Reading Material Lecture 1

CLICK TO OPEN PDF FILE

Article 1:
http://dosequis.colorado.edu/Courses/MicroNano/articles/Lecture1_Article1.pdf

Article 2:
http://dosequis.colorado.edu/Courses/MicroNano/articles/Lecture1_Article2.pdf

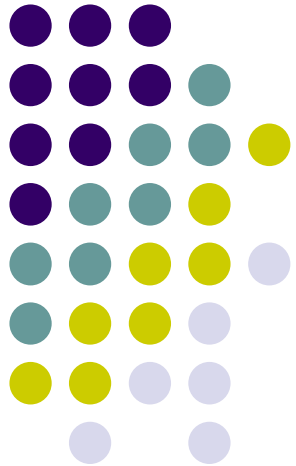
Article 3:
http://dosequis.colorado.edu/Courses/MicroNano/articles/Lecture1_Article3.pdf

Article 4:
http://dosequis.colorado.edu/Courses/MicroNano/articles/Lecture1_Article4.pdf

Moc/Bio and Nano/Micro

Lee and Stowell

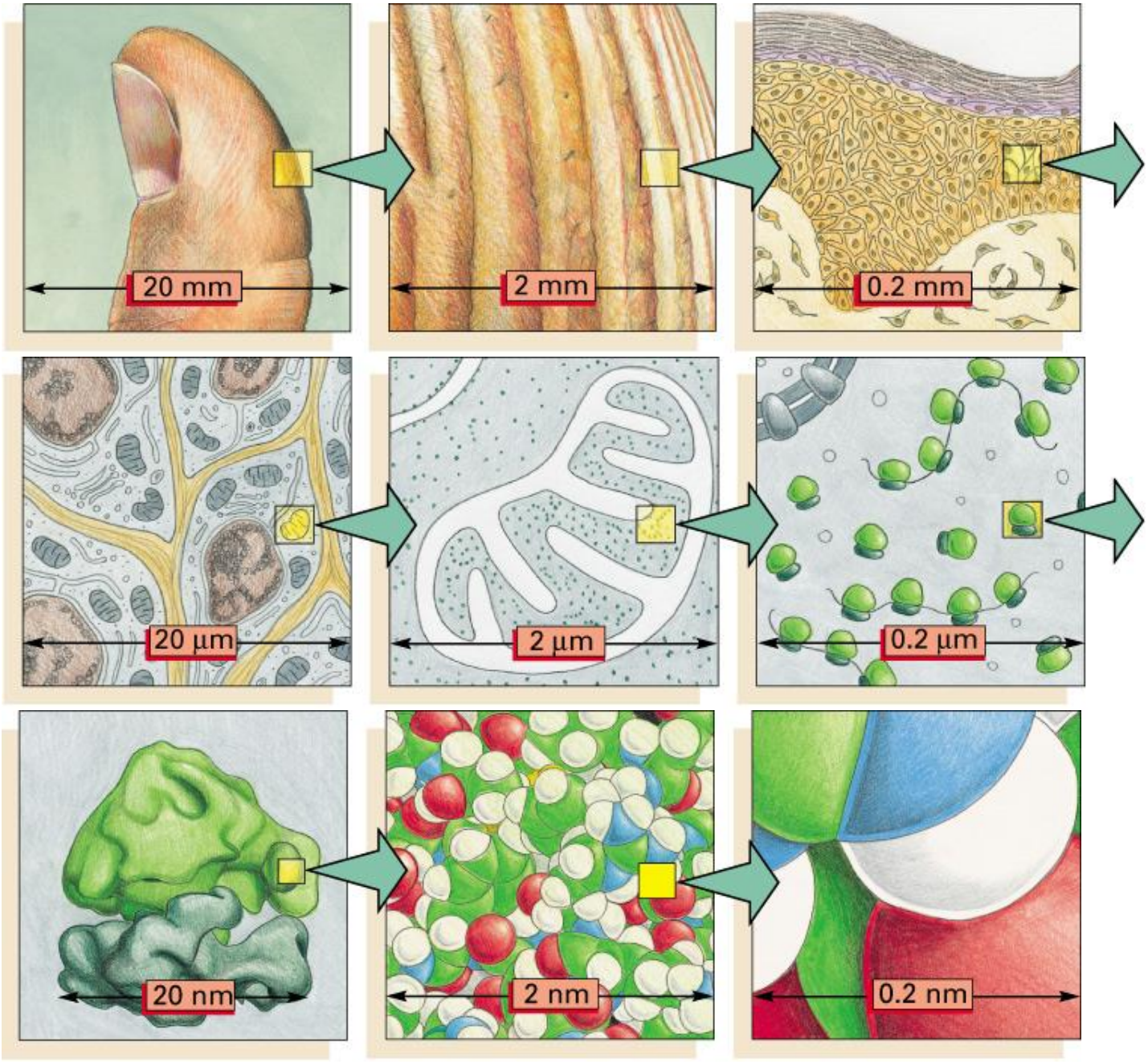
Moc/Bio-Lecture 1



Biological Molecules
- **Nucleic Acids (nucleotides)**
- **Proteins (amino acids)**
- **Carbohydrates (sugars)**
- **Lipids (fatty acids)**

Chemistry of Biomolecules
- **Peptides**
- **Phosphates**
- **Esters**
- **etc**

The size of life



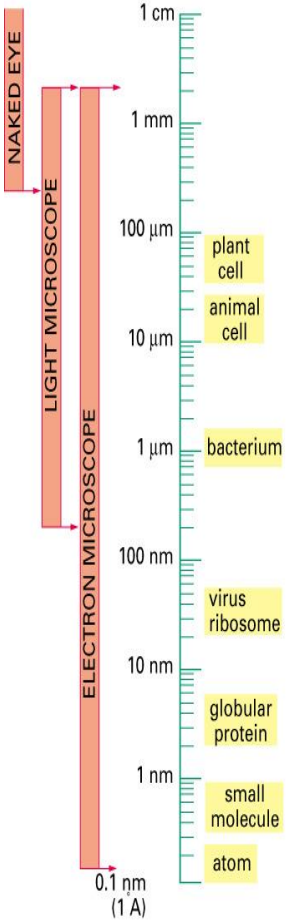


Figure 9–2. Molecular Biology of the Cell, 4th Edition.

The chemistry of life

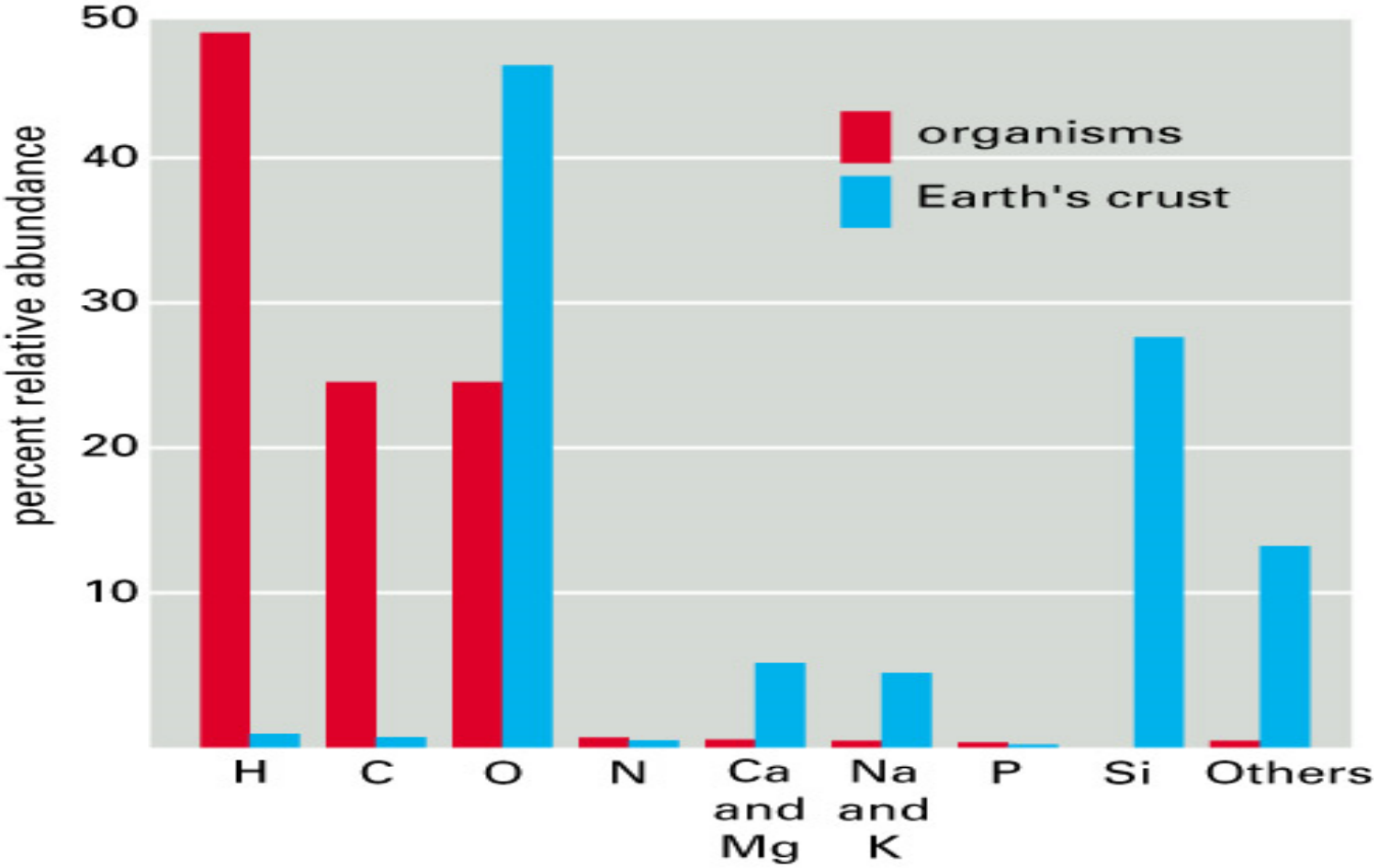
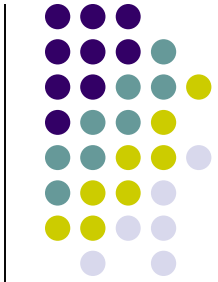


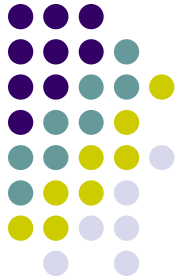
Figure 2–3. Molecular Biology of the Cell, 4th Edition.

Something about 4



- There are four fundamental elements in biology
  - Carbon
  - Nitrogen
  - Oxygen
  - Hydrogen
- There are four fundamental molecules in biology
  - Nucleic acids
  - Amino acids
  - Carbohydrates
  - Fatty acids
- The flow of information and function in the cell is
  - From DNA
  - To RNA
  - To proteins
  - To function

Chemical Bonds



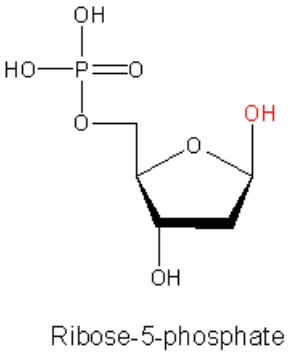
- Covalent Bonds
  - C-C
- Ionic Bonds
  - $Na^{+}Cl^{-}$
- Hydrogen Bonds
  - water
- Van der Waals
  - oils

Nucleic acids

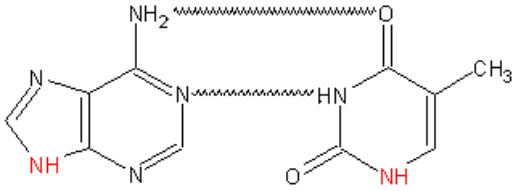
- Deoxyribonucleic acids (DNA)
  - Structure
  - Function
- Ribonucleic acids (RNA)
  - Structure
  - Function

DNA-structure

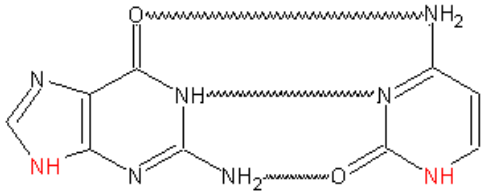
- Deoxyribonucleic acids



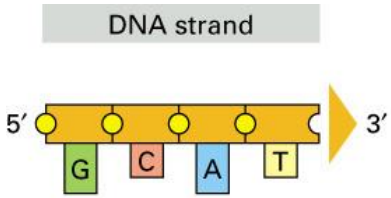
Ribose-5-phosphate



Adenine Thymine



Guanine Cytosine



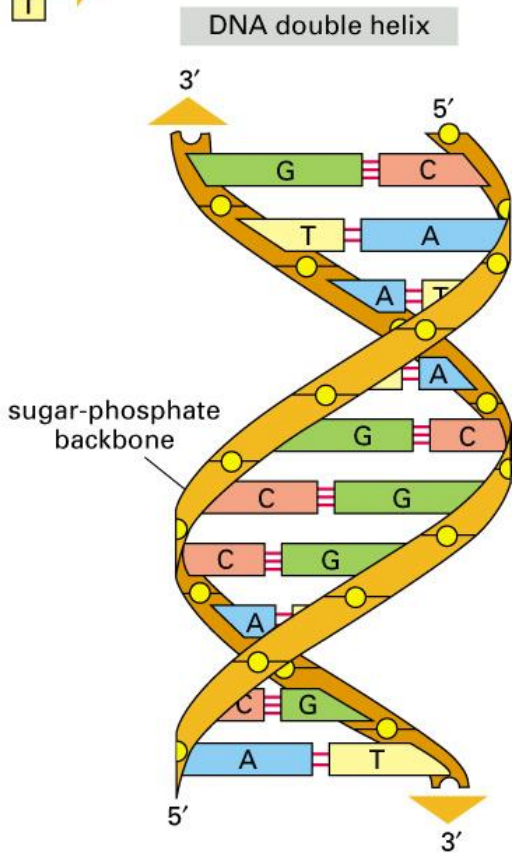


Figure 4–3 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

- Double helix (Watson, Crick, Wilkins and Franklin)
  - A=T, G=C Chargaff

Chemical recognition

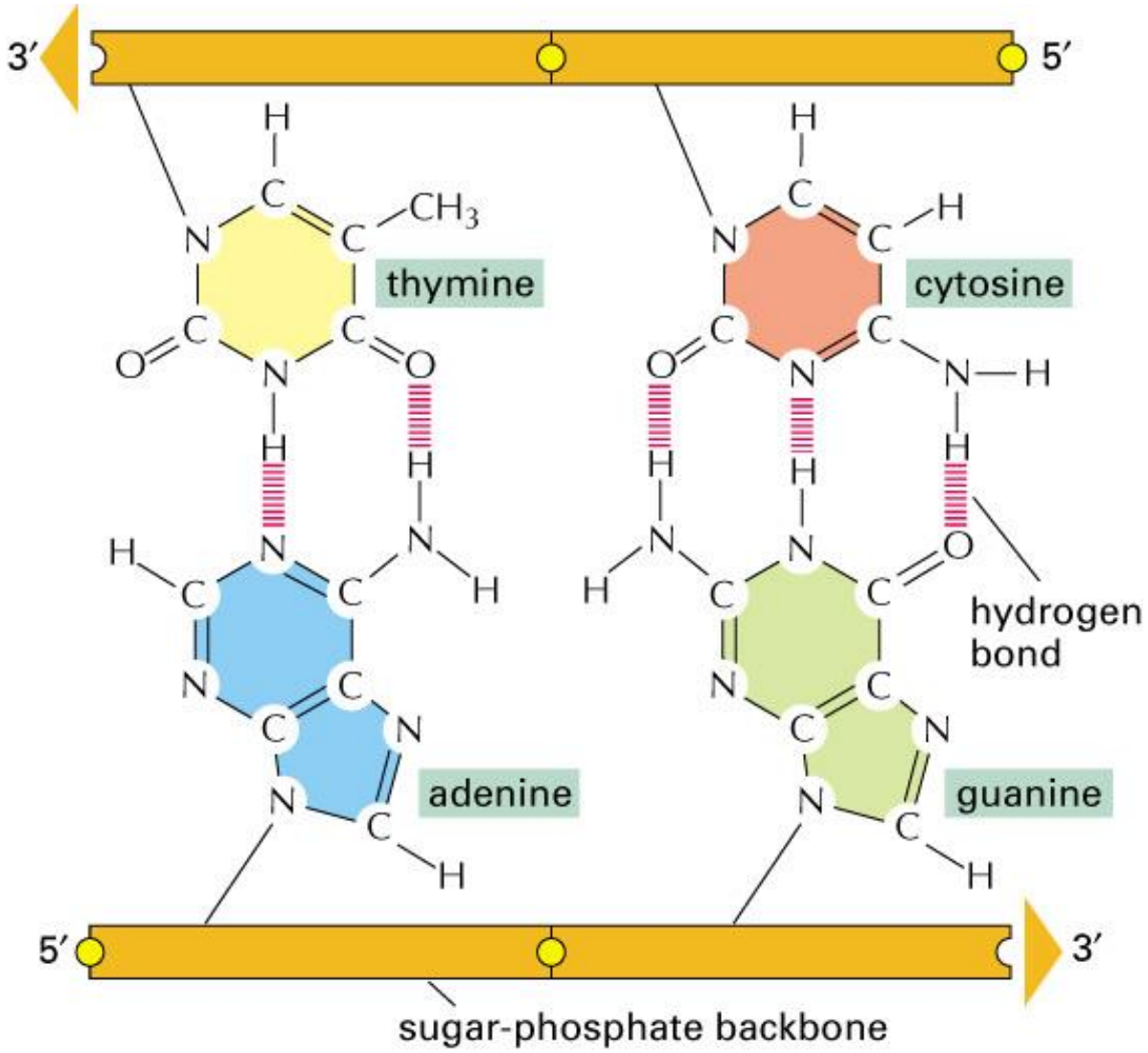


Figure 4–4. Molecular Biology of the Cell, 4th Edition.

Pyrimidine

Purine

Structure of duplex DNA

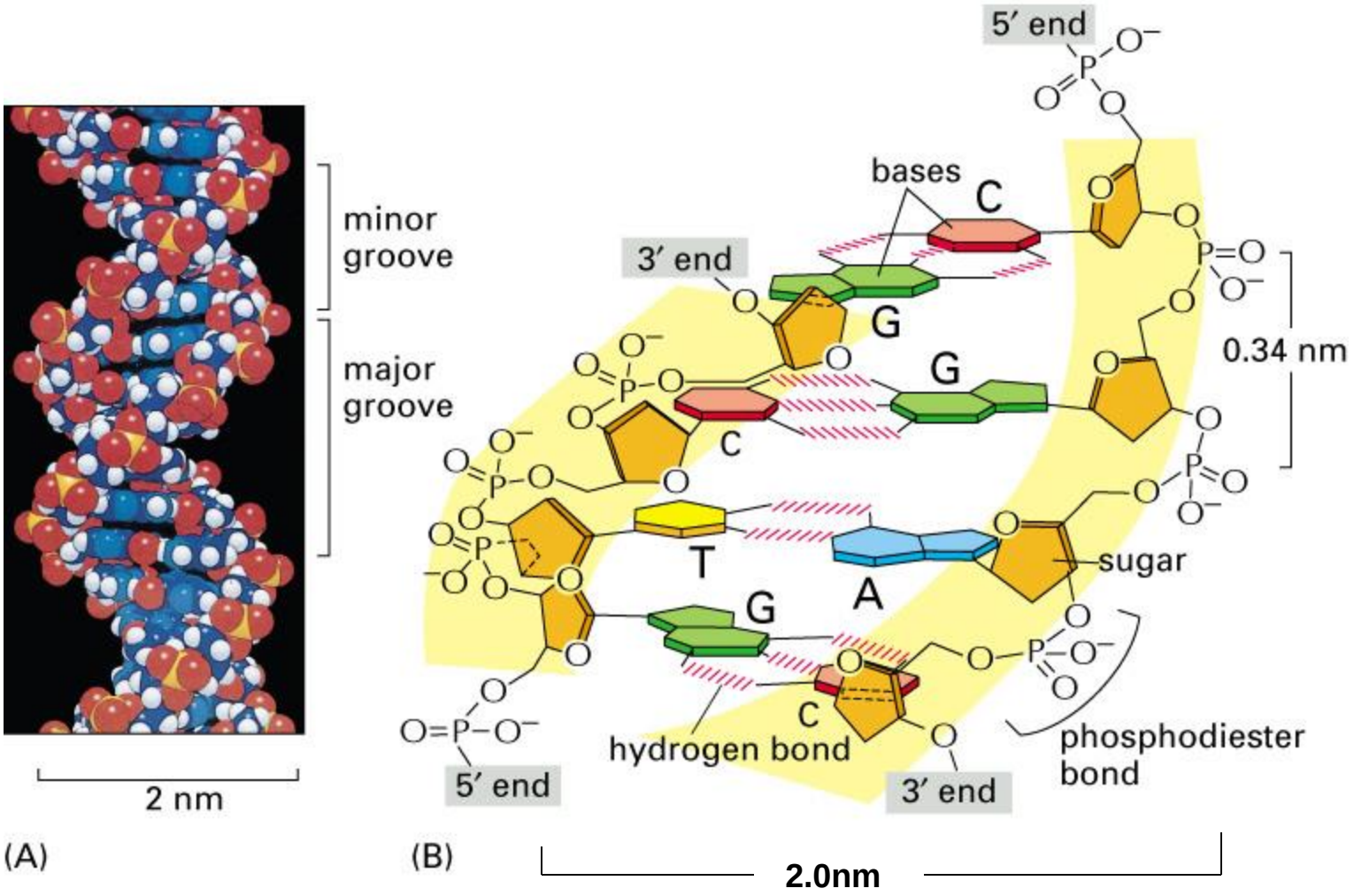


Figure 4–5. Molecular Biology of the Cell, 4th Edition.

Major Minor differences

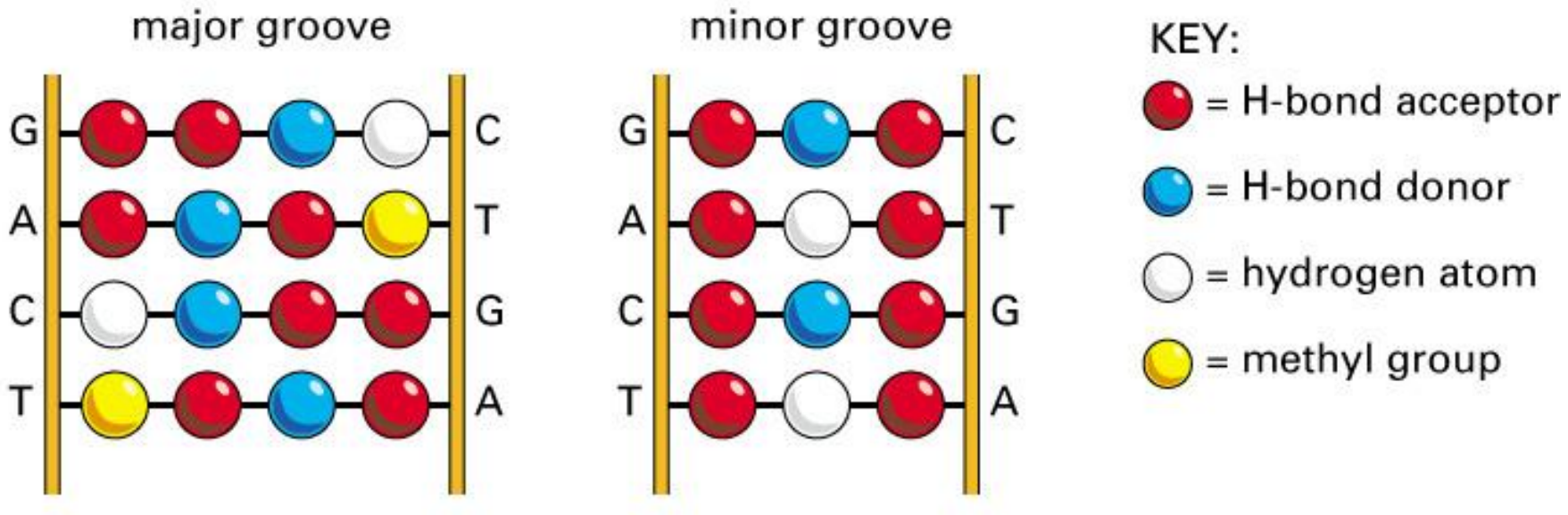


Figure 7–8. Molecular Biology of the Cell, 4th Edition.

Recognition

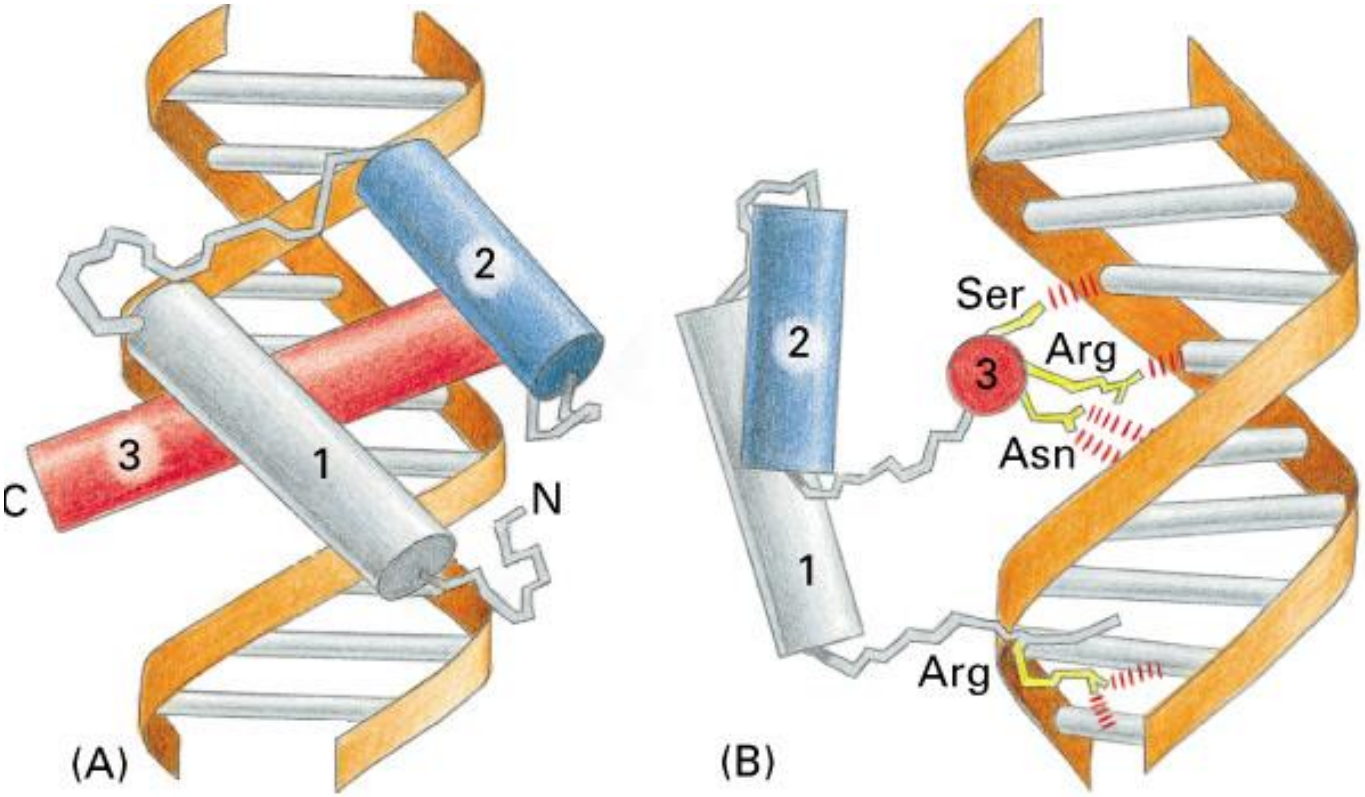


Figure 7–16. Molecular Biology of the Cell, 4th Edition.

DNA-biology

- Storage and replication of genetic information
  - Coding and noncoding strand
  - High fidelity replication
- Encodes for proteins and the regulation of protein expression
- Encodes for siRNA’s

Storage of information

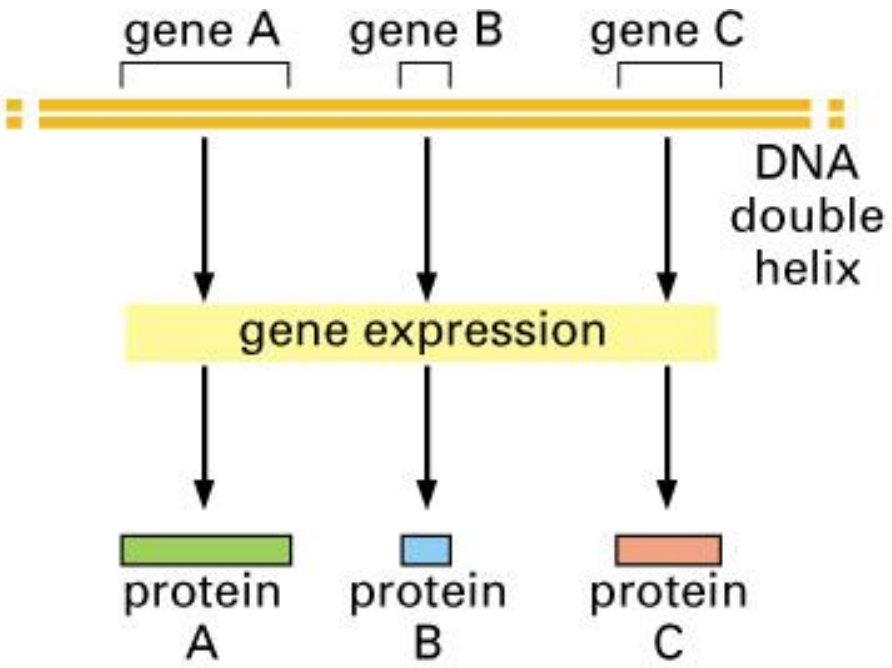


Figure 4–6. Molecular Biology of the Cell, 4th Edition.

High fidelity replication

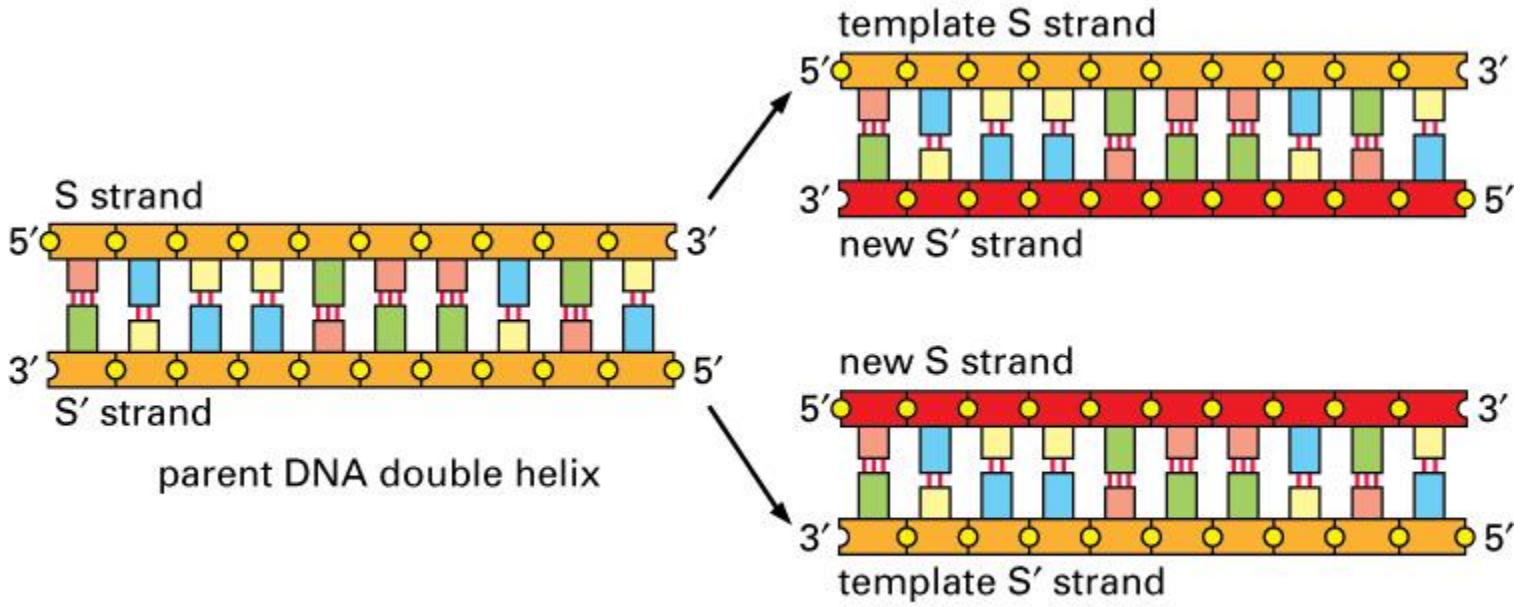
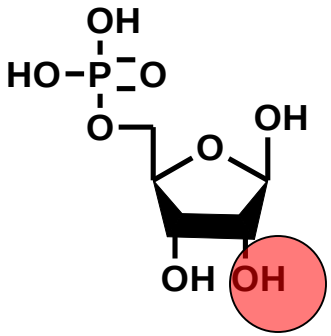


Figure 4–8. Molecular Biology of the Cell, 4th Edition.

Only 1 in 10^9 ! errors

RNA-structure

- Ribonucleic acid



- Also complements sequence (G-C A-U)
- Fold into more complex 3D structures
  - tRNA's, ribozymes, regulatory loops

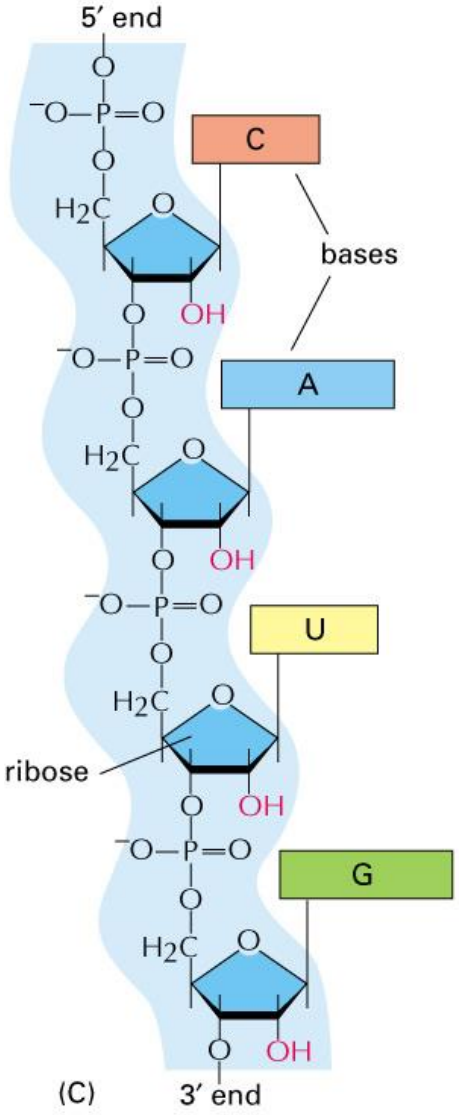


Figure 6–4 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

RNA bases

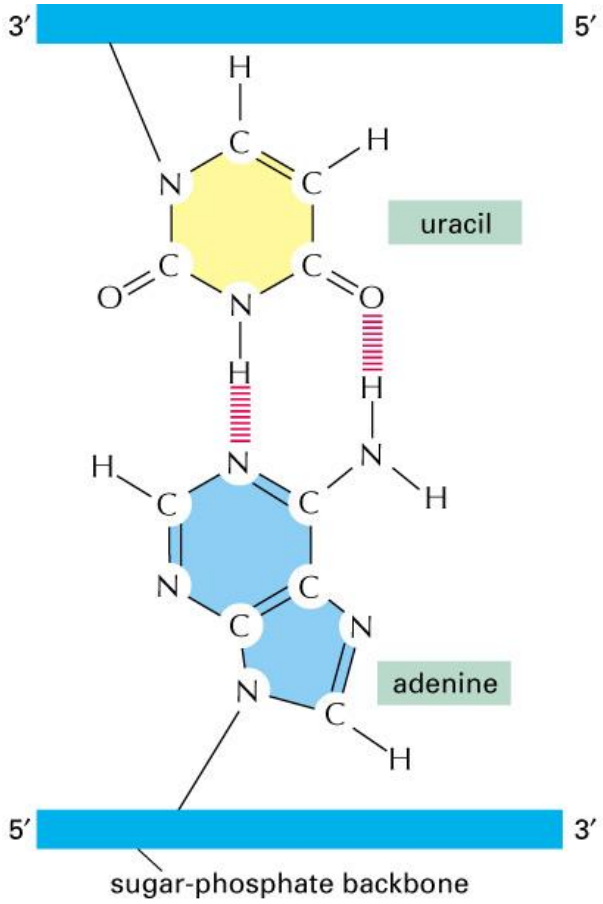


Figure 6–5. Molecular Biology of the Cell, 4th Edition.

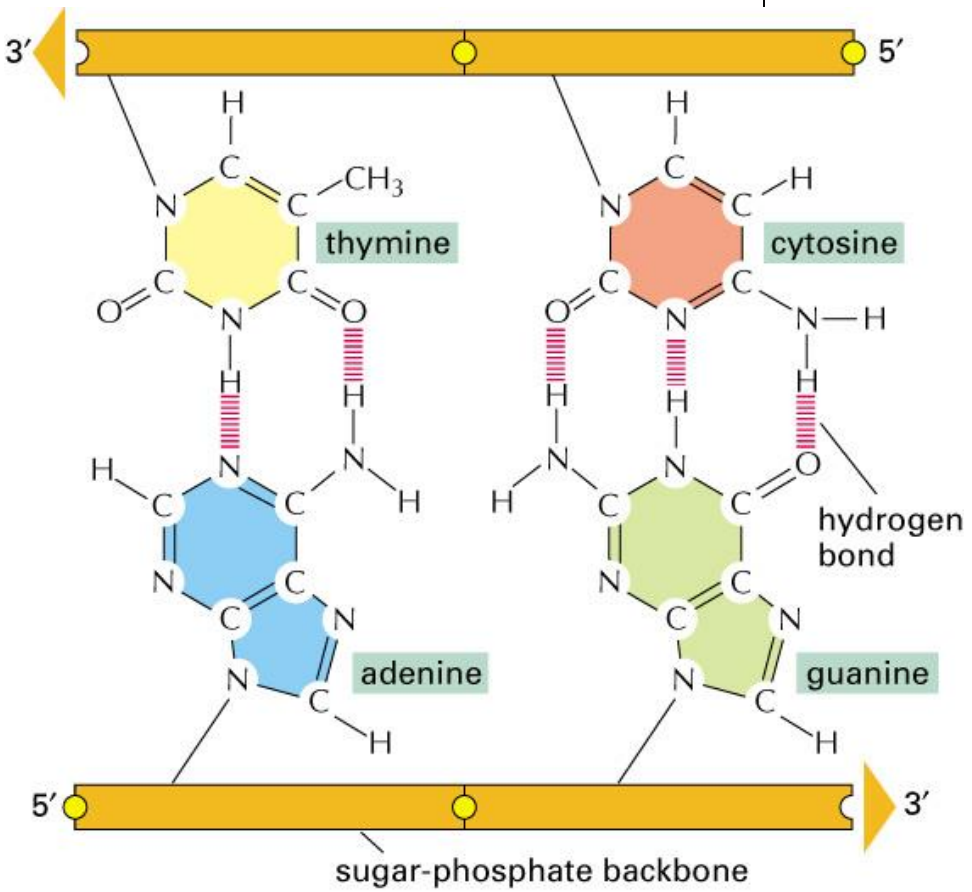


Figure 4–4. Molecular Biology of the Cell, 4th Edition.

RNA structures

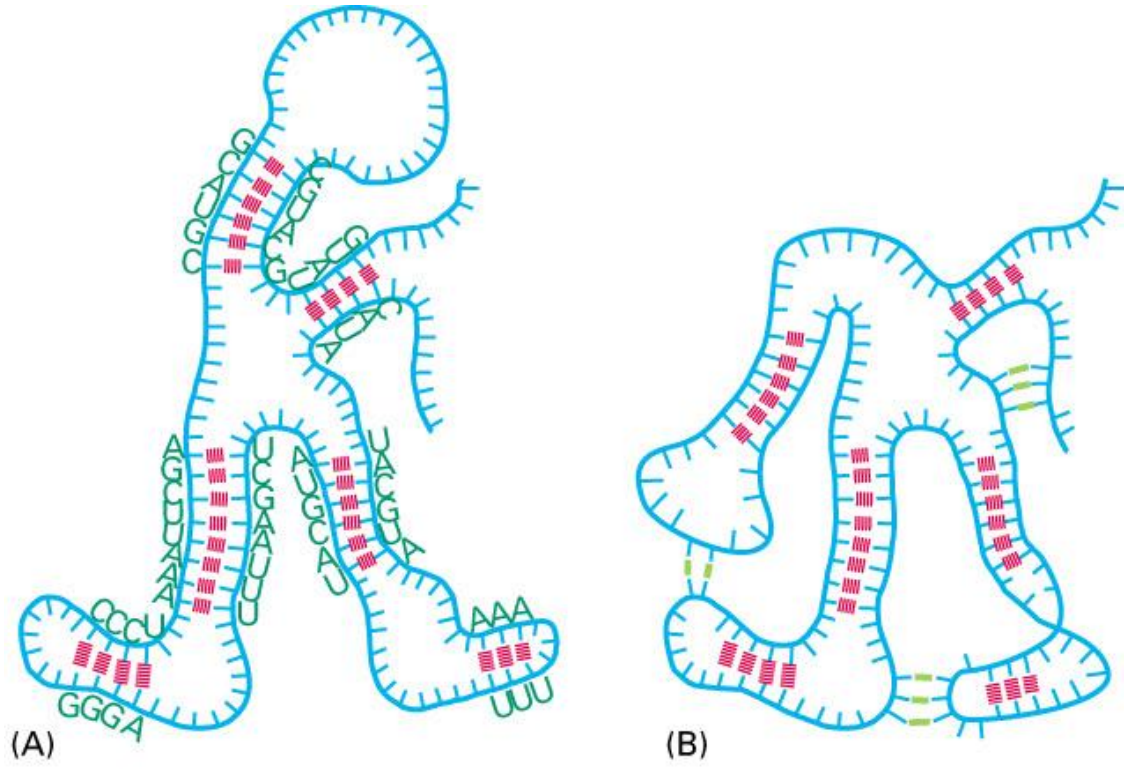


Figure 6–6 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

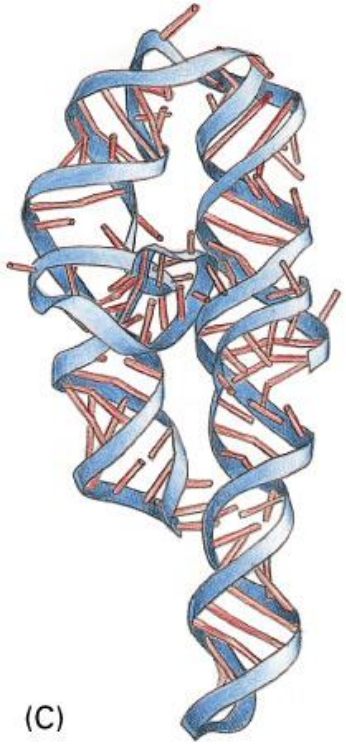


Figure 6–6 part 2 of 2. Molecular Biology of t

The ultimate ribozyme

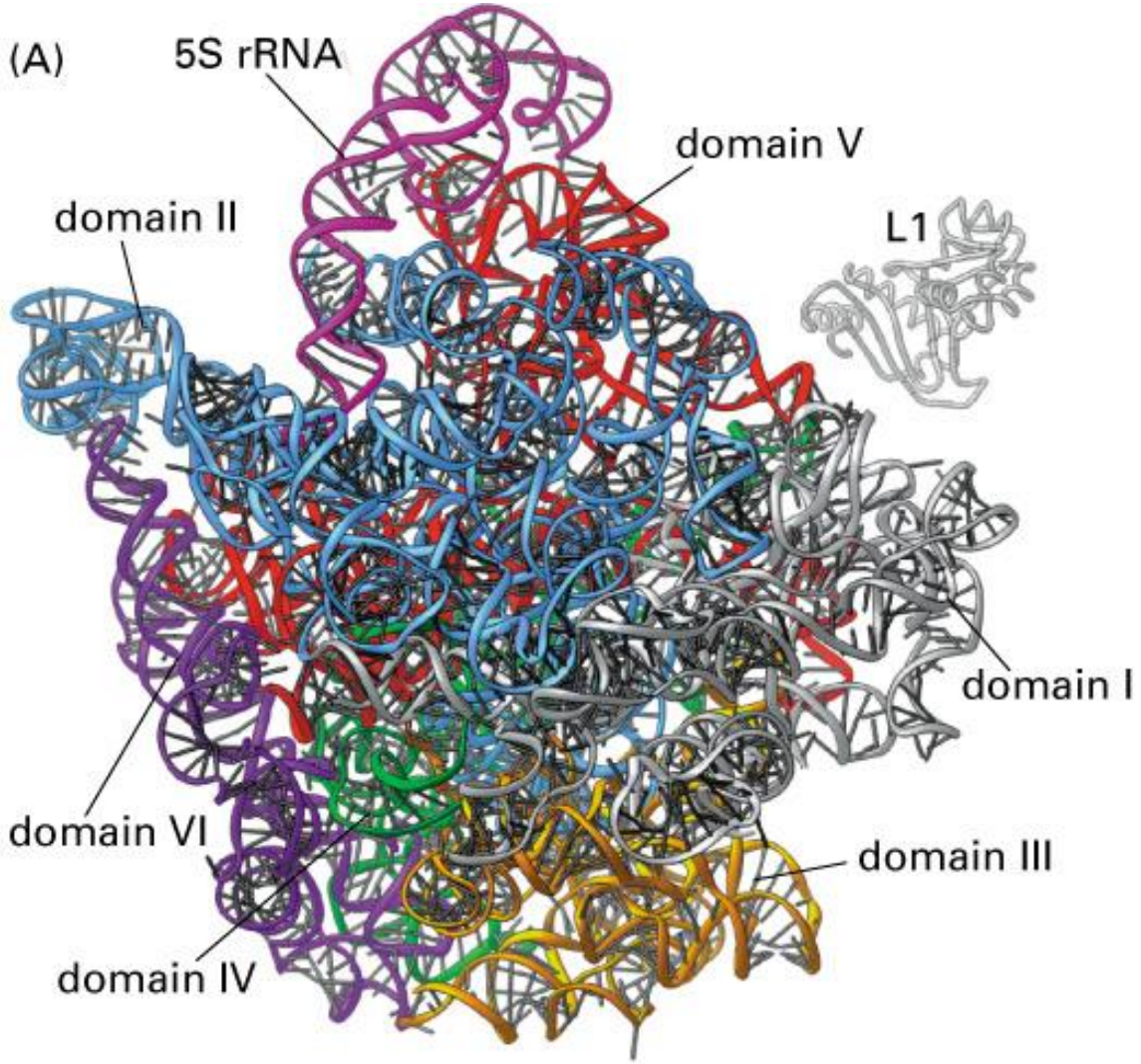
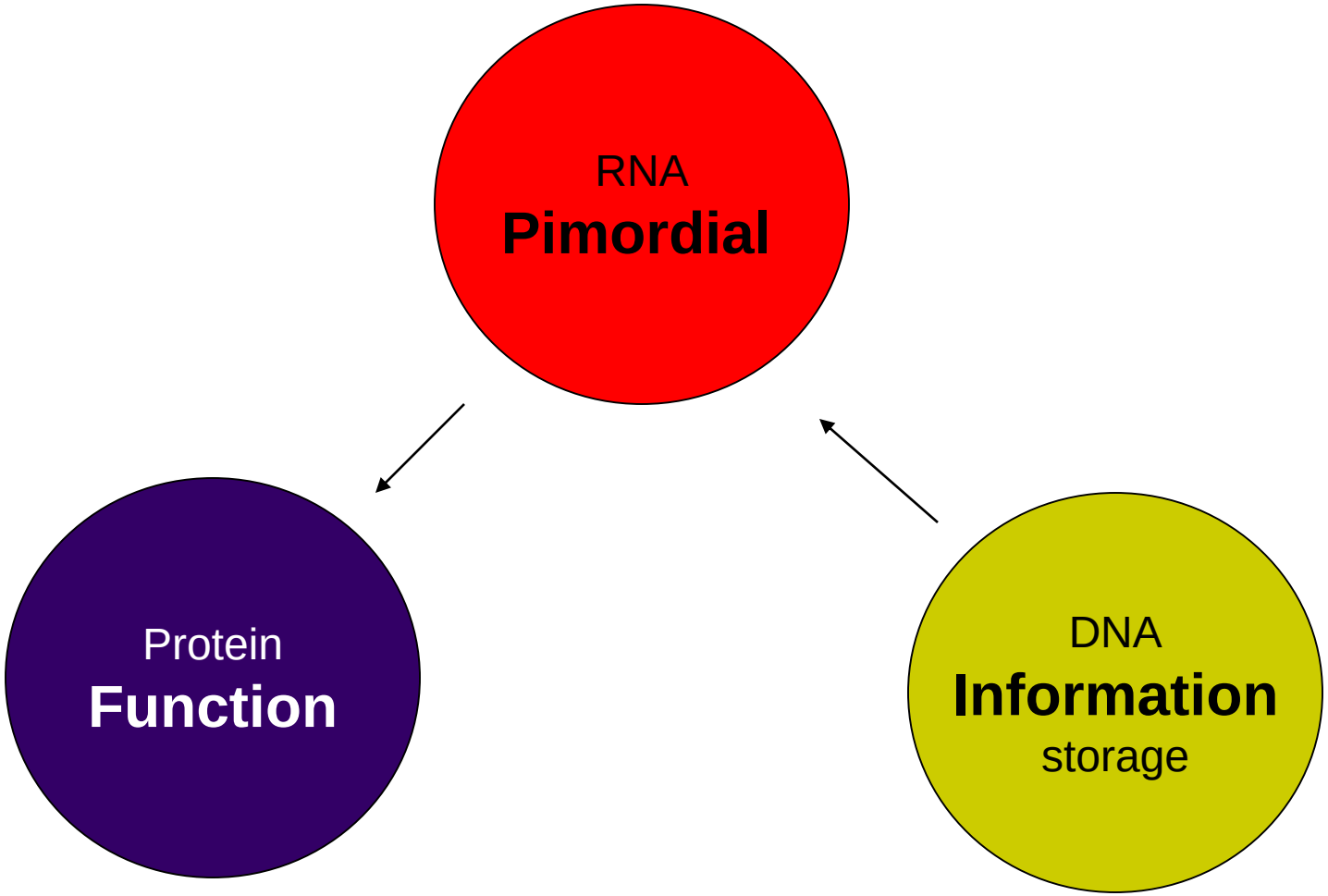


Figure 6–67 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

RNA-biology

- Primordial life
  - The first enzymes were ribozymes
- Intermediate for protein expression
- Catalyzes peptide synthesis
- Second level of protein regulation

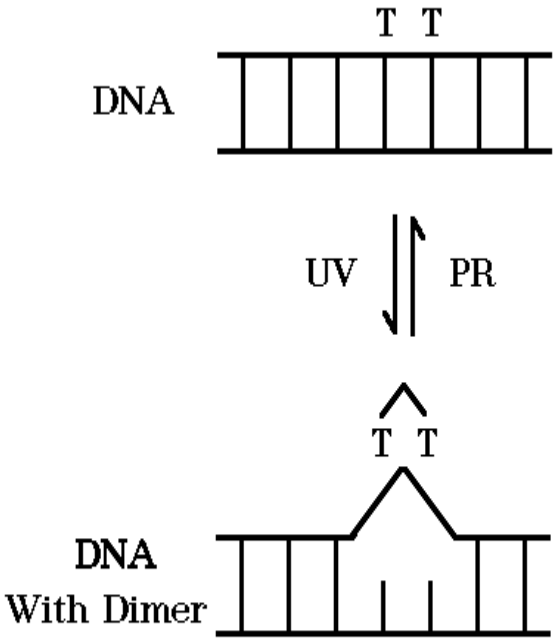
Tripartite division of labor

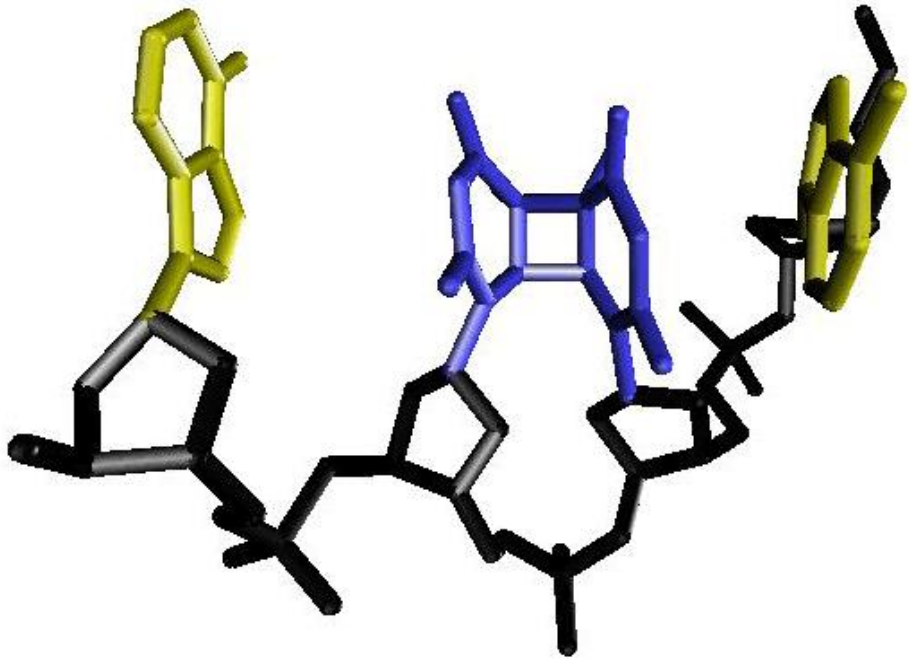


Reactions of Nucleotides

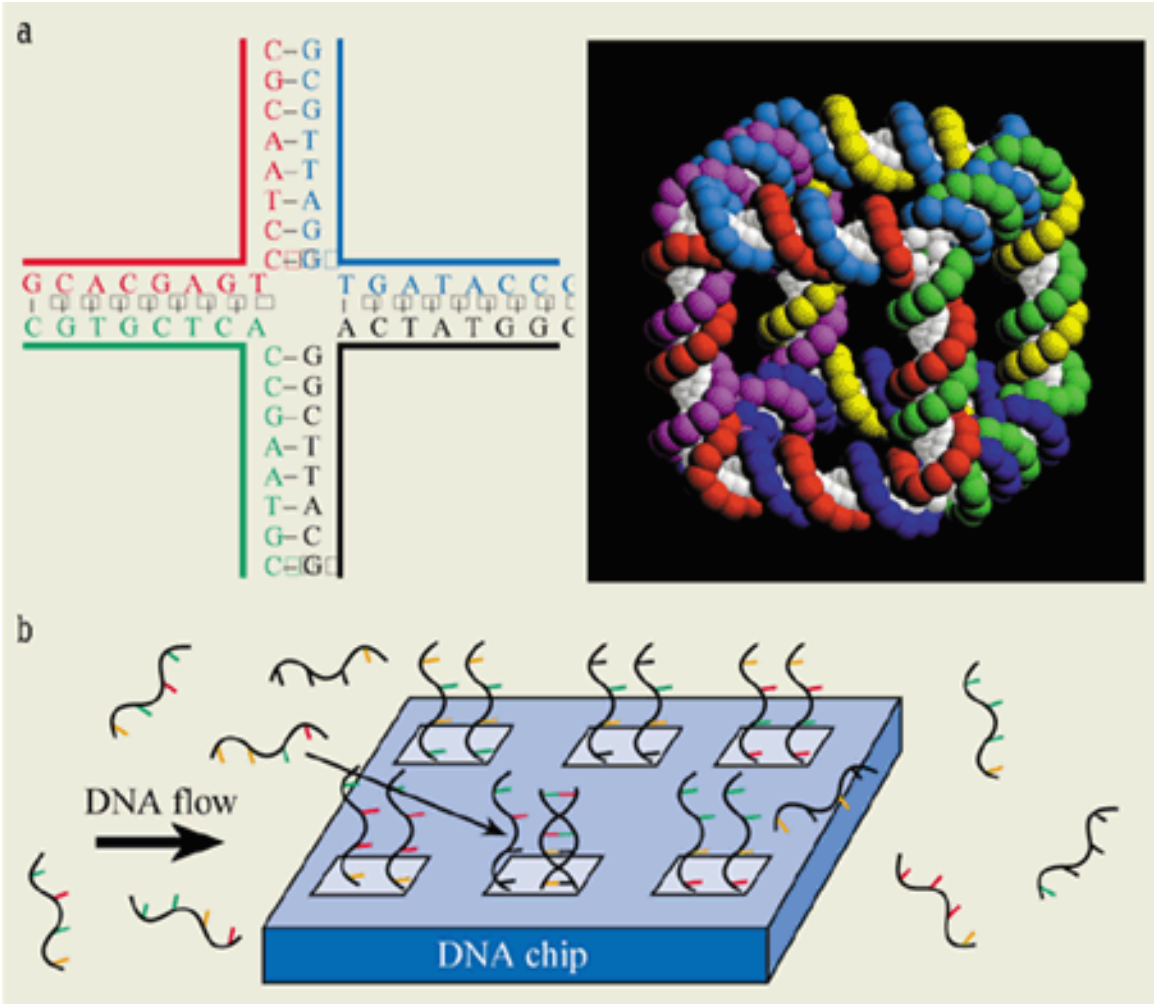
- Chemical hydrolysis
  - RNA phosphoryl hydrolysis greater than DNA
  - Cleaves both the phosphoryl and the N-glycosidic
- Oxidative damage
  - Most prevalent
  - Deoxyribose cleavage and base loss
  - Heterocycle cleavage
- Photo induced dimer formation
  - T-T formation from T T in sequence
  - Repair enzyme photolyase

Thymidine dimer and photolyase





Examples: Exploiting base pair specificity



NATURE | VOL 421 | 23 JANUARY 2003 | *Proc. Natl. Acad. Sci. U.S.A.* **94** (24).

L-Amino Acids-protein

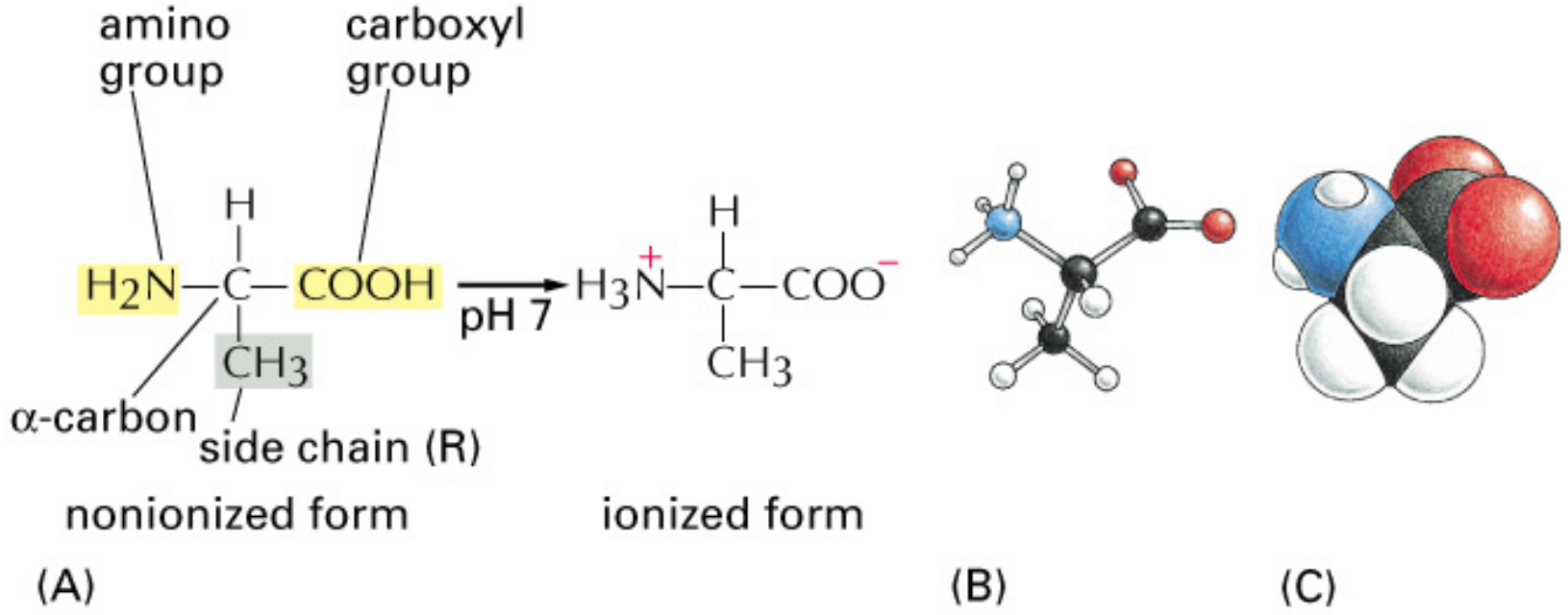


Figure 2–23. Molecular Biology of the Cell, 4th Edition.

The natural amino acids

AMINO ACID			SIDE CHAIN
Aspartic acid	Asp	D	negative
Glutamic acid	Glu	E	negative
Arginine	Arg	R	positive
Lysine	Lys	K	positive
Histidine	His	H	positive
Asparagine	Asn	N	uncharged polar
Glutamine	Gln	Q	uncharged polar
Serine	Ser	S	uncharged polar
Threonine	Thr	T	uncharged polar
Tyrosine	Tyr	Y	uncharged polar

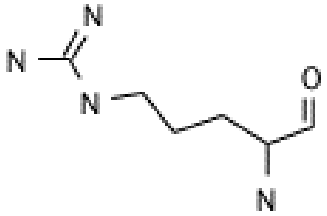
POLAR AMINO ACIDS

AMINO ACID			SIDE CHAIN
Alanine	Ala	A	nonpolar
Glycine	Gly	G	nonpolar
Valine	Val	V	nonpolar
Leucine	Leu	L	nonpolar
Isoleucine	Ile	I	nonpolar
Proline	Pro	P	nonpolar
Phenylalanine	Phe	F	nonpolar
Methionine	Met	M	nonpolar
Tryptophan	Trp	W	nonpolar
Cysteine	Cys	C	nonpolar

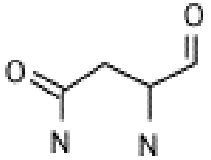
NONPOLAR AMINO ACIDS

Figure 3–3. Molecular Biology of the Cell, 4th Edition.

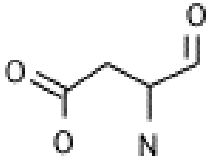
Alanyl
[Ala]



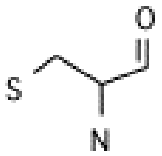
Arginyl
[Arg]



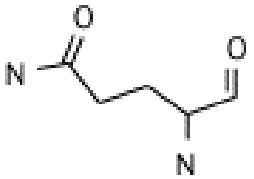
Asparaginyl
[Asn]



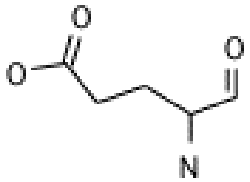
Aspartyl
[Asp]



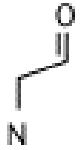
Cysteinyl
[Cys]



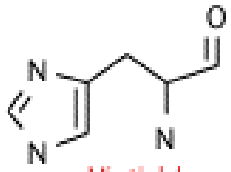
Glutaminyl
[Gln]



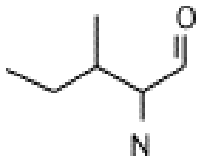
Glutamyl
[Glu]



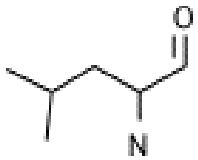
Glycyl
[Gly]



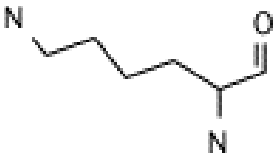
Histidyl
[His]



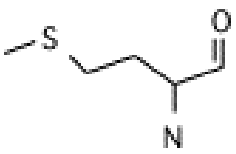
Isoleucyl
[Ile]



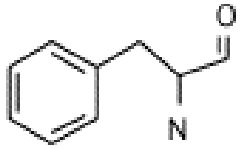
Leucyl
[Leu]



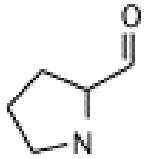
Lysyl
[Lys]



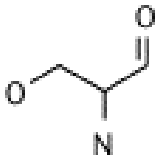
Methionyl
[Met]



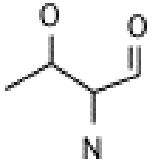
Phenylalanyl
[Phe]



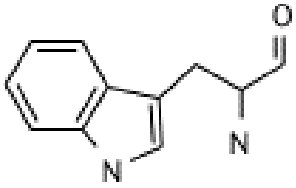
Prolyl
[Pro]



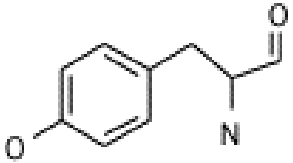
Seryl
[Ser]



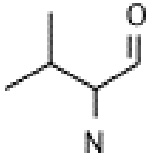
Threonyl
[Thr]



Tryptophanyl
[Trp]



Tyrosyl
[Tyr]



Valyl
[Val]

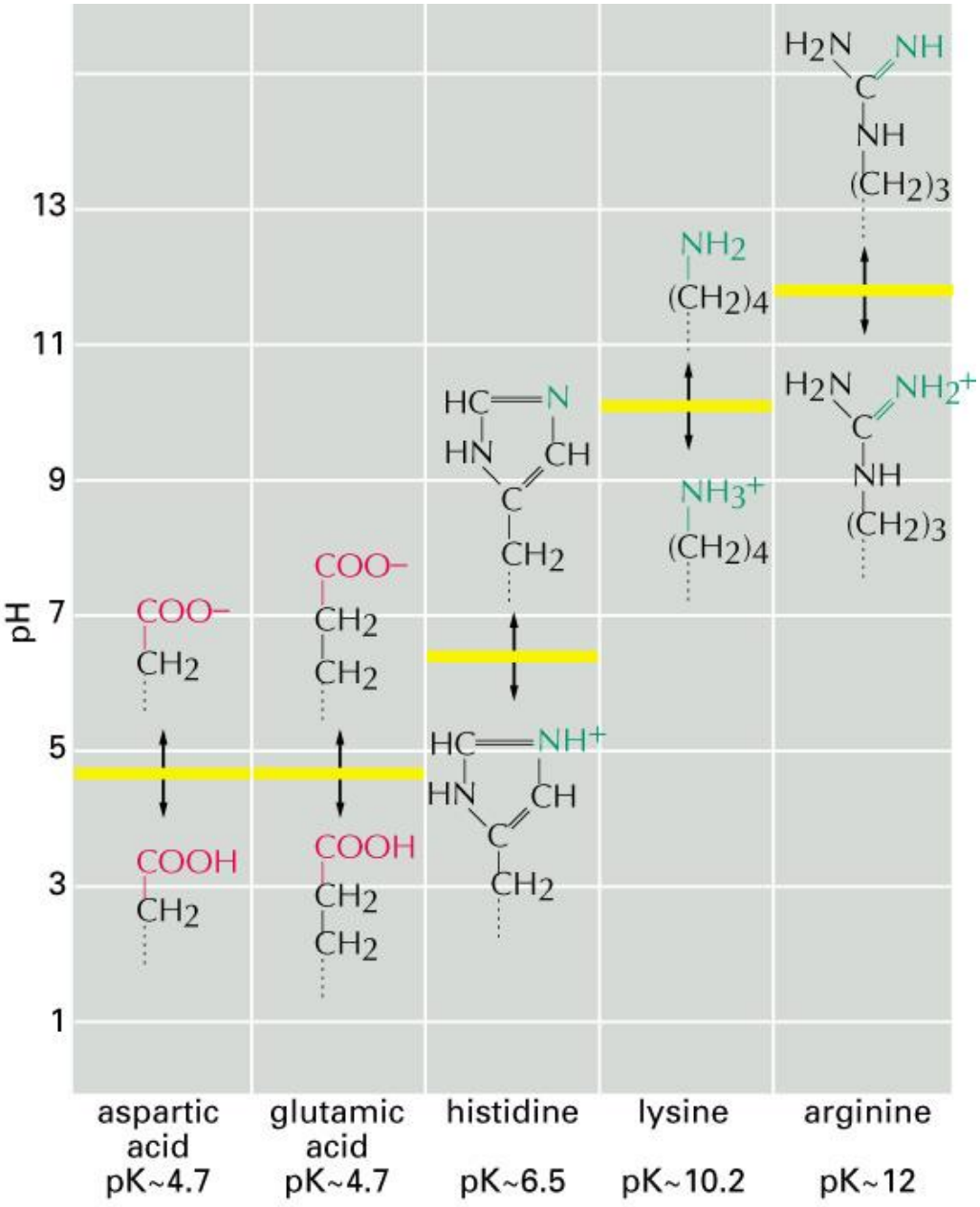


Figure 2–25. Molecular Biology of the Cell, 4th Edition.

Variance

Polypetides (proteins)

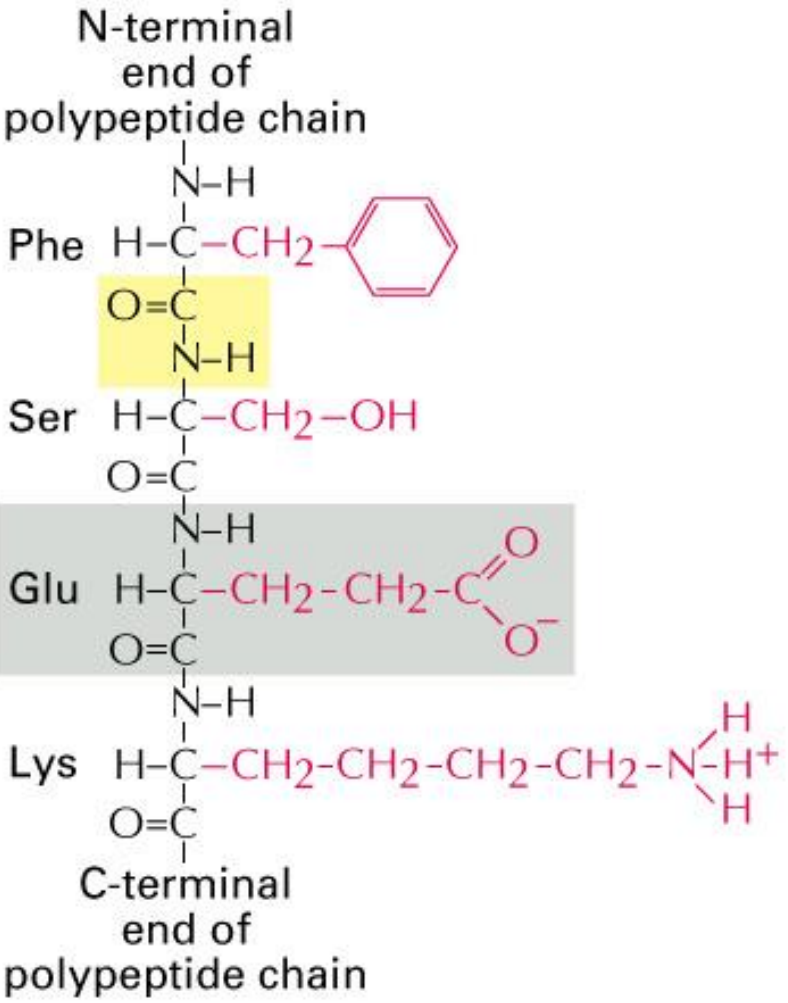


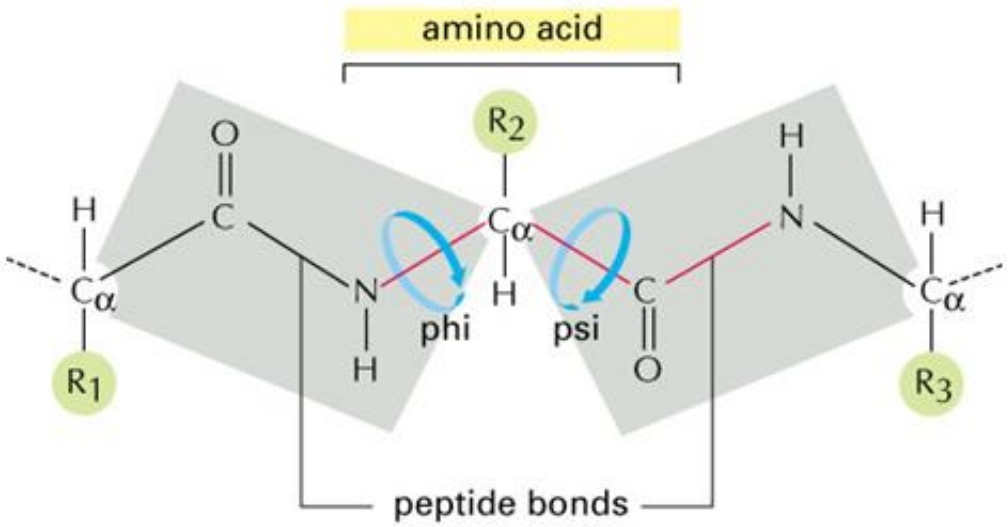
Figure 2–24. Molecular Biology of the Cell, 4th Edition.

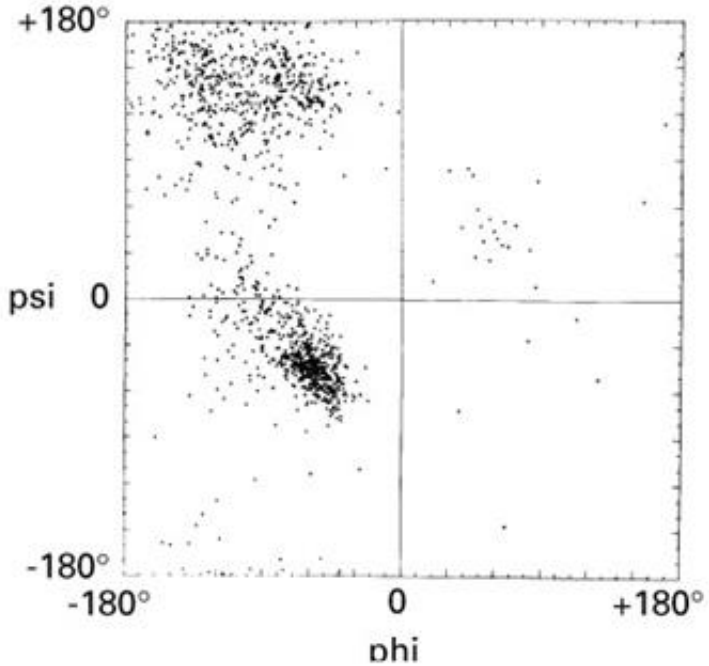
Proteins-structure

- Primary structure
  - Peptide bond
- Secondary structure
  - H-bond
  - Helix, sheet, extended
- Tertirary structure
  - Globular folds
  - VDW-forces

The peptide bond

Resonance





The helix

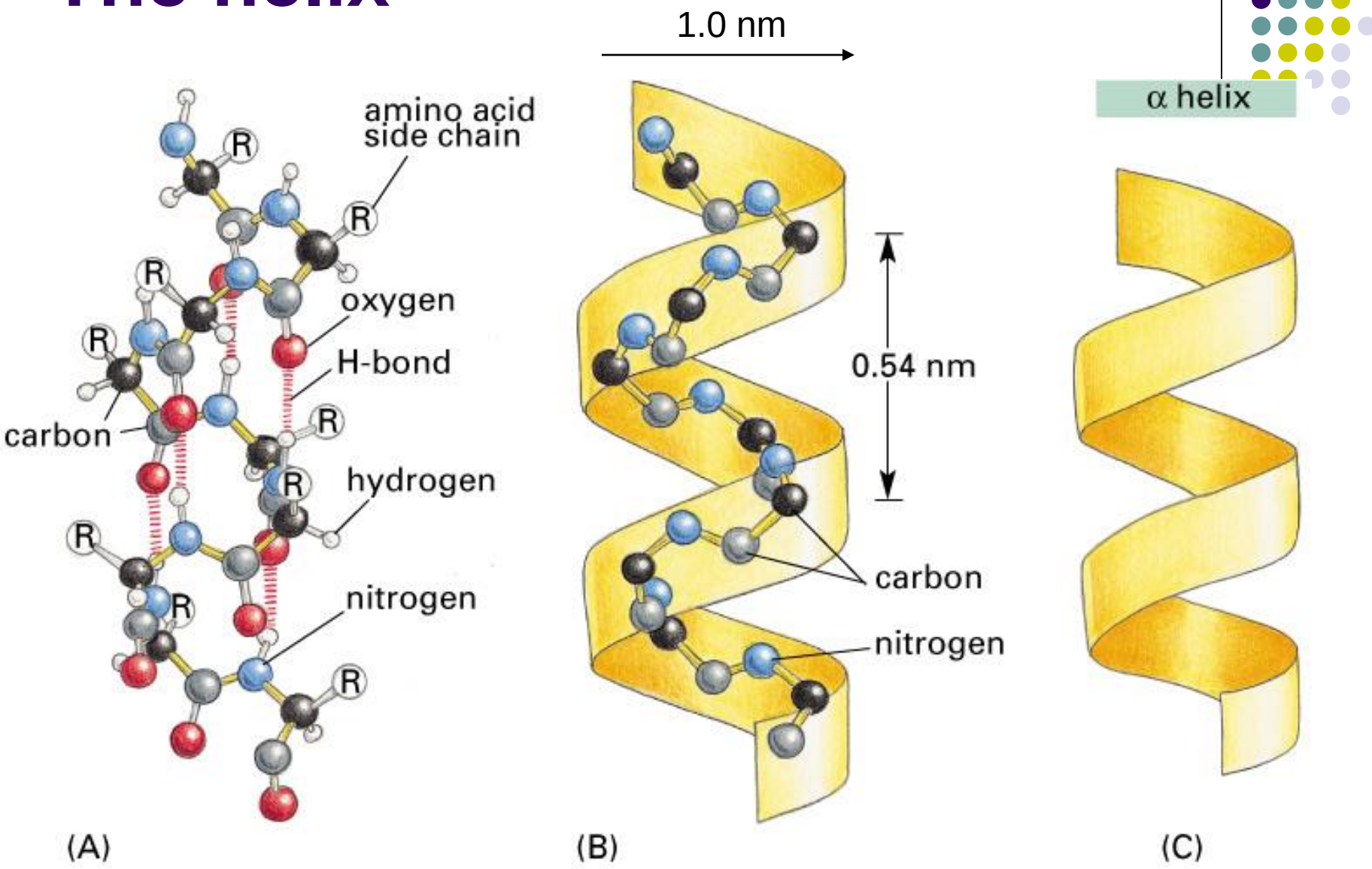


Figure 3–9 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

The sheet

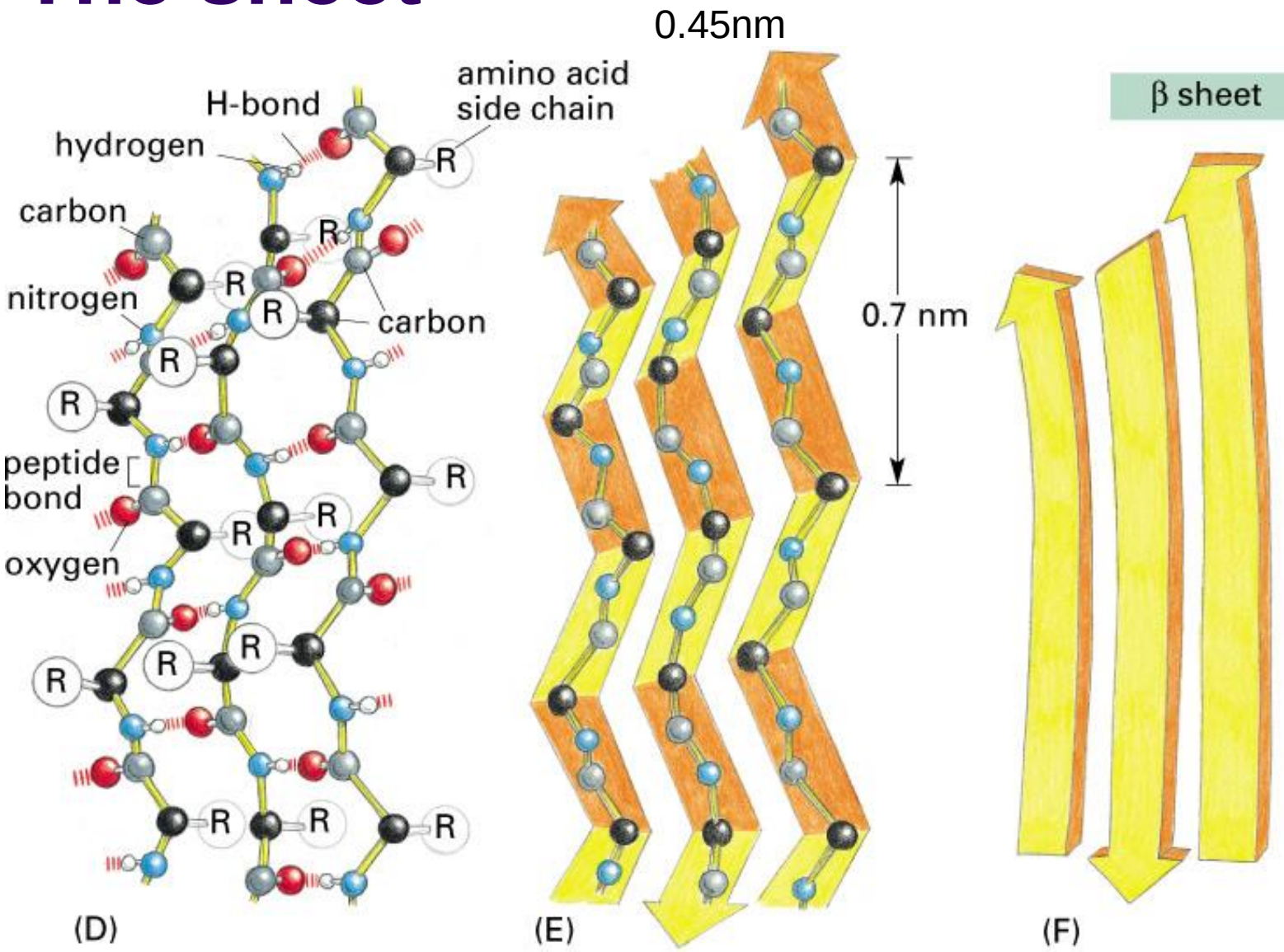


Figure 3–9 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

Add them together and….

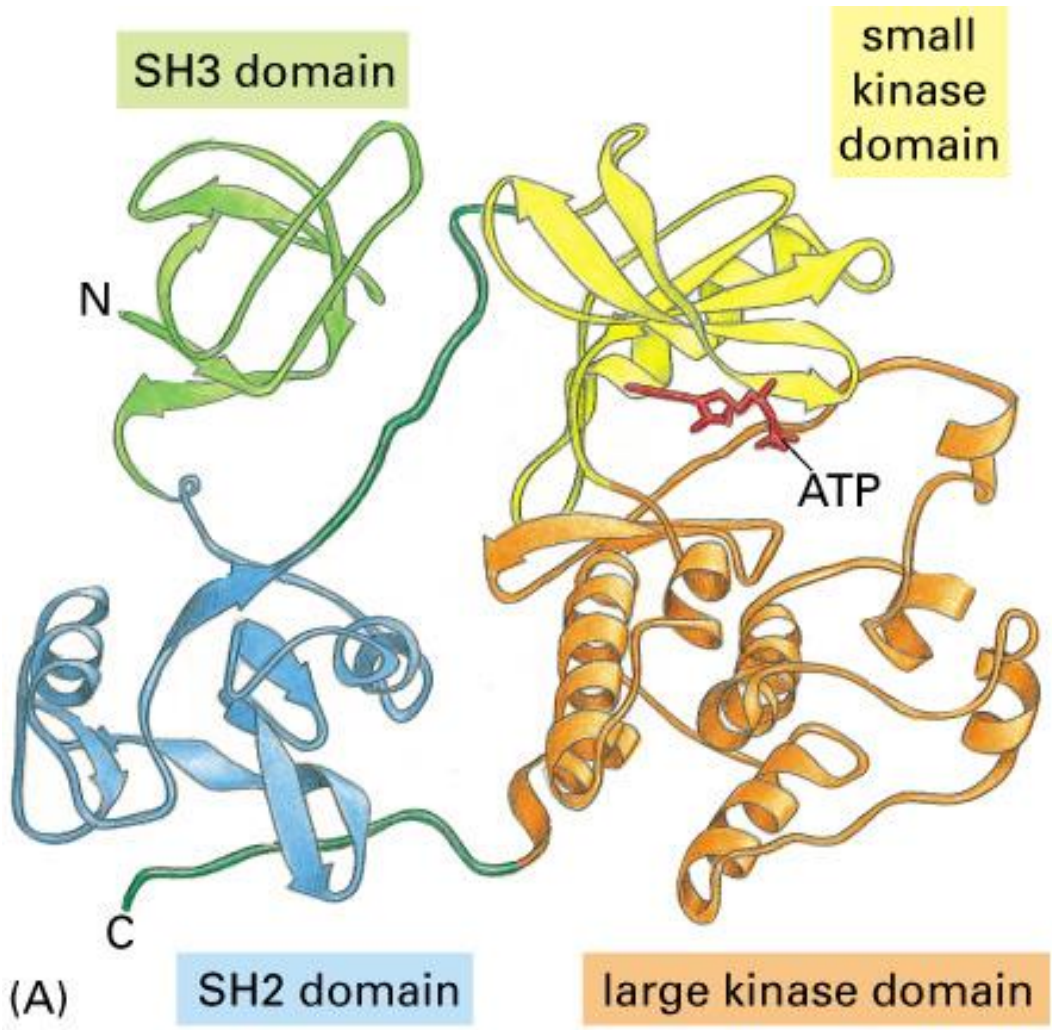


Figure 3–12 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

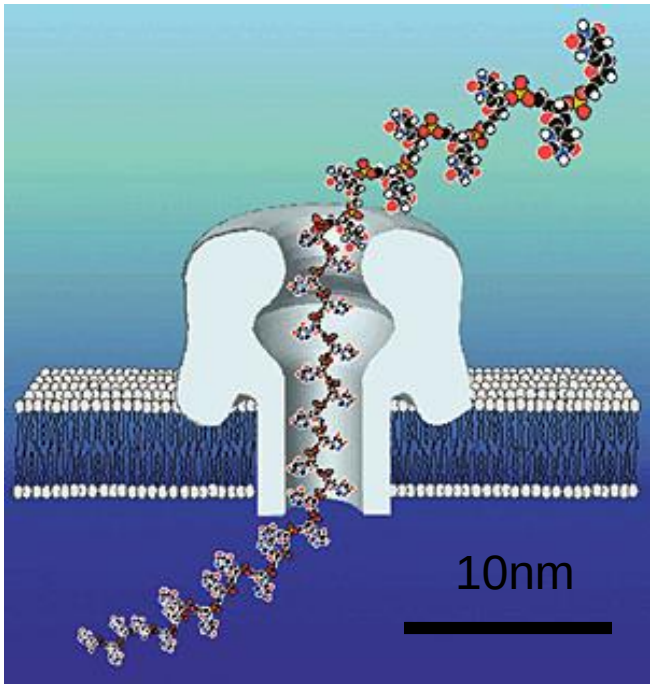
Proteins-biology

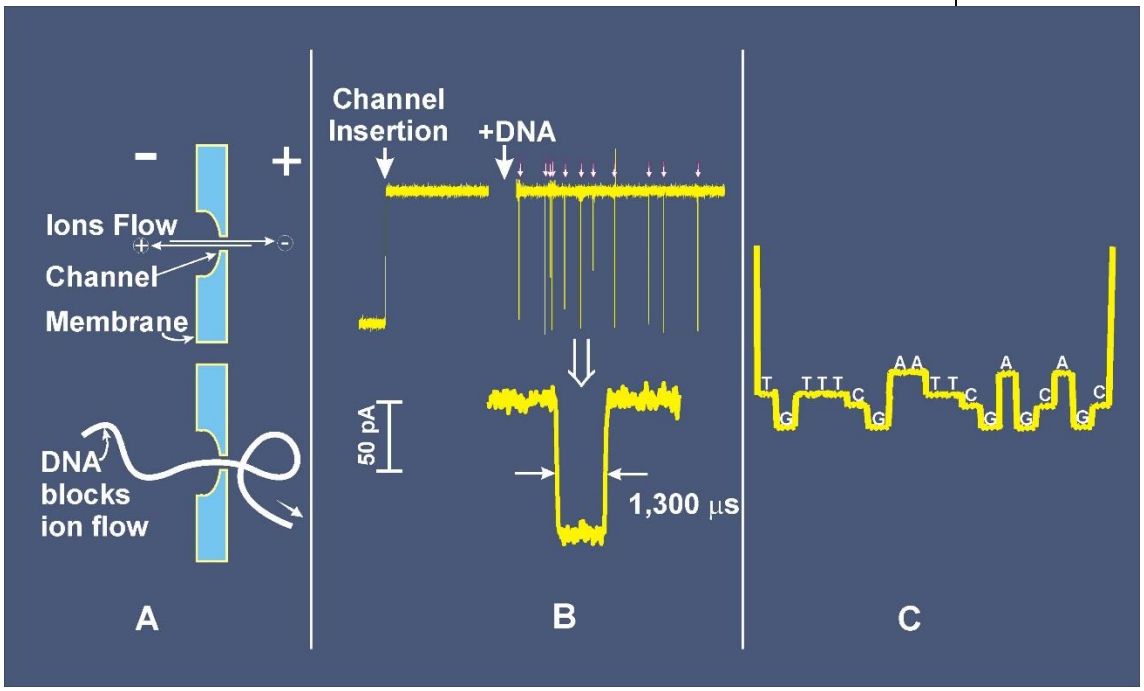
- The workhorses of the cell
  - Catalysts
  - Energy production
  - Regulation
  - Assembly
  - Motility
  - Repair
  - Etc, etc…….

Reactions of proteins

- Sulfur oxidation (Cys disulfides, S-thiolation; Met sulfoxide)
- Protein carbonyls (side chain aldehydes, ketones)
- Tyrosine crosslinks, chlorination, nitrosation, hydroxylation
- Tryptophane oxidation
- Hydro(pero)xy derivatives of aliphatic amino acids
- Chloramines, deamination
- Amino acid interconversions (*e.g.*, His to Asn; Pro to OH-Pro)
- Amino acid oxidation adducts (*e.g.*, *p*-hydroxyphenylacetaldehyde)
- Glycoxidation adducts (*e.g.*, carboxymethyllysine)
- Cross-links, aggregation, peptide bond cleavage

Nano-DNA-sequencer





US patent # 5,795,782

Proc Natl Acad Sci USA **93** (24)

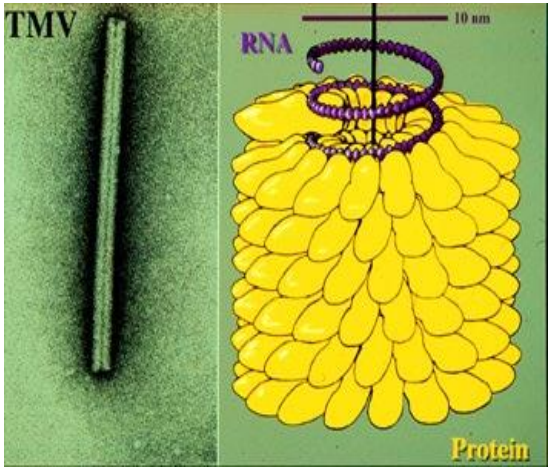
DNA encodes for Proteins

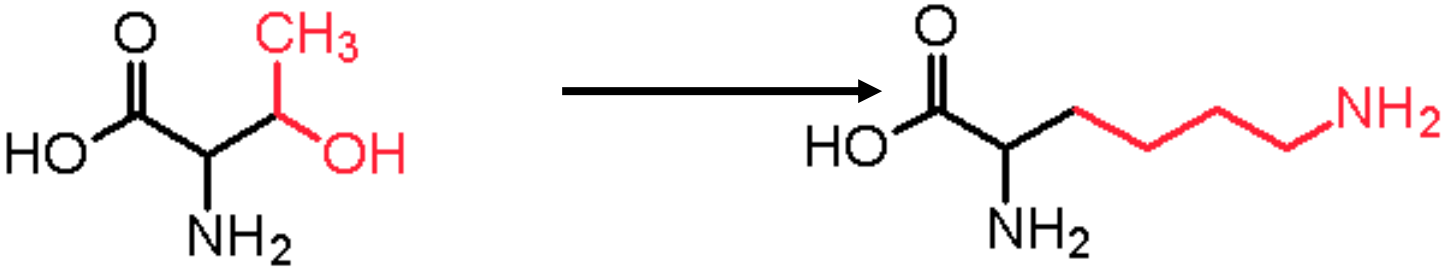
- 3 bases make a codon
- Each codon encodes a single amino acid
- Change the codon → change the amino acid

Example: Alter the chemistry of a known biomolecule.

- **The three potential external labeling positions**
  - **N-terminus**
  - **C-terminus**
  - **63-66 loop**
- **Conversion of Threonine to Lysine**

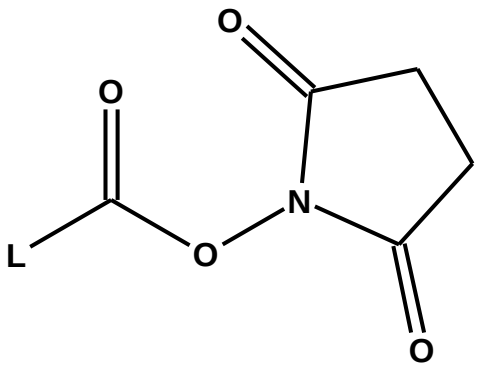
  Change DNA-Codon from ACC to AAG

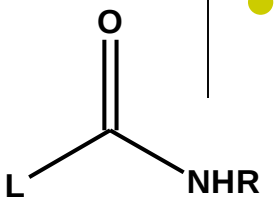




Nanotechnology **13** (2002) 541–544

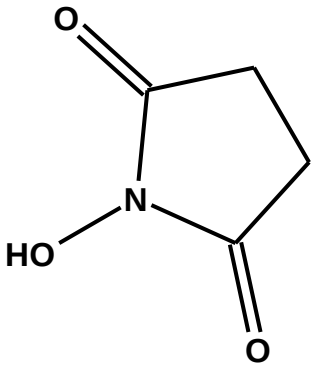
N-Hydroxy-Succinamide

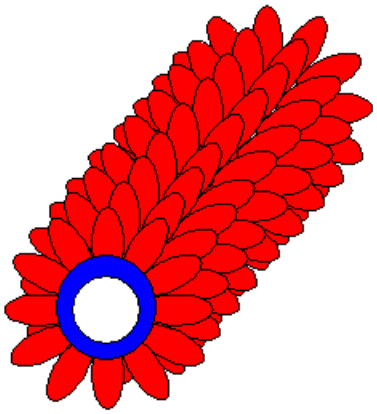




>99%

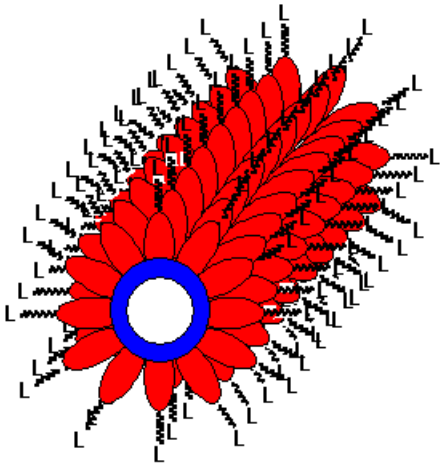
RNH_2





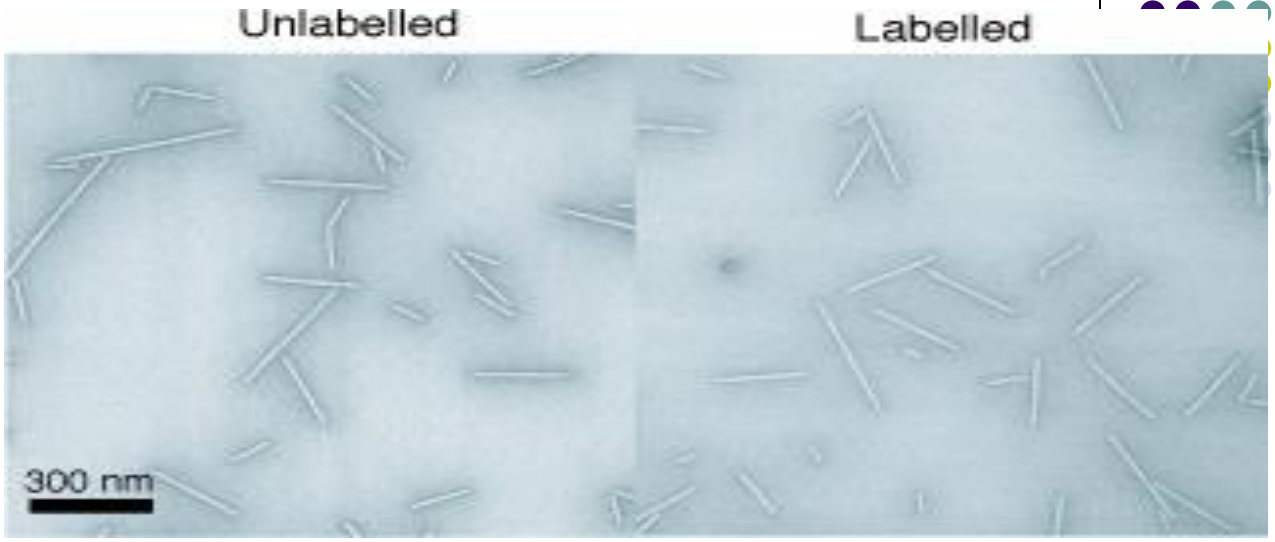
NHS-Ligand

PBS pH 7.4 25°C 60 min

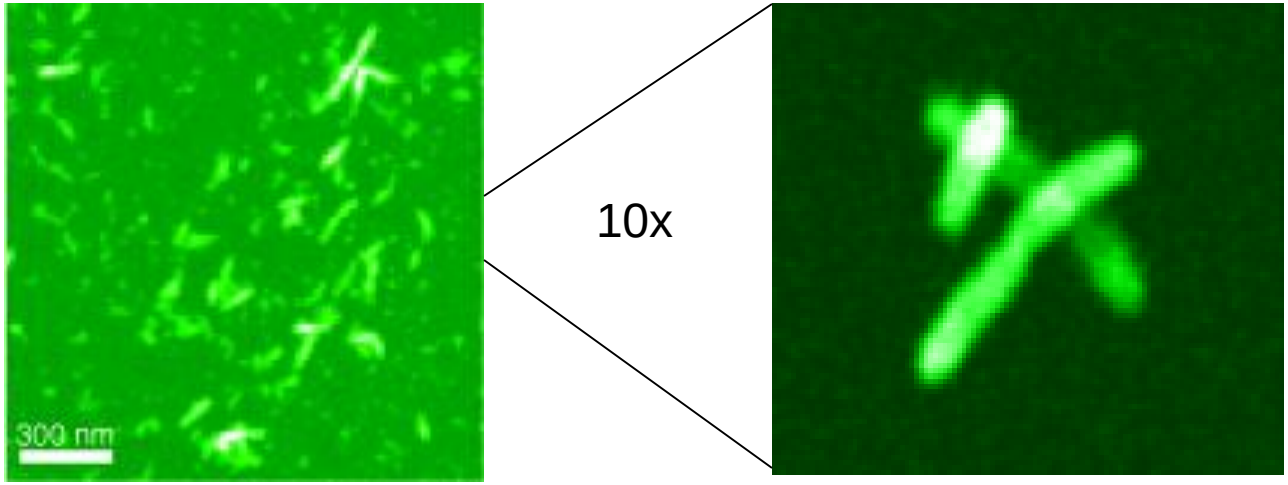


Fluorescent labeling

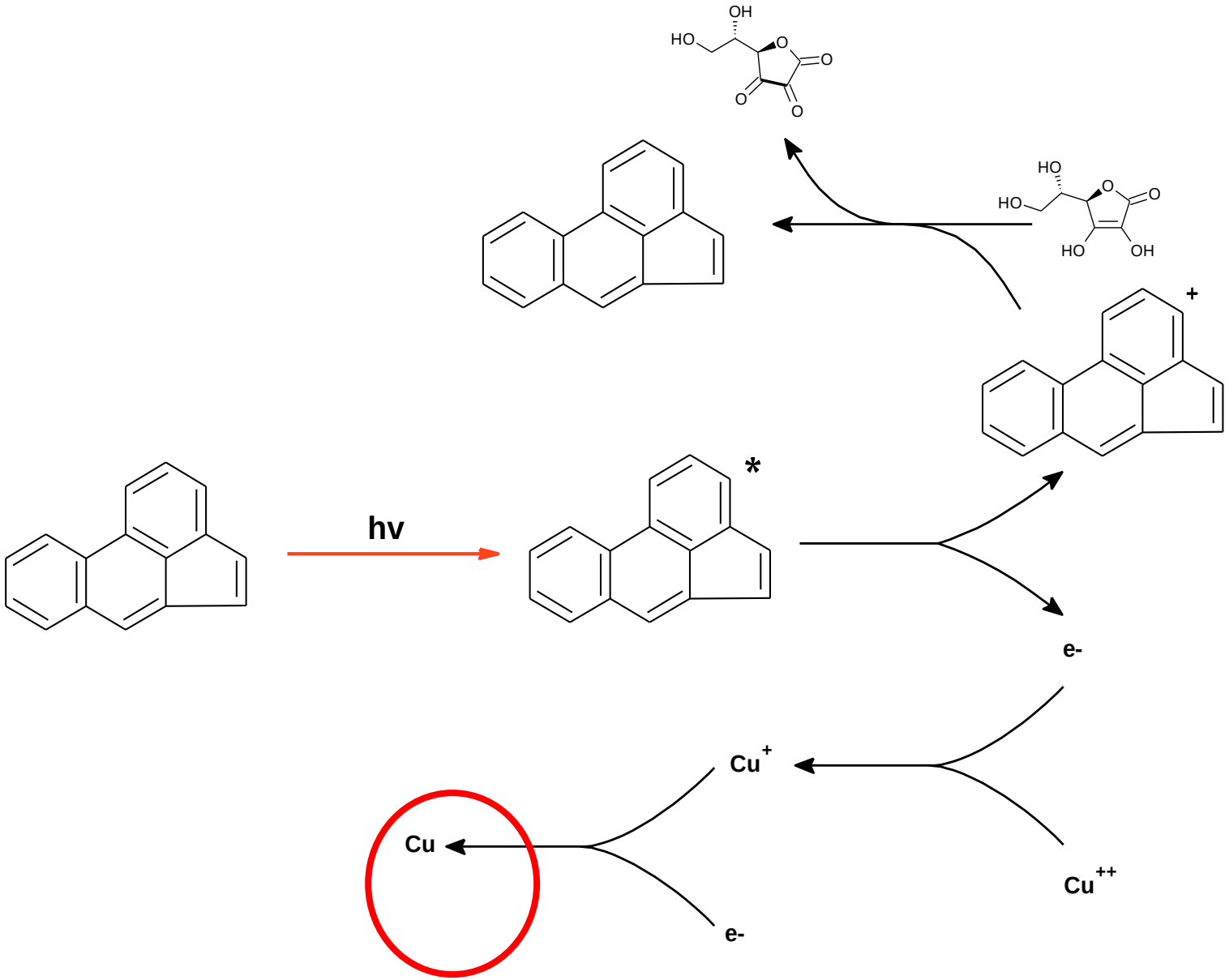
EM



Fluorescence Confocal

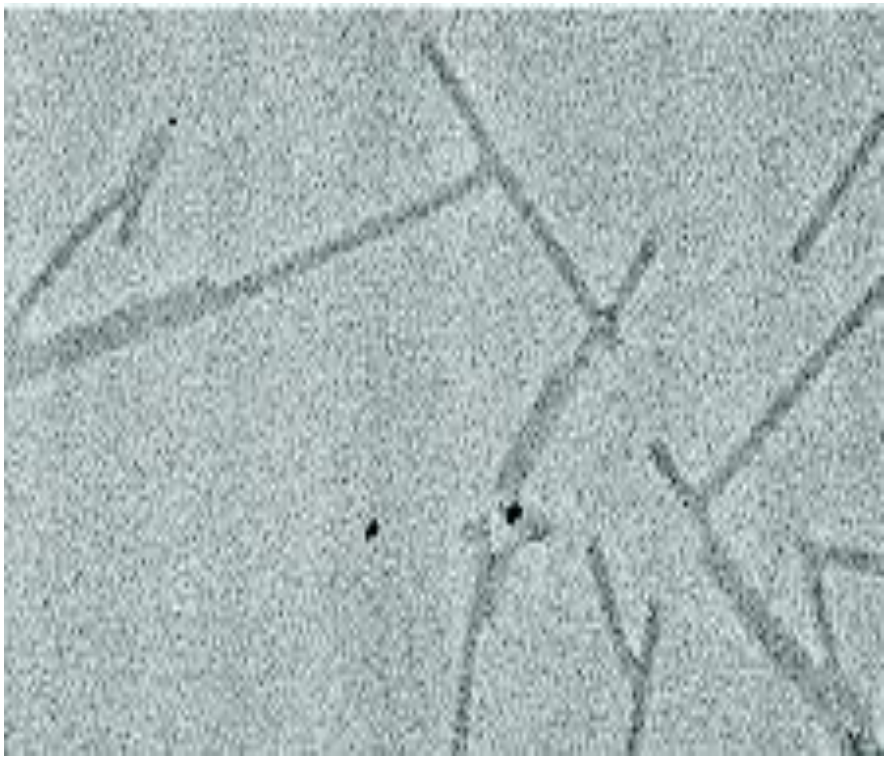


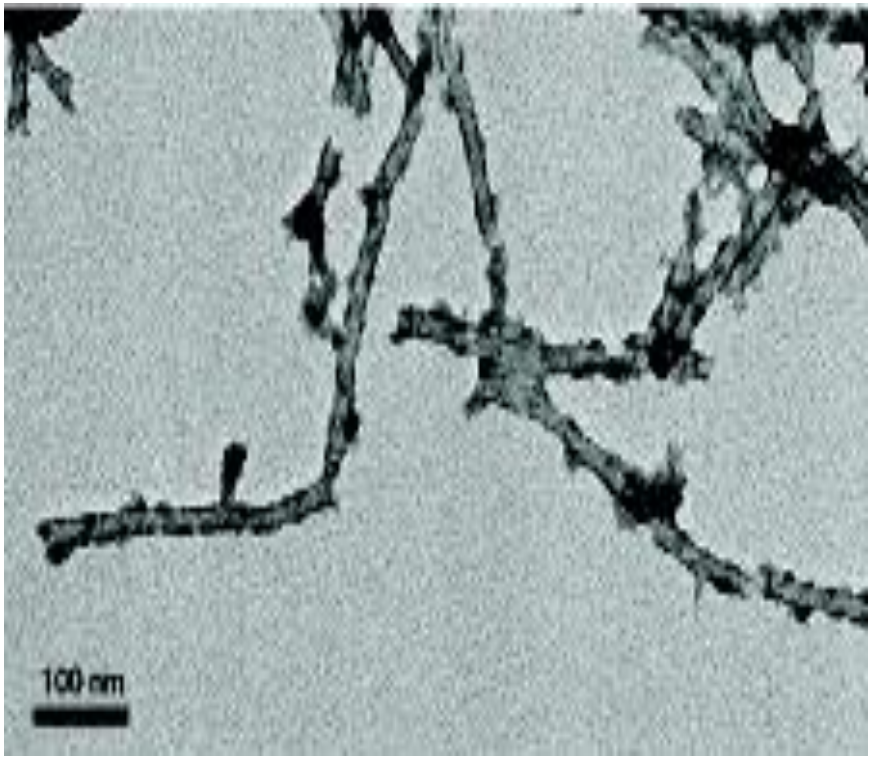
Metal coating via in situ photoreduction



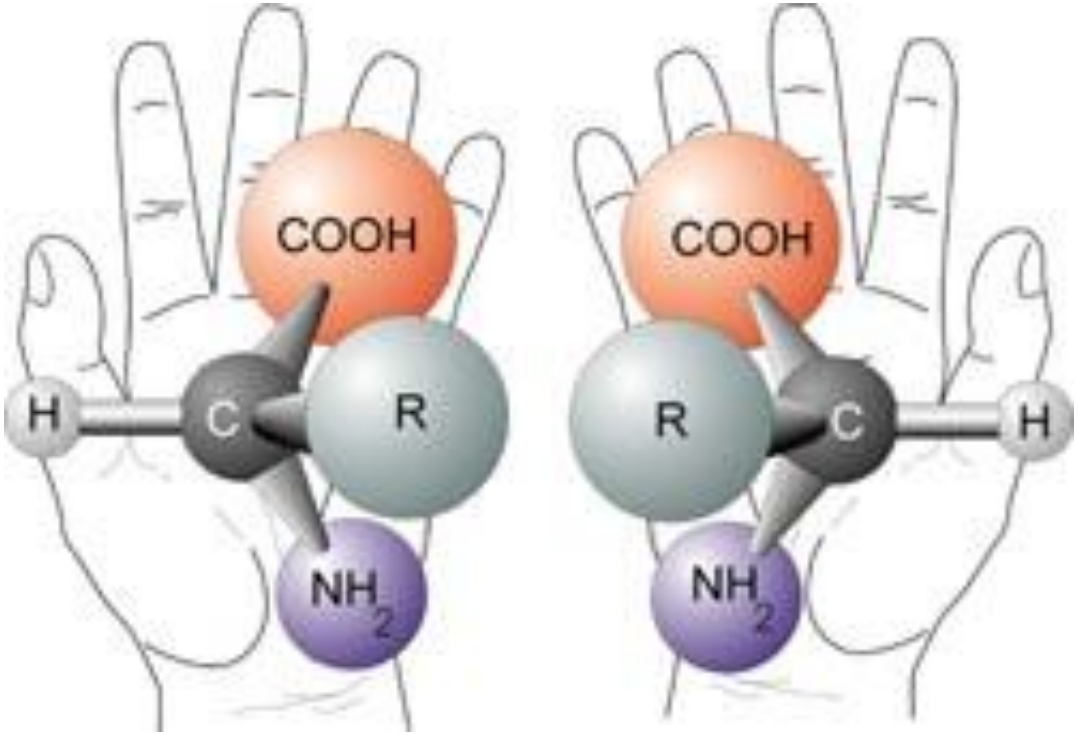
Metal coated TMV

-hν **+hν**





Workshop Question?



Why L-amino acids? Proteins from living organism consist of exclusively L-amino acids. If I synthesized a D-amino acid version of a known enzyme what might you predict about this enzyme.

Carbos structure

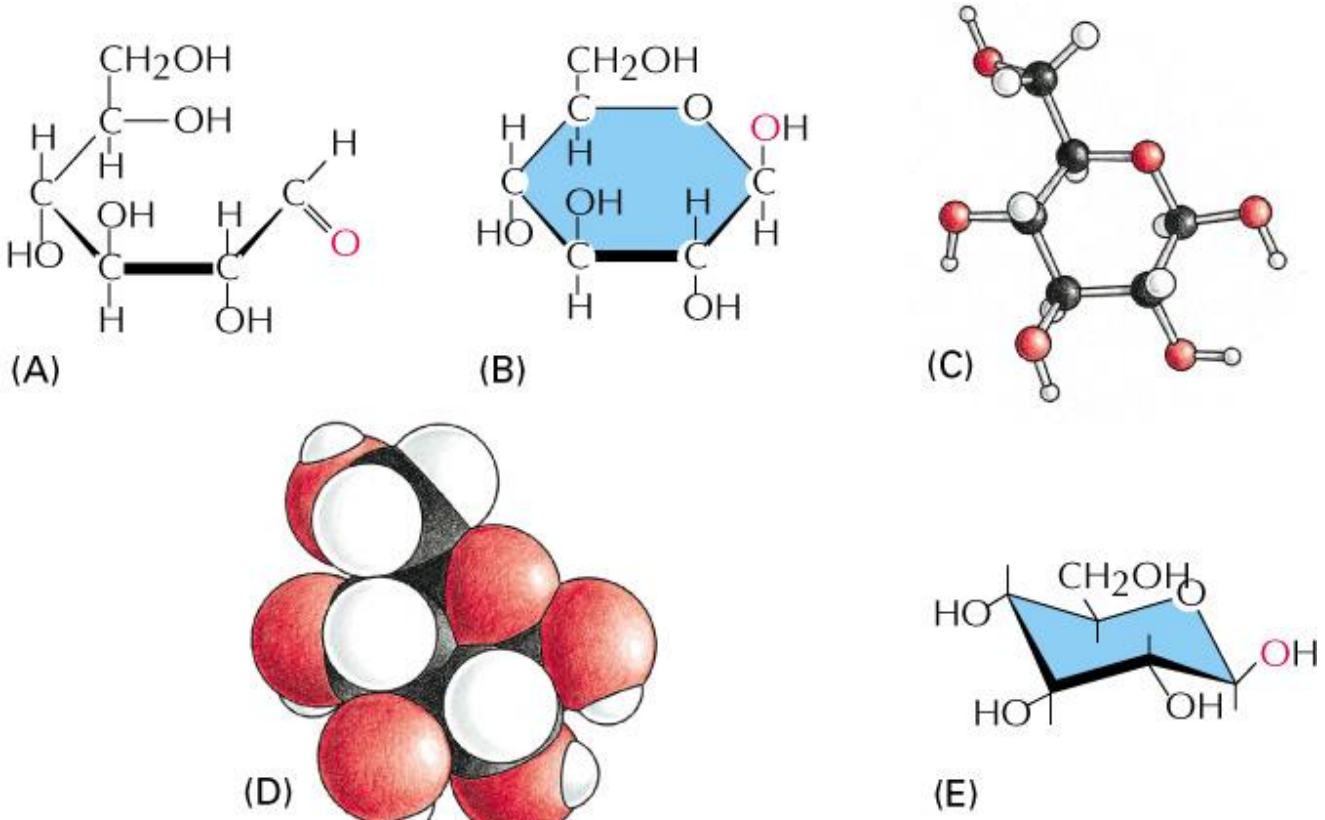


Figure 2–18. Molecular Biology of the Cell, 4th Edition.

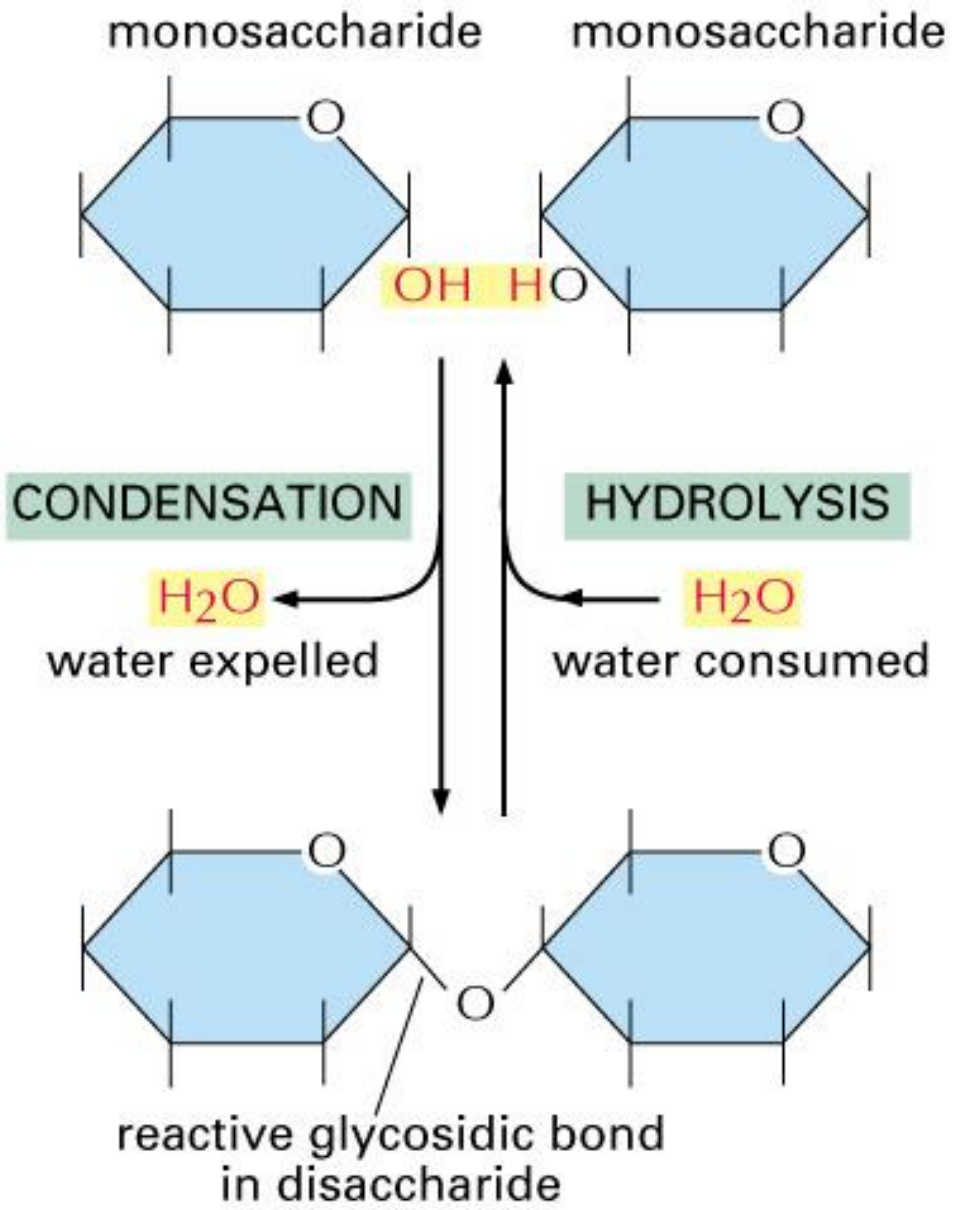


Figure 2–19. Molecular Biology of the Cell, 4th Edition.

Reactions of carbos

- Primary oxidation as in Nucleotides
- Hydrolysis to shorter chain polys

Carbohydrates-biology

- Polysaccharides
  - Protein modification
  - Cell surface modification
  - The food stuff of the cell

Protein modification

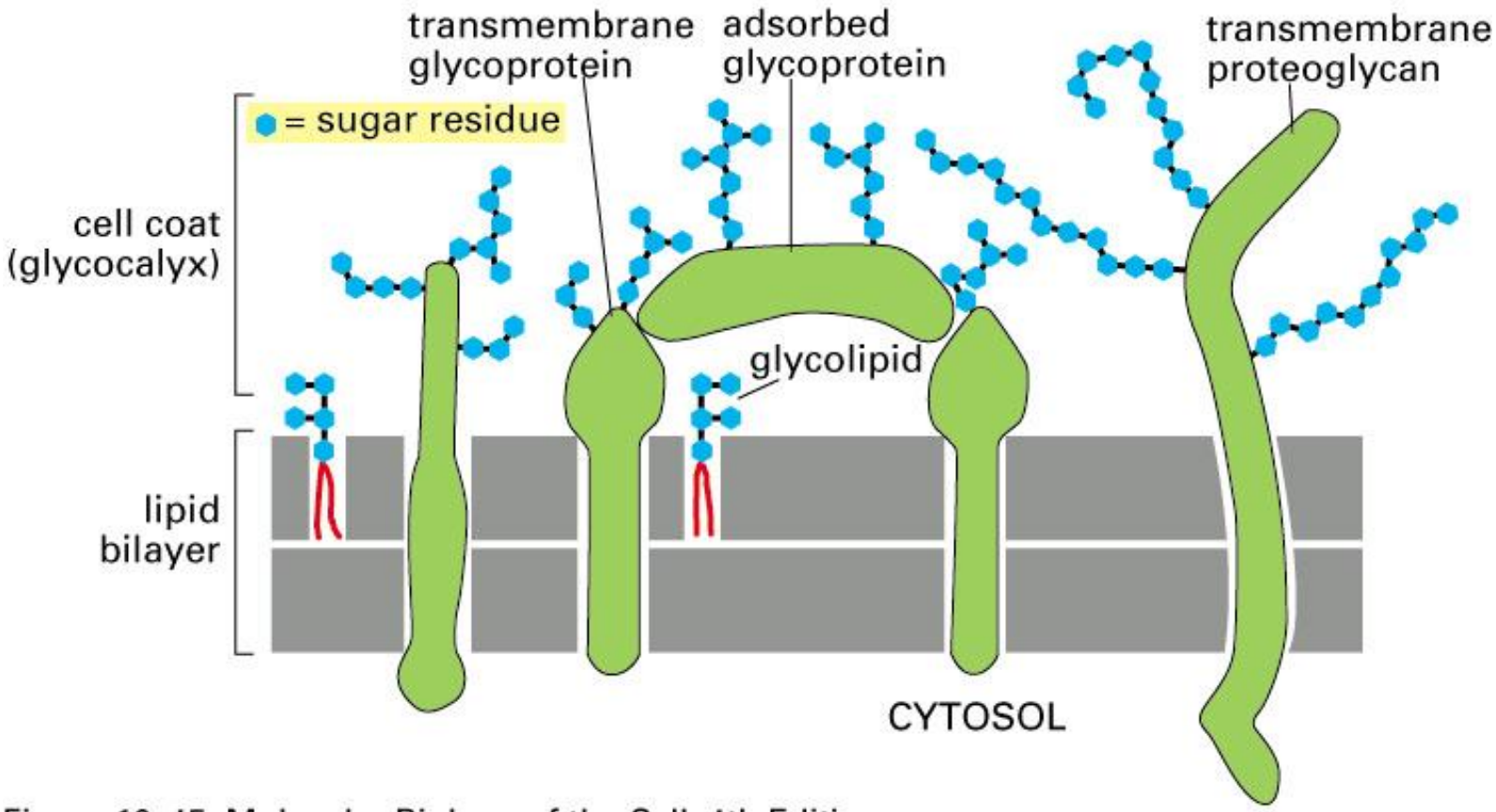


Figure 10–45. Molecular Biology of the Cell, 4th Edition.

Fatty acids

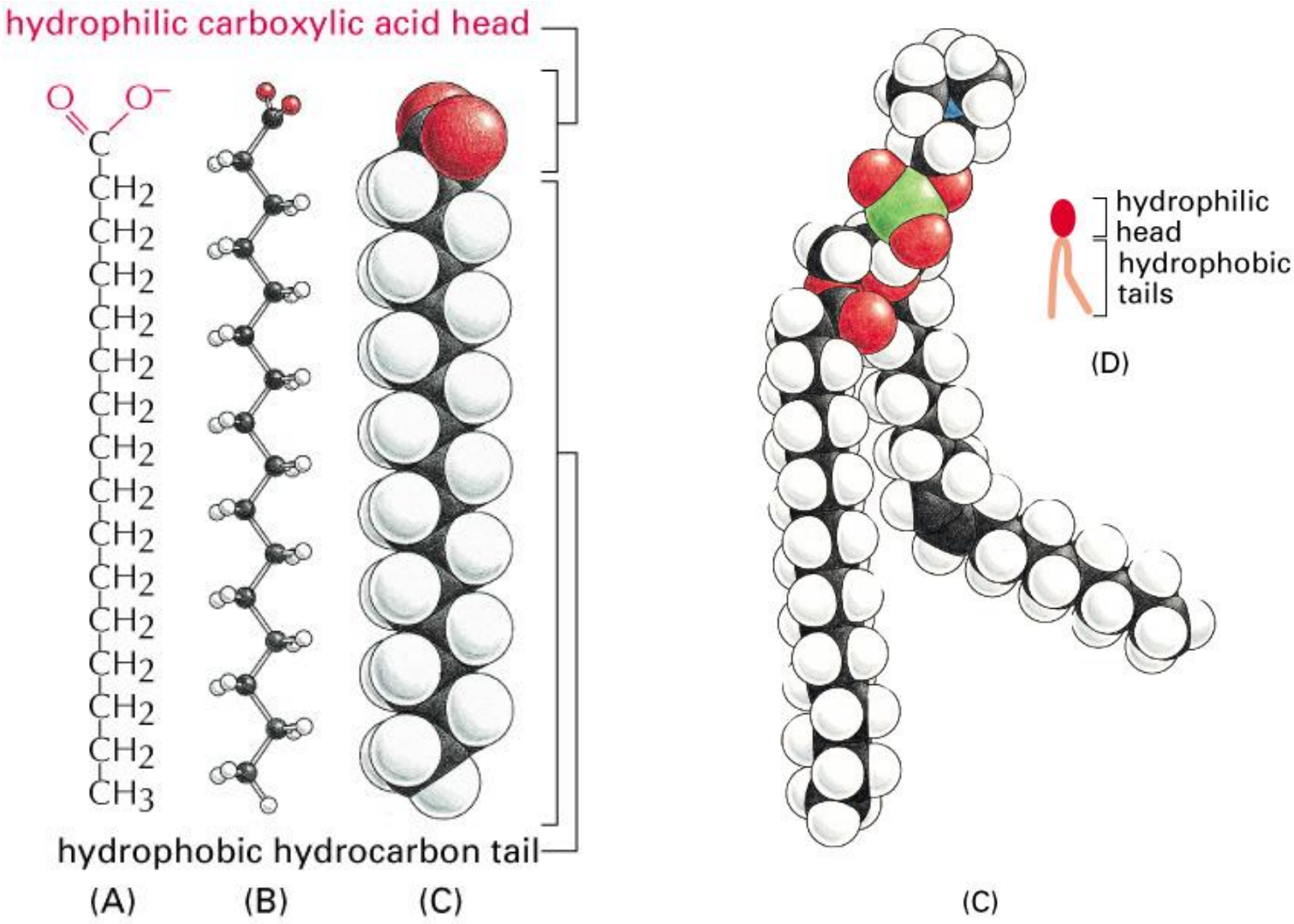


Figure 2–21. Molecular Biology of the Cell, 4th Editic Figure 10–2 part 3 of 3. Molecular Biology of the Cell, 4th Edition.

The cell membrane

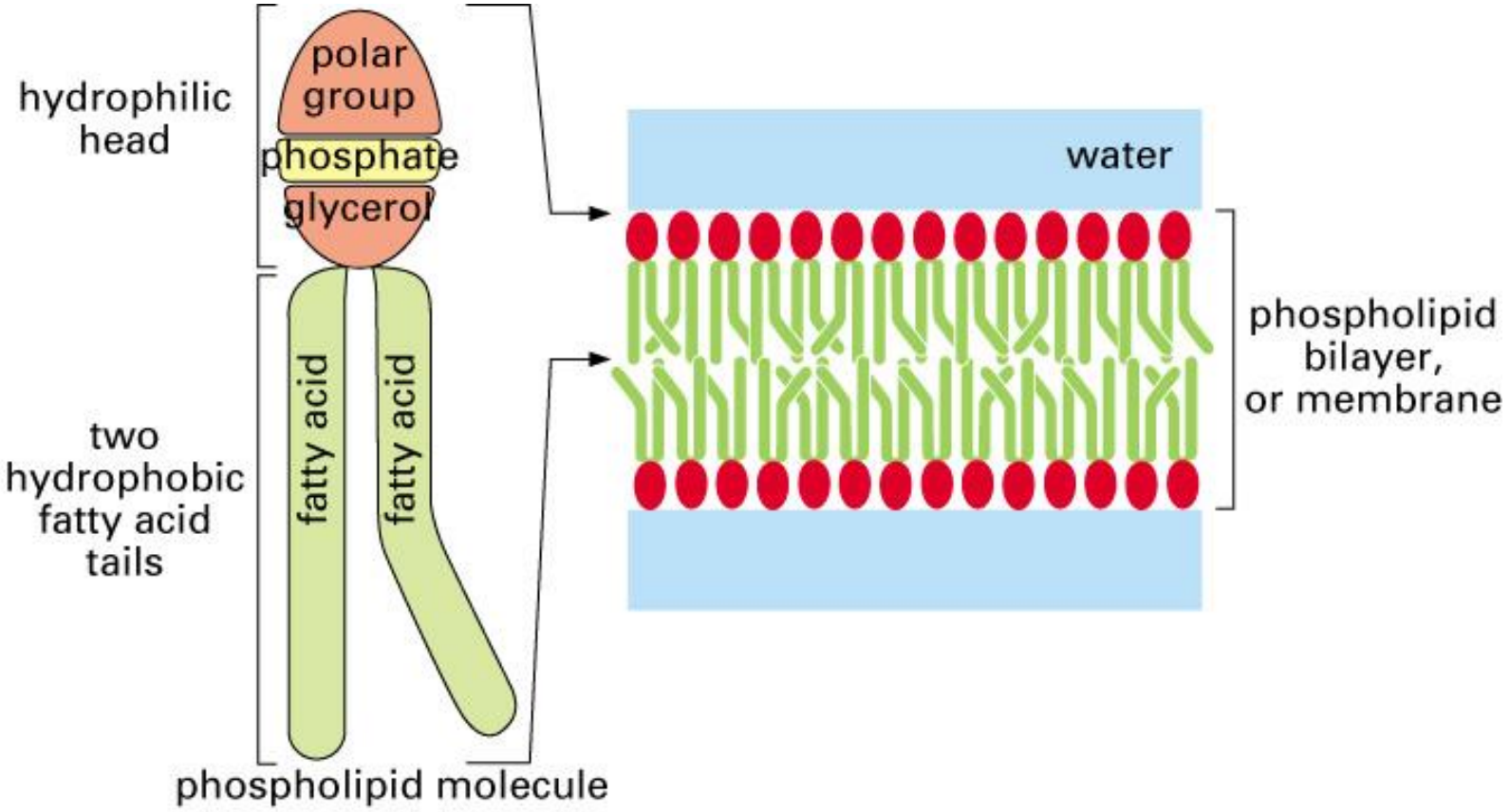


Figure 2–22. Molecular Biology of the Cell, 4th Edition.

Lipid variation-head to tail

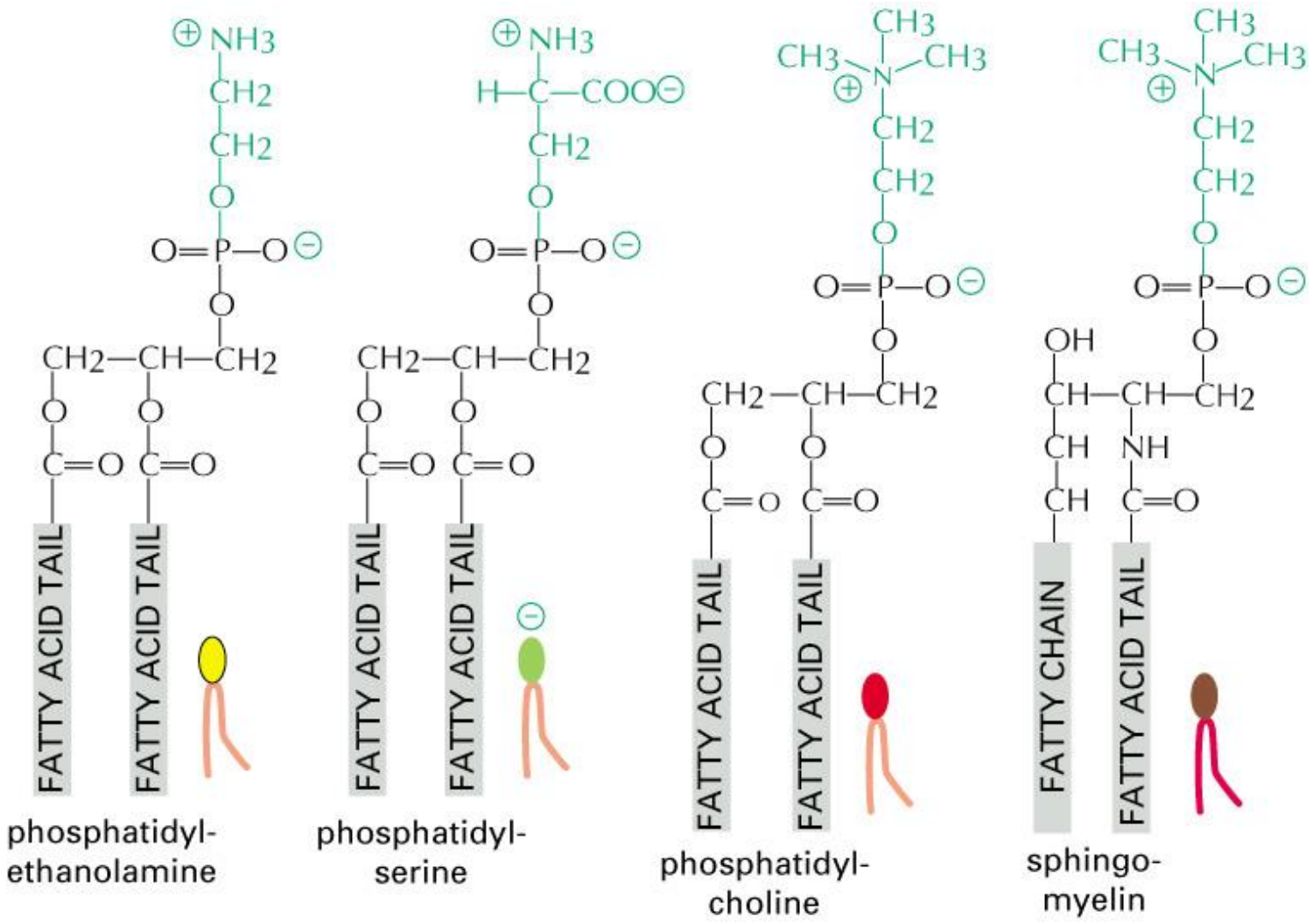
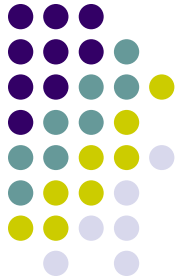


Figure 10–12. Molecular Biology of the Cell, 4th Edition.

Fatty-acids biology



- The cell membrane (barrier to the outside)
  - Regulates uptake of nutrients and waste
- Regulate membrane proteins
  - Modification
  - Stabilization

The membrane

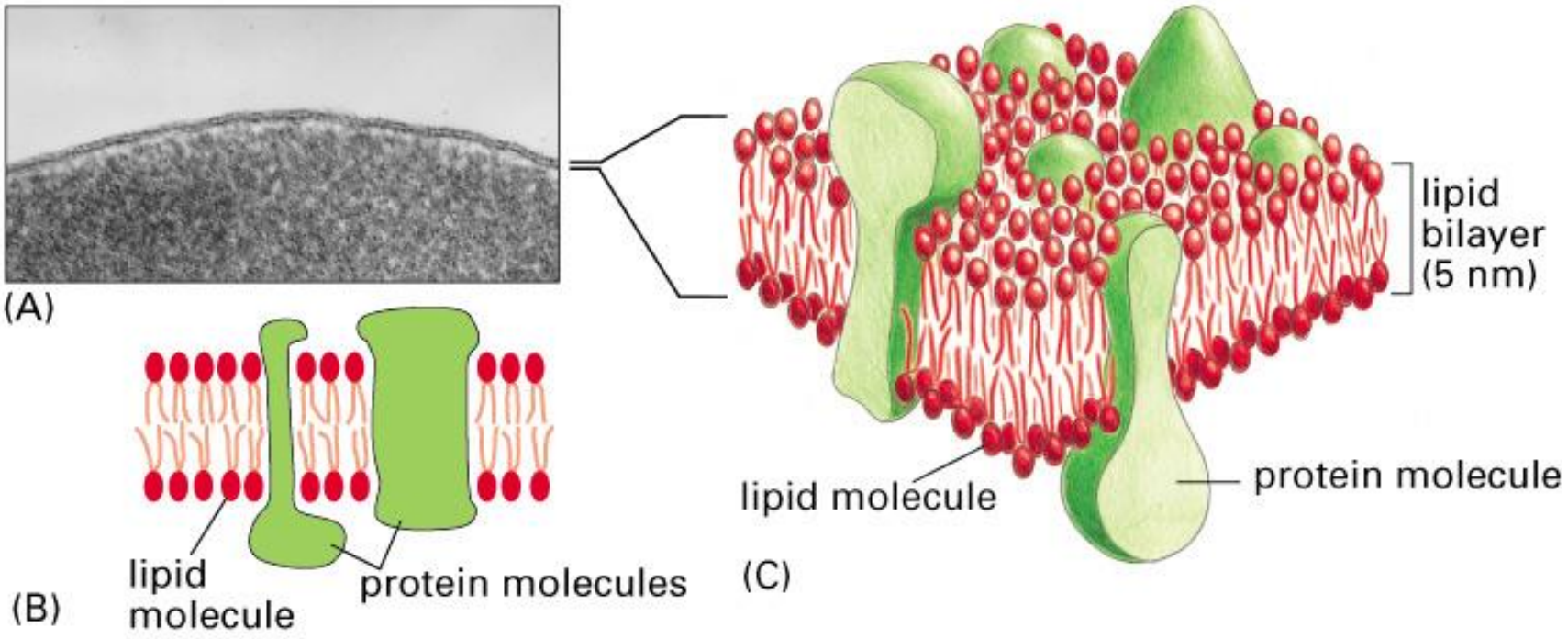
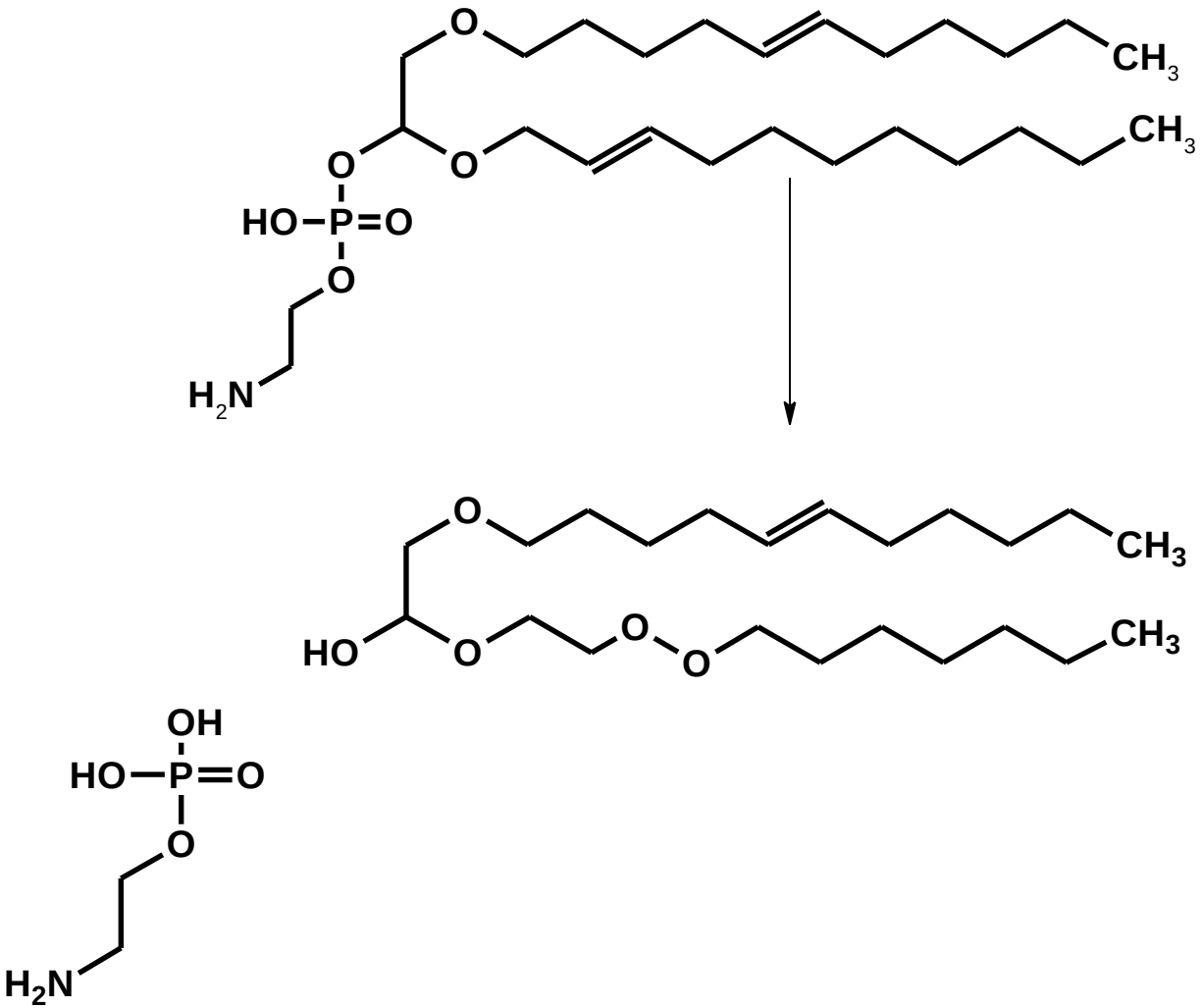


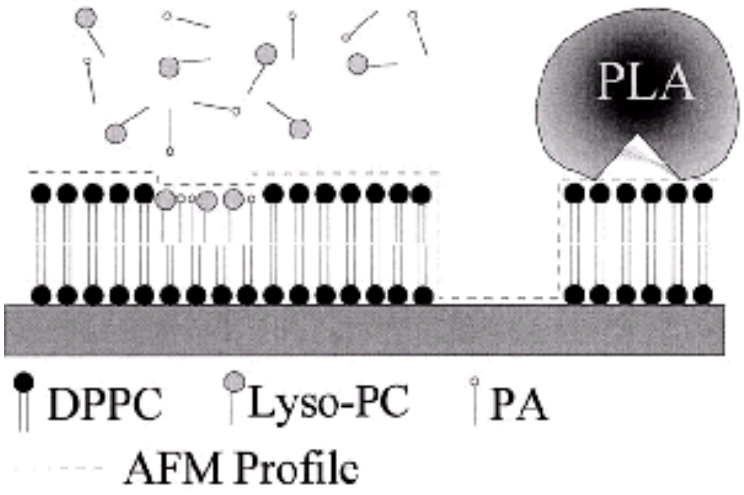
Figure 10–1. Molecular Biology of the Cell, 4th Edition.

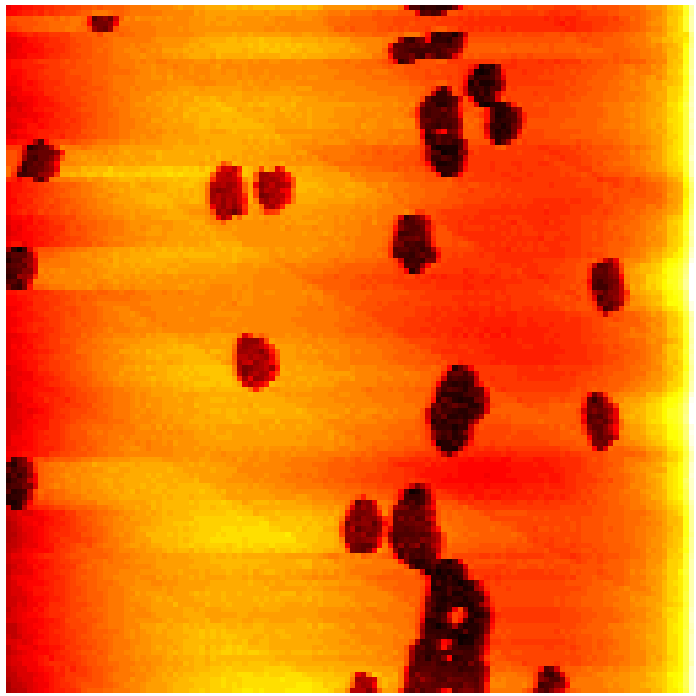
Fatty acids chemistry

- Hydrolysis of the glycerol backbone
- Oxidation of unsaturated alkyl chains



NanoPen





PLA: phospholipase-A

*Biomembranes.*1420, P.266, (1999)

Cellular chemistry

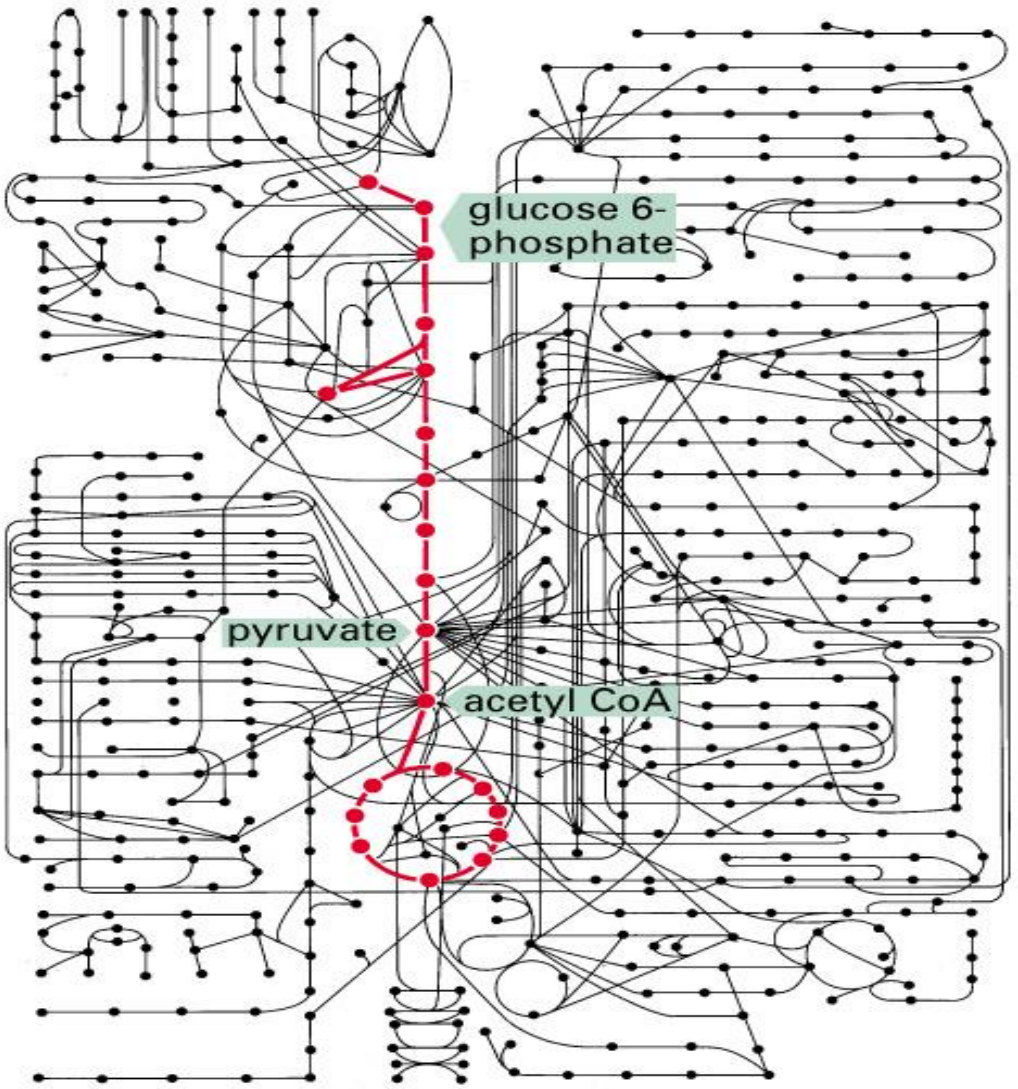
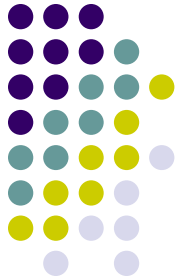


Figure 2–88. Molecular Biology of the Cell, 4th Edition.

The extreme chemistry of life



- pH 0 to10
- NaCl 0 to 2M
- Temp -2 to 110 Celsius
- 0.1 to 110 Mpa
- 0 to 100,000 rem (acceptable dose limit for humans is about 5 rem/year)