteins and homones



Some common motifs of α-helix



Protein folding: secondary structure
β-strand & sheets

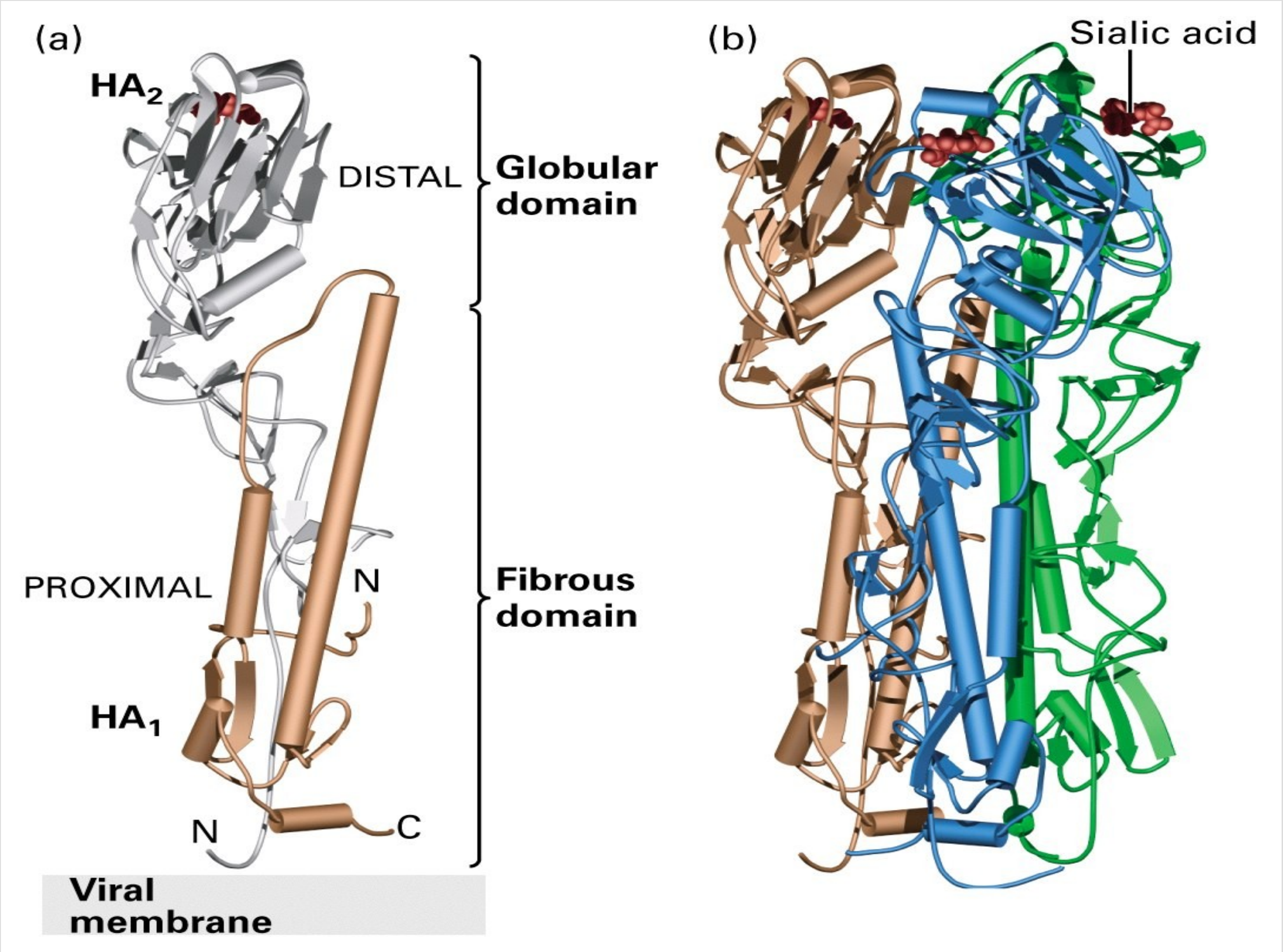


β-strand & sheets -2

- β-strand: a locally planar arrangement formed by lateral hydrogen bonding often forming a twisted pleated sheet
- β-strand can form sheets when more strands hydrogen bond laterally
- β-sheets can be open or closed
- Can have opposite faces hydrophobic or hydrophilic based on radical properties
- Various combinations of α-helices and β-sheets

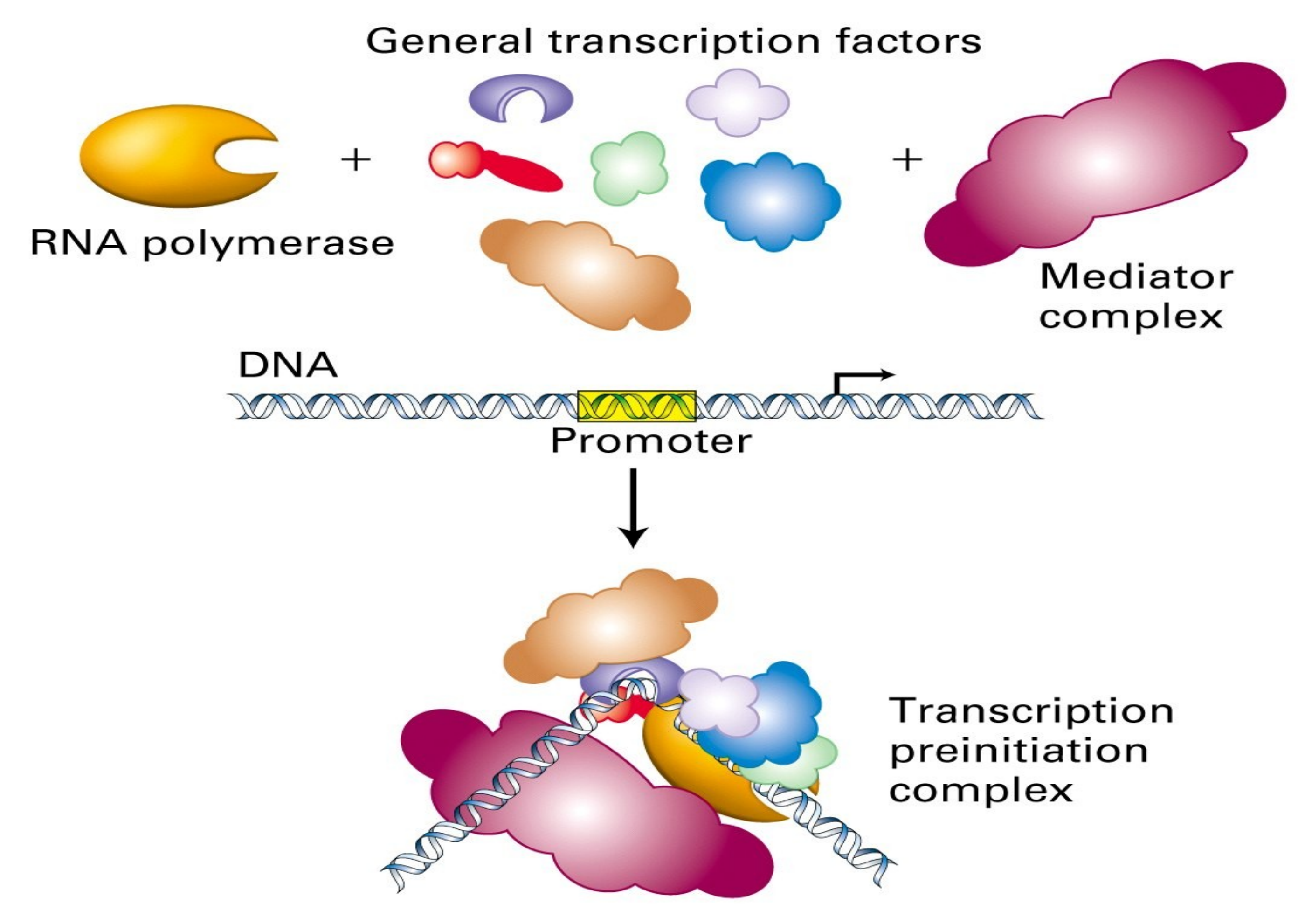
Protein folding: tertiary structure

Stabilized by disulfide, hydrogen, ionic bonds and hydrophilic/hydrophobic interactions



Protein structure: quarterary structure

A conglomeration of several molecules



Classification of proteins

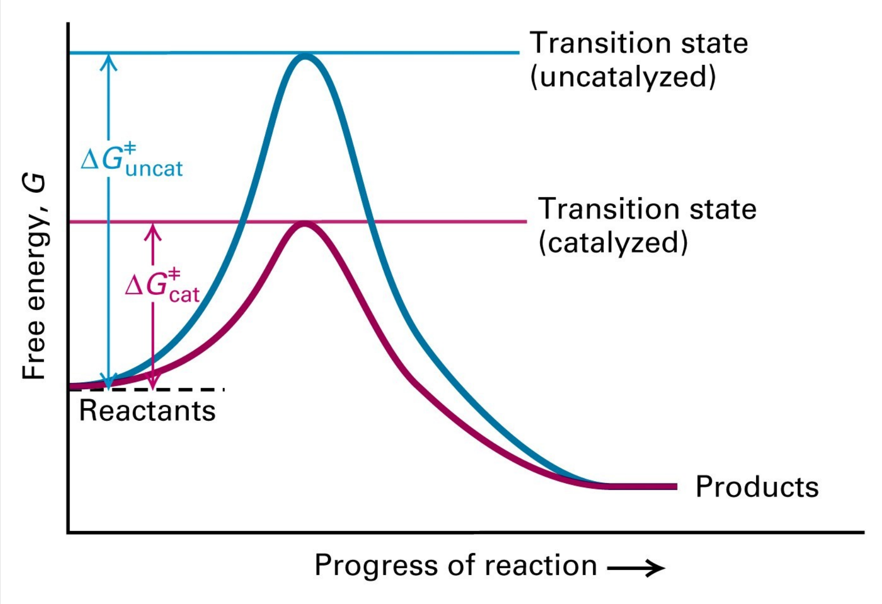
- Globular proteins (also called spheroproteins)
  - Almost all are soluble and many are enzymes
- Fibrous proteins (also called scleroproteins)
  - Rod or wire-like and are non-soluble & inert and act as structural material in connective tissues, tendons, bone matrix & muscle
- Membrane proteins
  - Attach to membranes and serve as signaling molecules or as channels

Some examples of proteins

A quick look of the immense variability of structure and function of proteins.
Also if a function is common, conservation of the core block across species.

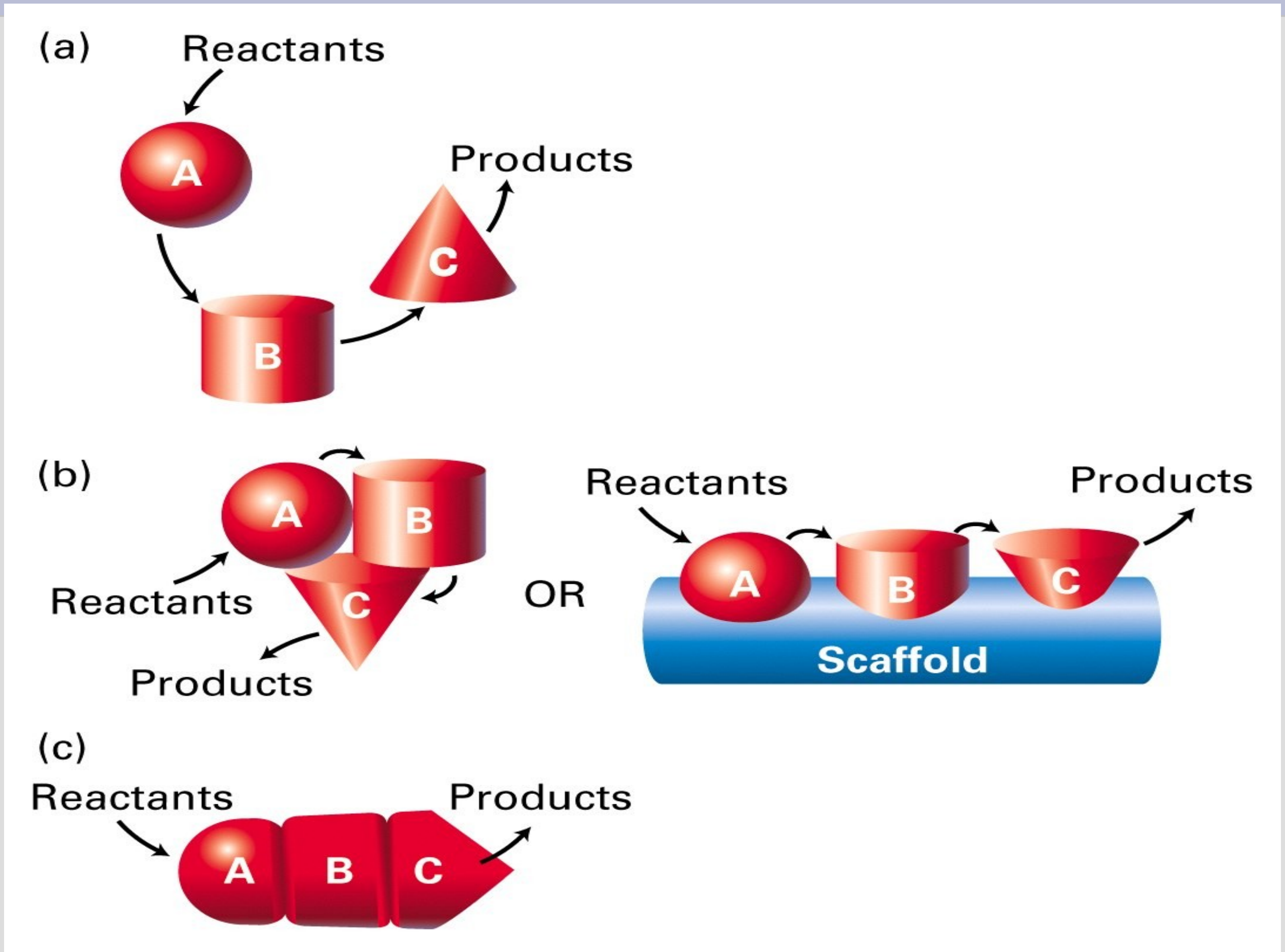
Enzyme catalyzed reactions -1

- Catalysis, reduces the activation energy for a reaction as shown in the adjacent figure
- This might be accomplished in many ways



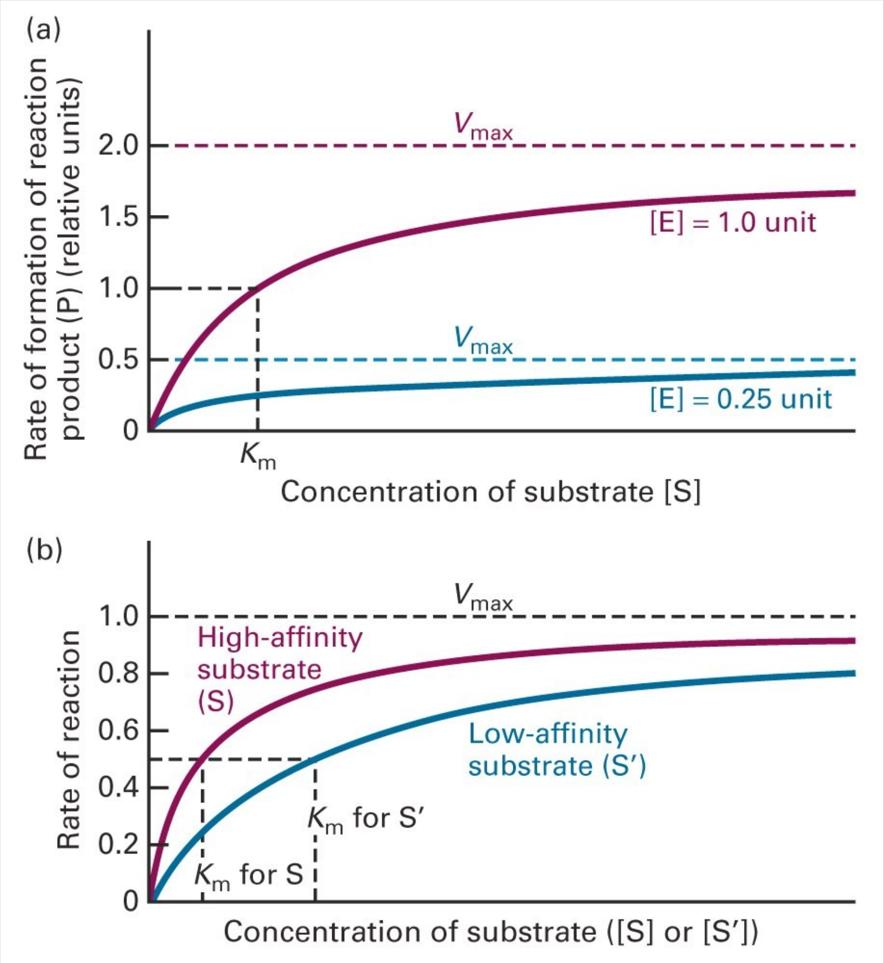
Enzyme catalyzed reactions -2

The reaction can be catalyzed in many ways

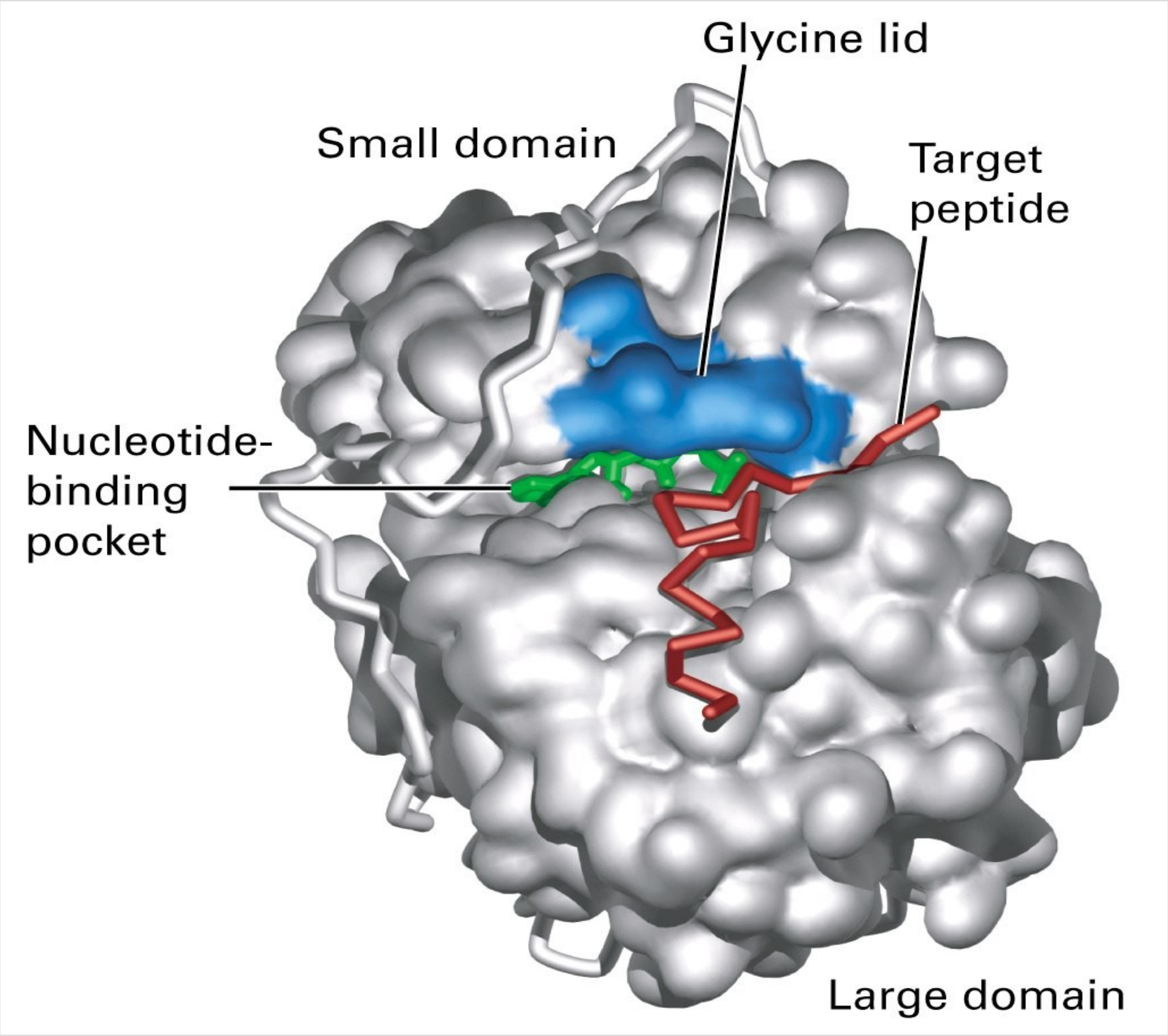


Enzyme catalyzed reactions -3

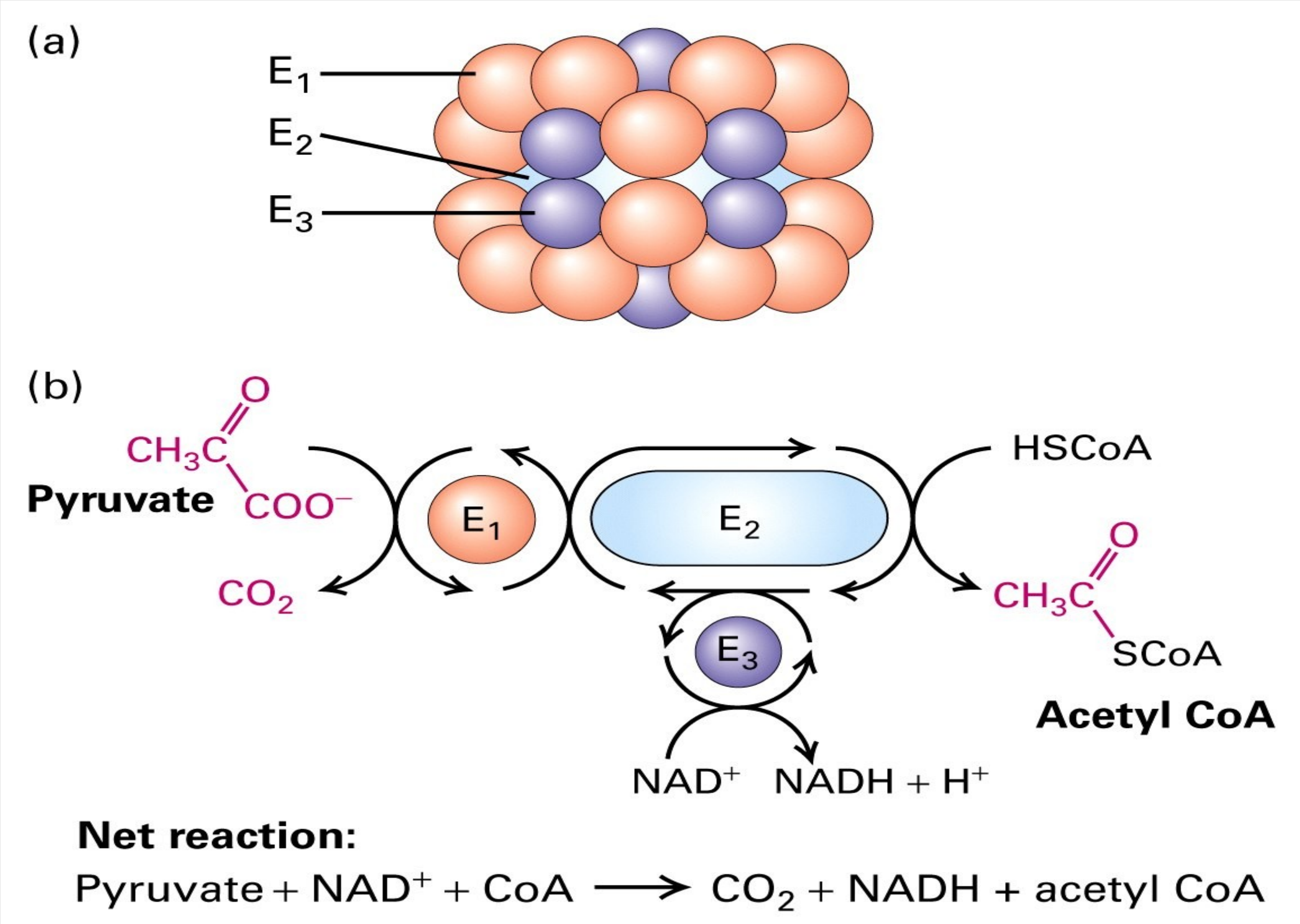
- Measuring reaction kinetics as a function of concentration can help one guess probable processes



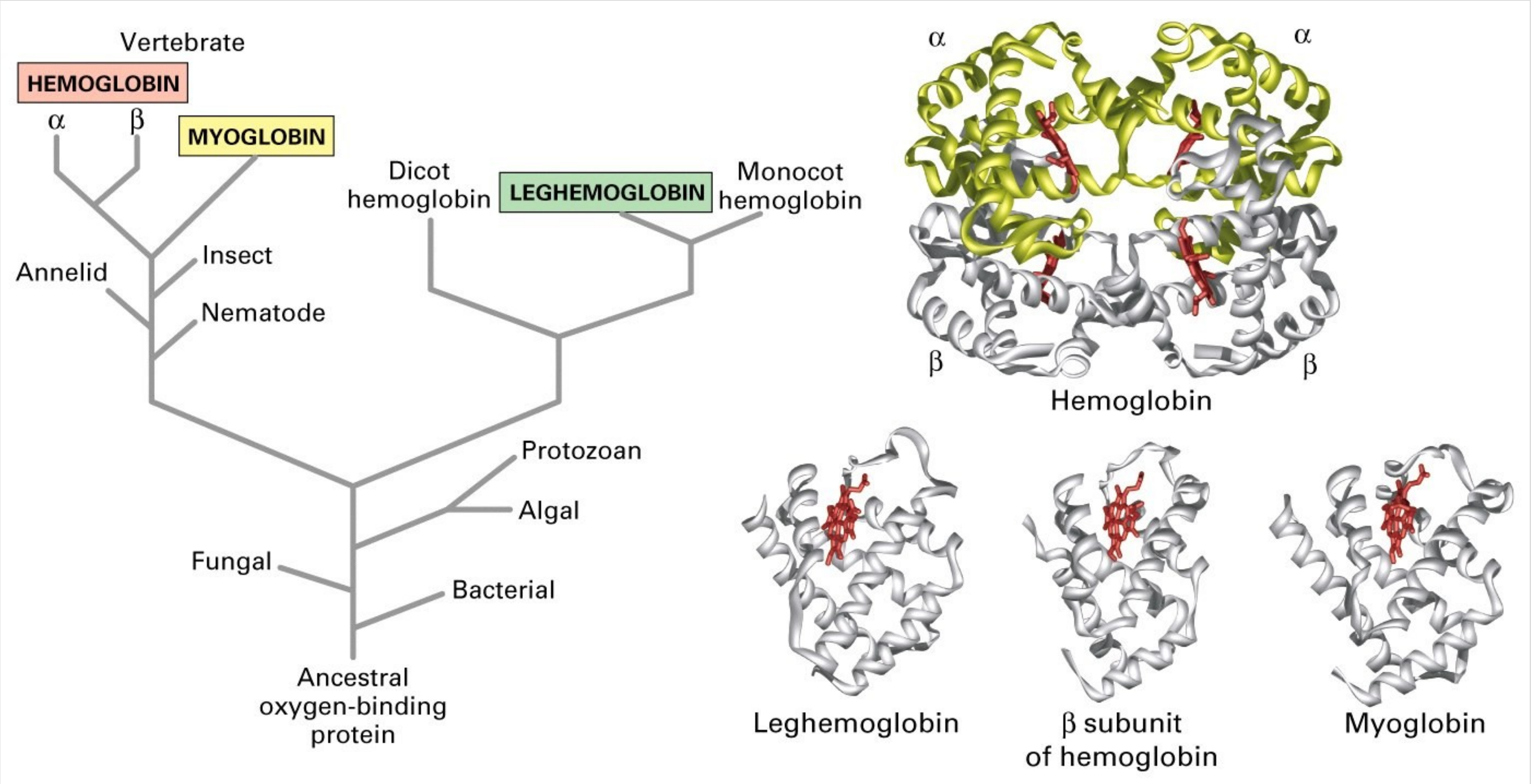
Structure of an enzyme
What does it do?



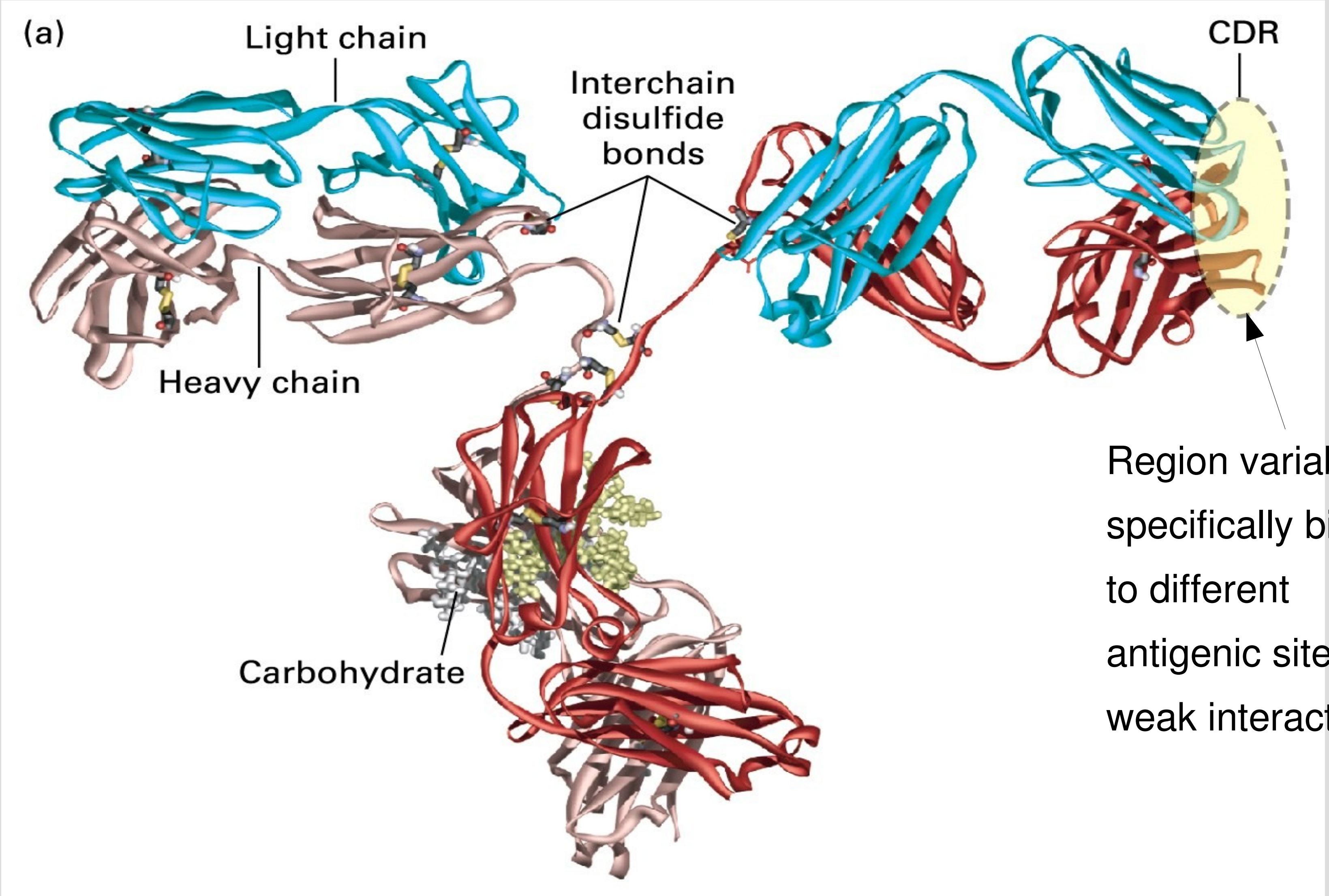
Enzyme examples:
Multi-enzyme process



Oxygen binding protein evolution

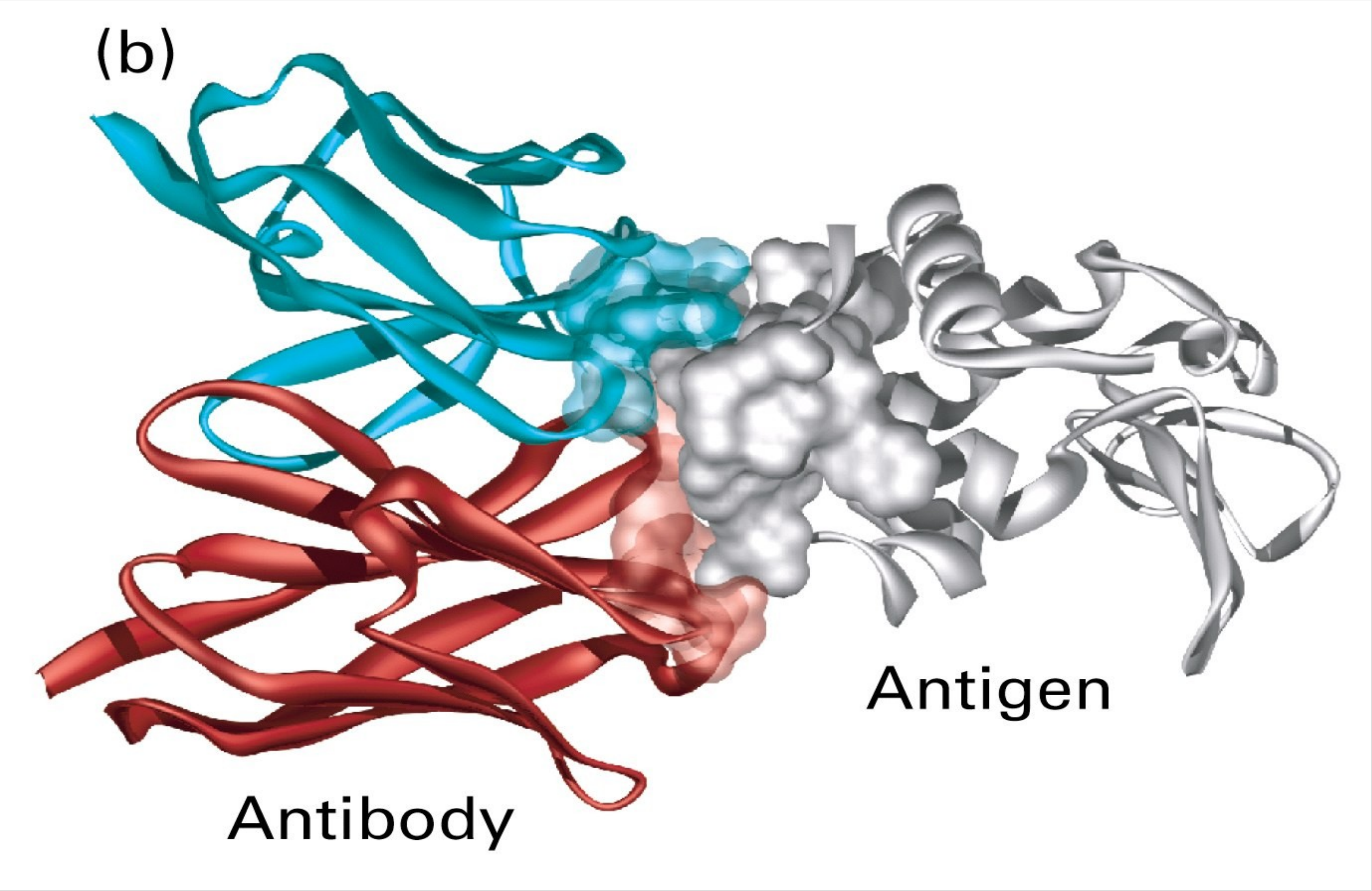


Antibodies



Region variable & specifically binds to different antigenic sites by weak interactions

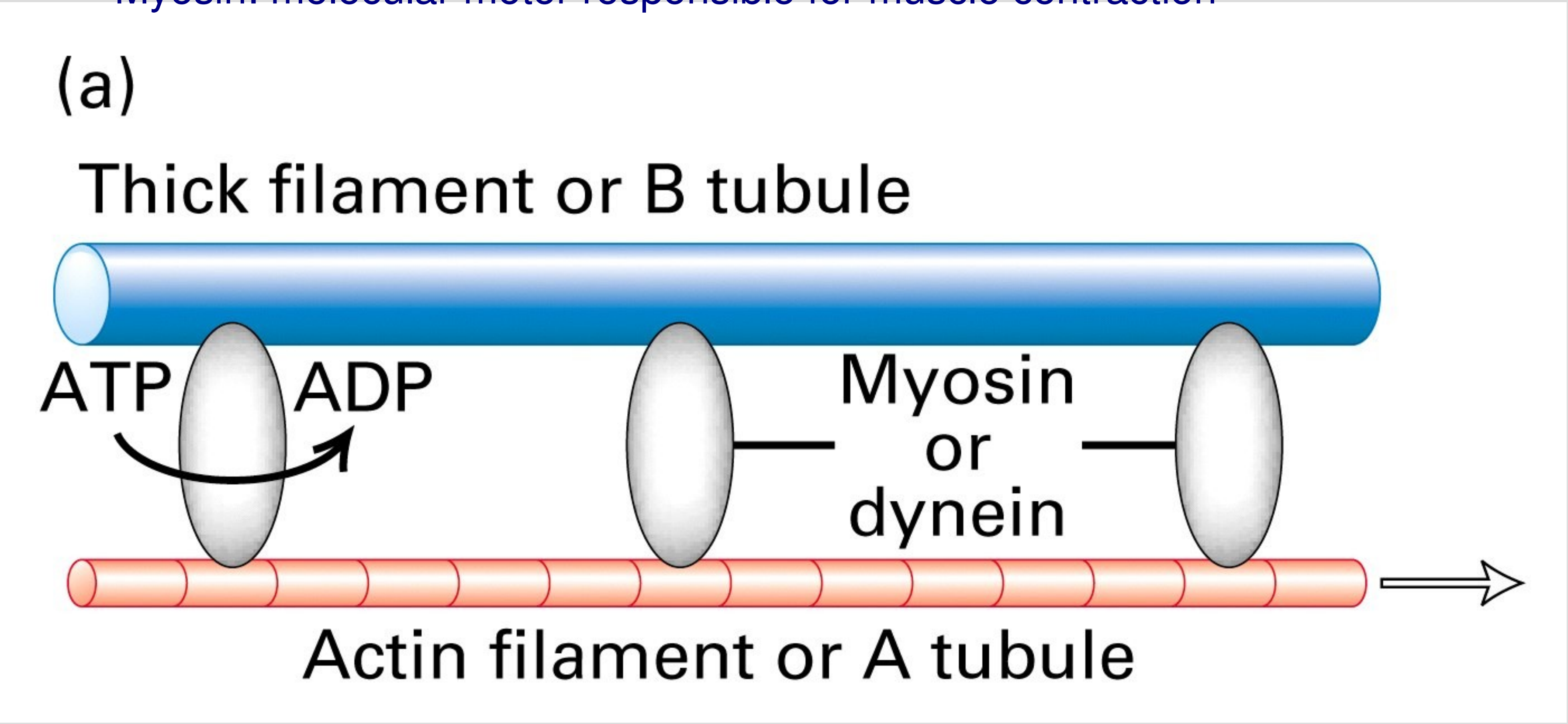
Antigen-antibody binding



Molecular motors -1
Fueled by ATP

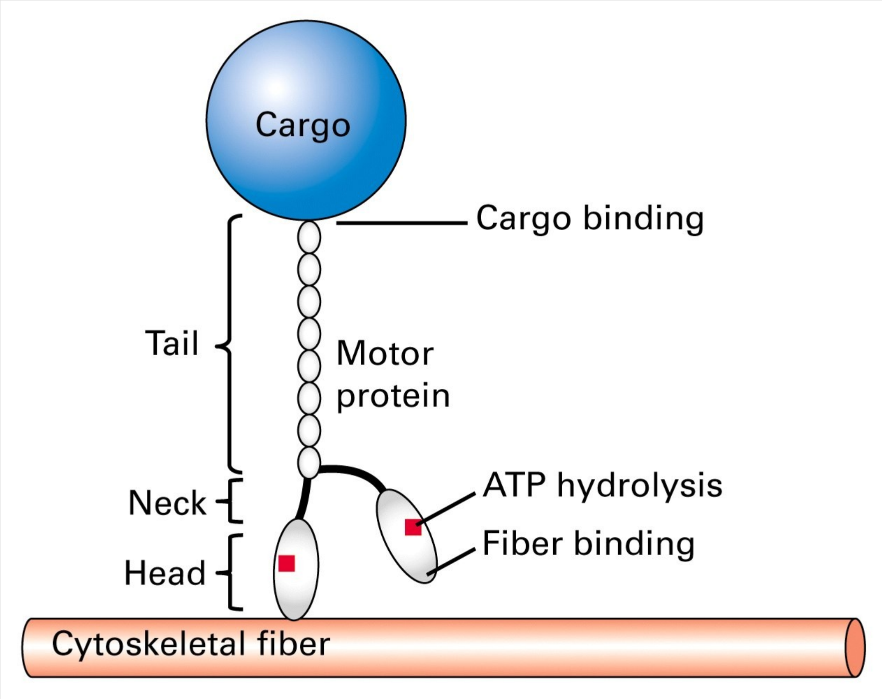
Dynein: molecular motor responsible for organelle transport along cyo-skeleton

Myosin: molecular motor responsible for muscle contraction

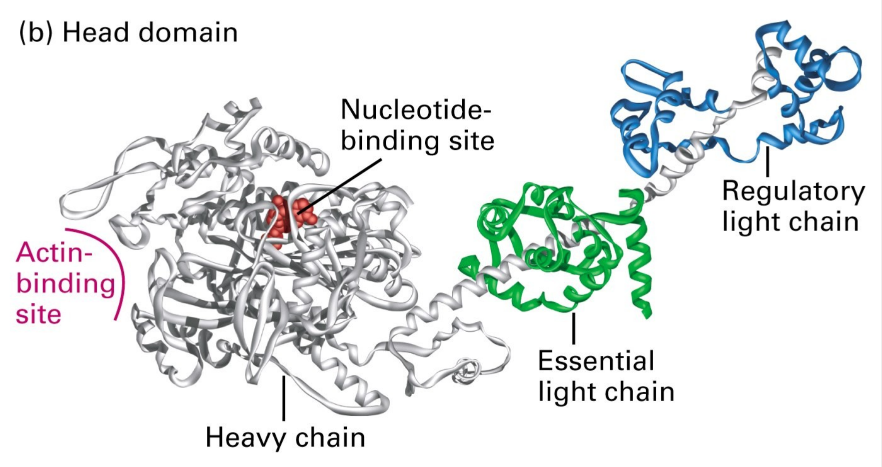


Molecular motors -2

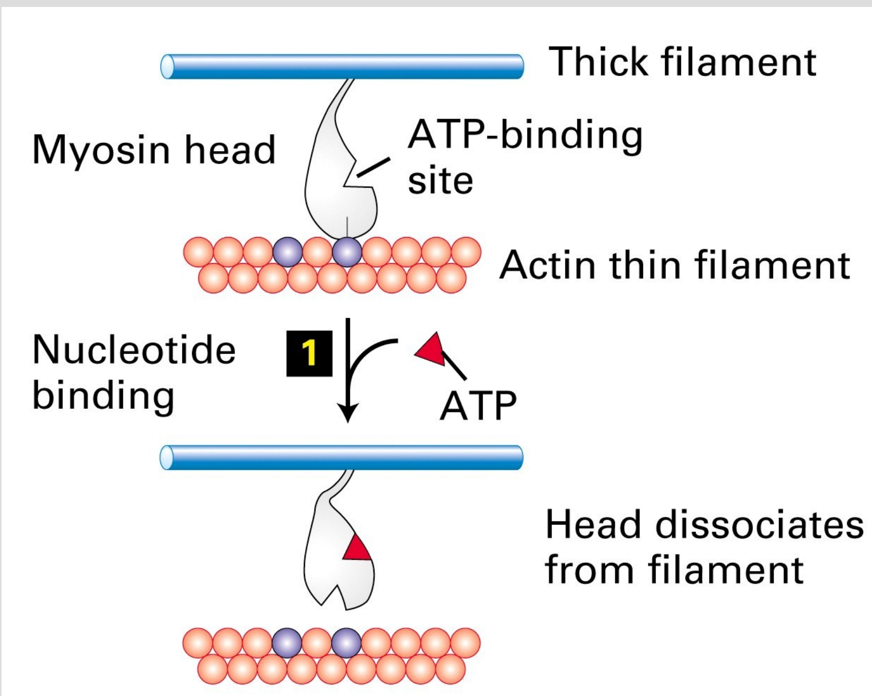
- Interesting new finding that has been recently confirmed with microscopy that molecules often transported within cell with molecular motors!

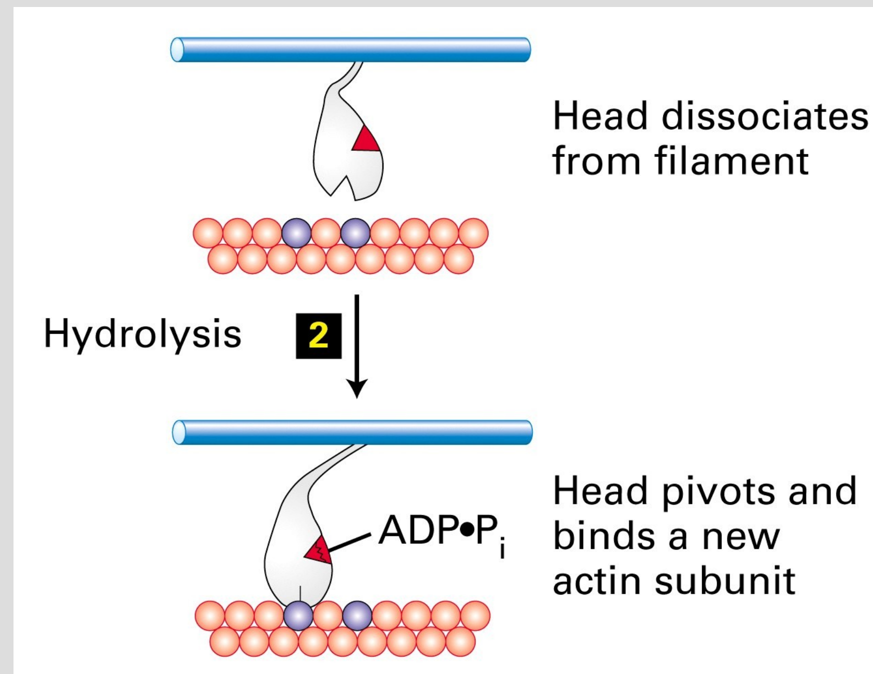


Molecular motors -3
Myosin well studied



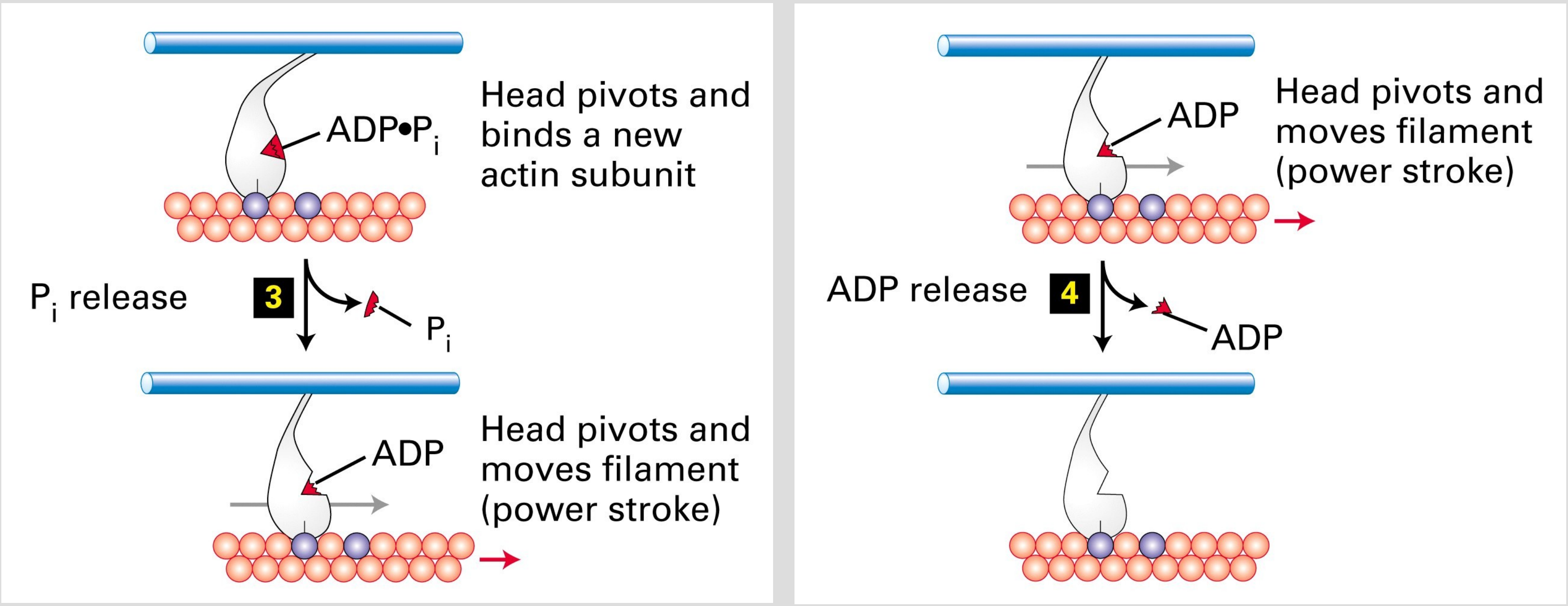
Molecular motors -4
Myosin – action sequence -1





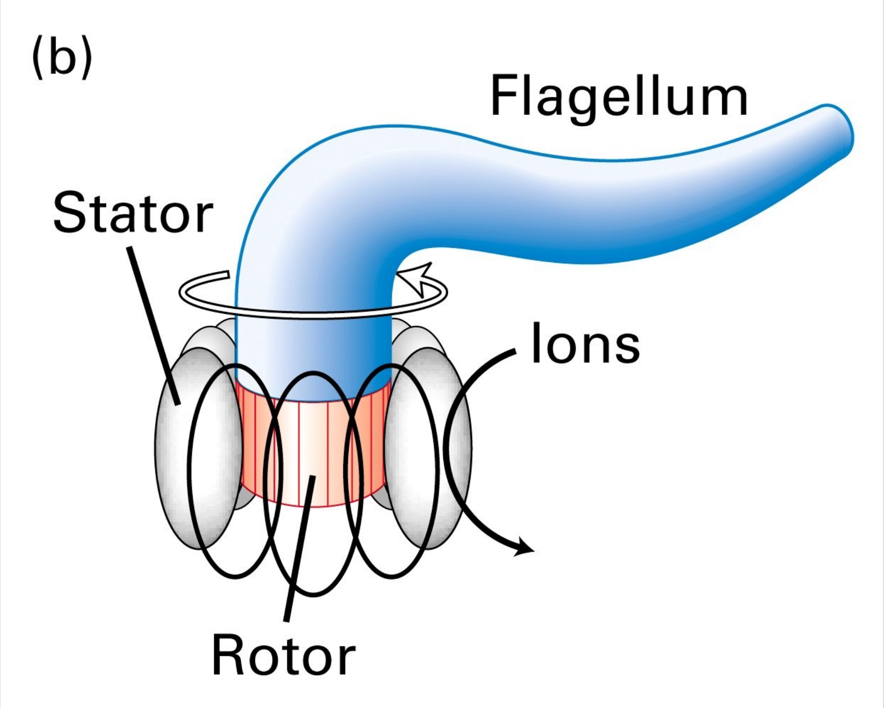
Molecular motors -5

Myosin – action sequence -2



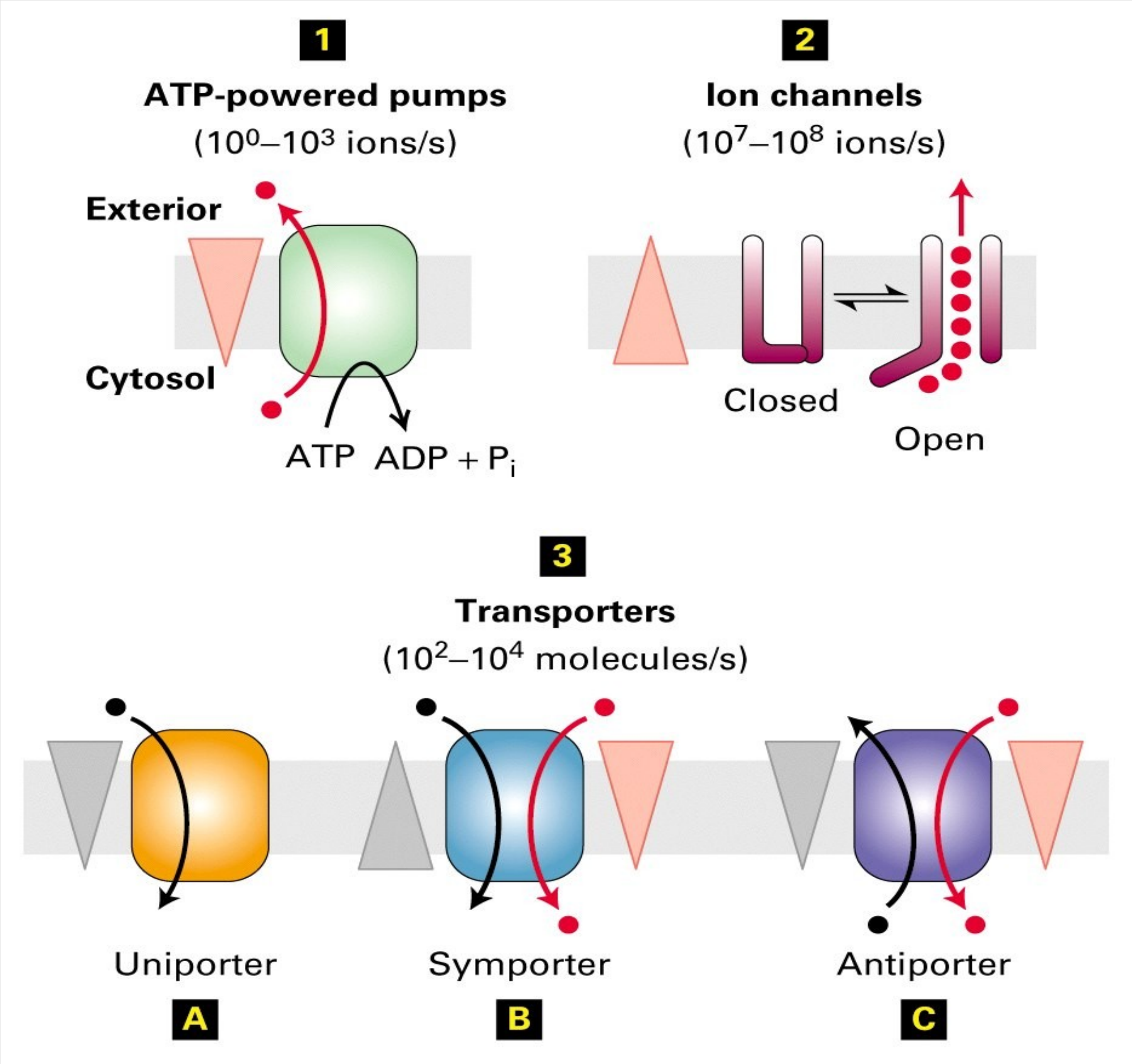
Molecular motor -6
Ionic gradient driven

- Motor of flagellum anchored in cell membrane
- Ionic gradients of either protons or sodium ions drive the rotor with respect to the stator
- Would be interesting to check out how the torque is generated!

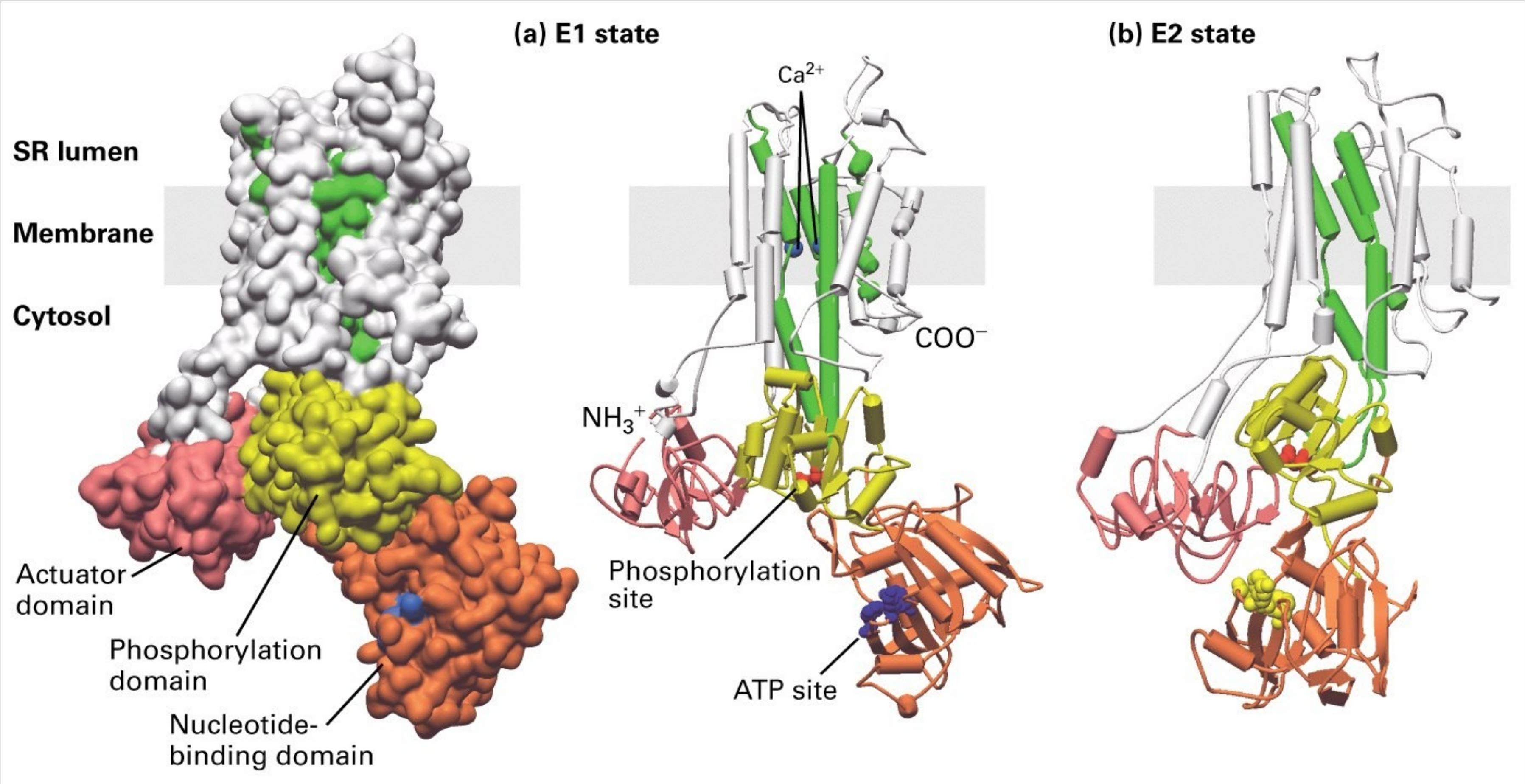


Transport across membranes

Classes of membrane proteins associated with transport

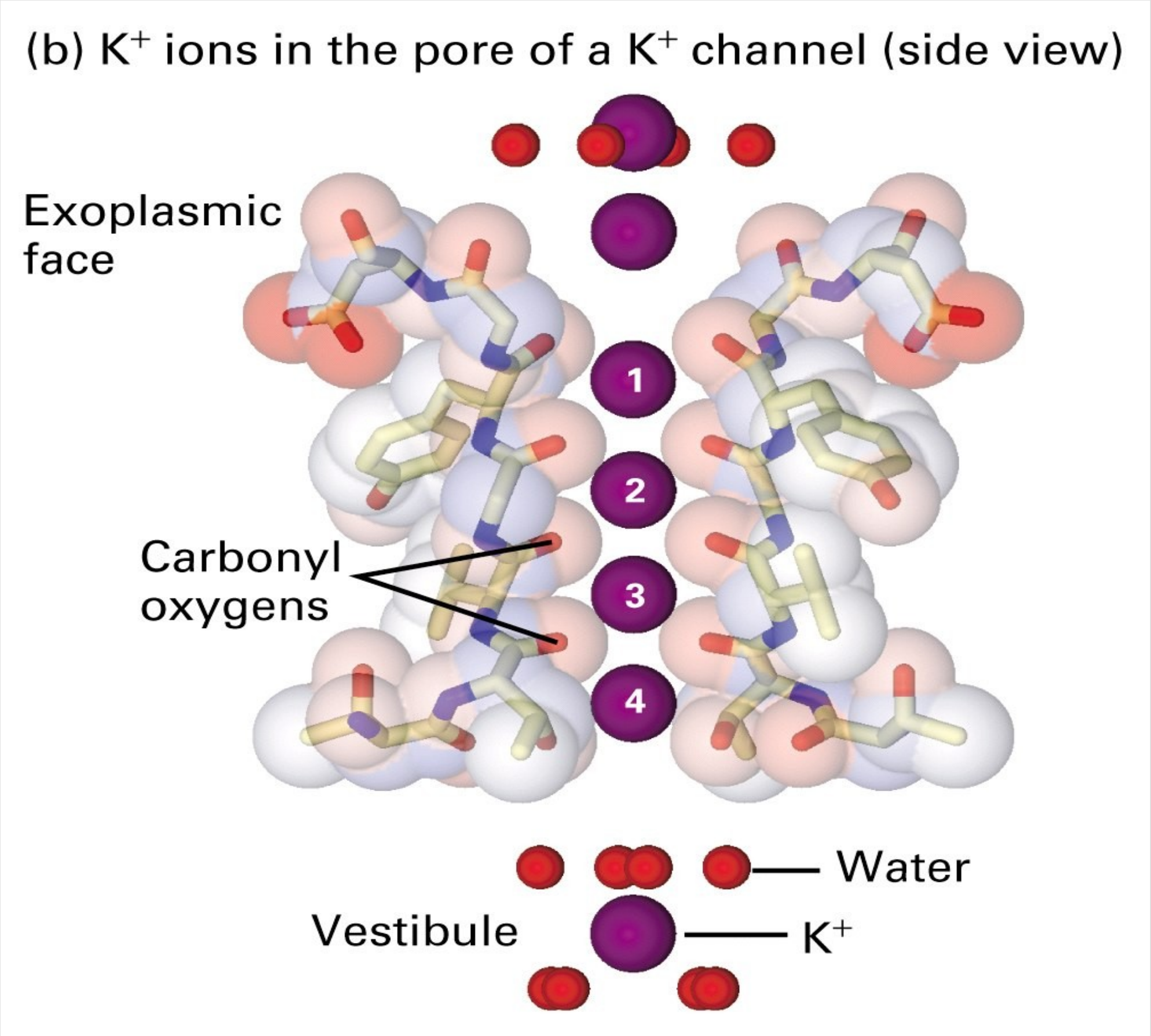


Example: ATP powered pump



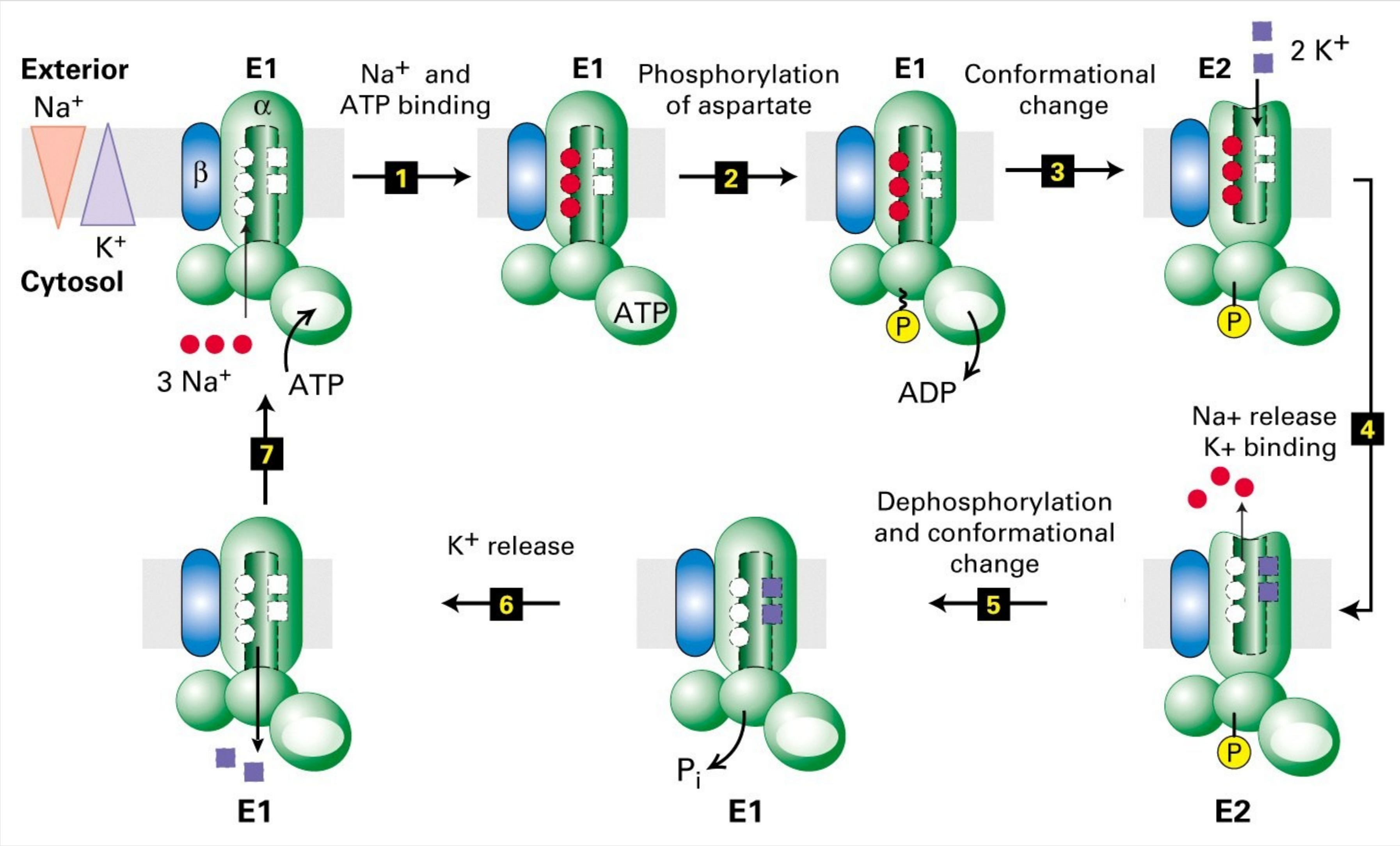
Example: Ion channel

Potassium channel (note in this case unsolvated ion diffuses through)



Example: Symporter

Transports sodium and potassium in opposite directions



Summary

- A great deal of cell function are carried out by polypeptides and proteins
- They are synthesized from amino acids as and when needed & degraded after use
- A great variety of molecule shape and function is possible to four levels of structural conformation
- We'll select some of these proteins for studying them in greater detail in their functional contexts