Nanobiotechnology

Place: IOP 1st Meeting Room
Time: 9:30-12:00

Reference: Review Papers

Grade: 40% midterm, 60% final report (oral + written)

Midterm: 5/18

Oral Presentation

1. 20 minutes each person
2. One major reference (2010-2012)
3. Source: Nature, Science, Nature Biotechnology
4. Other journals: Nano Letter, Advanced Materials, PNAS, JACS, PRL

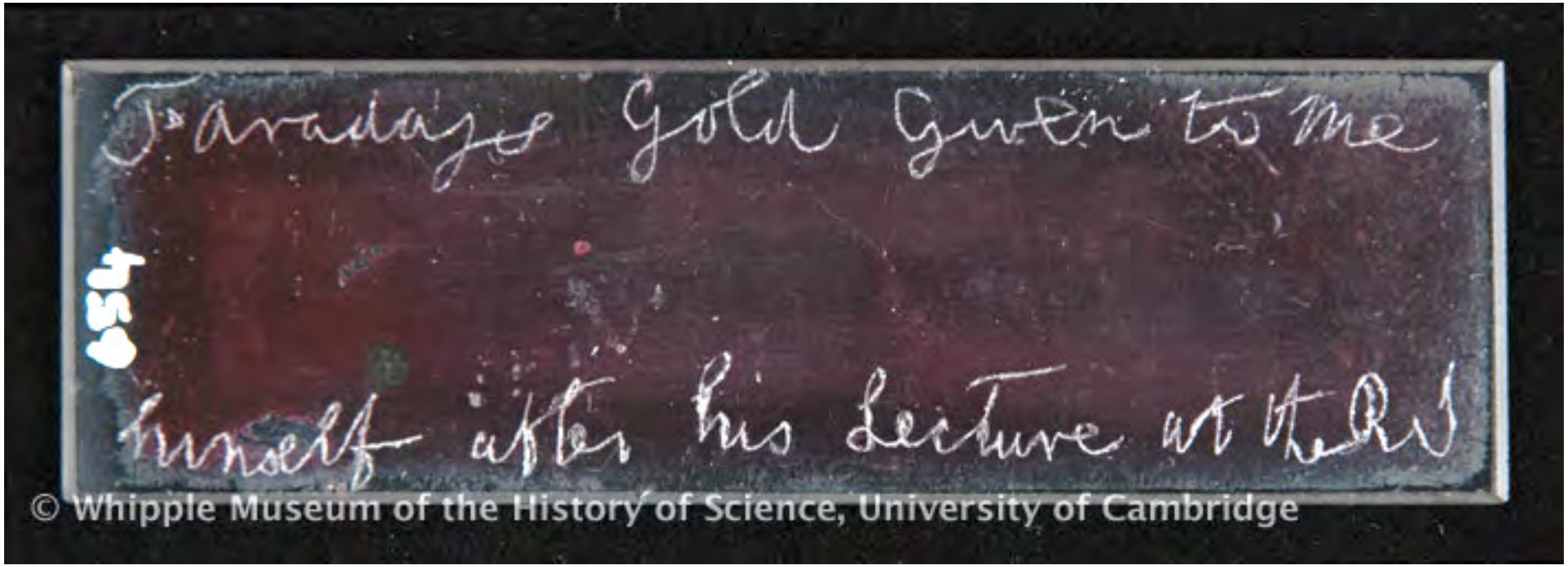
History

- Atom
- Earth, Air, Water Fire

SEM: 20-40 nm
Silver 66.2%
Gold 31.2%
Copper 2.6%

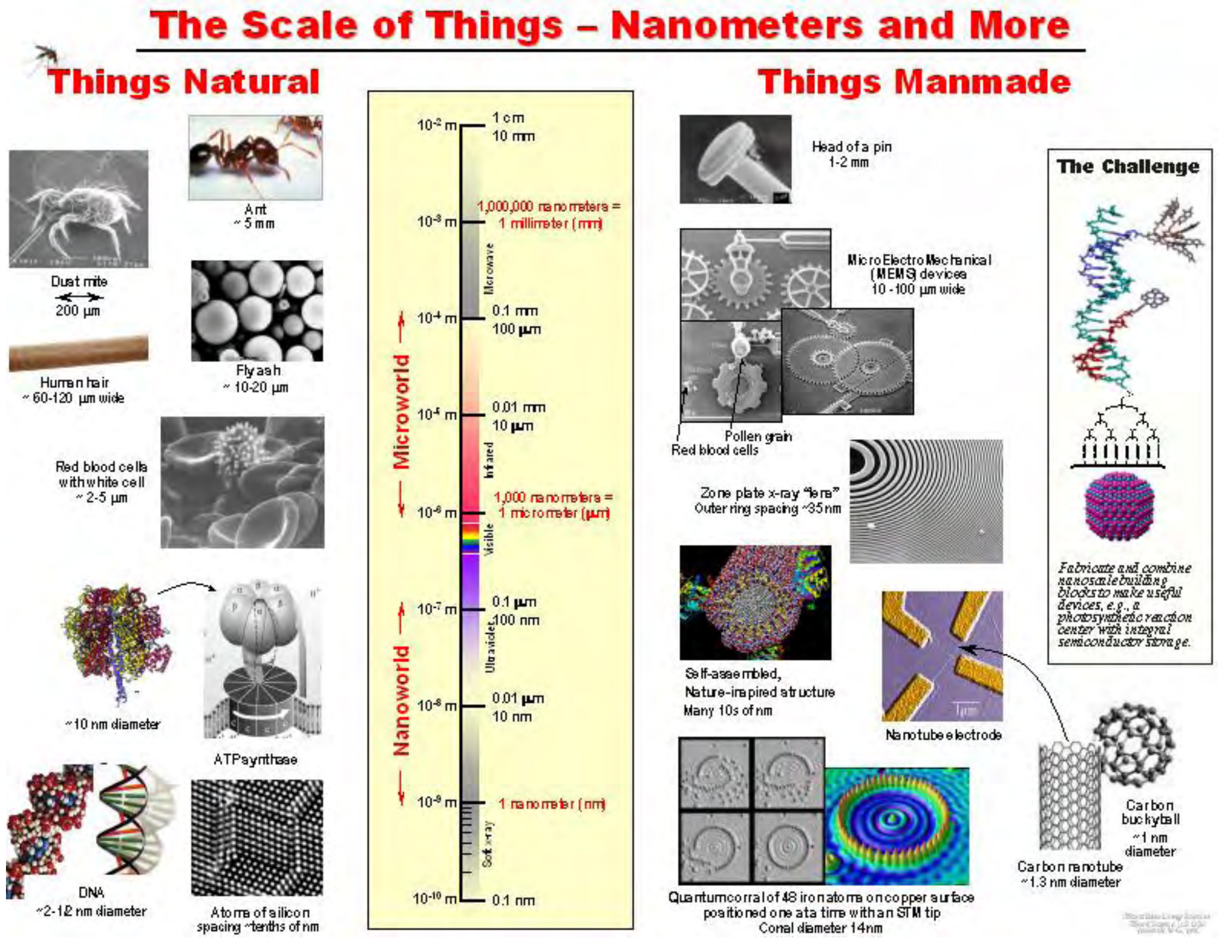
Red – gold at 520 nm
Purple- larger nanoparticles
Green- scattering >40nm

Faraday’s Gold Sol



1856
20-40 nm gold

What is nano?



http://cohesion.rice.edu/CentersAndInst/CNST/emplibrary/Scale%20of%20Nanotechnology.jpg

Nanosciences and Nanotechnology

- Science
  - Theory
  - Experiment
- Technology
  - Development
  - Applications
  - Commercialization

Nanotechnolgy

- Top-Down Approach
- Lithographic, Manipulation, Industrial process

- Bottom-Up
- Self-assembly, natural process

What is nanobiotechnology

- Nano + Bio
- Nano-fabrication => nanopatterning, NEMs
- Nano-manipulation => optical, electrical, acoustic, thermal, magnetic, mechanical
- Nanomaterials => Q-dots, SERS, Plasmon, Magnetic
- Nano-imaging => SPM, optical tool, EM

What is nanobiotechnology

- Bio + nano
- DNA assembly
- Cell factory
- Molecular motor
- Energy

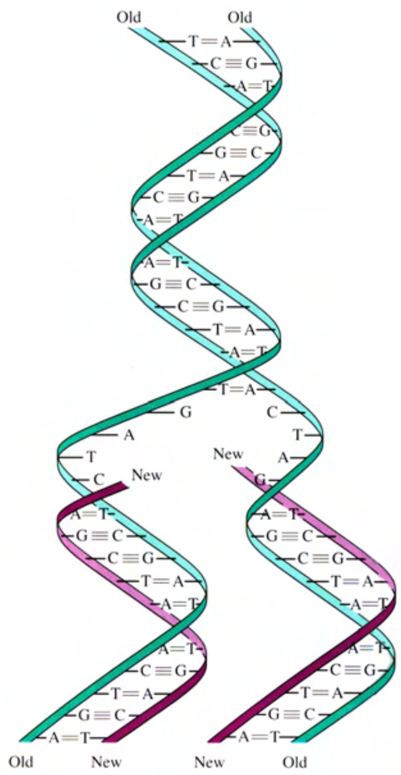
Building Block

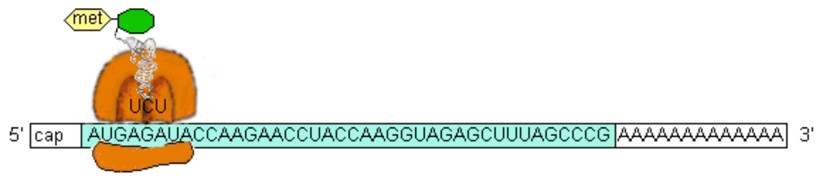
- Log, Brick
- High energy physicist –quark
- Physicist-proton, neutron, electron
- ➔periodic table
- Chemist- molecule
- Biologist- cells

How to assemble them

- Thermodynamic
- Chemical bond
- Hydrogen bond
- Electrostatic
- Van der Waals interaction
- Other interactions

Self-Assembly Process in Nature





Topics

Fundamental Knowledge and Current Literatures

- Analytical Chemistry
  - Spectroscopic tools
  - Microarray
  - Cell-surface interaction
    Ultrasensitive detection
- Physical Chemistry
  - Single molecular behavior (Optical and AFM)
  - Optical properties of Q-dot
  - SERS
  - Surface plasmon
- Material Chemistry:
  - Nanomaterials: Q-dot, nanoparticle, DNA assembly
  - Surface functionalization
  - Drug delivery
  - DNA, Protein, Cell interactions
-

1. Review of biochemistry and cell biology

- Building blocks
  - Lipid
  - Carbohydrate
  - Amino acid
  - Nuclear acid
- Structural function relation
- Central dogma
- Enzymatic reactions
- Cells
- Virus and bacteria

2. Micro- and Nano- Fabrication and Characterization Techniques

- Photolithography
- Soft-lithography
- E-beam lithography
- AFM/STM
- Interferences
- MEMs and NEMs

2. Micro- and Nano- Fabrication and Characterization Techniques

- Optical
- Electron
- Scanning Probe
- Spectroscopy
- Thermal
- Surface

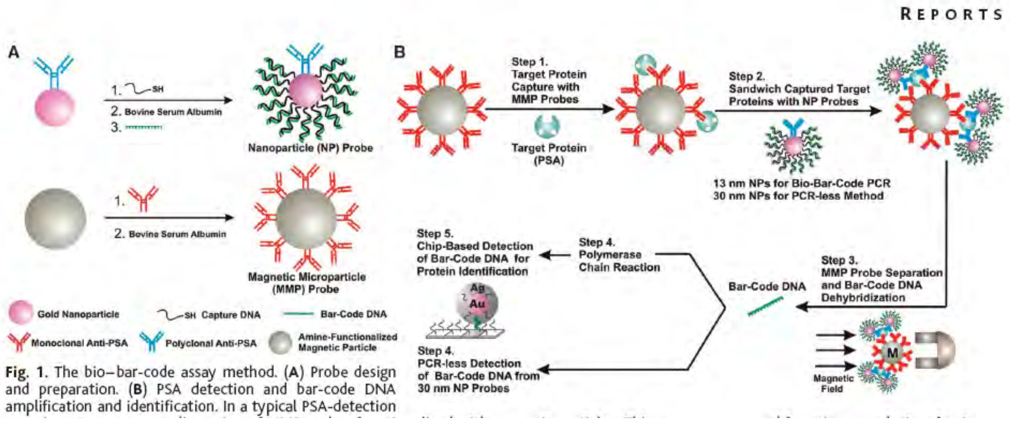
3. Synthesis and Modifications

- Carbon-based nanomaterials
- Metallic nanoparticles
- Quantum dots
- Polymers
- Chemical interactions at nano-scale
- Synthesis and modification of nanomaterials

4. Properties

- Materials, structure and nanosurface
- Energy at nano scale
- Material Continuum
- Nano-thermodynamics

5. Applications of nanoparticle in biotechnology



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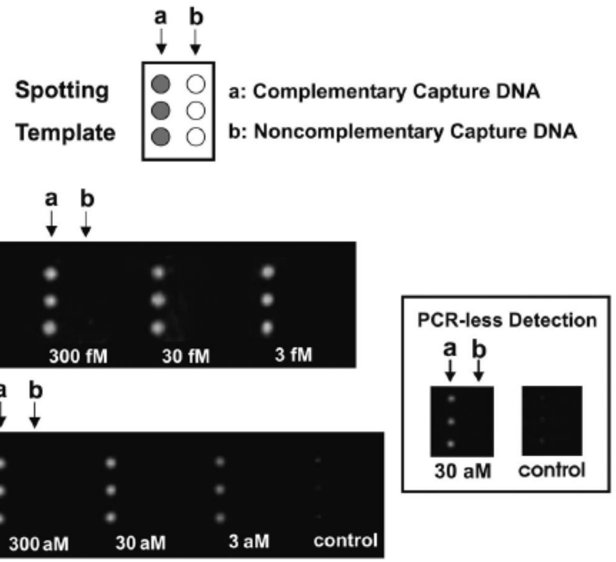
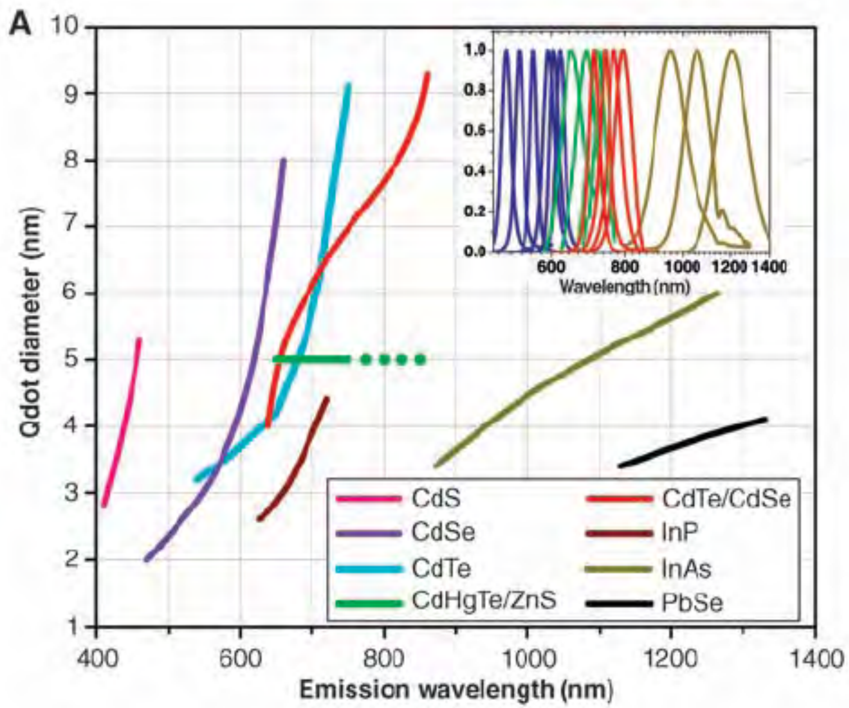
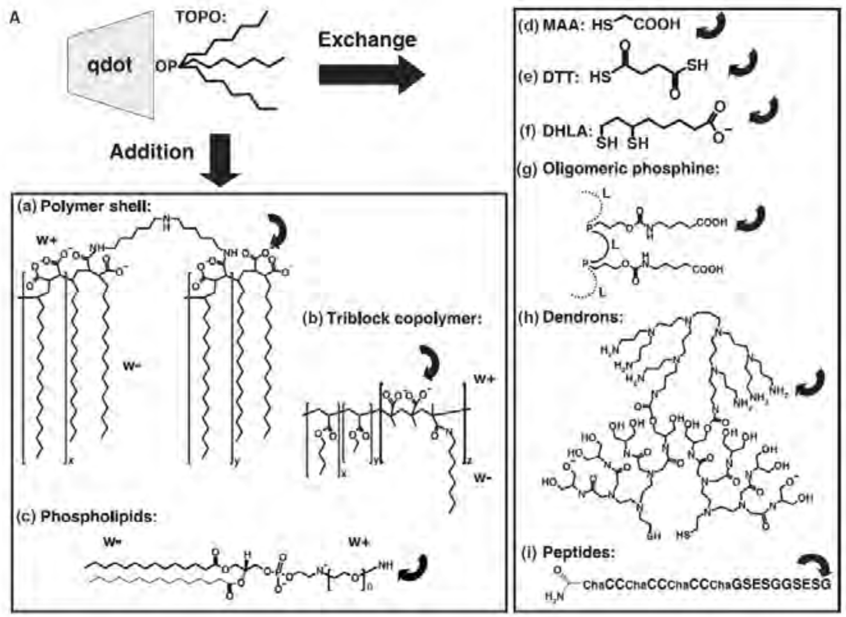
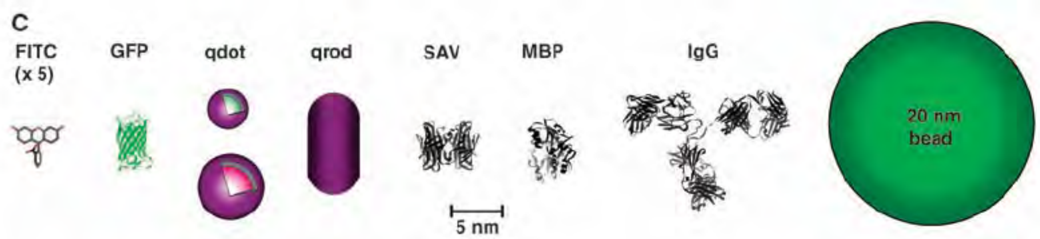


6. Optical properties of nanoparticles- Fluorescence







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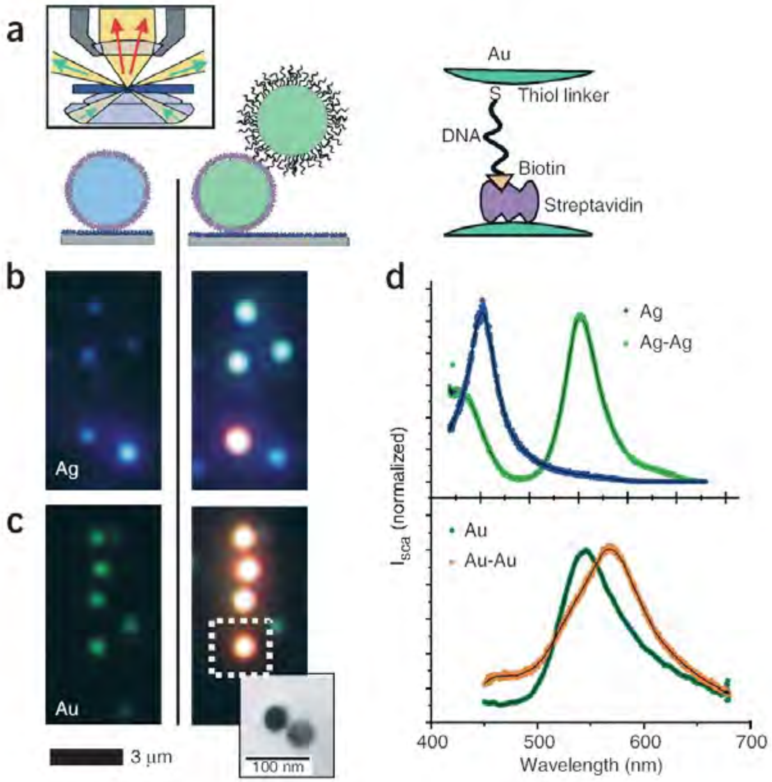
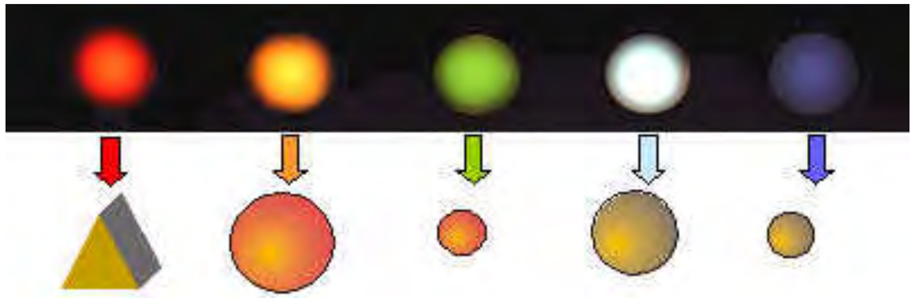
7. Plasmonic





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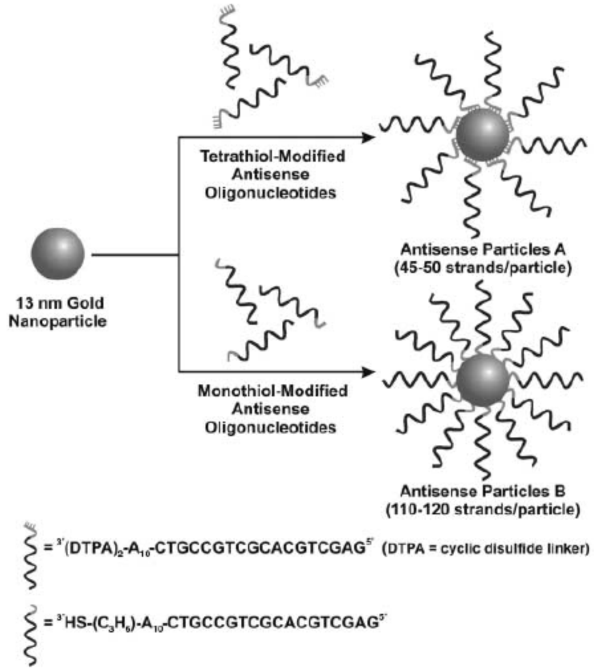
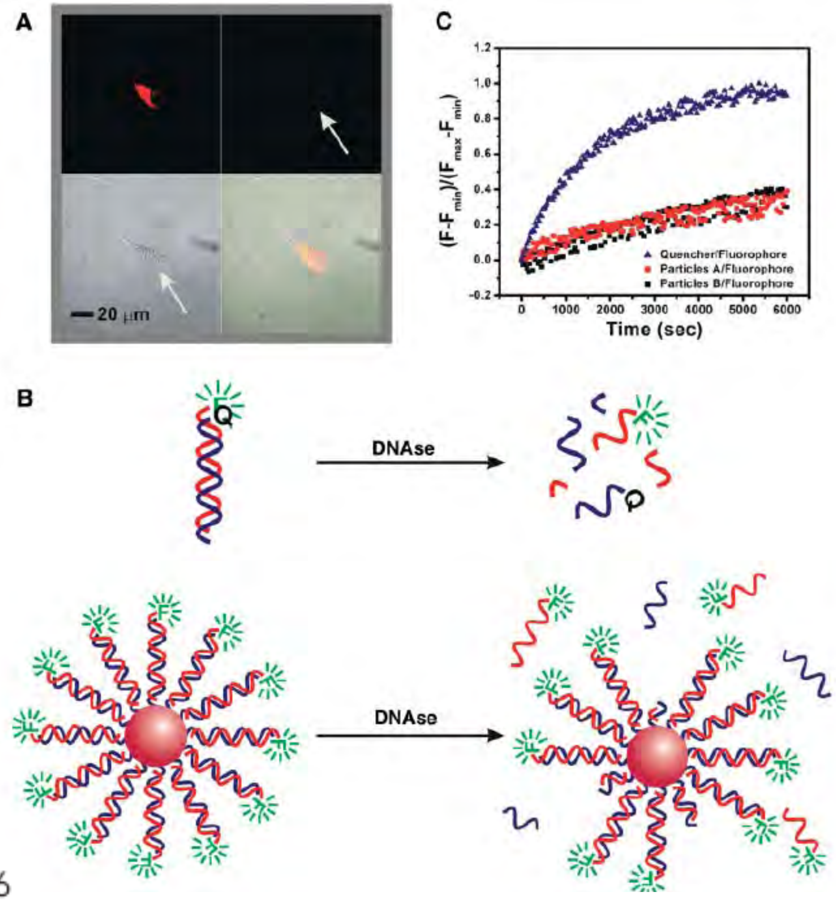
8. Interaction between nanoparticles and cells





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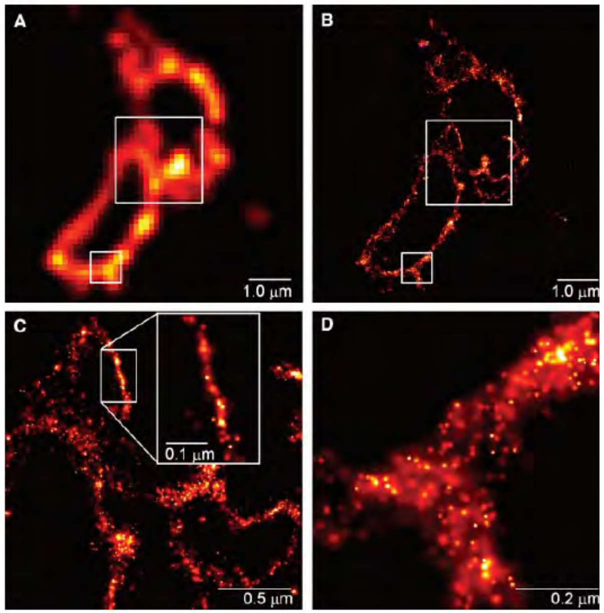
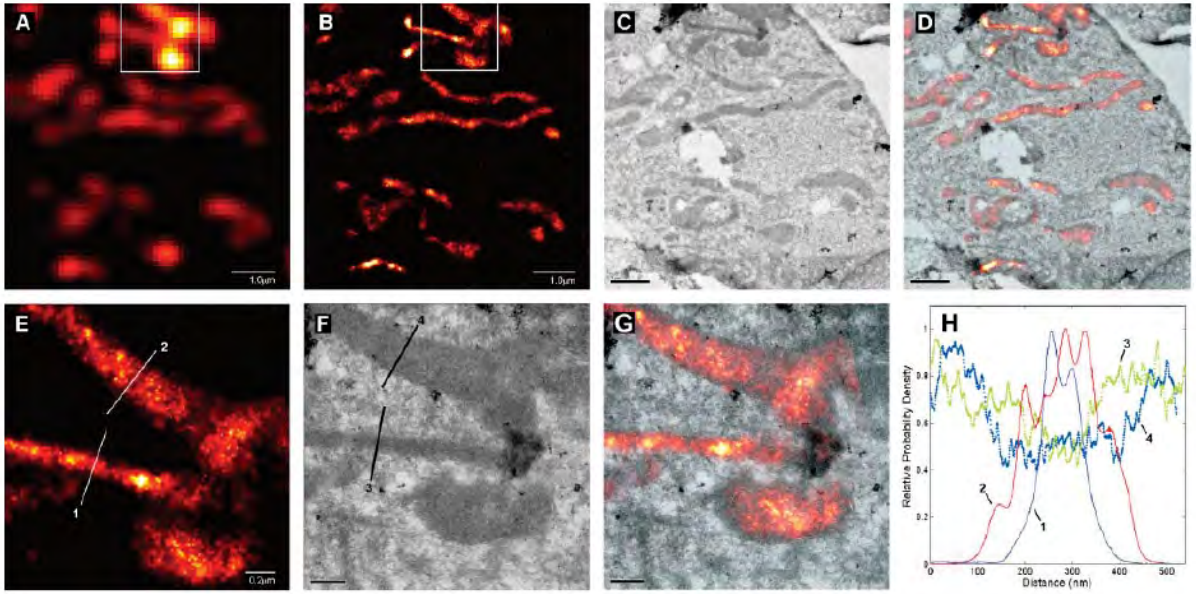
9. Super-resolution optical imaging





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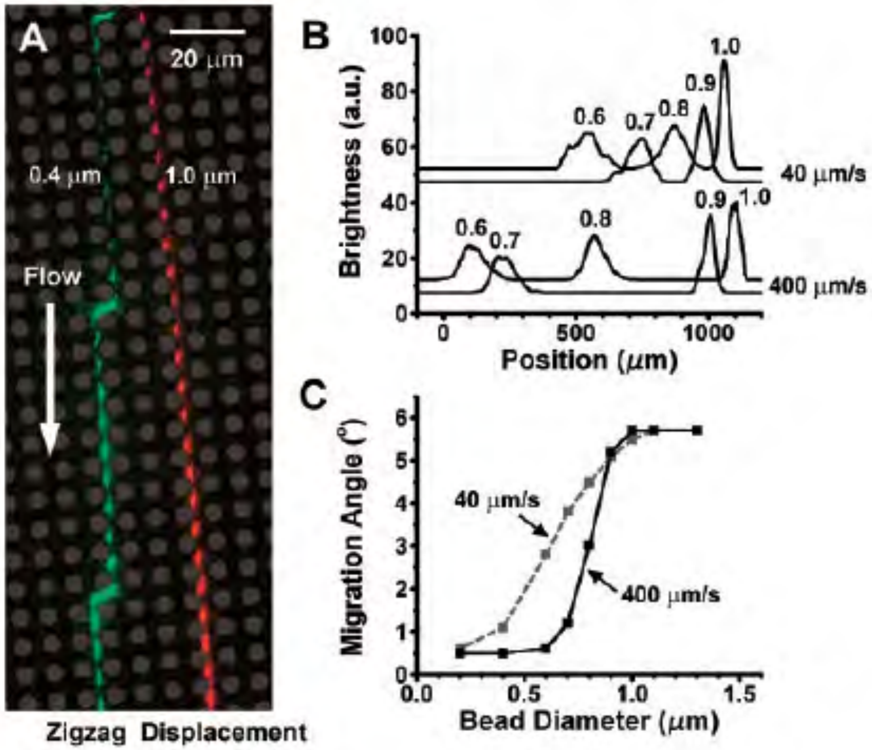
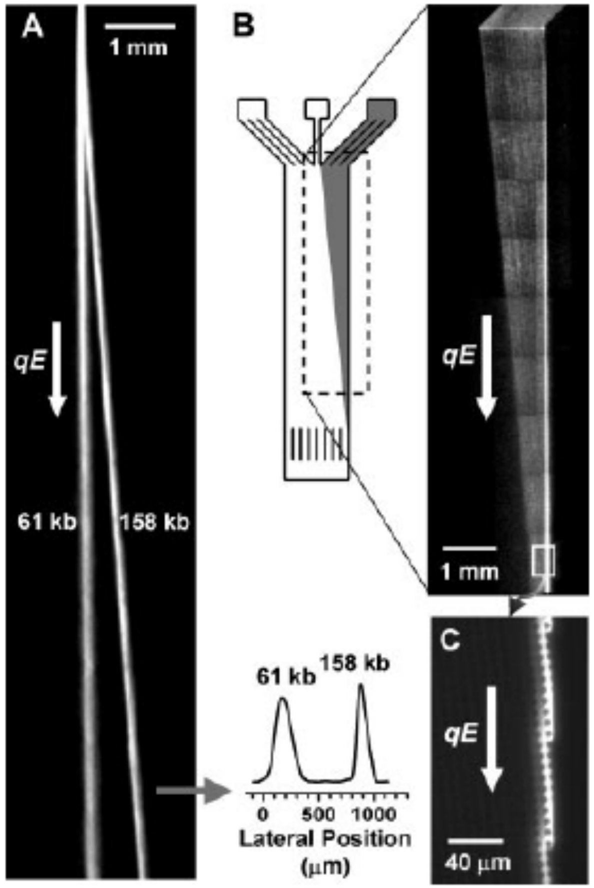
11. Micro- and Nano-fluidic





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Review of Biochemistry

Periodic Table of Elements

	IA	IIA	IIIB	IVB	VB	VIB	VIIB	VII	VII	VII	IB	IB	IIIA	IVA	VA	VIA	VIIA	0
1	1 H																	2 He
2	3 Li	4 Be											5 B	6 C	7 N	8 O	9 F	10 Ne
3	11 Na	12 Mg											13 Al	14 Si	15 P	16 S	17 Cl	18 Ar
4	19 K	20 Ca	21 Sc	22 Ti	23 V	24 Cr	25 Mn	26 Fe	27 Co	28 Ni	29 Cu	30 Zn	31 Ga	32 Ge	33 As	34 Se	35 Br	36 Kr
5	37 Rb	38 Sr	39 Y	40 Zr	41 Nb	42 Mo	43 Tc	44 Ru	45 Rh	46 Pd	47 Ag	48 Cd	49 In	50 Sn	51 Sb	52 Te	53 I	54 Xe
6	55 Cs	56 Ba	57 *La	72 Hf	73 Ta	74 W	75 Re	76 Os	77 Ir	78 Pt	79 Au	80 Hg	81 Tl	82 Pb	83 Bi	84 Po	85 At	86 Rn
7	87 Fr	88 Ra	89 +Ac	104 Rf	105 Ha	106 106	107 107	108 108	109 109	110 110								

* Lanthanide Series	58 Ce	59 Pr	60 Nd	61 Pm	62 Sm	63 Eu	64 Gd	65 Tb	66 Dy	67 Ho	68 Er	69 Tm	70 Yb	71 Lu
+ Actinide Series	90 Th	91 Pa	92 U	93 Np	94 Pu	95 Am	96 Cm	97 Bk	98 Cf	99 Es	100 Fm	101 Md	102 No	103 Lr

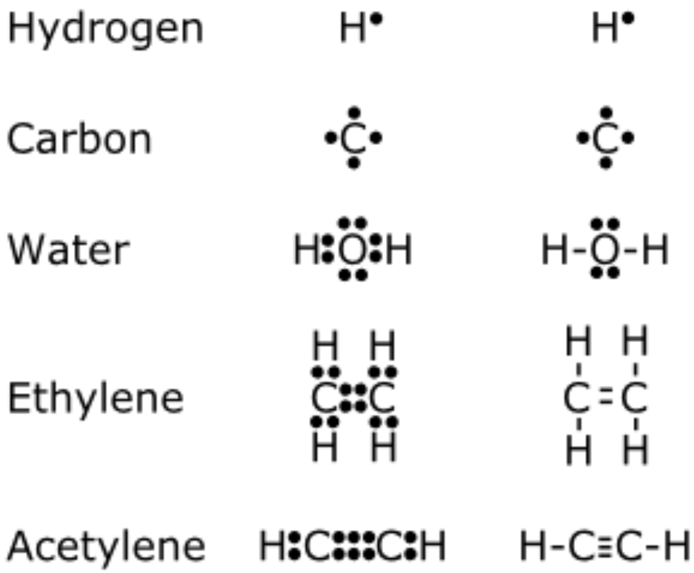
Legend - click to find out more...

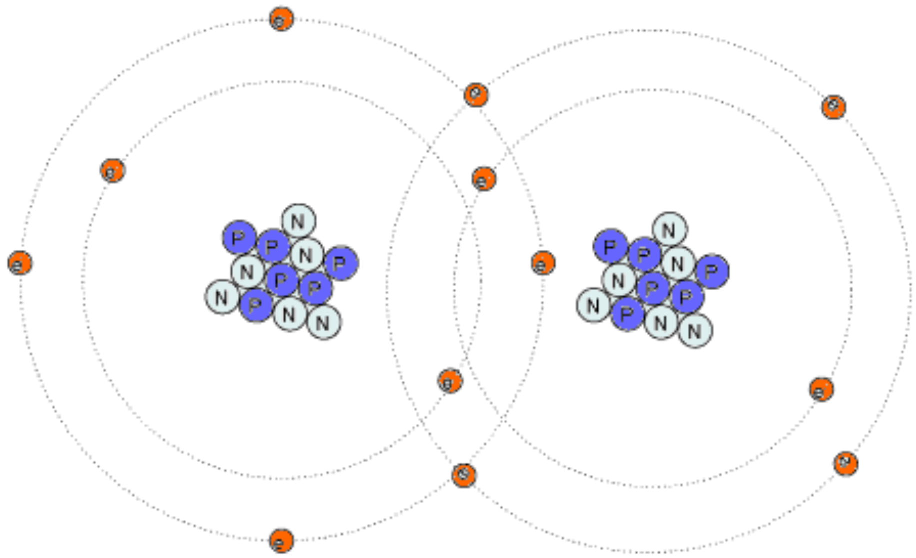
H - gas | Li - solid | Br - liquid | Tc - synthetic

Non-Metals | Transition Metals | Rare Earth Metals | Halogens

Alkali Metals | Alkali Earth Metals | Other Metals | Inert Elements

Chemical bond





Functional Groups

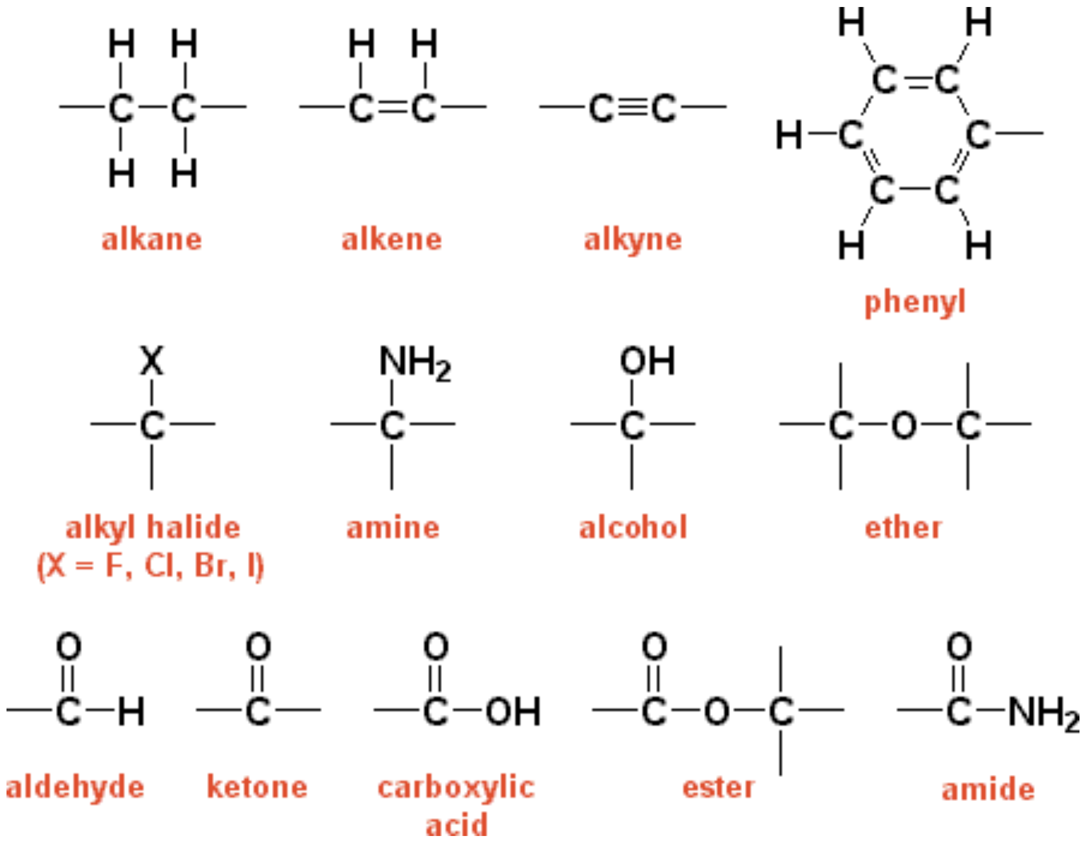
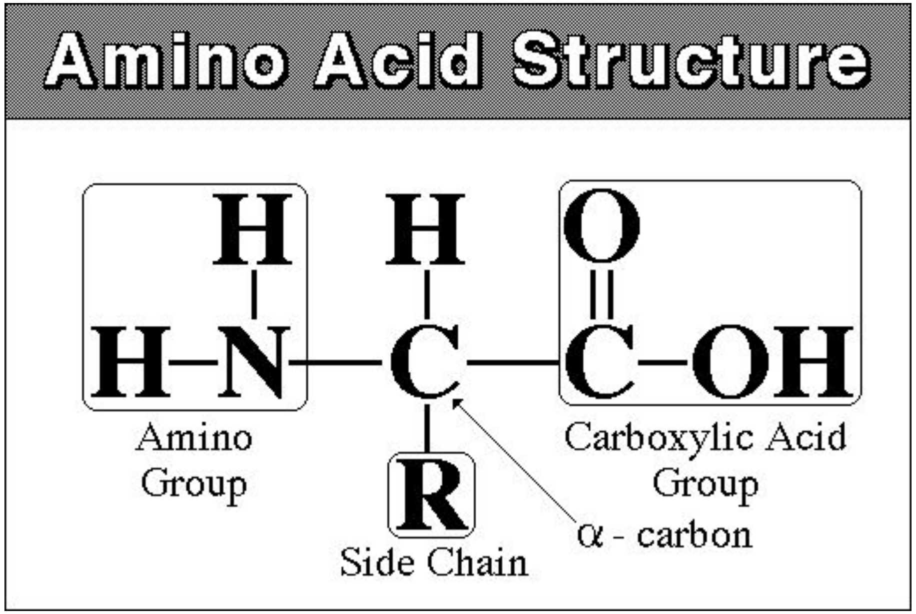
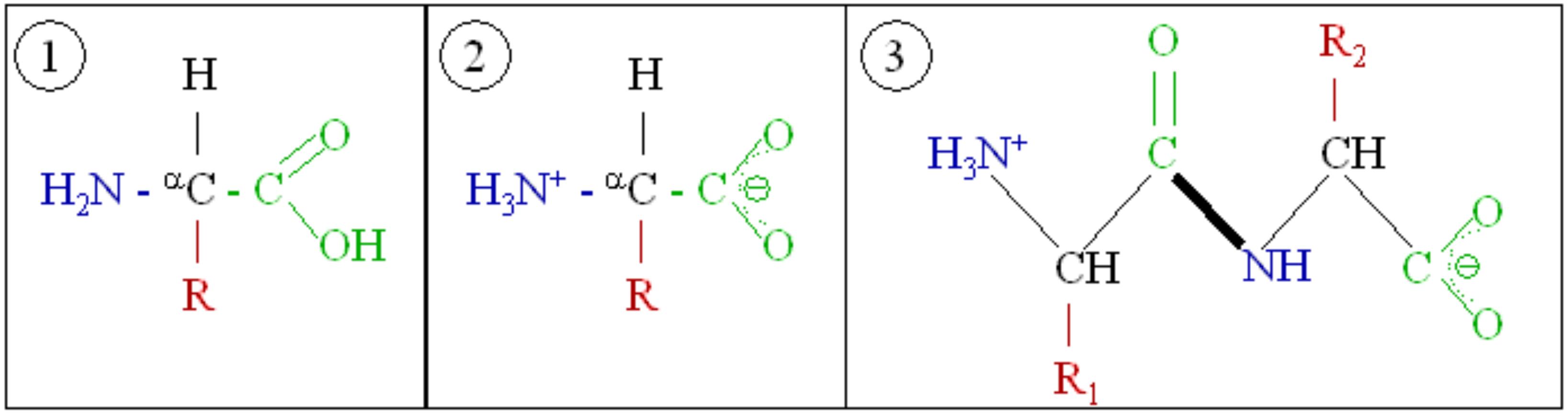


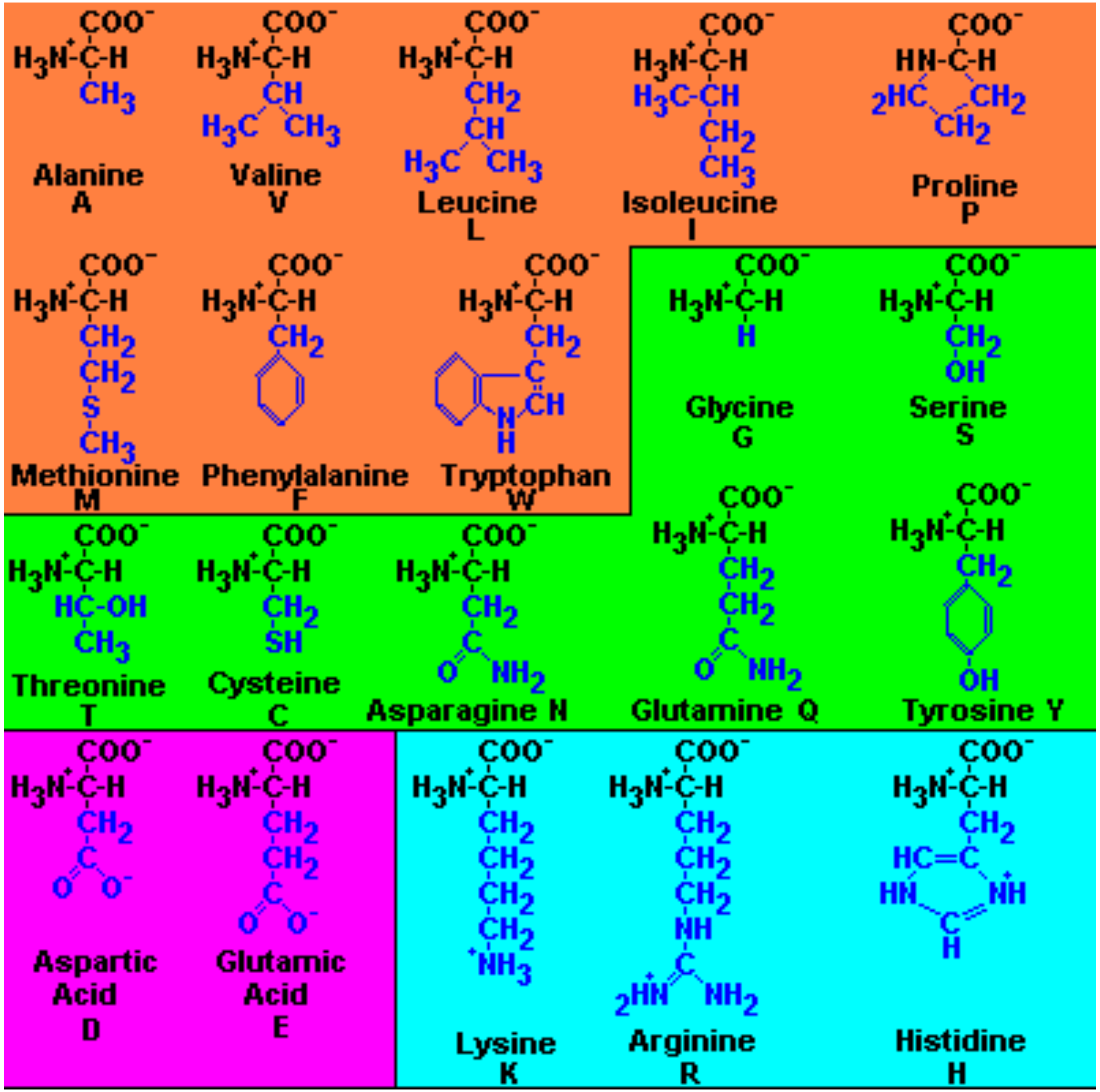
TABLE 18.1 Functional Groups of Importance in Biochemical Molecules

Functional Group	Structure	Type of Biomolecule
Amino group	$-NH_3^+$, $-NH_2$	Amino acids and proteins (Sections 18.3, 18.7)
Hydroxyl group	$-OH$	Monosaccharides (carbohydrates) and glycerol: a component of triacylglycerols (lipids) (Sections 22.4, 24.2)
Carbonyl group	$-C(=O)-$	Monosaccharides (carbohydrates); in acetyl group (CH_3CO) used to transfer carbon atoms during catabolism (Sections 22.4, 21.4, 21.8)
Carboxyl group	$-C(=O)-OH$, $-C(=O)-O^-$	Amino acids, proteins, and fatty acids (lipids) (Sections 18.3, 18.7, 24.2)
Amide group	$-C(=O)-N(-)-$	Links amino acids in proteins; formed by reaction of amino group and carboxyl group (Section 18.7)
Carboxylic acid ester	$-C(=O)-O-R$	Triacylglycerols (and other lipids); formed by reaction of carboxyl group and hydroxyl group (Section 24.2)
Phosphates, mono-, di-, tri-	$-\overset{\mid}{\underset{\mid}{C}}-O-P(=O)(O^-)-O^-$ $-\overset{\mid}{\underset{\mid}{C}}-O-P(=O)(O^-)-O-P(=O)(O^-)-O^-$ $-\overset{\mid}{\underset{\mid}{C}}-O-P(=O)(O^-)-O-P(=O)(O^-)-O-P(=O)(O^-)-O^-$	ATP and many metabolism intermediates (Sections 17.8, 21.5, and throughout metabolism sections)
Hemiacetal group	$-\overset{\mid}{C}(OR)-OH$	Cyclic forms of monosaccharides; formed by a reaction of carbonyl group with hydroxyl group (Sections 16.7, 22.4)
Acetal group	$-\overset{\mid}{C}(OR)-OR$	Connects monosaccharides in disaccharides and larger carbohydrates; formed by reaction of carbonyl group with hydroxyl group (Sections 16.7, 22.7, 22.9)

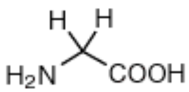
Amino Acid


Amino Acid Structure
H H O
H–N–C–C–OH
R
Amino
Group
Carboxylic Acid
Group
Side Chain
α - carbon

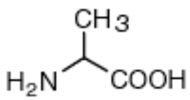

1
H
H2N - αC - C
O
OH
R
2
H
H3N+ - αC - C
O
O
R
3
O
R2
H3N+
C
CH
CH
NH
C
O
O
R1


Alanine A
Valine V
Leucine L
Isoleucine I
Proline P
Methionine M
Phenylalanine F
Tryptophan W
Glycine G
Serine S
Threonine T
Cysteine C
Asparagine N
Glutamine Q
Tyrosine Y
Aspartic Acid D
Glutamic Acid E
Lysine K
Arginine R
Histidine H

Small

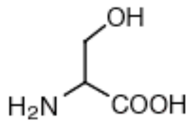


Glycine (Gly, G)
MW: 57.05

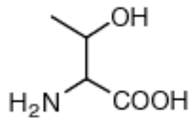


Alanine (Ala, A)
MW: 71.09

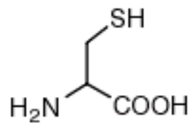
Nucleophilic



Serine (Ser, S)
MW: 87.08, pK_a ~ 16

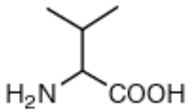


Threonine (Thr, T)
MW: 101.11, pK_a ~ 16

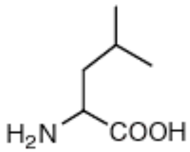


Cysteine (Cys, C)
MW: 103.15, pK_a = 8.35

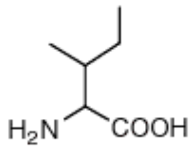
Hydrophobic



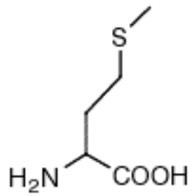
Valine (Val, V)
MW: 99.14



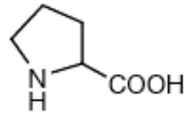
Leucine (Leu, L)
MW: 113.16



Isoleucine (Ile, I)
MW: 113.16

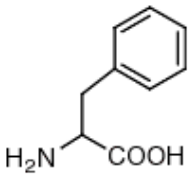


Methionine (Met, M)
MW: 131.19

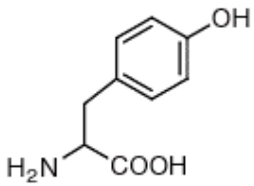


Proline (Pro, P)
MW: 97.12

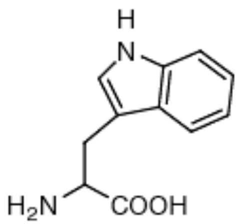
Aromatic



Phenylalanine (Phe, F)
MW: 147.18

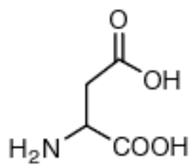


Tyrosine (Tyr, Y)
MW: 163.18

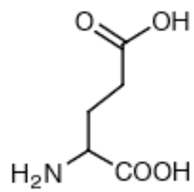


Tryptophan (Trp, W)
MW: 186.21

Acidic

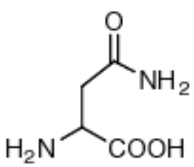


Aspartic Acid (Asp, D)
MW: 115.09, pK_a = 3.9

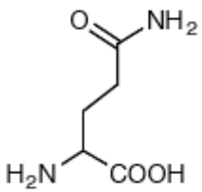


Glutamic Acid (Glu, E)
MW: 129.12, pK_a = 4.07

Amide

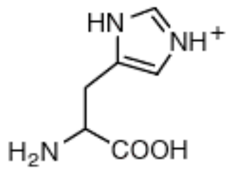


Asparagine (Asn, N)
MW: 114.11

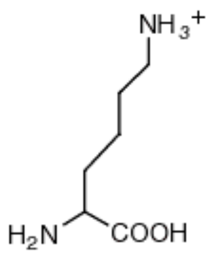


Glutamine (Gln, Q)
MW: 128.14

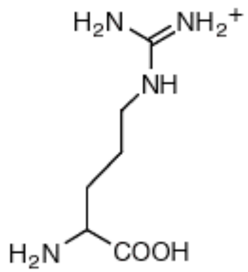
Basic



Histidine (His, H)
MW: 137.14, pK_a = 6.04



Lysine (Lys, K)
MW: 128.17, pK_a = 10.79

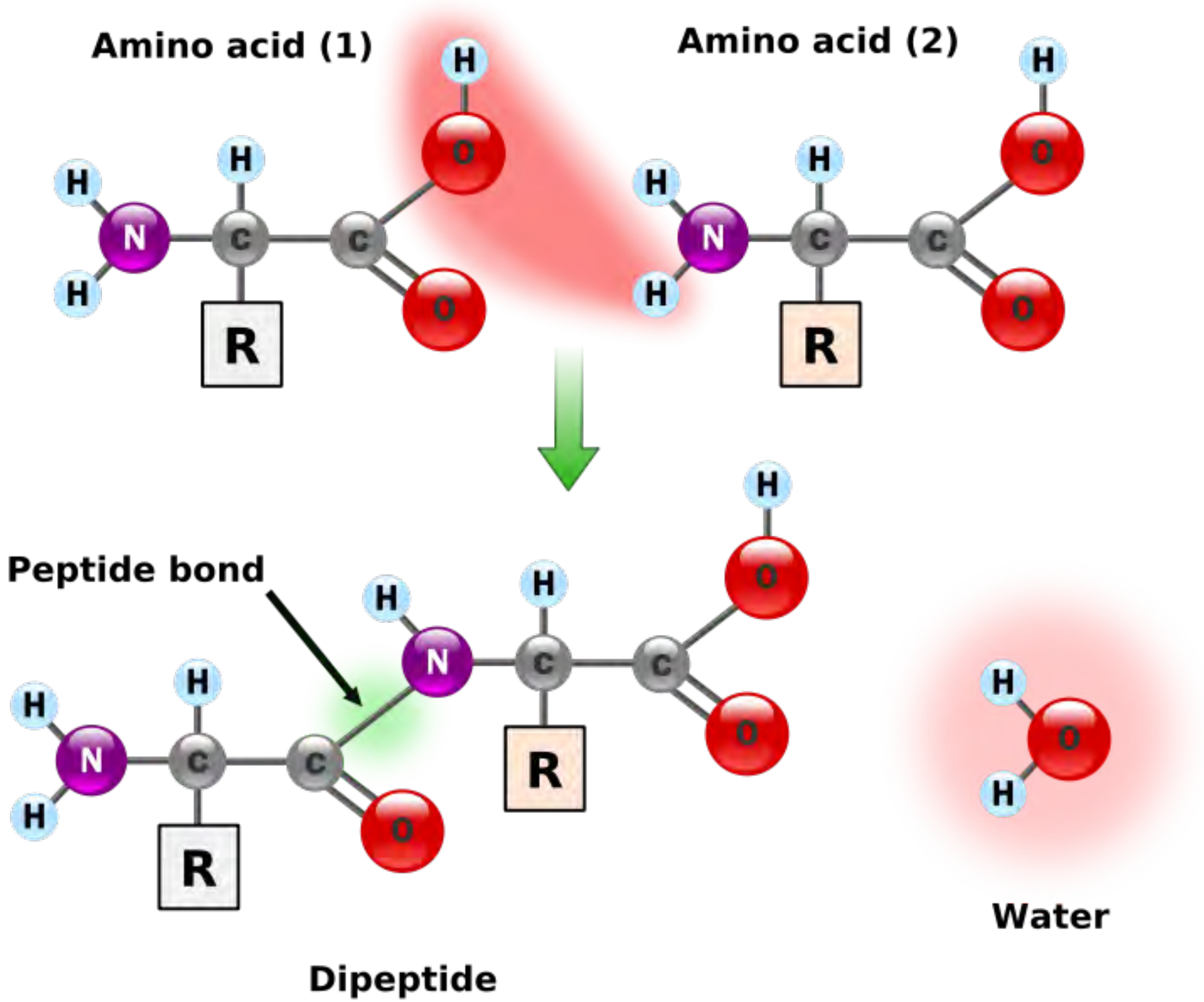


Arginine (Arg, R)
MW: 156.19, pK_a = 12.48

Protein Structure and Function

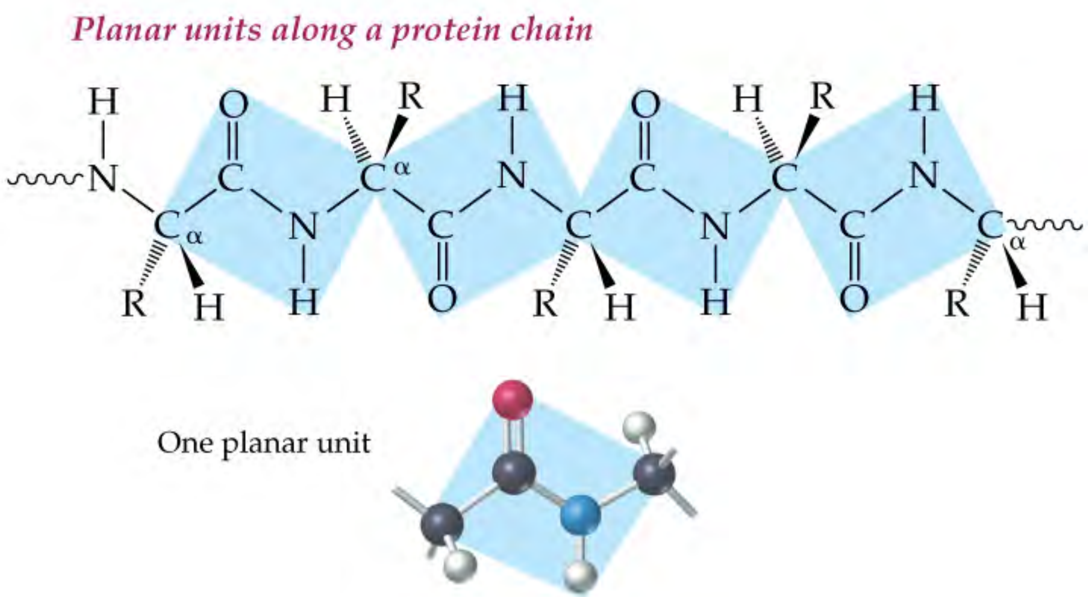
- Proteins are polymers of amino acids.
- Each amino acids in a protein contains a amino group, -NH_2, a carboxyl group, -COOH, and an R group, all bonded to the central carbon atom. The R group may be a hydrocarbon or they may contain functional group.
- All amino acids present in a proteins are *α-amino acids* in which the amino group is bonded to the carbon next to the carboxyl group.
- Two or more amino acids can join together by forming amide bond, which is known as a ***peptide bond*** when they occur in proteins.

Peptide bond



Primary Protein Structure

- Primary structure of a proteins is the sequence of amino acids connected by peptide bonds. Along the backbone of the proteins is a chain of alternating peptide bonds and α-carbons and the amino acid side chains are connected to these



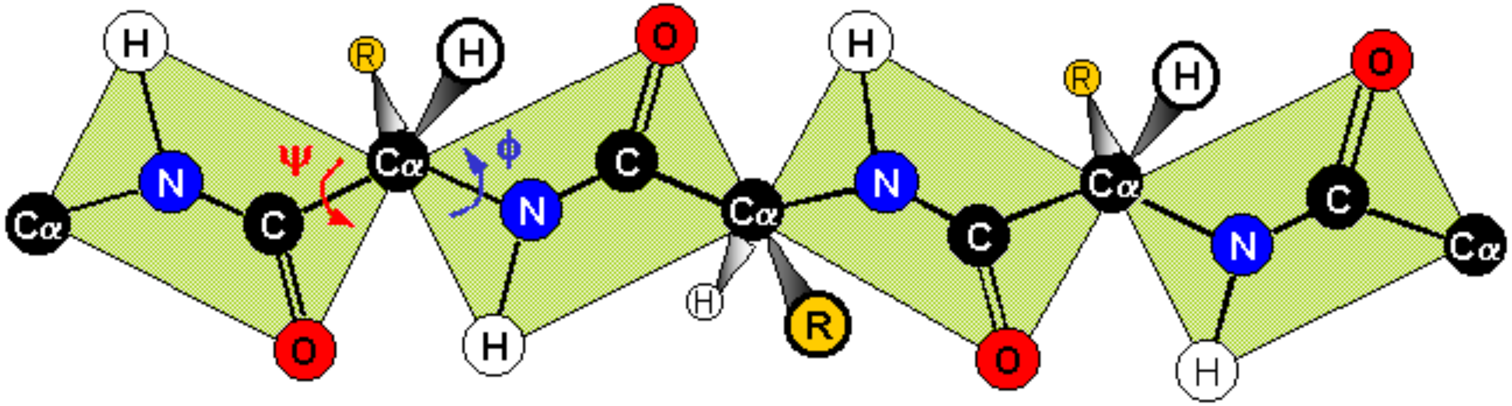
- By convention, peptides and proteins are always written with the amino terminal amino acid (N-terminal) on the left and carboxyl-terminal amino acid (C-terminal) on the right.

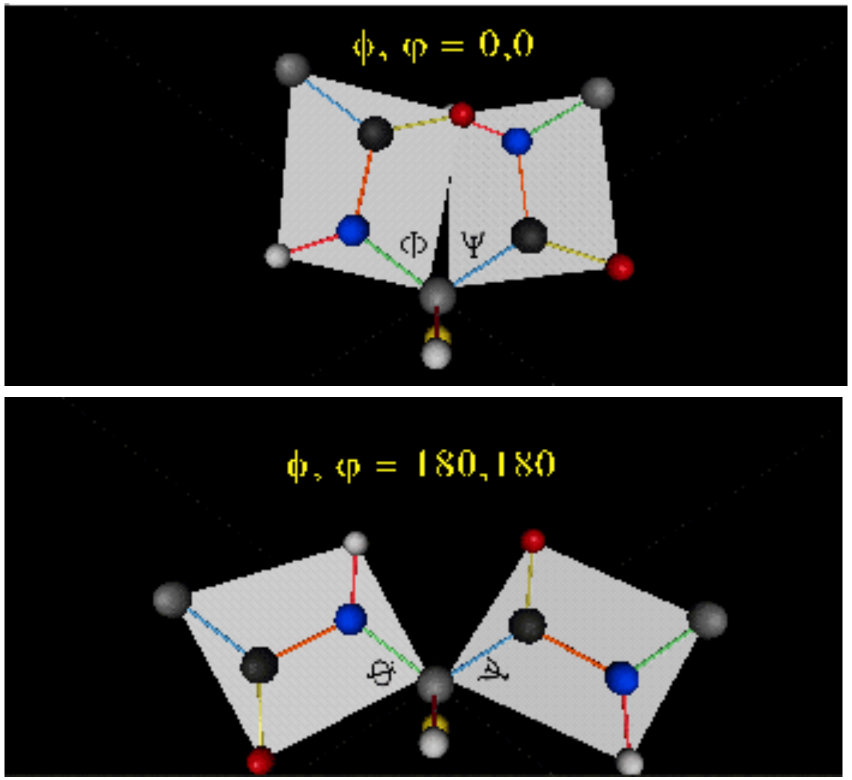
N → C

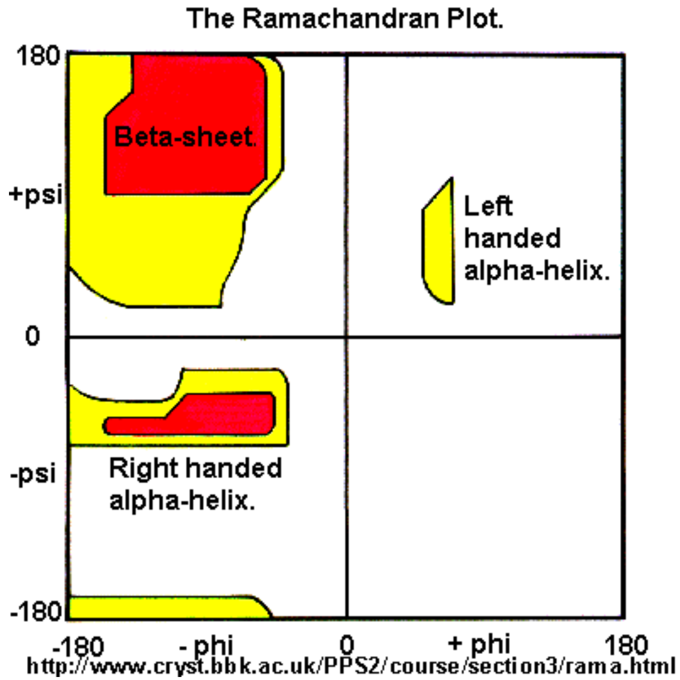
Secondary Protein Structure

- Secondary structure of a protein is the arrangement of polypeptide backbone of the protein in space. The secondary structure includes two kinds of repeating pattern known as the *α-helix* and *β-sheet*.
- Hydrogen bonding between backbone atoms are responsible for both of these secondary structures.

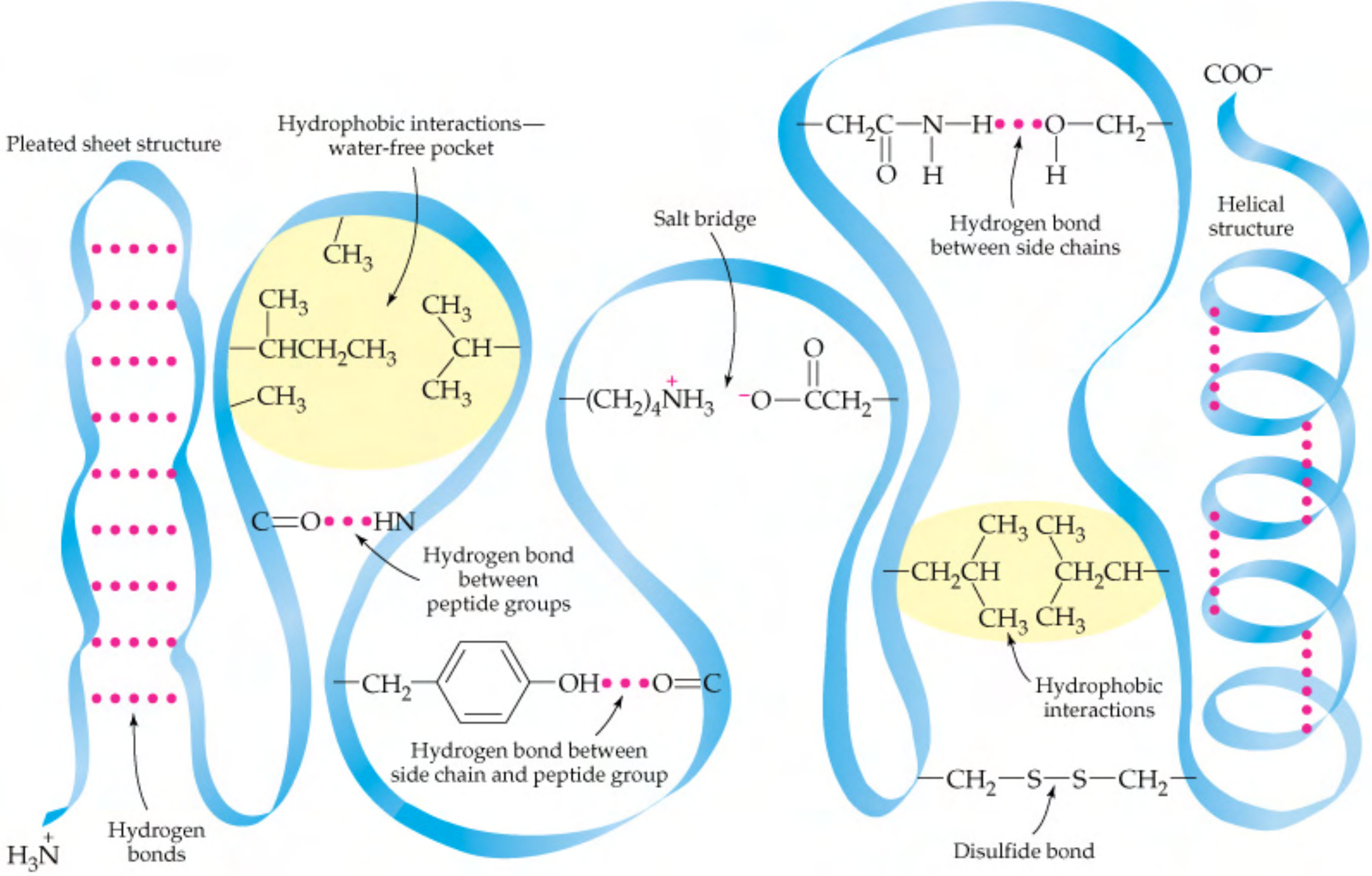
FULLY EXTENDED POLYPEPTIDE CHAIN



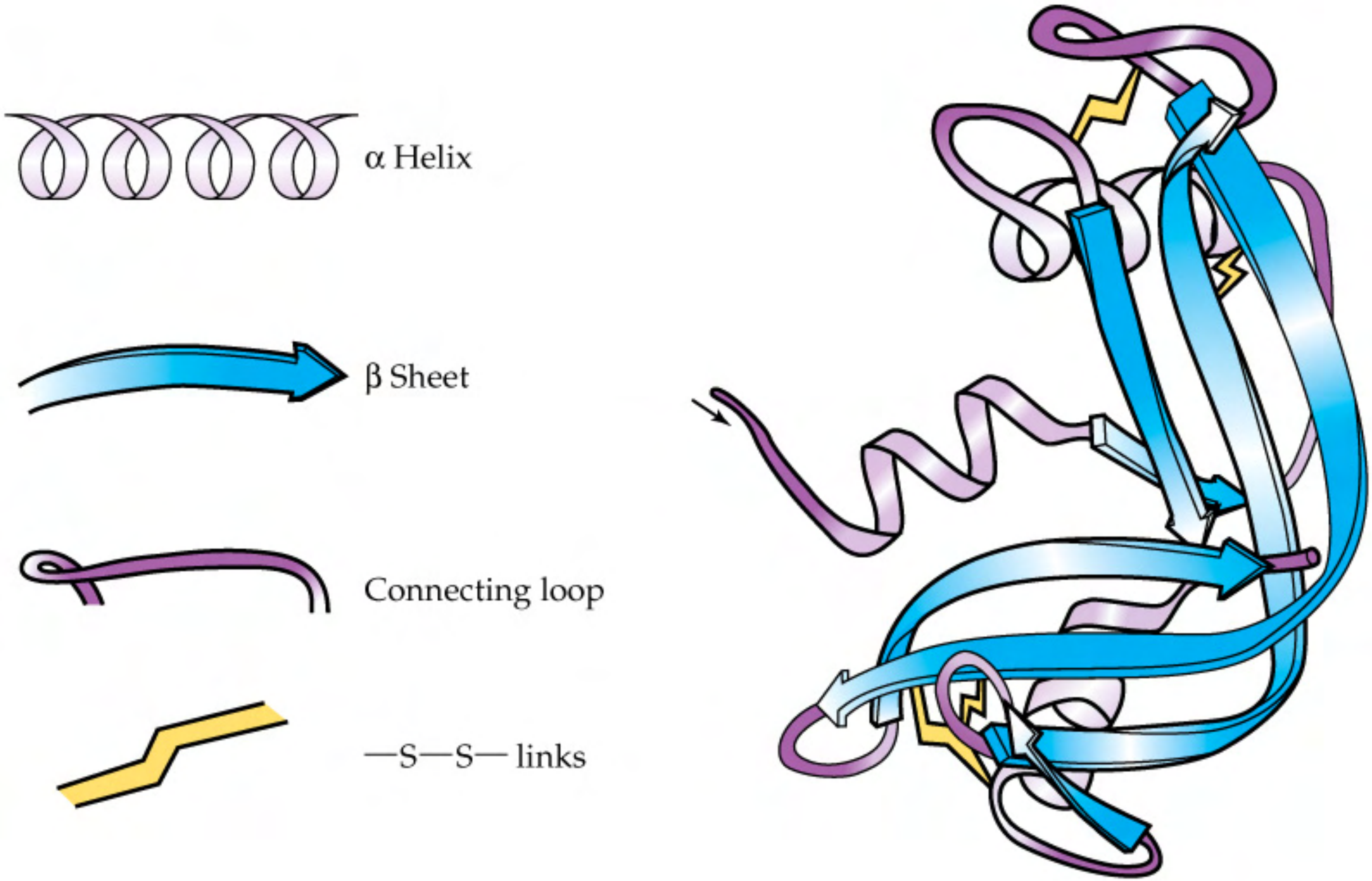




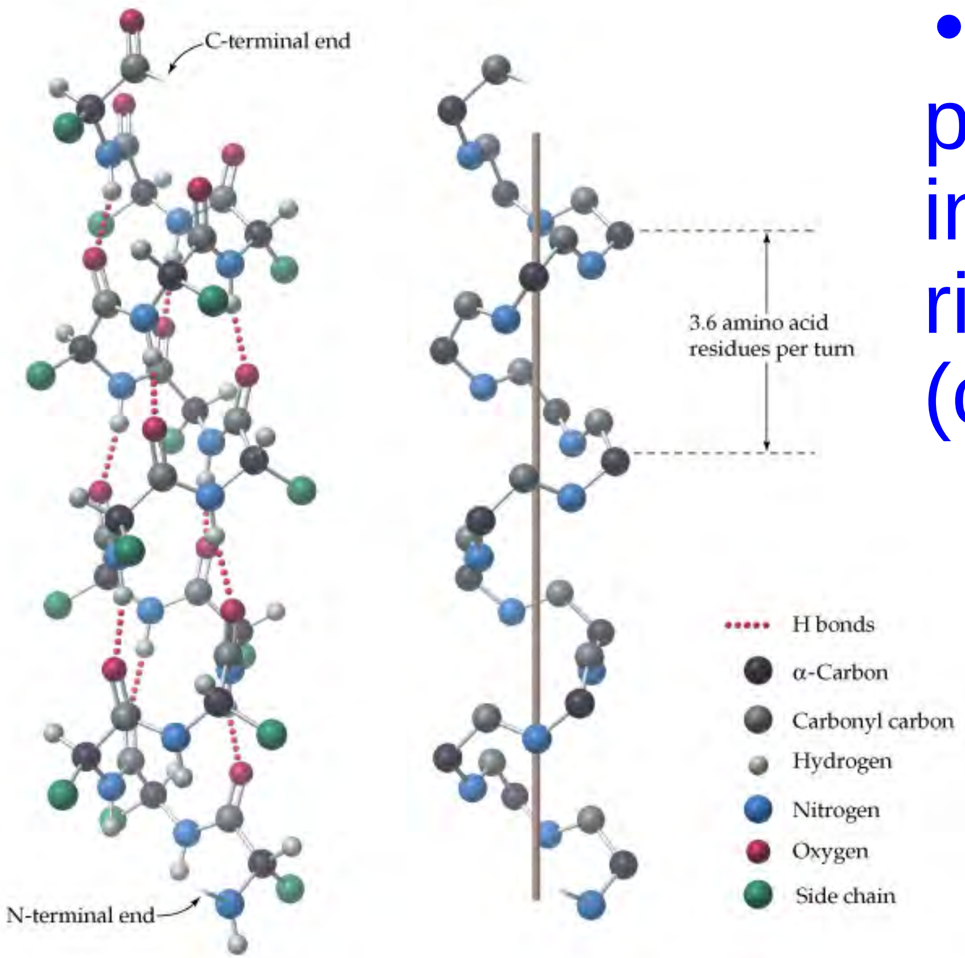
- Protein shape determining interactions are summarized below:
- Hydrogen bond between neighboring backbone segments.
- Hydrogen bonds of side chains with each other or with backbone atoms.
- Ionic attractions between side chain groups or salt bridge.
- Hydrophobic interactions between side chain groups.
- Covalent sulfur-sulfur bonds.



Pleated sheet structure
Hydrophobic interactions—
water-free pocket
Salt bridge
Hydrogen bond
between side chains
Helical
structure
COO⁻
Hydrogen bond
between
peptide groups
Hydrogen bond between
side chain and peptide group
Hydrophobic
interactions
Disulfide bond
Hydrogen
bonds
H₃N⁺

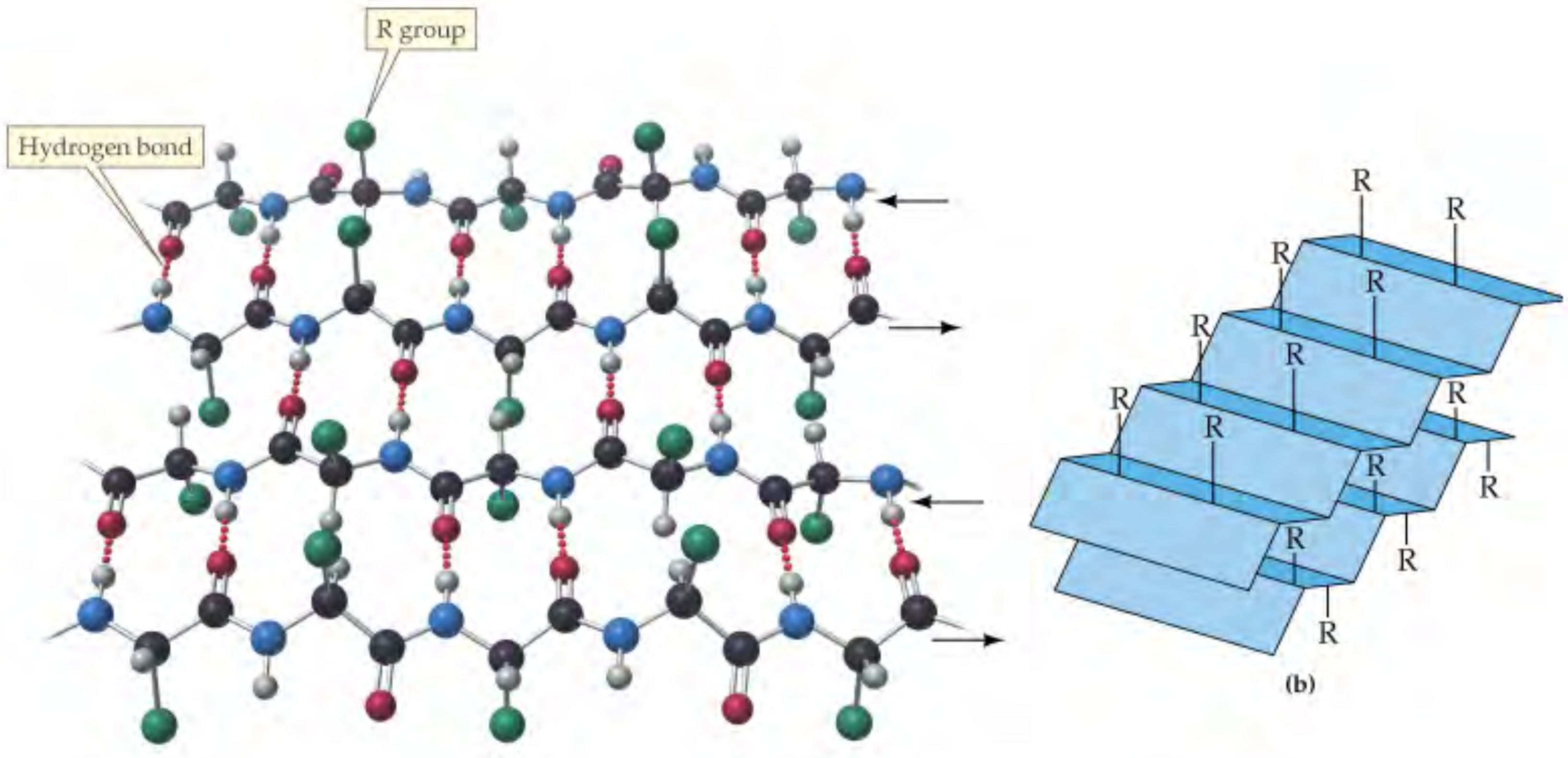


Ribonuclease



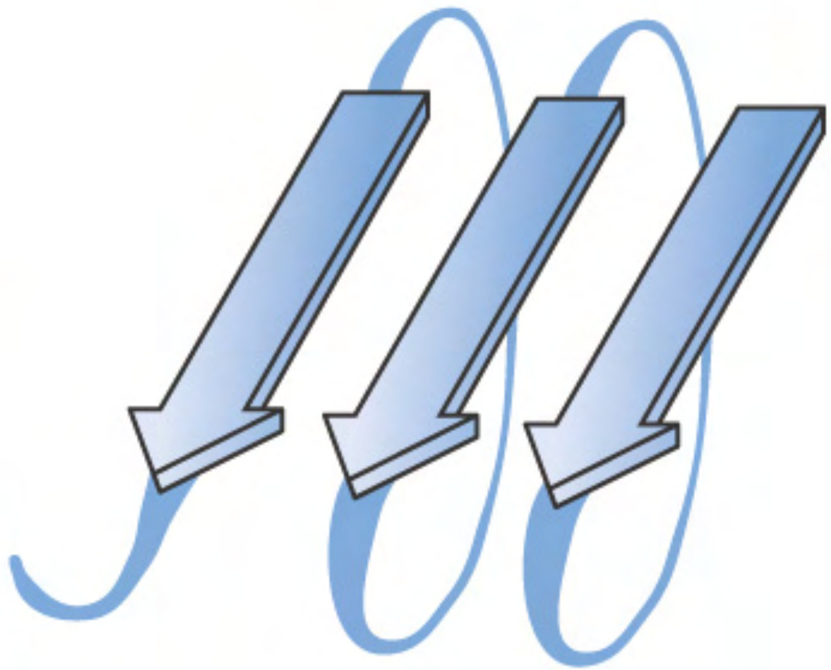
• ***α-Helix:*** A single protein chain coiled in a spiral with a right-handed (clockwise) twist.

•***β*-Sheet:** The polypeptide chain is held in place by hydrogen bonds between pairs of peptide units along neighboring backbone segments.



(a) (b)

α helix



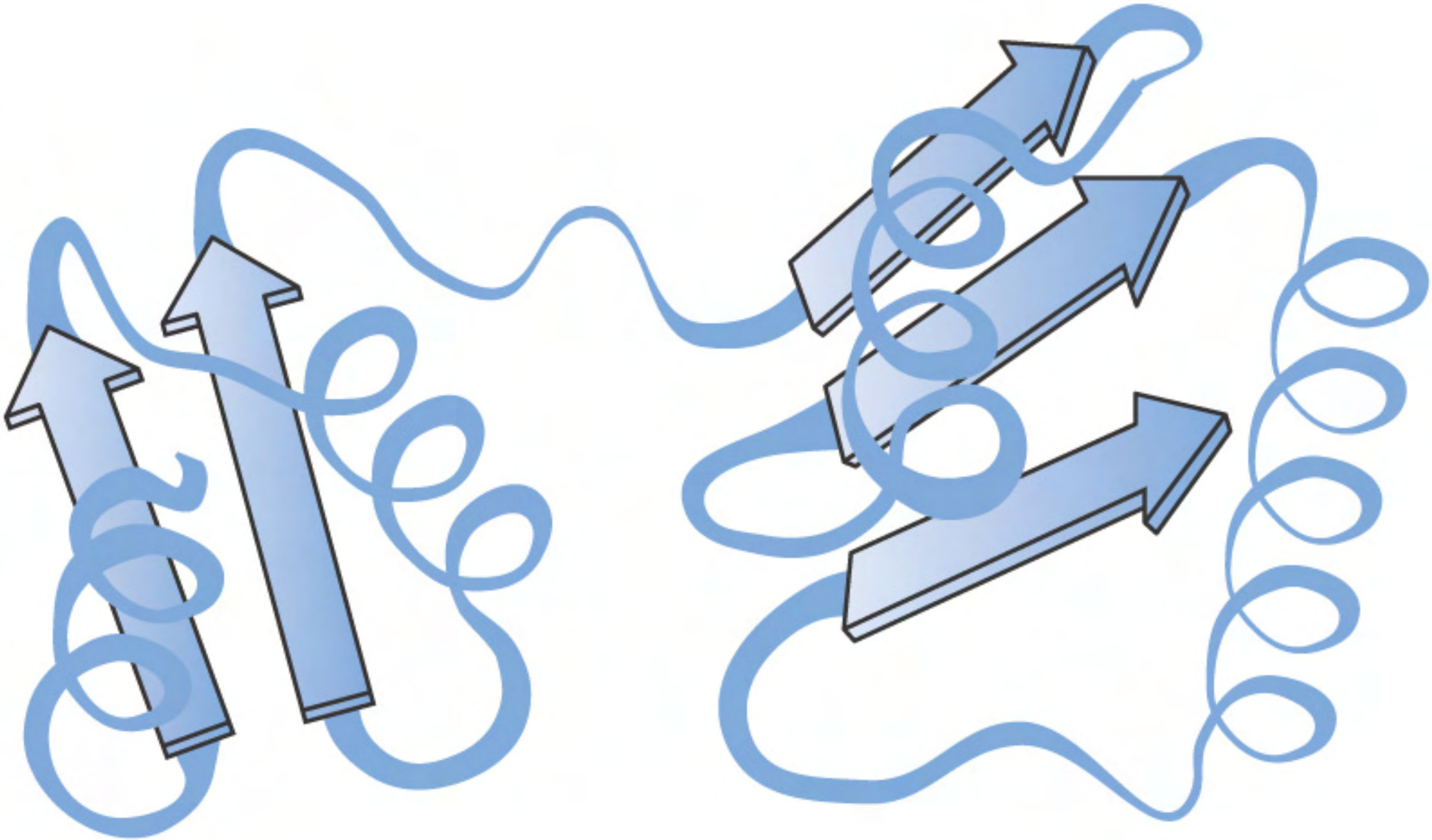
β sheet

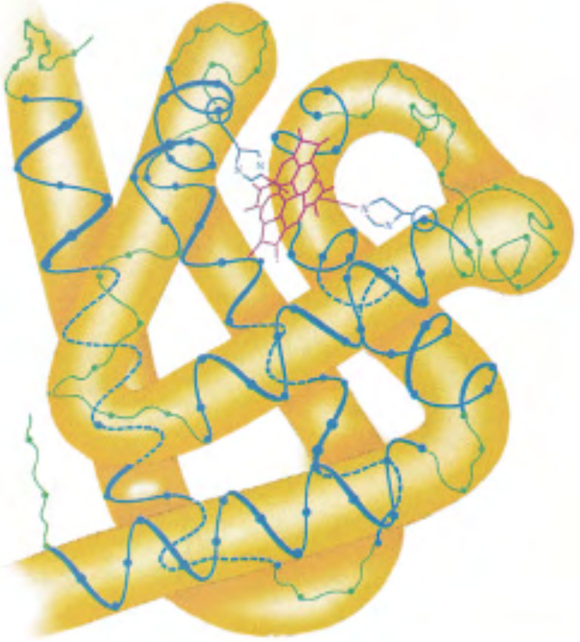
Shape-Determining Interactions in Proteins

- The essential structure-function relationship for each protein depends on the polypeptide chain being held in its necessary shape by the interactions of atoms in the side chains.

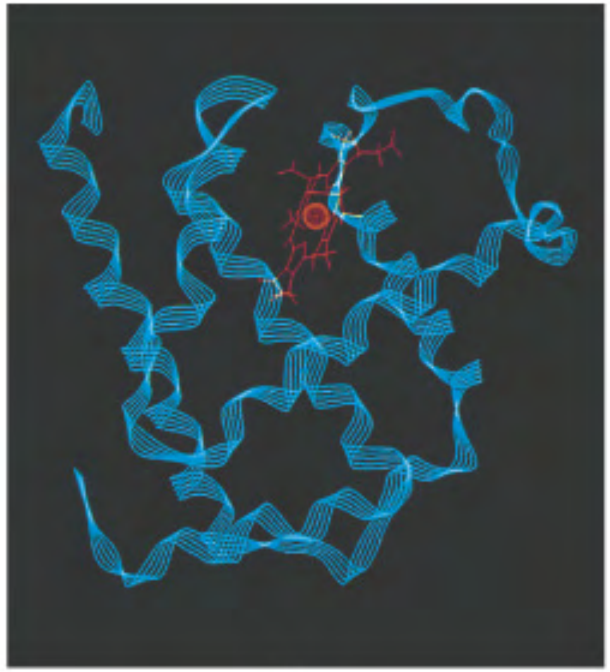
Tertiary Protein Structure

- ***Tertiary Structure of a proteins*** The overall three dimensional shape that results from the folding of a protein chain. Tertiary structure depends mainly on attractions of amino acid side chains that are far apart along the same backbone. Non-covalent interactions and disulfide covalent bonds govern tertiary structure.
- A protein with the shape in which it exist naturally in living organisms is known as a *native protein.*

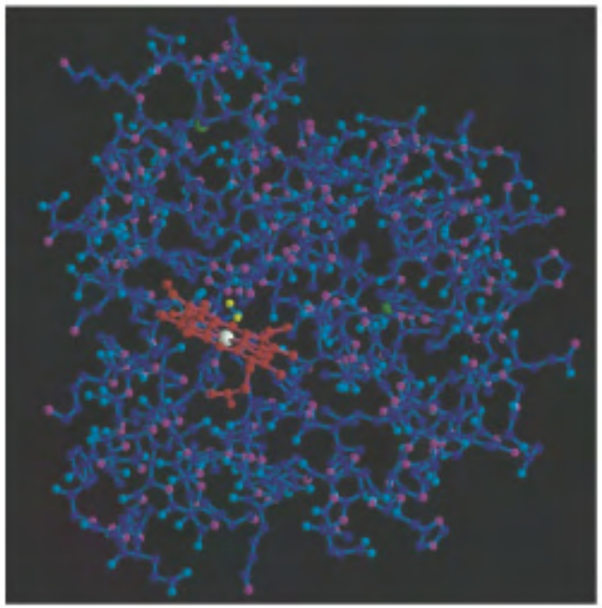




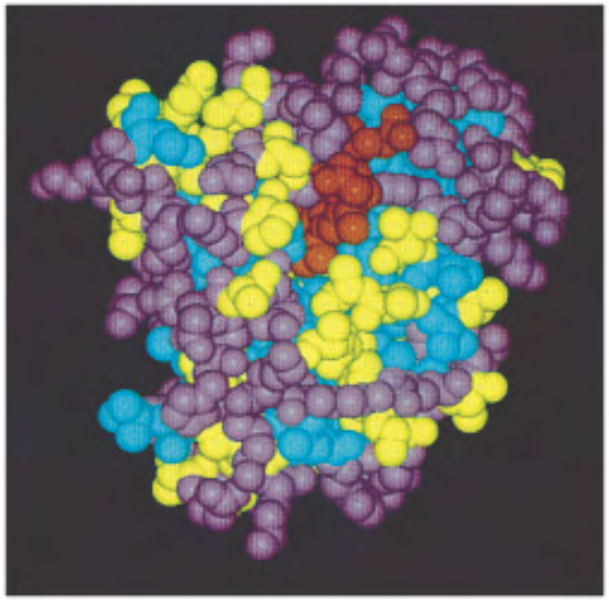
(a)



(b)



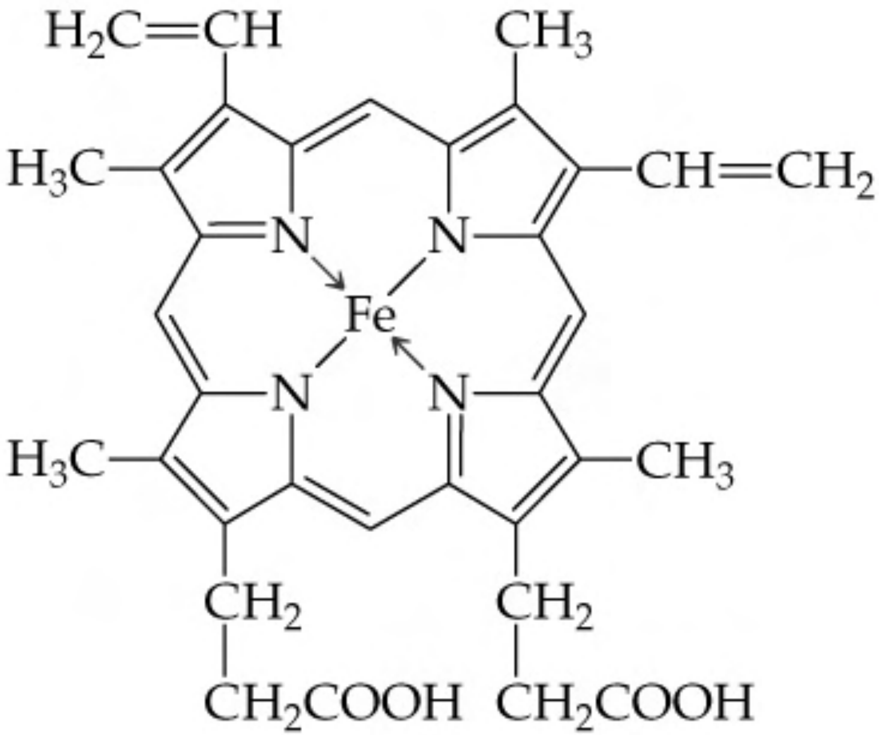
(c)



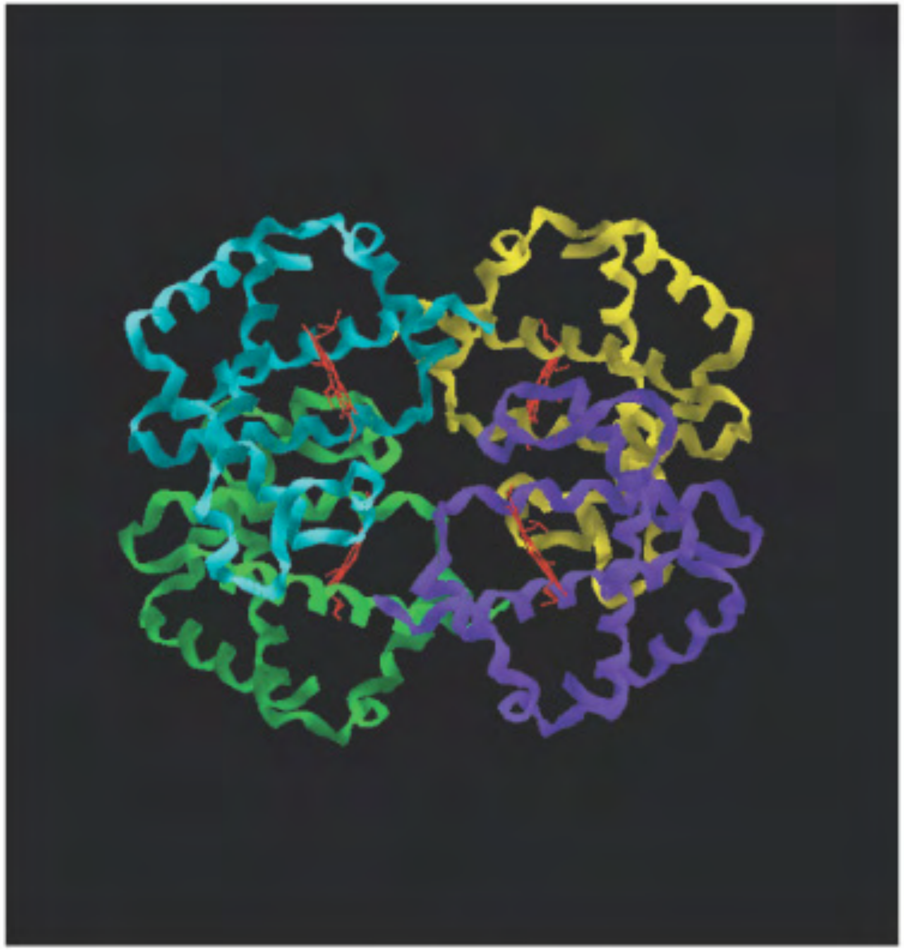
(d)

Quaternary Protein Structure

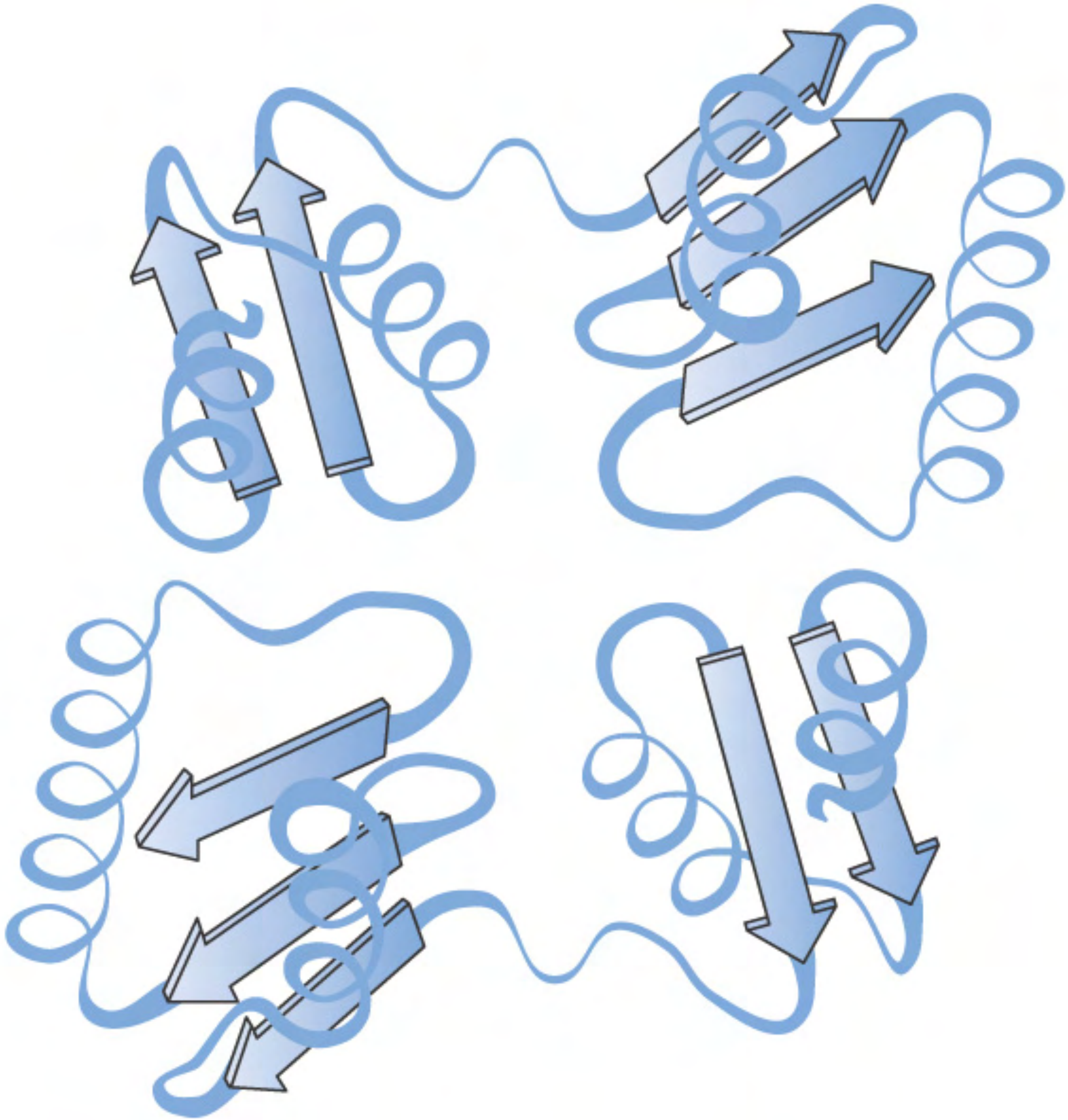
- ***Quaternary protein structure***: The way in which two or more polypeptide sub-units associate to form a single three-dimensional protein unit. Non-covalent forces are responsible for quaternary structure essential to the function of proteins.

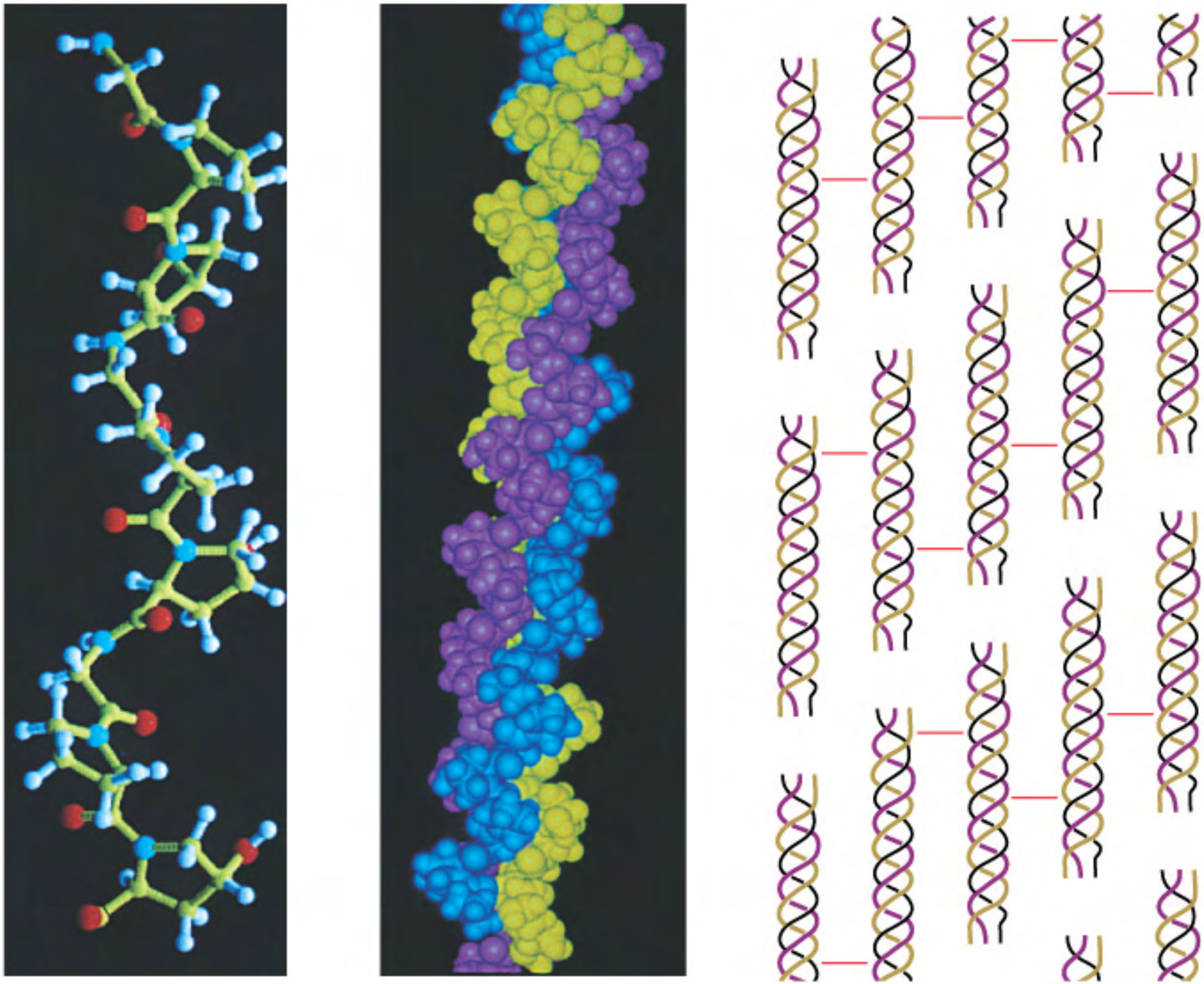


(a)



(b)



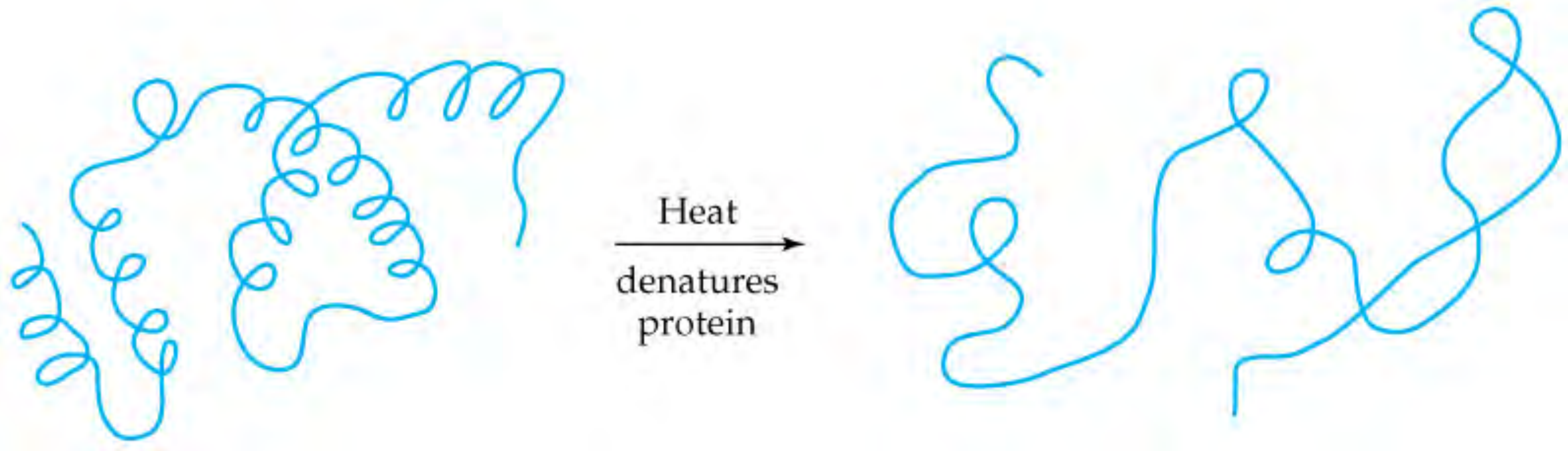


(a) (b) (c)

Chemical Properties of Proteins

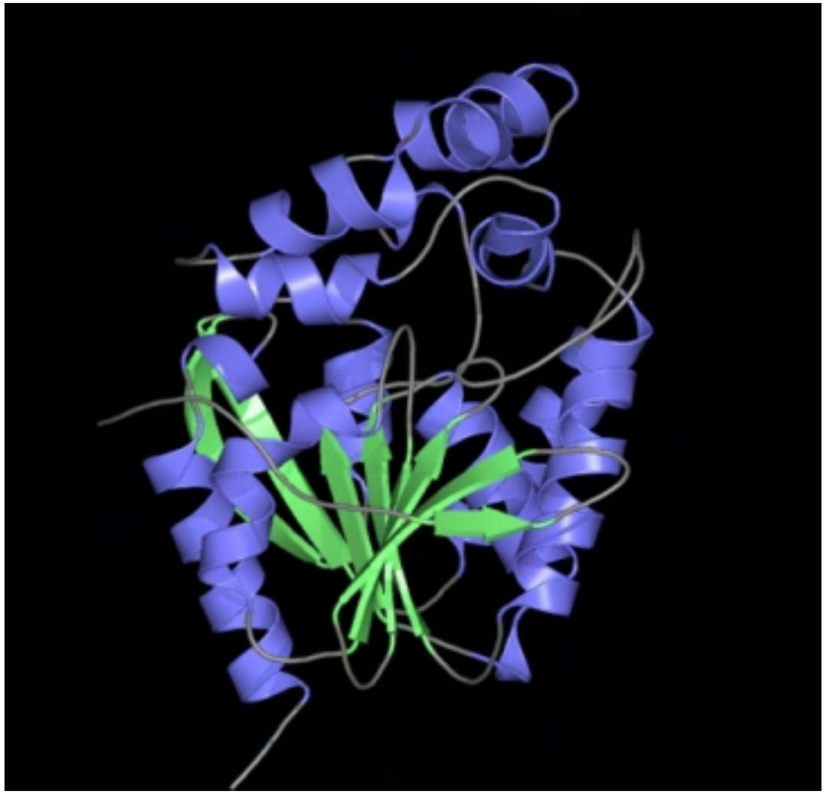
- *Protein hydrolysis:* In protein hydrolysis, peptide bonds are hydrolyzed to yield amino acids. This is reverse of protein formation.

- *Protein* *denaturation*: The loss of secondary, tertiary, or quaternary protein structure due to disruption of non-covalent interactions and or disulfide bonds that leaves peptide bonds and

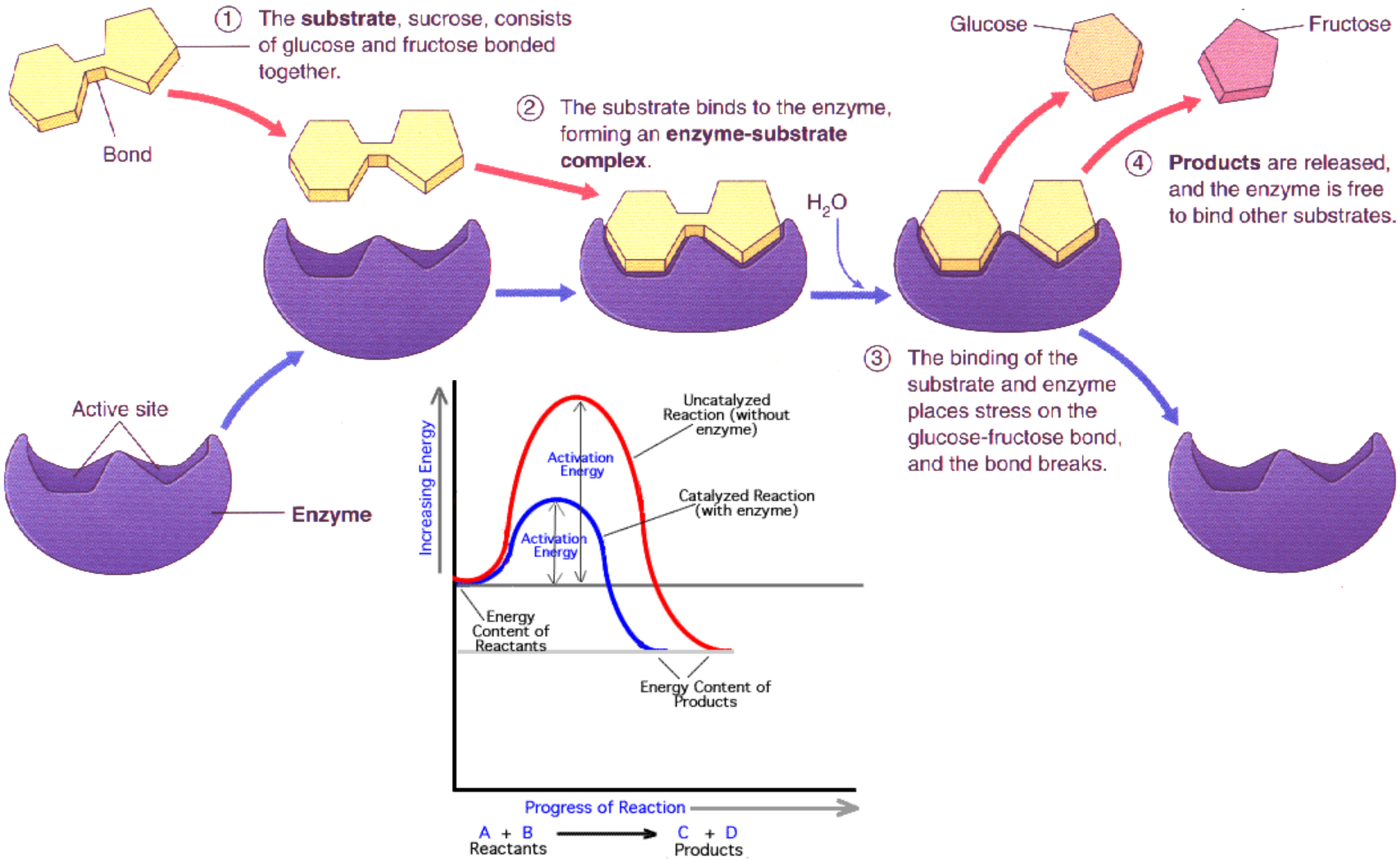


Catalysis by Enzymes

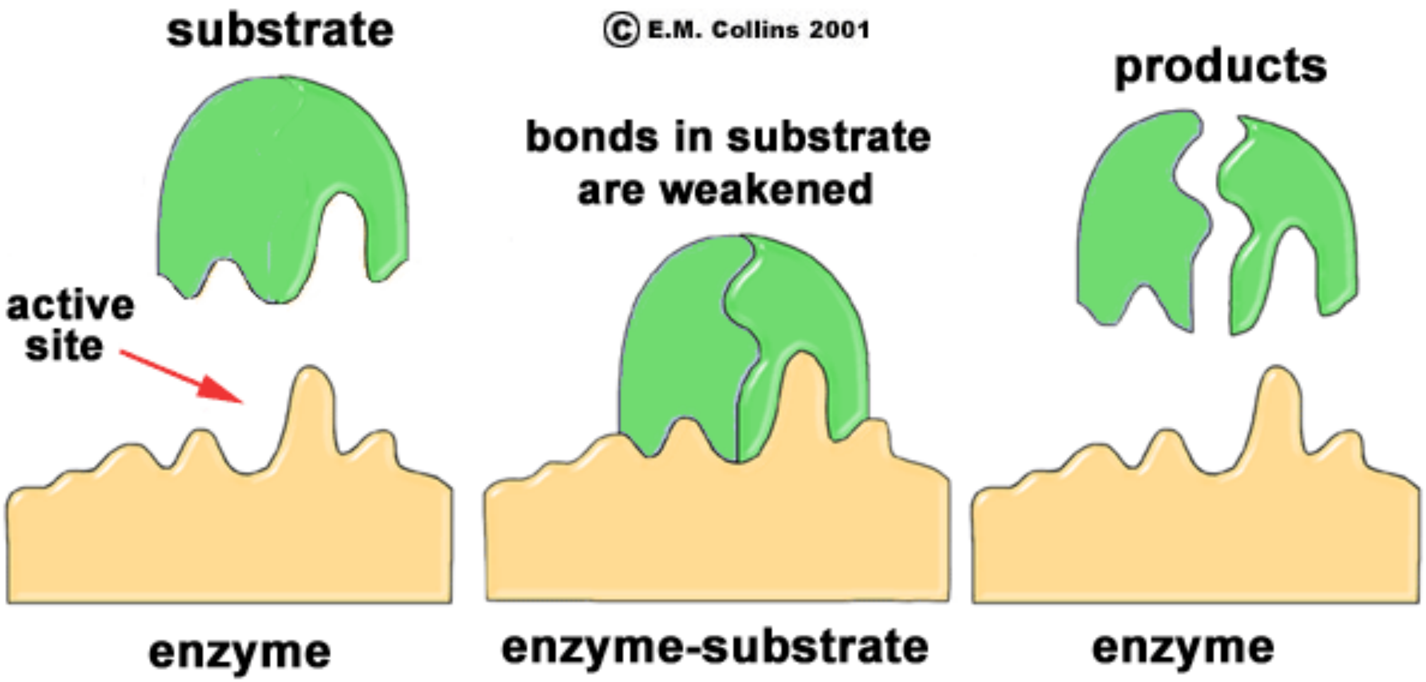
- ***Enzyme*** A protein that acts as a catalyst for a biochemical reaction.



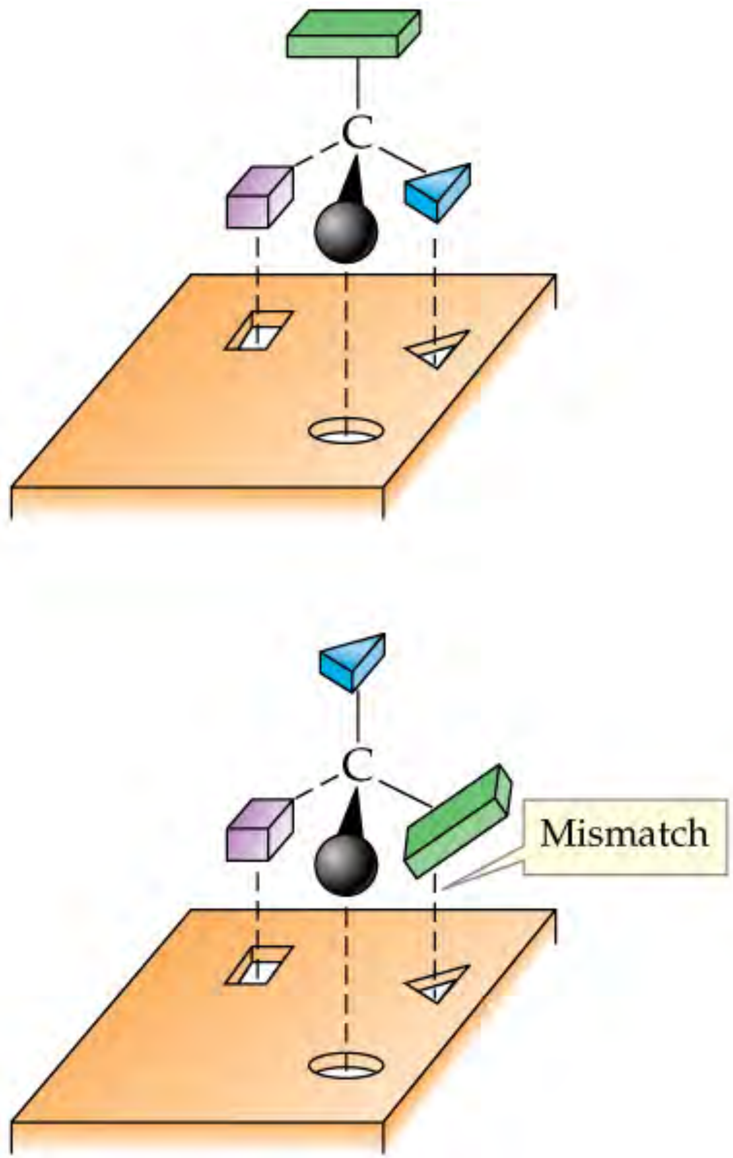
Enzymatic Reaction



Specificity



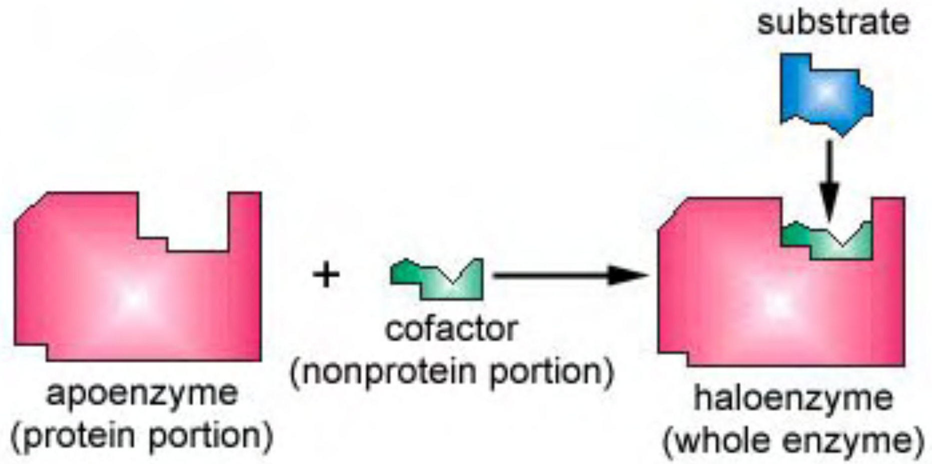
The specificity of an enzyme for one of two enantiomers is a matter of fit. One enantiomer fits better into the active site of the enzyme than the other enantiomer. Enzyme catalyzes reaction of the enantiomer that fits better into the active site of the enzyme.

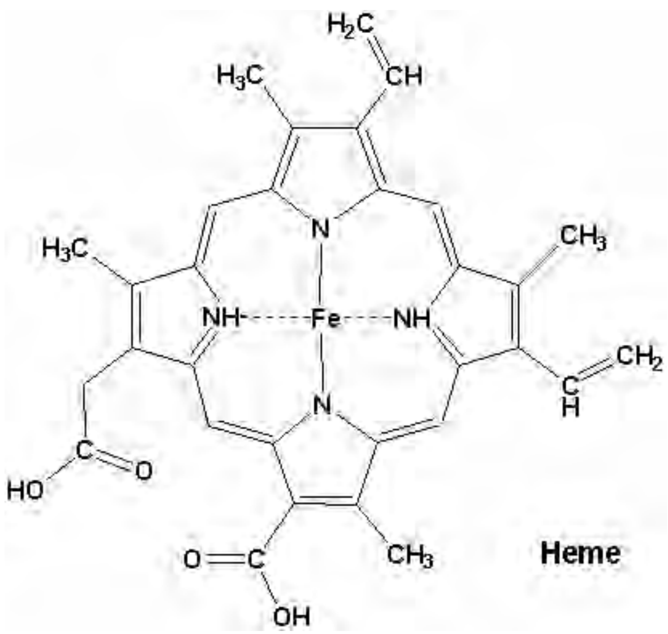


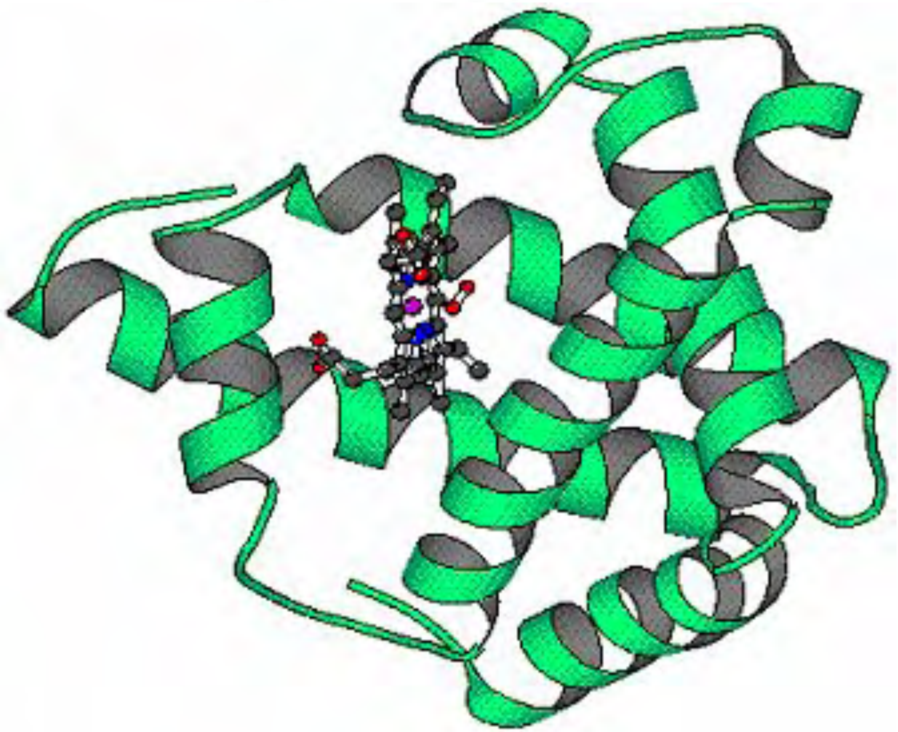
Enzyme Cofactors

- Many enzymes are conjugated proteins that require nonprotein portions known as ***cofactors***.
- Some cofactors are metal ions, others are nonprotein organic molecules called ***coenzymes***.
- An enzyme may require a metal-ion, a coenzyme, or both to function.

Cofactor


substrate
apoenzyme
(protein portion)
cofactor
(nonprotein portion)
haloenzyme
(whole enzyme)

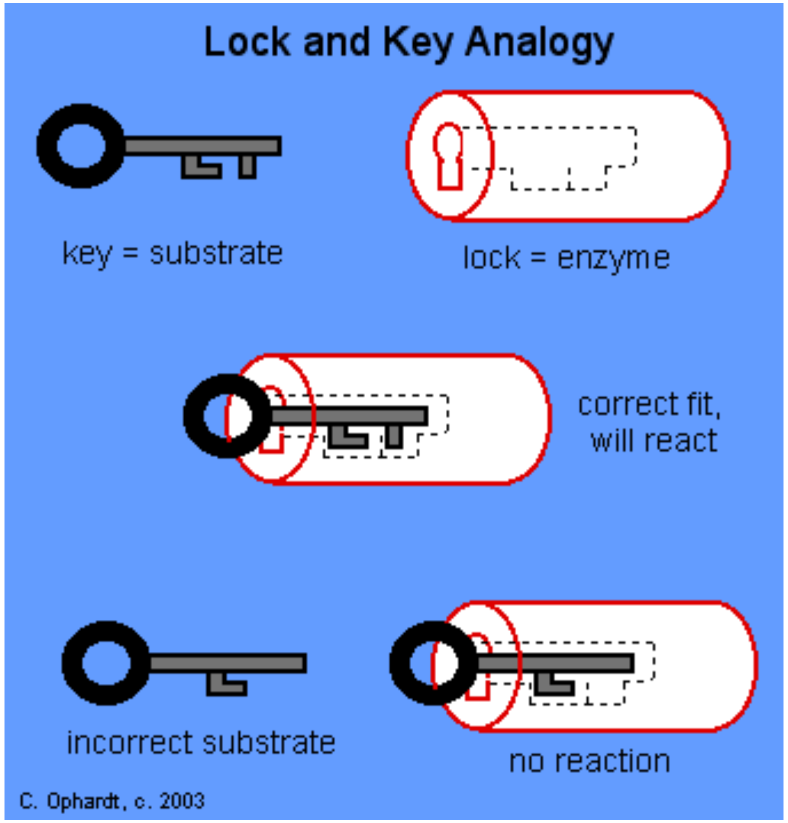

Heme

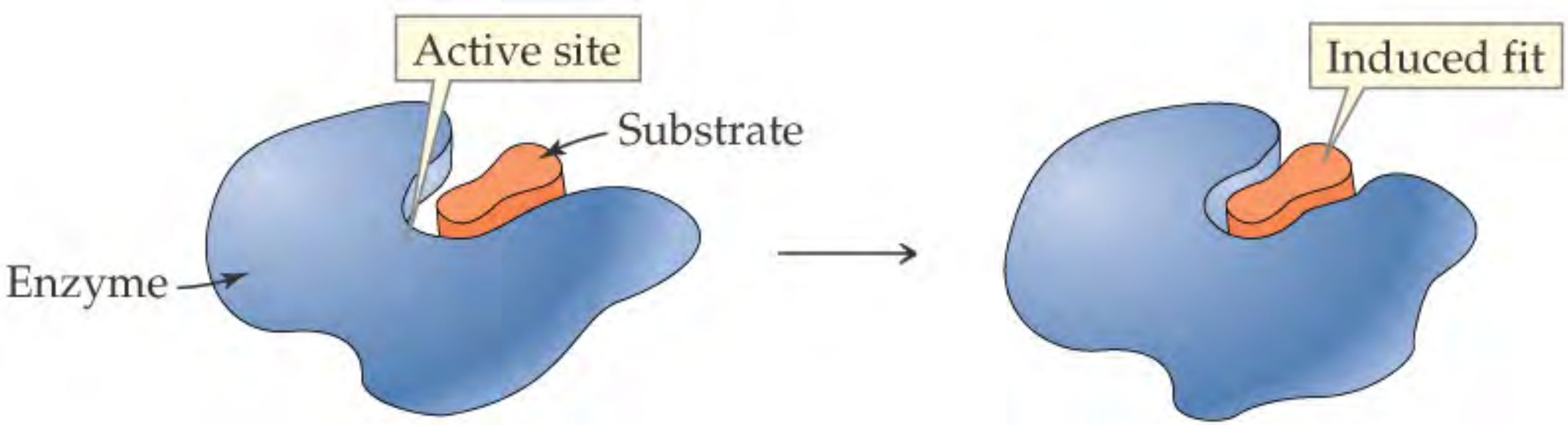


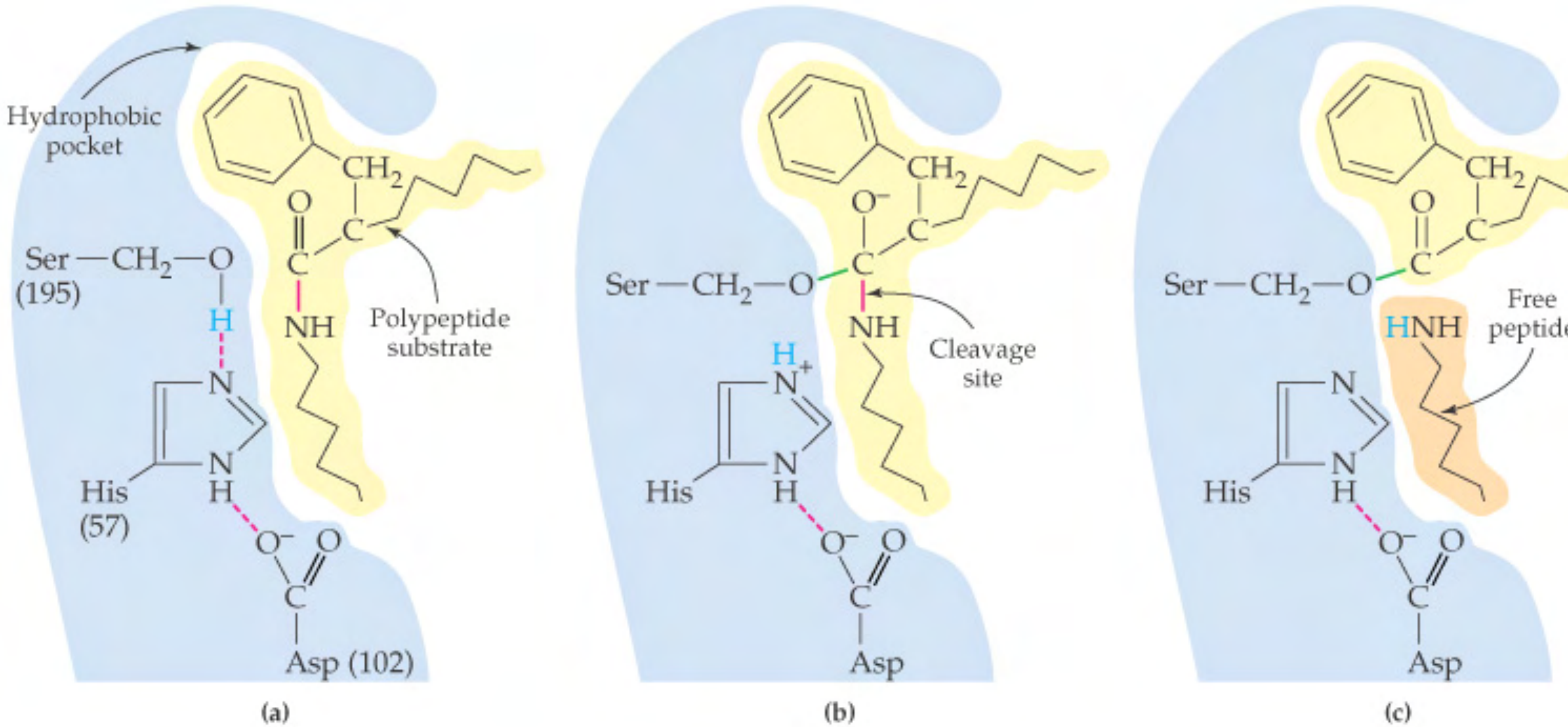
- Cofactors provide additional chemically active functional groups which are not present in the side chains of amino acids that made up the enzyme.
- Metal ions may anchor a substrate in the active site or may participate in the catalyzed reaction.

How Enzyme Work

- Two modes are invoked to represent the interaction between substrate and enzymes. These are:
- ***Lock-and-key model***: The substrate is described as fitting into the active site as a key fit into a lock.
- ***Induced-fit-model***: The enzyme has a flexible active site that changes shape to accommodate the substrate and facilitate the reaction.


Lock and Key Analogy
key = substrate
lock = enzyme
correct fit,
will react
incorrect substrate
no reaction
C. Ophardt, c. 2003


Active site
Substrate
Enzyme
Induced fit



Hydrophobic pocket
Ser — CH2 — O
(195)
H
Polypeptide substrate
N
N
H
His
(57)
O⁻ O
C
Asp (102)
CH2
O
C
C
NH
(a)
Ser — CH2 — O
O⁻
C
C
CH2
NH
Cleavage site
H+
N
N
H
His
O⁻ O
C
Asp
(b)
Ser — CH2 — O
CH2
O
C
C
HNH
Free peptide
N
N
H
His
O⁻ O
C
Asp
(c)