THE UNIVERSITY *of* TEXAS

HEALTH SCIENCE CENTER AT HOUSTON

SCHOOL *of* HEALTH INFORMATION SCIENCES

Introduction to Biomolecular Structure

For students of HI 6327 “Biomolecular Modeling”

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http://biomachina.org/courses/modeling/02.html

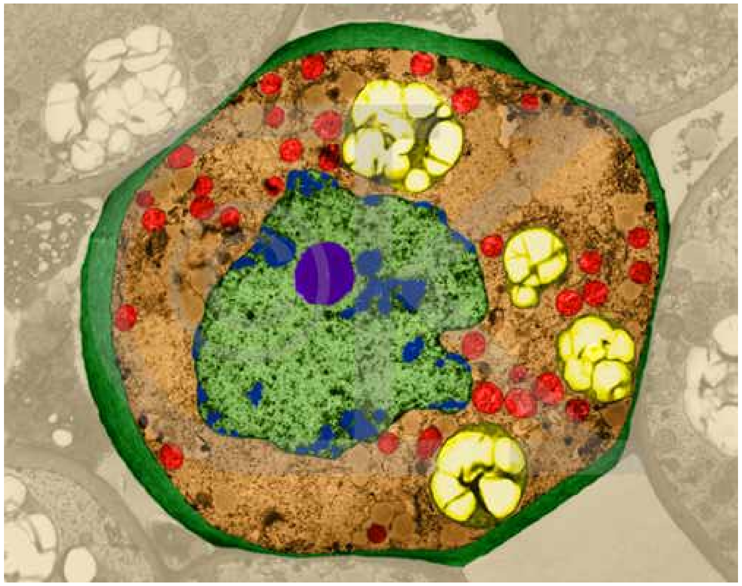
Early Life on Earth

Time (Myr ago)	Event
4600	Formation of the approximately homogeneous solid Earth by planetesimal accretion
4300	Melting of the Earth due to radioactive and gravitational heating which leads to its differentiated interior structure as well as outgassing of molecules such as water, methane, ammonia, hydrogen, nitrogen, and carbon dioxide
4000	Bombardment of the Earth by planetesimals stops
3800	The Earth's crust solidifies--formation of the oldest rocks found on Earth. Condensation of atmospheric water into oceans
3500-2800	**Prokaryotic cell organisms develop**
3500-2800	**Beginning of photosynthesis by blue-green algae which releases oxygen molecules into the atmosphere**

Stromatolites are layered mounds, columns, and sheets found in the rock. They were originally formed by the growth of layer upon layer of *cyanobacteria*, a single-celled photosynthesizing microbe growing on a sea floor. Photo by Marjory Martin, Deakin Univ, Australia.

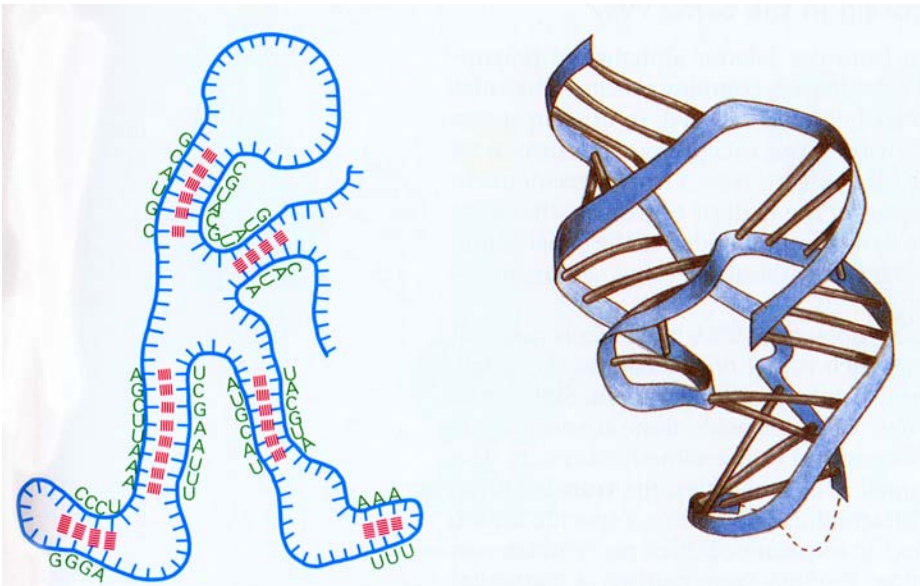
Early Life on Earth

Time (Myr ago)	Event
1500-600	**Eukaryotic cell organisms develop, rise of multicellular organisms**
430	Waxy coated algae begin to live on land
420	Millipedes have evolved--first land animals
375	The Appalachian mountains are formed via a plate tectonic collision between North America, Africa, and Europe
200	Appearance of mammals
65	K-T (Kreide-Tertiär = Cretaceous-Tertiary) Boundary--extinction of the dinosaurs and beginning of the reign of mammals
20-12	The chimpanzee and hominid lines evolve
0.05-0	*Homo sapiens sapiens* exist

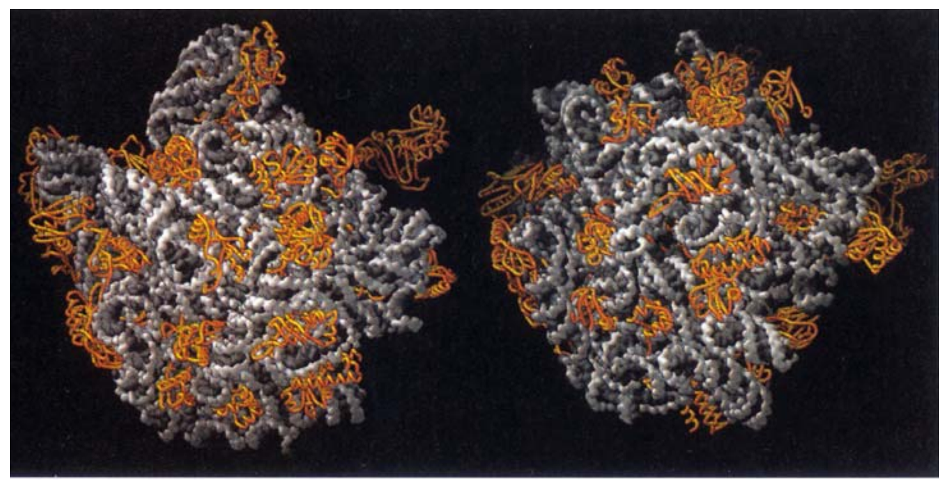


Lily Parenchyma Cell (cross-section) (TEM x7,210). Note the large nucleus and nucleolus in the center of the cell, mitochondria and plastids in the cytoplasm. Photo by Dennis Kunkel at www.DennisKunkel.com

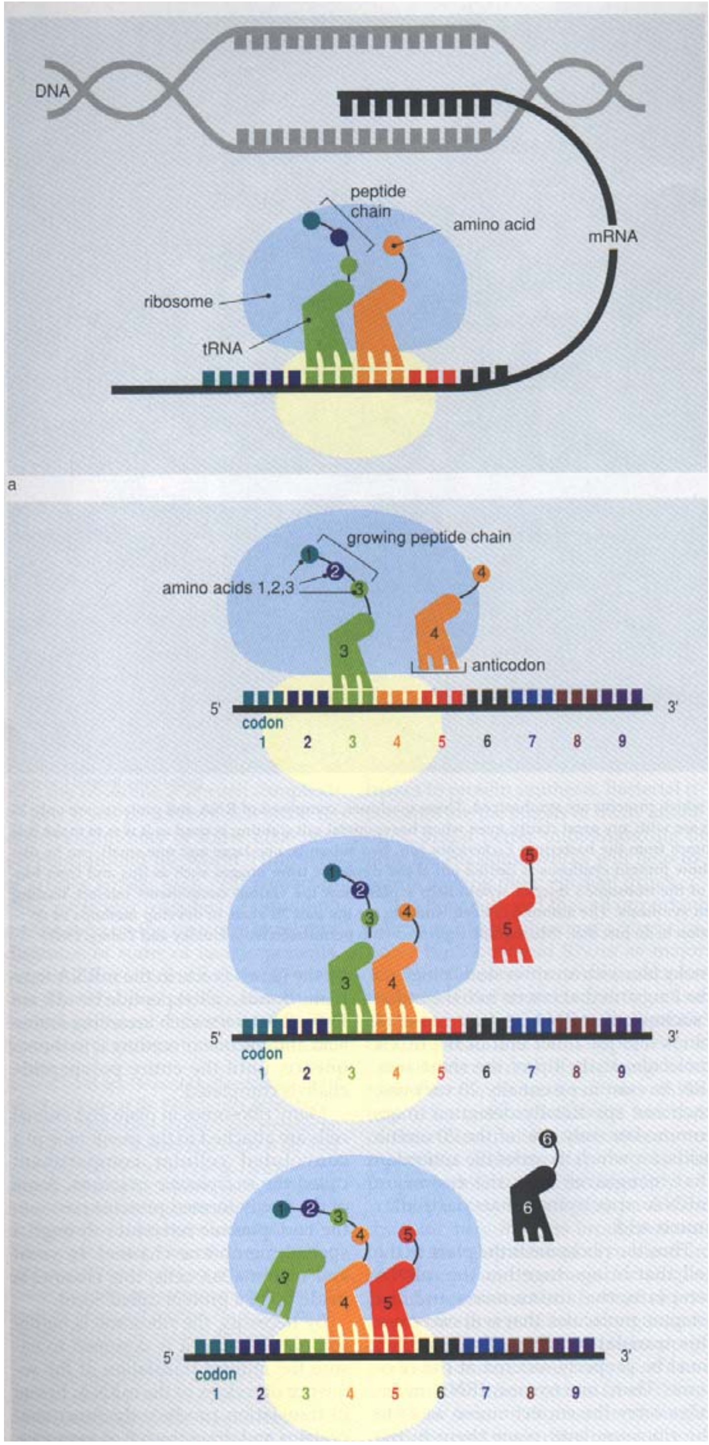
The First Enzymes: RNA



The conformation of an RNA molecule: Nucleotide pairing and 3D structure. © Alberts et al. The Cell.



Location of the protein components (gold) in the ribosome, that consists mainly of RNA (grey). © Ban et al. Science.



Protein Synthesis in the Ribosomal Translation Cycle

1. mRNA synthesis with RNA polymerase

2. aa-tRNA (1 anticodon - 3b) acts as adapter

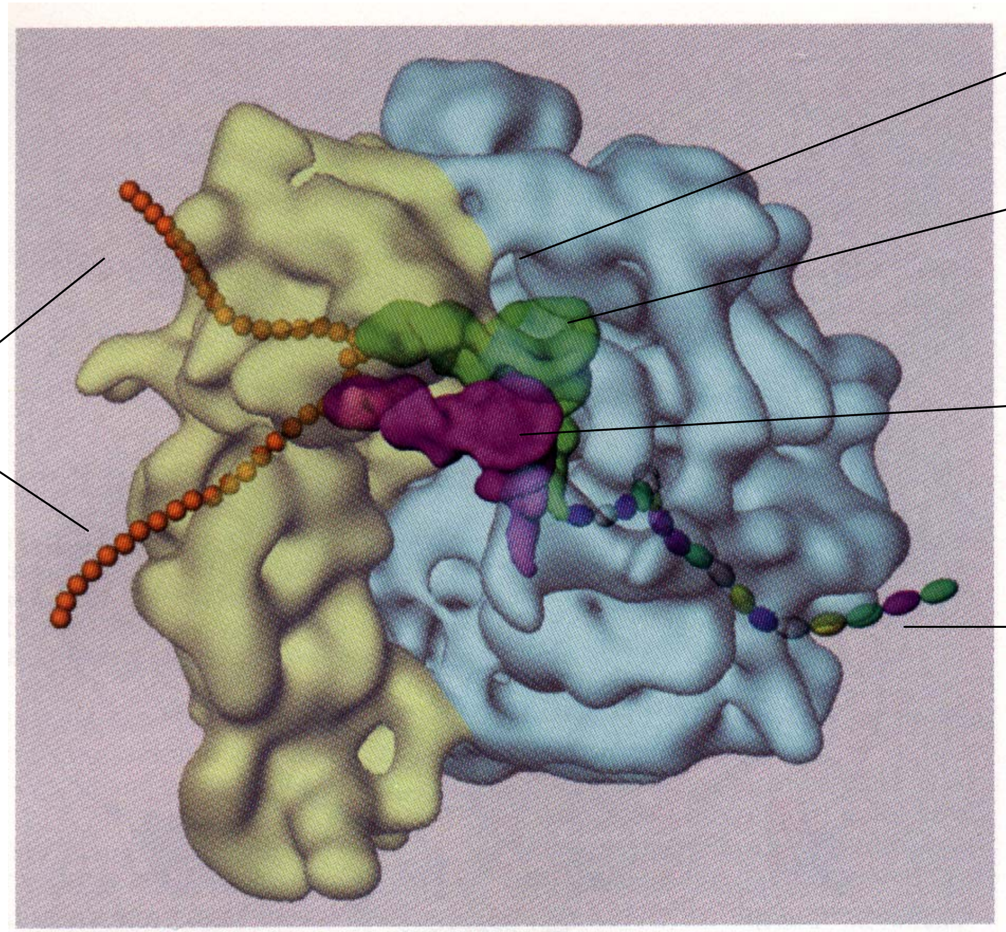
3. anticodon matches codon on mRNA

4. aa binds to polypeptide chain

5. release of tRNA

6. new tRNA binds

EM Map of the Ribosome at 15Å Resolution

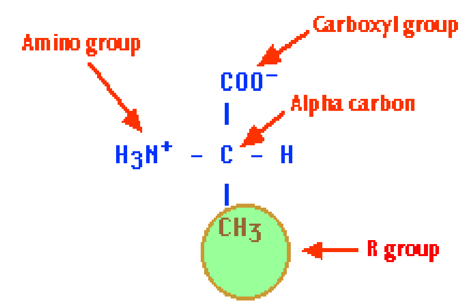


The Amino Acids

- **Proteins are polymers of the 20 naturally occurring amino acids**
- **A.a. are abbreviated by 3 and 1 letter codes (learn these!)**
- **A.a. can be grouped based on electrostatic and size of side chain R**

Aliphatic:

Alanine	Ala A
Valine	Val V
Leucine	Leu L
Isoleucine	Ile I



© Kimball's Biology Pages

Polar:

Asparagine	Asn N
Glutamine	Gln Q
Serine	Ser S
Threonine	Thr T

Non-polar:

Glycine	Gly G
Proline	Pro P
Cysteine	Cys C
Methionine	Met M

Aromatic:

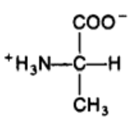
Histidine	His H
Phenylalanine	Phe F
Tyrosine	Tyr Y
Tryptophan	Trp W

Charged:

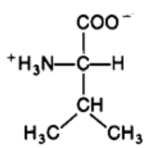
Lysine	Lys K
Arginine	Arg R
Aspartic Acid	Asp D
Glutamic Acid	Glu E

2D Structures of Amino Acids

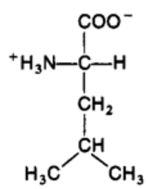
Aliphatic



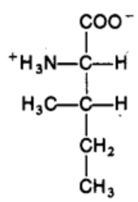
Alanine
(Ala)



Valine
(Val)

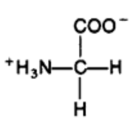


Leucine
(Leu)

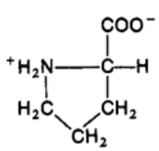


Isoleucine
(Ile)

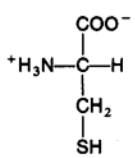
Nonpolar



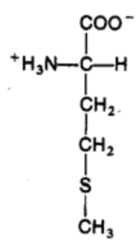
Glycine
(Gly)



Proline
(Pro)

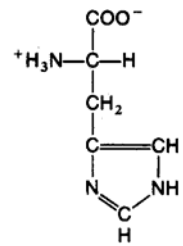


Cysteine
(Cys)

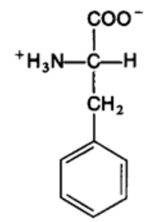


Methionine
(Met)

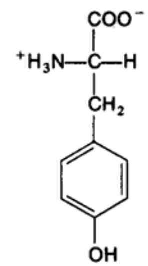
Aromatic



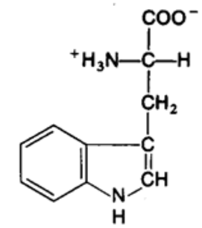
Histidine
(His)



Phenylalanine
(Phe)

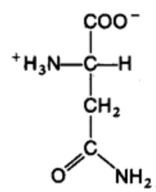


Tyrosine
(Tyr)

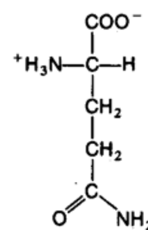


Tryptophan
(Trp)

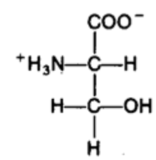
Polar



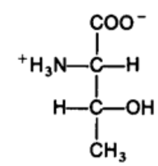
Asparagine
(Asn)



Glutamine
(Gln)

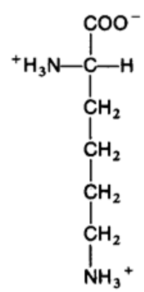


Serine
(Ser)

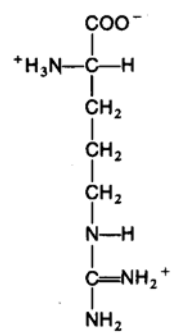


Threonine
(Thr)

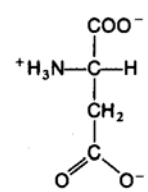
Charged



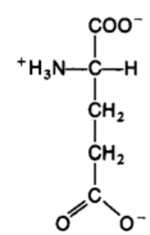
Lysine
(Lys)



Arginine
(Arg)

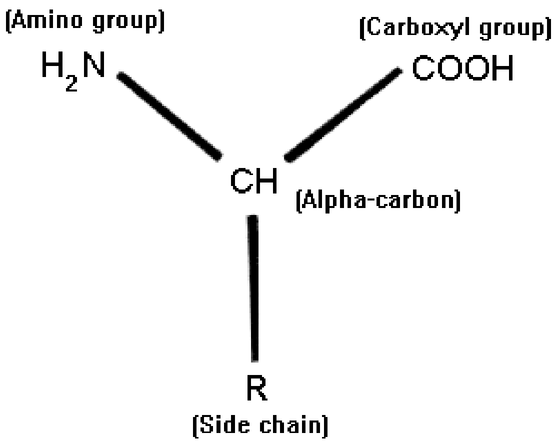


Aspartate
(Asp)

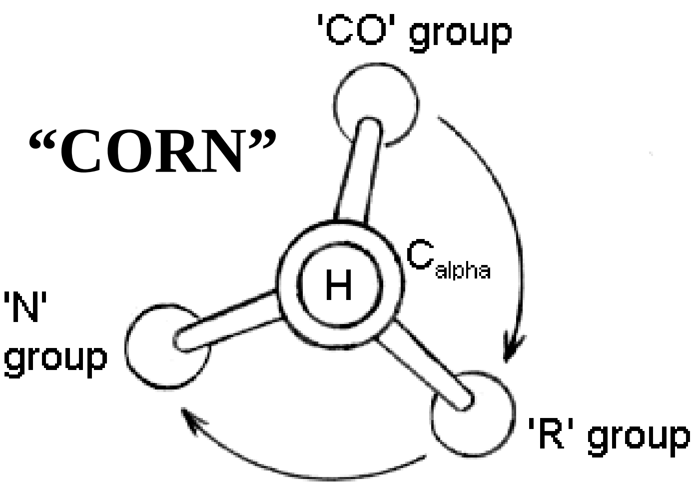


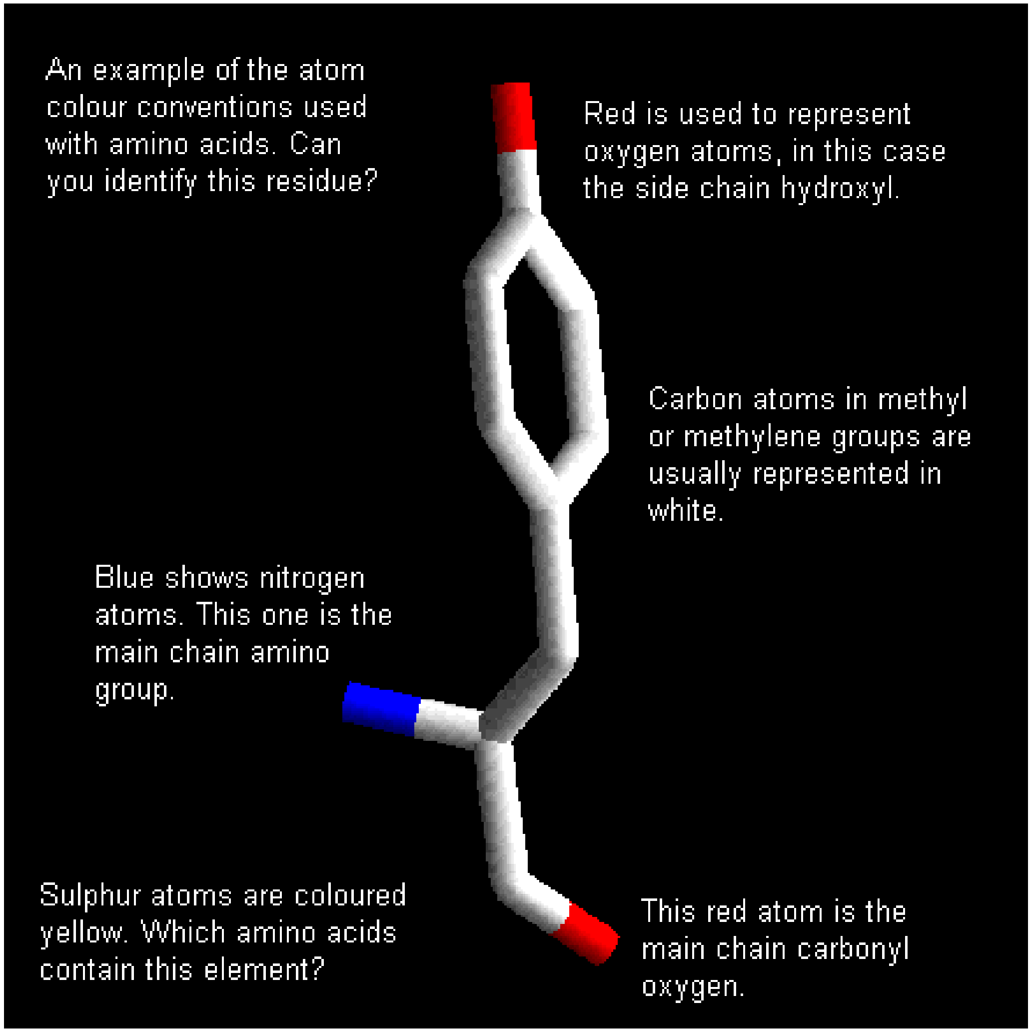
Glutamate
(Glu)

3D Structure



“CORN”



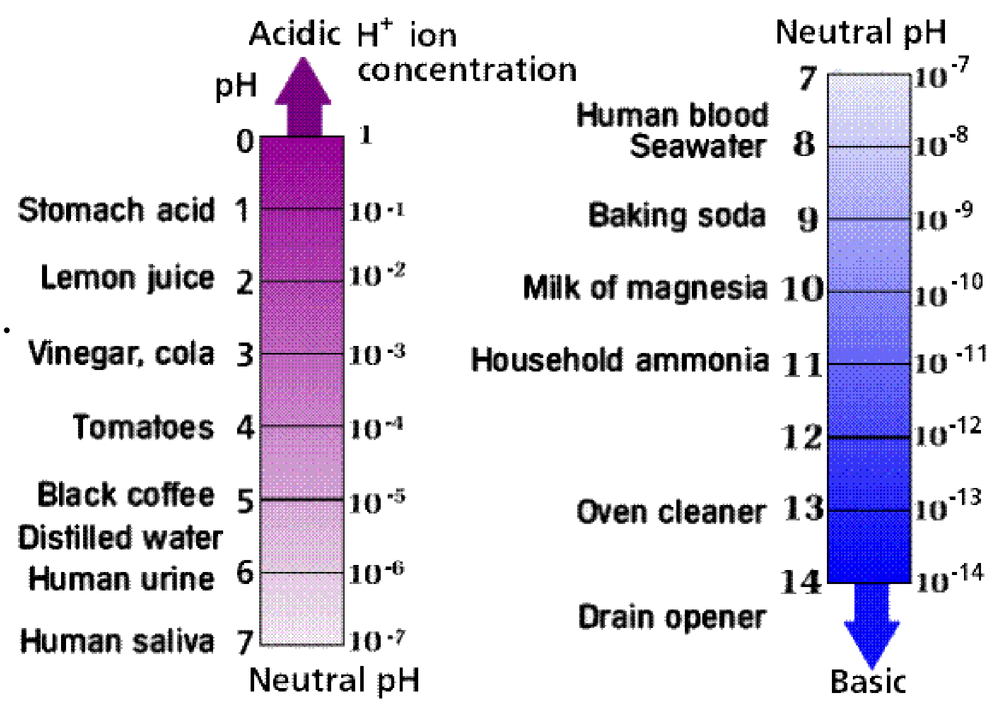


Side Chain Protonation and pH

- pH measures the concentration of H+ ions in solution.
- H+ from dissociation of an acid when this is dissolved in water.

The pH value is the negative logarithm of the H+ concentration in mol/L:
$pH = -\log10[H+]$
The [H+] in pure water is 10^-7; therefore the neutral pH of pure water is:
$pH = 7$

- Below pH 7: higher [H+] acidic.
- Above pH 7: lower [H+] basic
- Cellular pH is approximately 7.2-7.4.



pH of some common items.
Image from Purves et al.,
Life: The Science of Biology

acid-base equilibrium

pKa

“dissociation point”

pH<pKa: H+ on

pH>pKa: H+ off

The ionization equilibrium of a weak acid is given by

$$HA \leftrightarrow H^{+} + A^{-}$$

The equilibrium constant K for this weak acid is

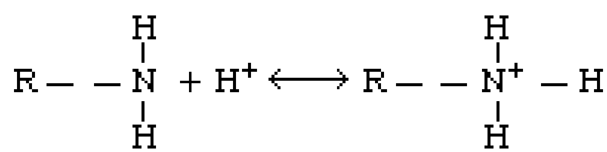
$$K = \frac{[H^{+}][A^{-}]}{[HA]}$$

The pK_a of an acid is defined as

$$pK_a = -\log K = \log\frac{1}{K}$$

By looking again at the 2nd equation, it can easily be shown that pK_a = pH when the acid is half dissociated, $[A^{-}] = [HA]$

The relationship between pH and pKa is very important to understand, because this relationship describes how chemicals change states in biological systems as the pH varies. For example, an amino group has two possible states representable by A^{-} and HA:



It is important to know which state of the equilibrium is favored at different pH's. This relationship between pH and pKa is described by the Henderson-Hasselbalch Equation:

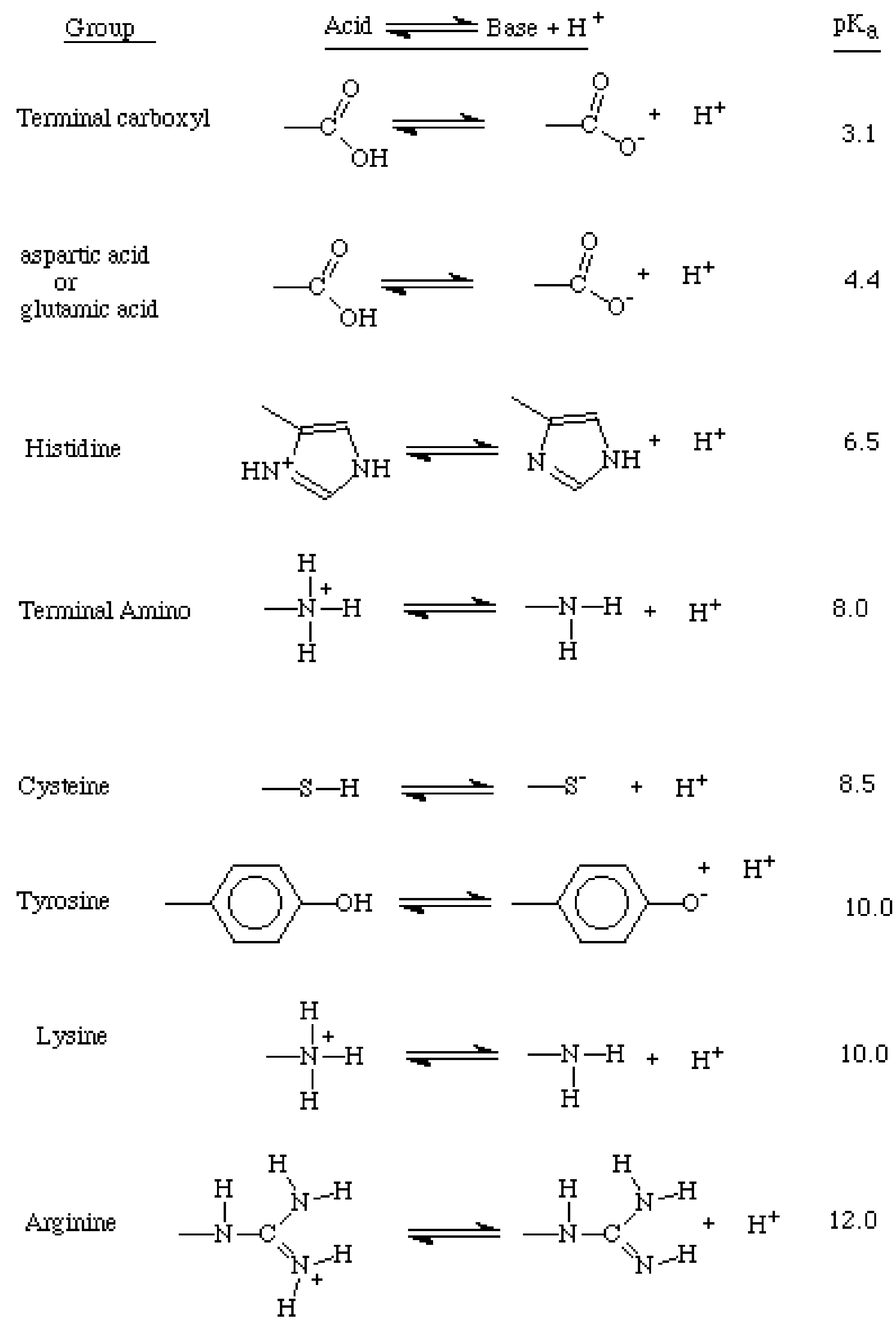
$$pH = pKa + \log\frac{[A^{-}]}{[HA]}$$

This equation is quite useful. With it you can now predict what state a molecule will be in at a given pH, among other things.

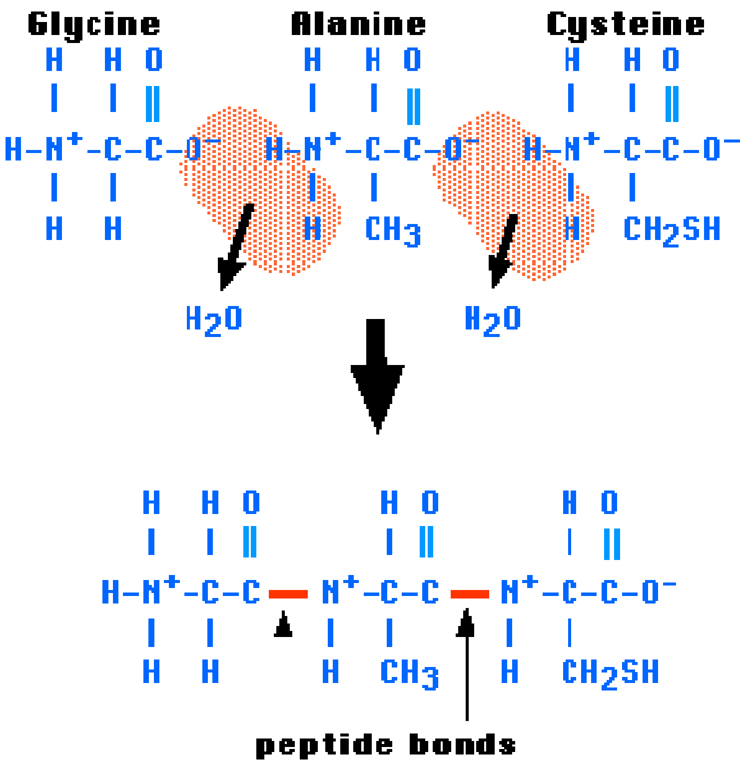
pKa Chart

for amino acids

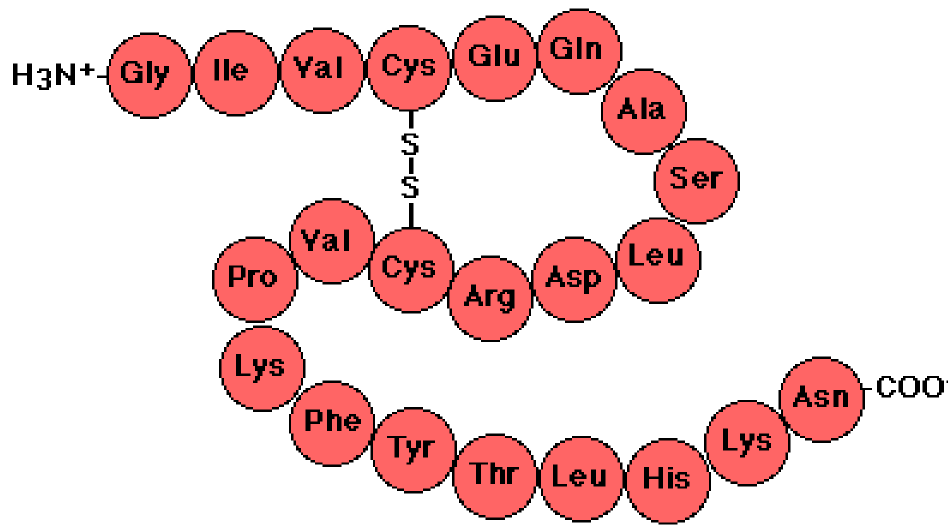
Note: Histidine protonation depends on protein environment (pKa shift) at neutral pH. Can have either N, or both, protonated.



Polypeptides



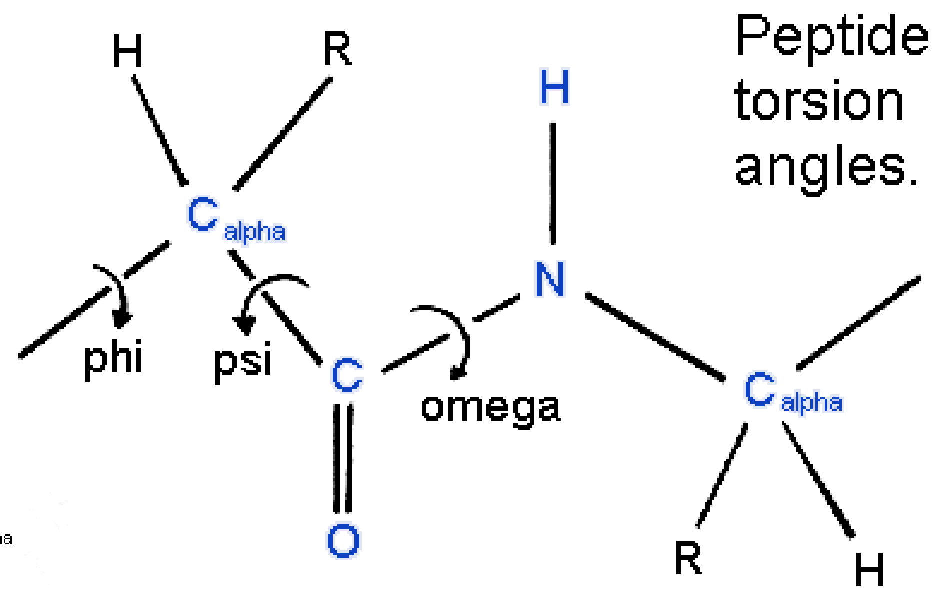
“N-terminus”

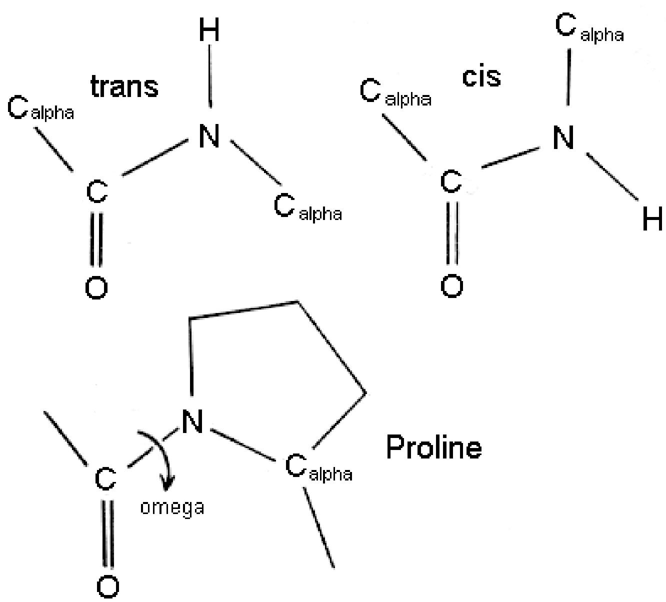


“C-terminus”

Planarity of the Peptide Bond

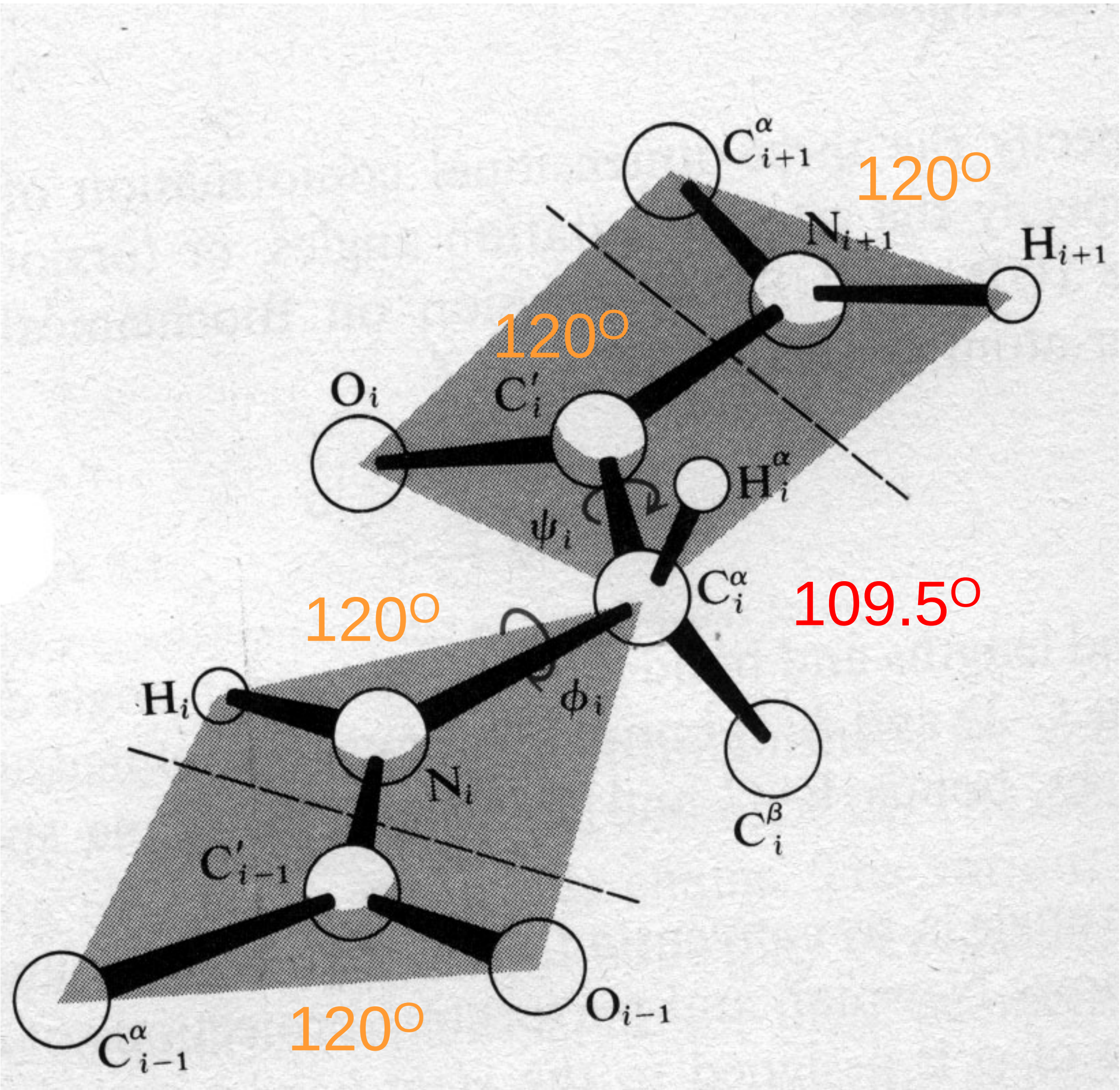
Calpha(i), C(i), O(i), N(i+1) H(i+1) and Calpha(i+1) are co-planar





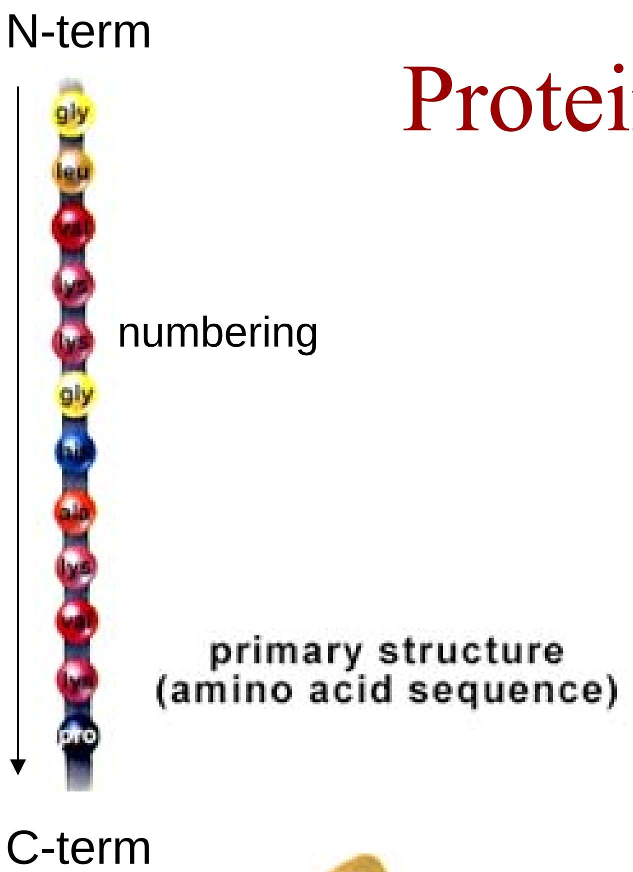
In all a.a. (except proline) steric hindrance favors the trans configuration (omega $=180^{O}$), in proline sometimes omega =0.

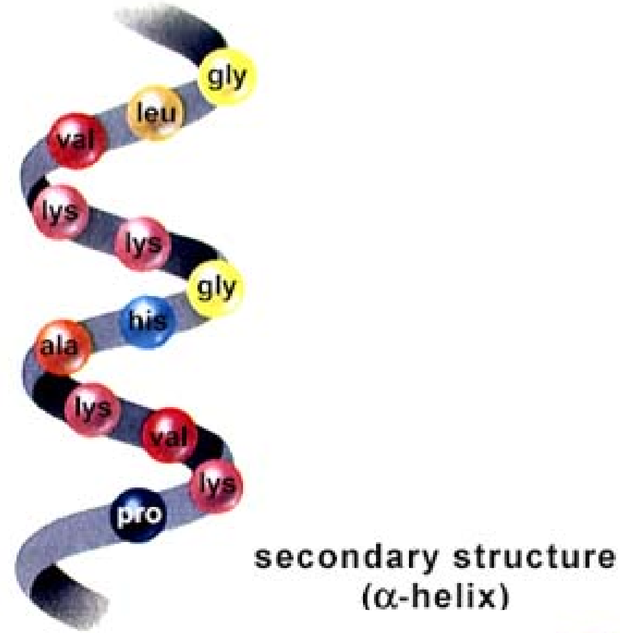
Peptide Bond in 3D

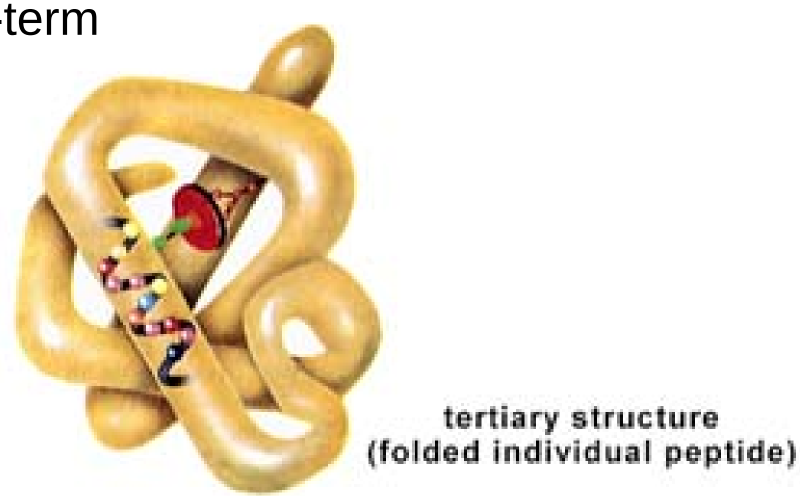


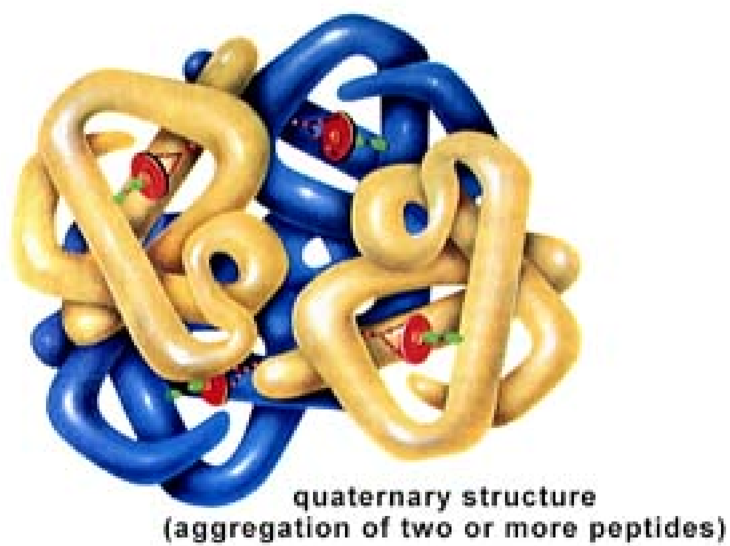
These angles are approximate and should be used in HW 1 http://www.biosci.uga.edu/almanac/bio_103/notes/may_14.html

Protein Structural Hierarchy

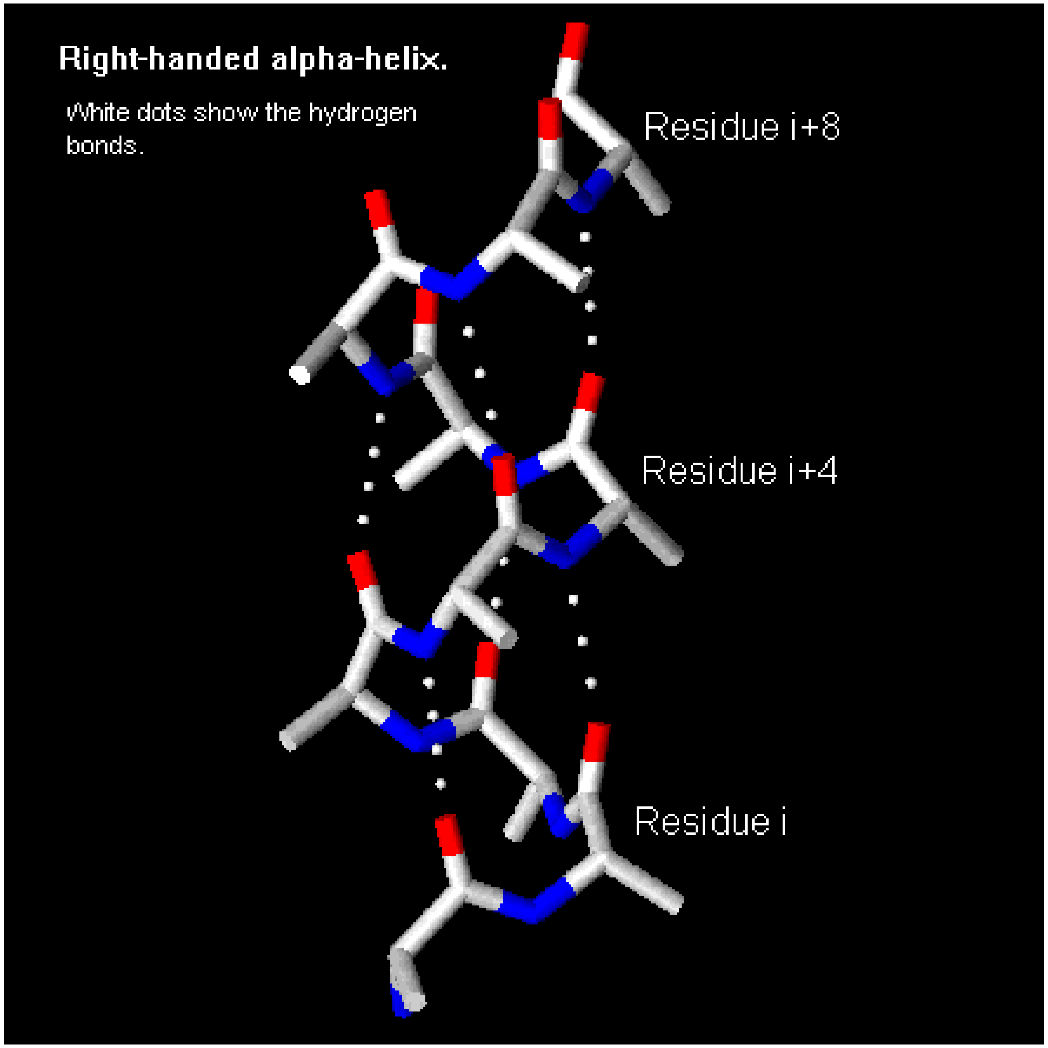


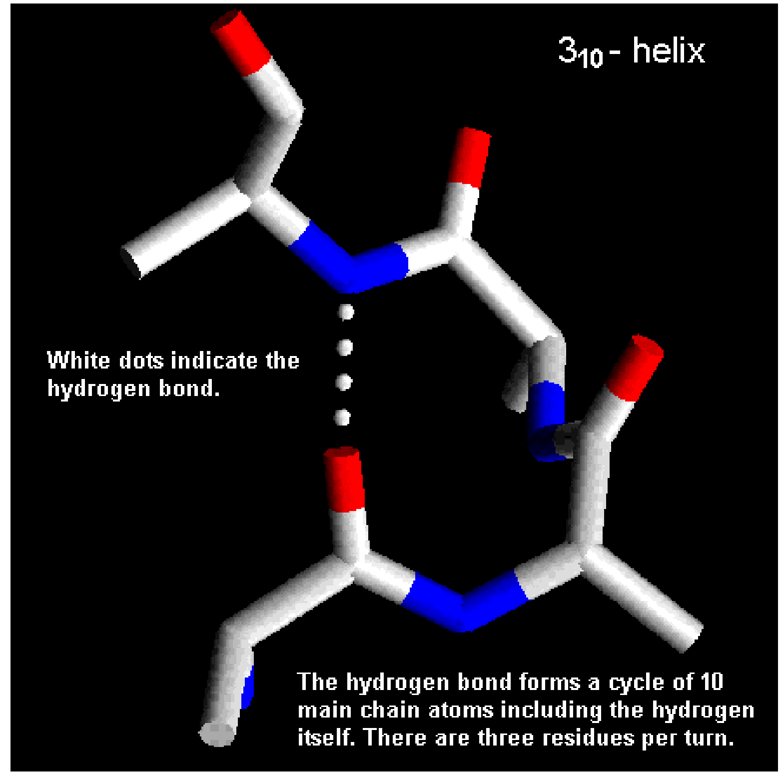






Secondary Structure: α-Helix

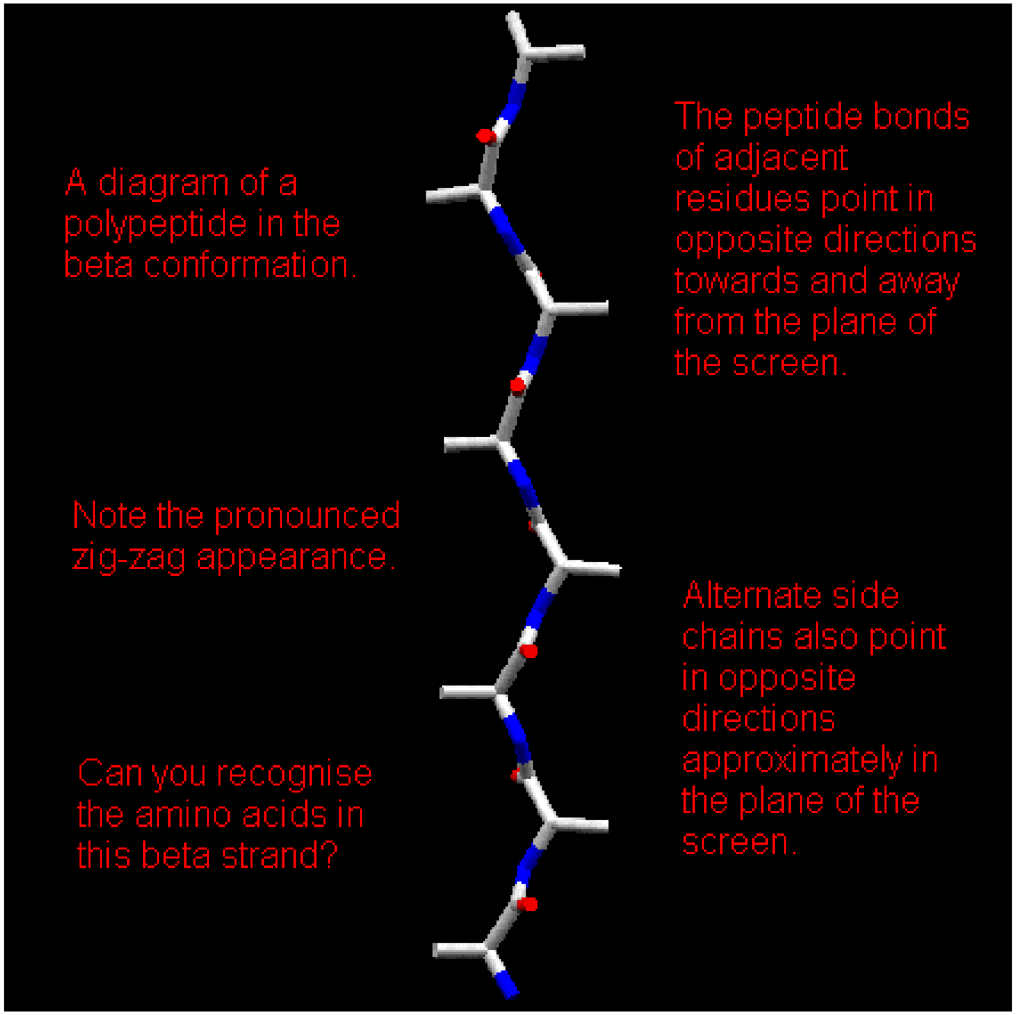




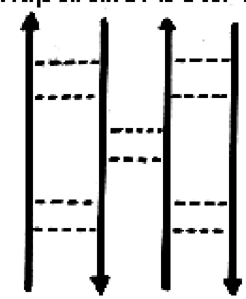
α -helix (R):

- repeats every 5.4Å,
- 3.6 a.a. per turn
- frequently terminated by 3(10) helix

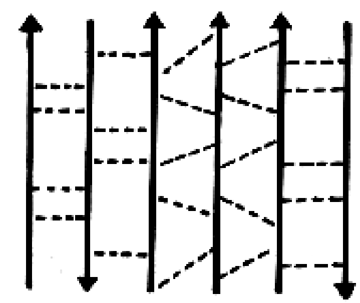
Secondary Structure: β -Sheet



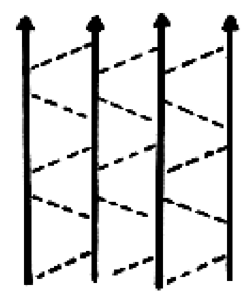
Antiparallel beta-sheet



The different types of beta-sheet. Dashed lines indicate main chain hydrogen bonds.

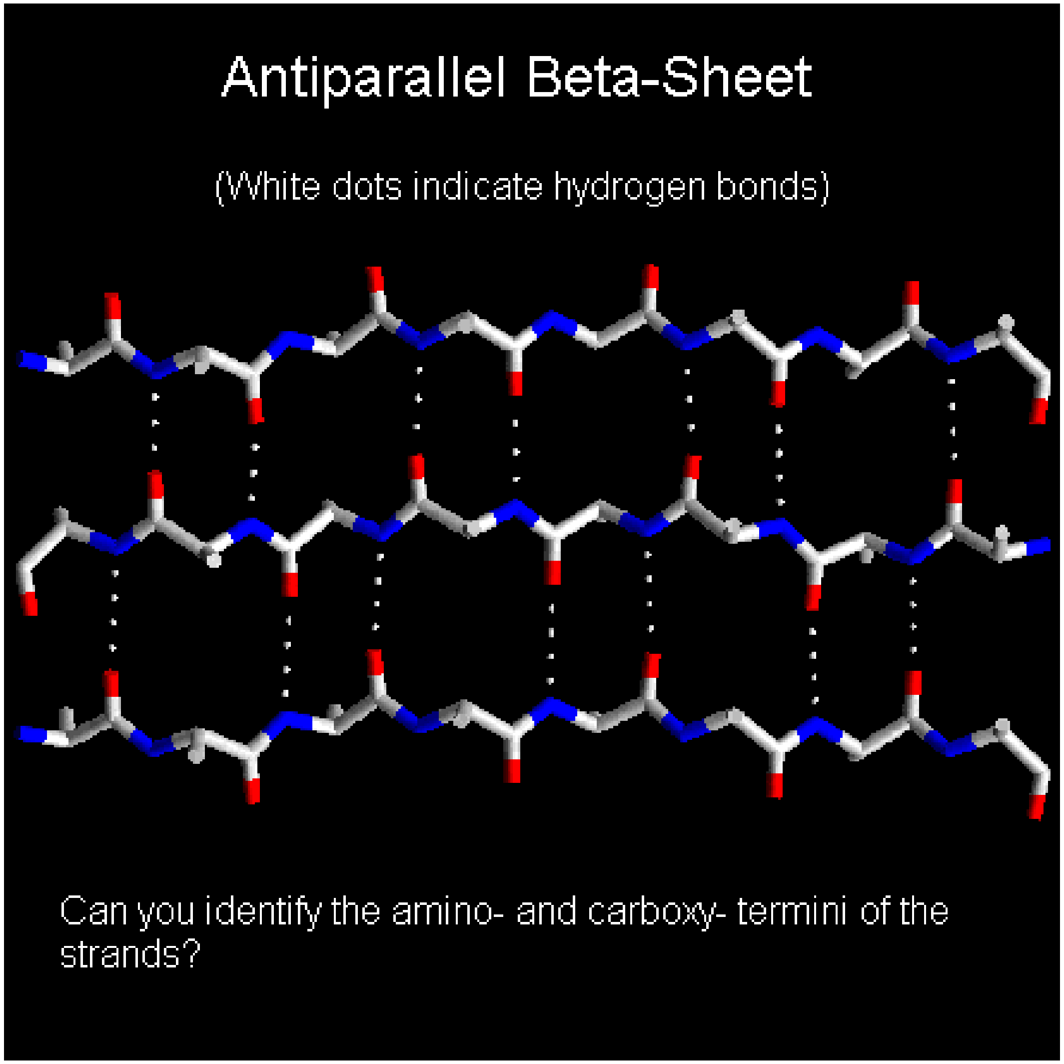


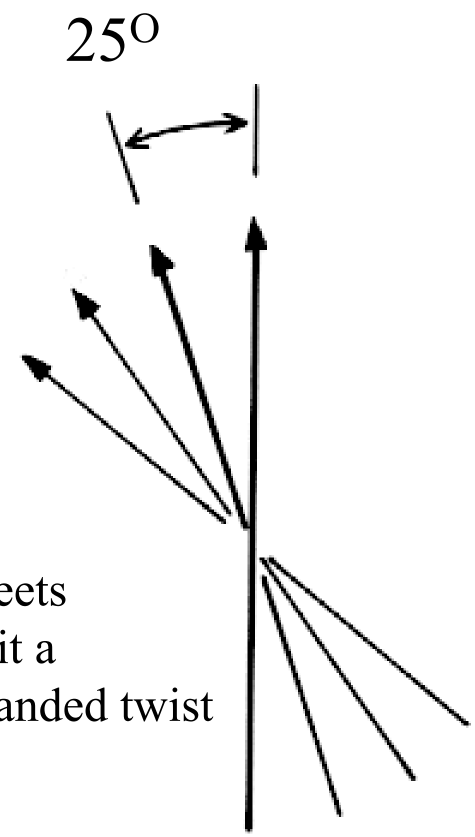
Mixed beta-sheet



Parallel beta-sheet

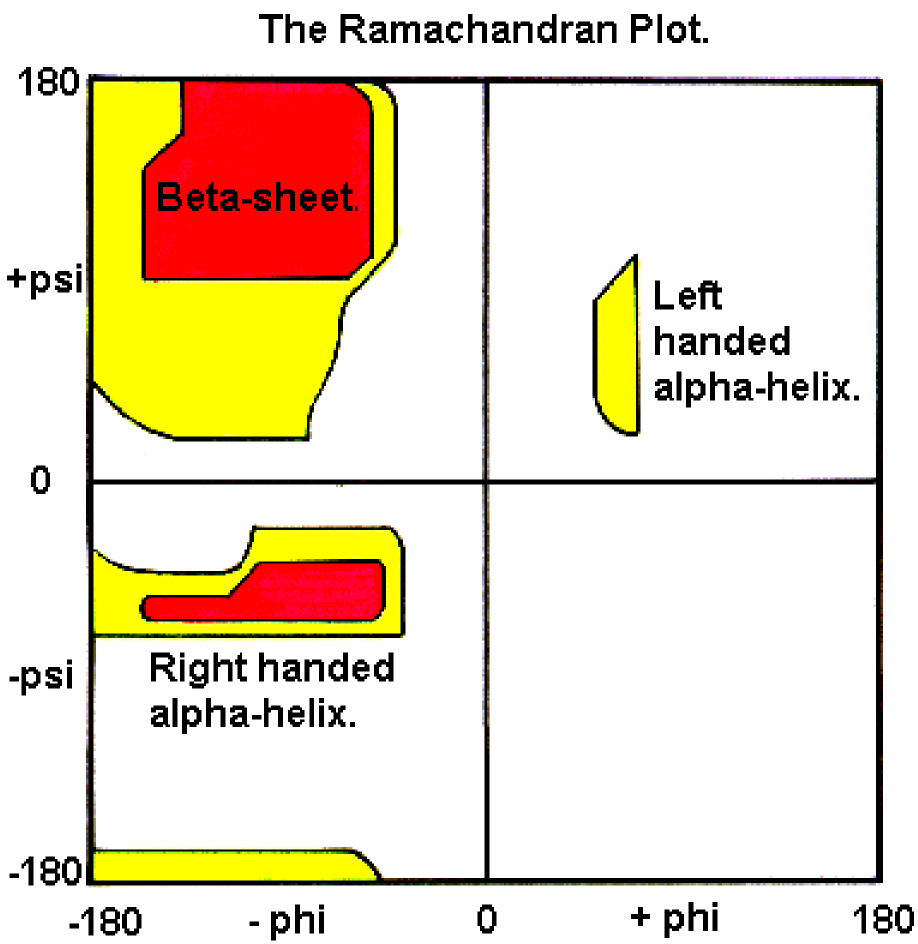
Secondary Structure: β -Sheet





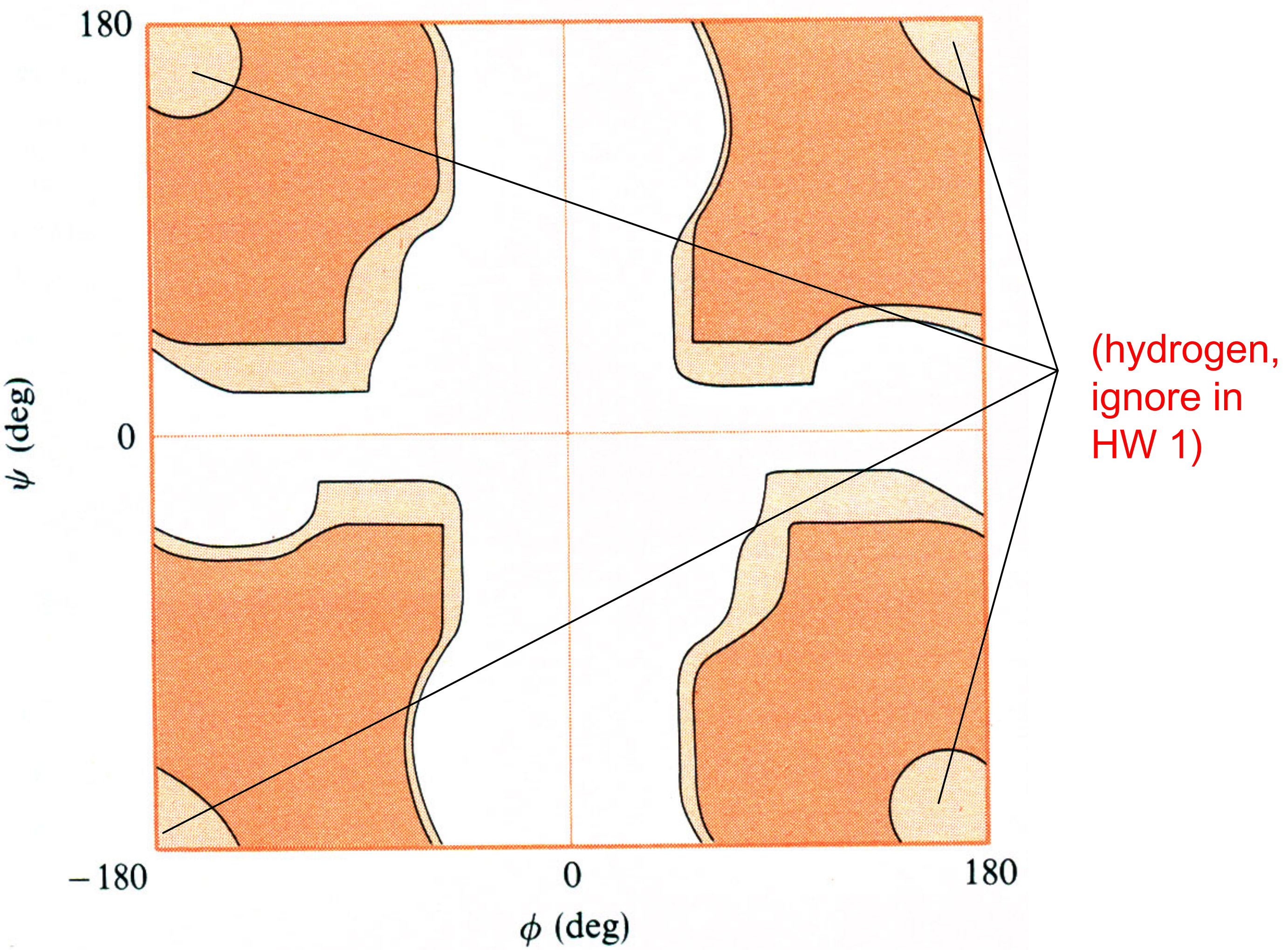
β –sheets exhibit a left-handed twist

The Ramachandran Plot

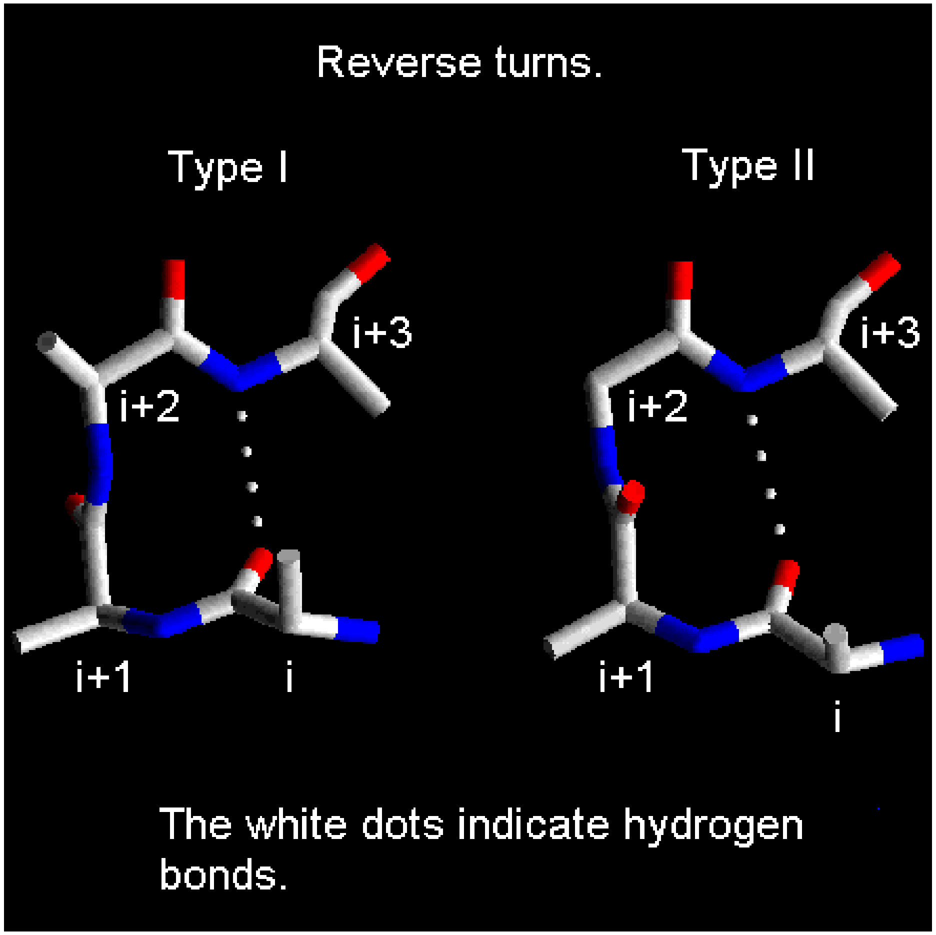


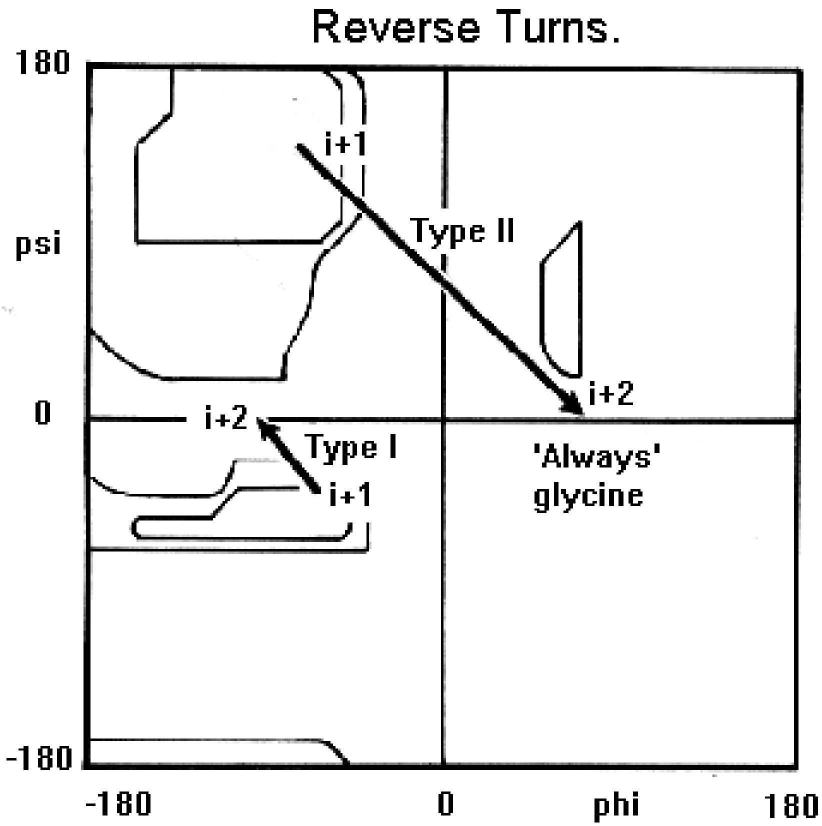
- hard-sphere model
- sterically disallowed regions
- valid for all a.a. except Gly
- Gly has no side chain

Glycine Ramachandran Plot



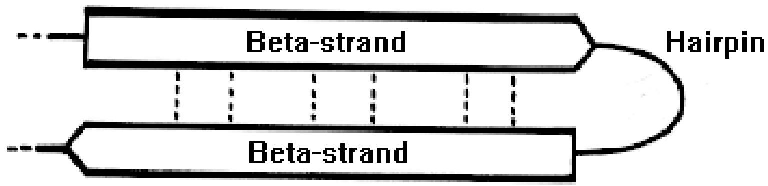
Reverse Turns



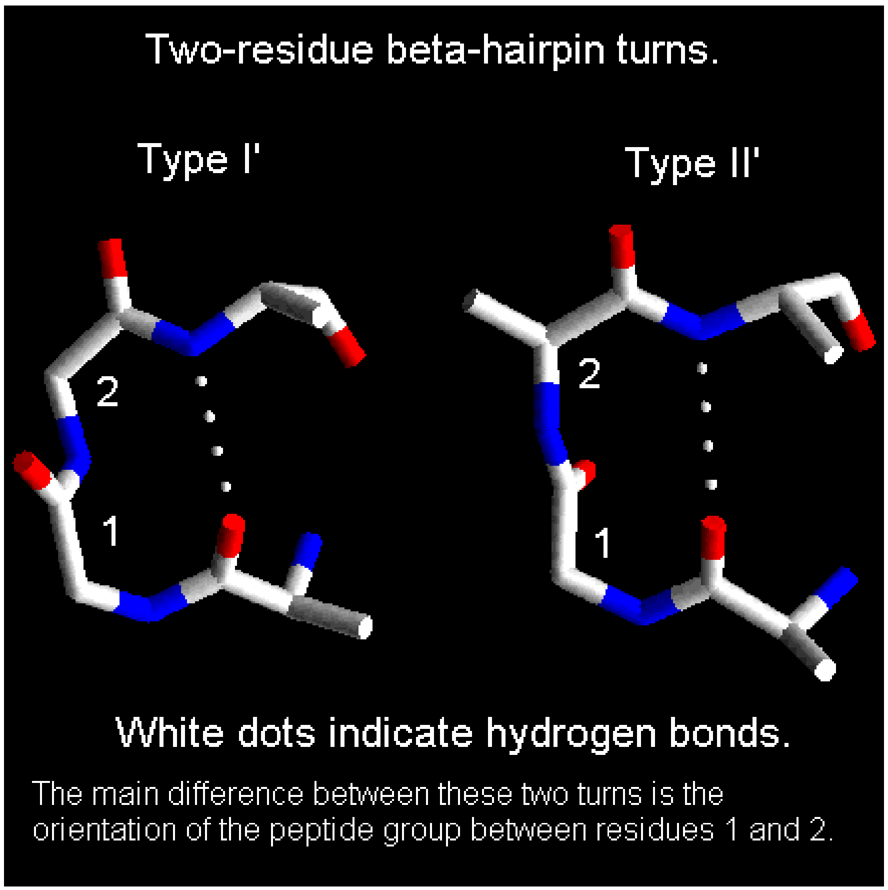


- abundant in globular proteins
- occur on surface of molecule
- possibly nucleation center for folding

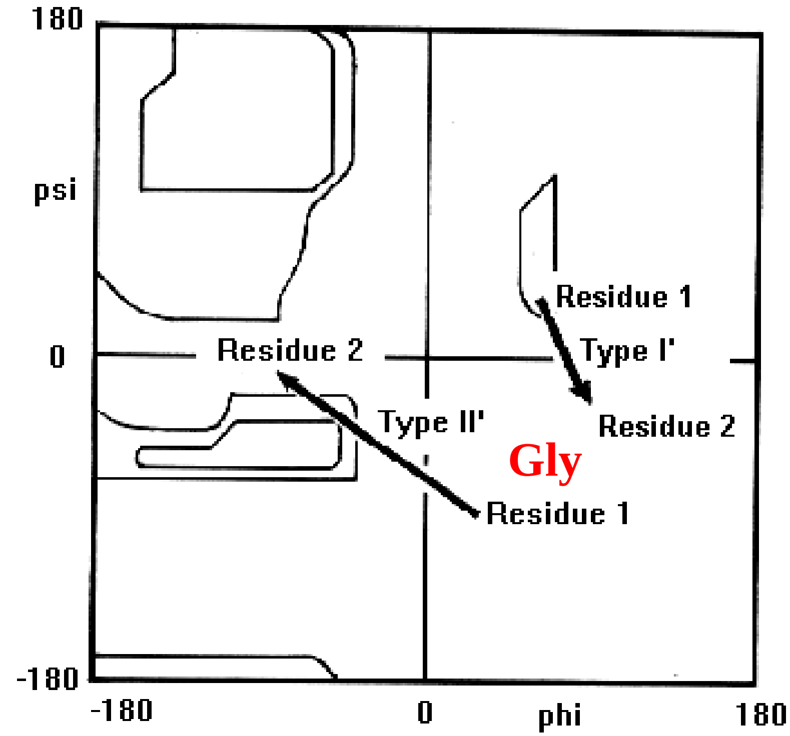
β –Hairpins



The dashed lines indicate main chain hydrogen bonds.

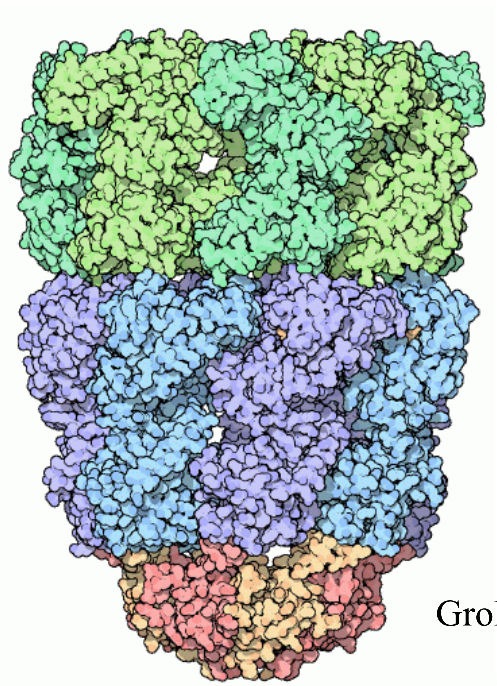


Two residue beta-hairpin turns.

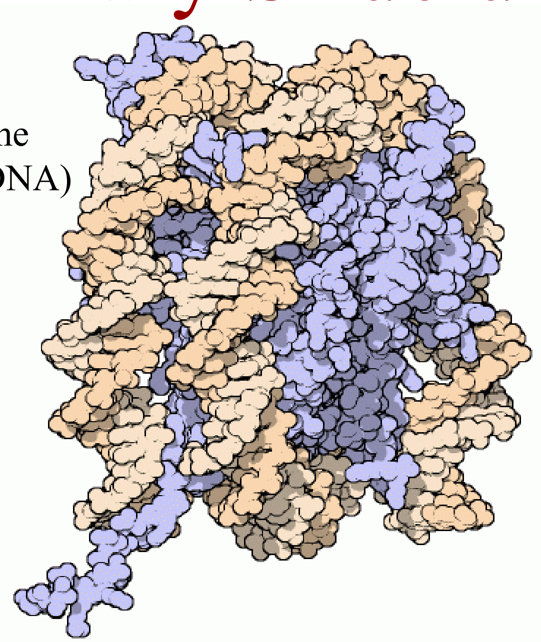


PDB molecules of the month

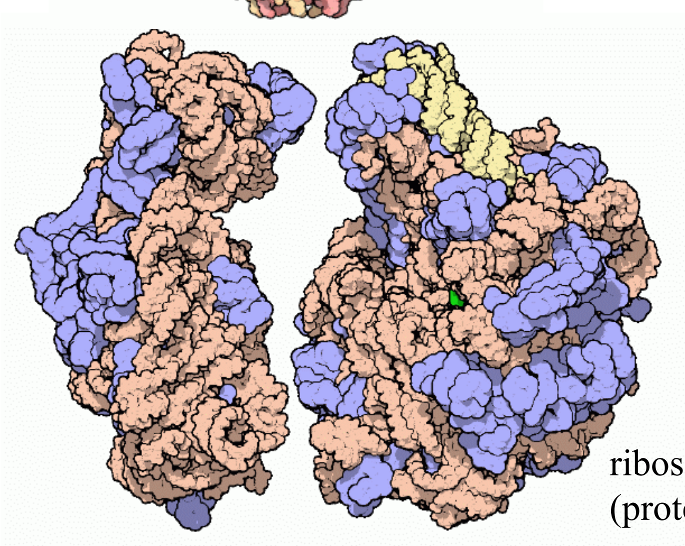
Tertiary and Quaternary Structure



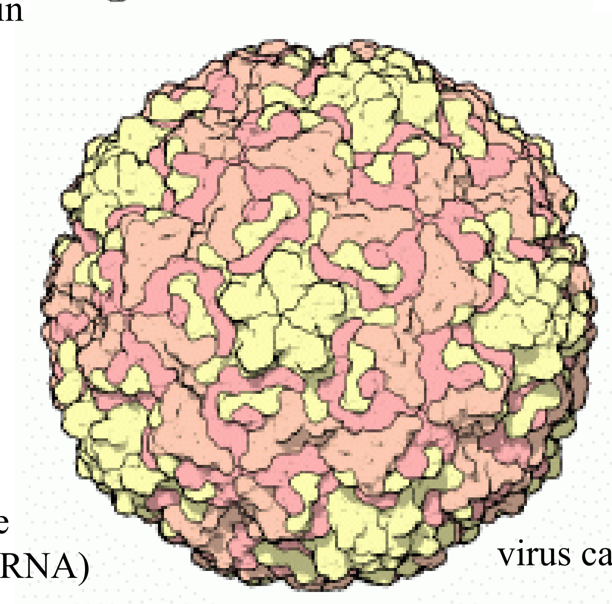
GroEL chaperonin



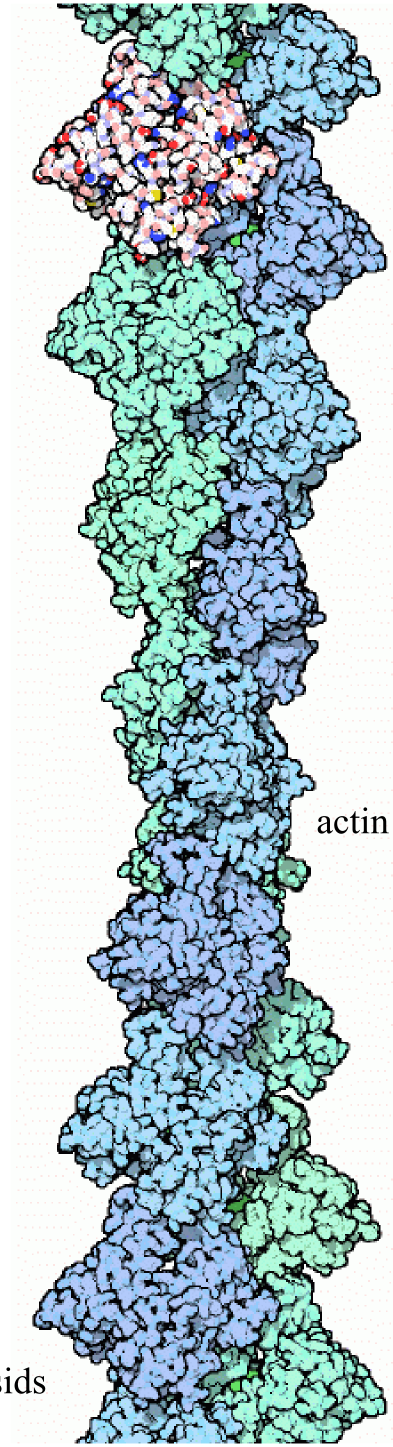
nucleosome
(protein/DNA)



ribosome
(protein/RNA)

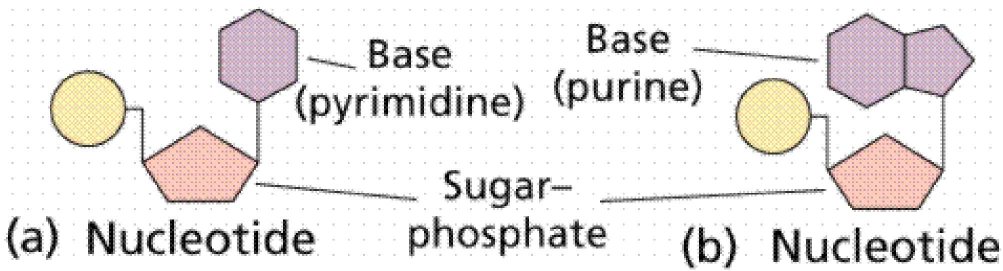


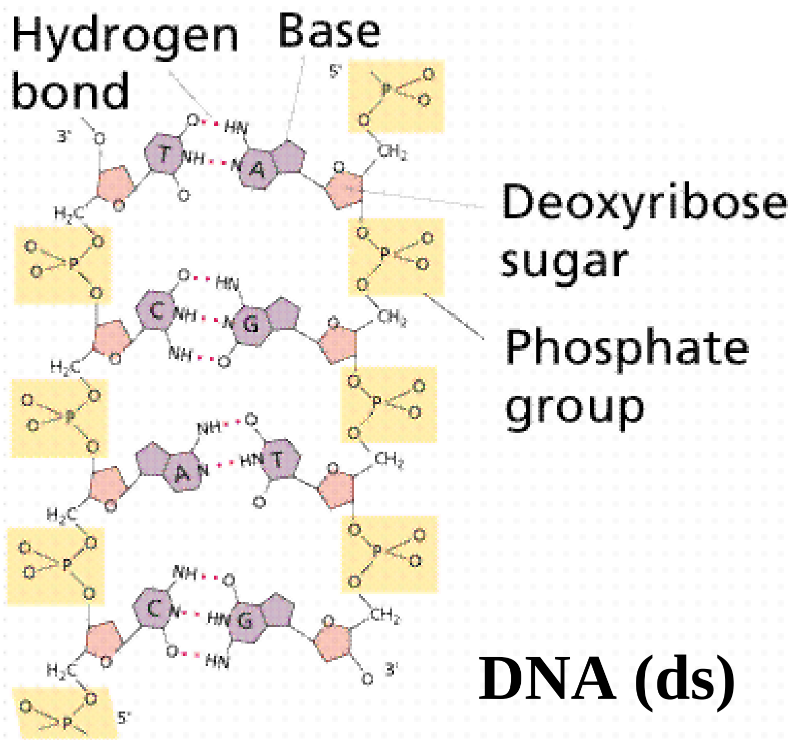
virus capsids



actin

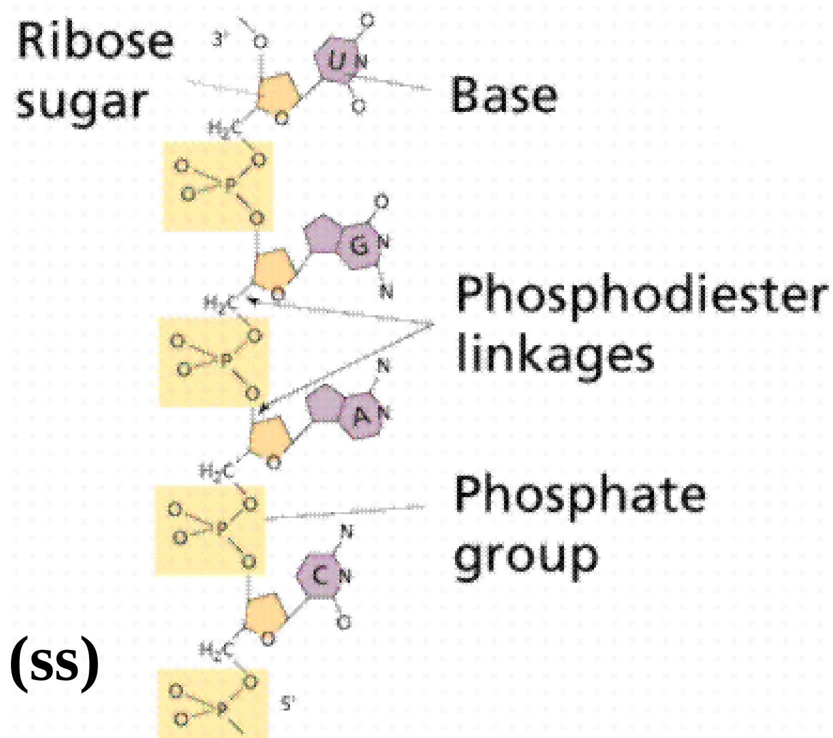
Polynucleotides





DNA (ds)

RNA (ss)

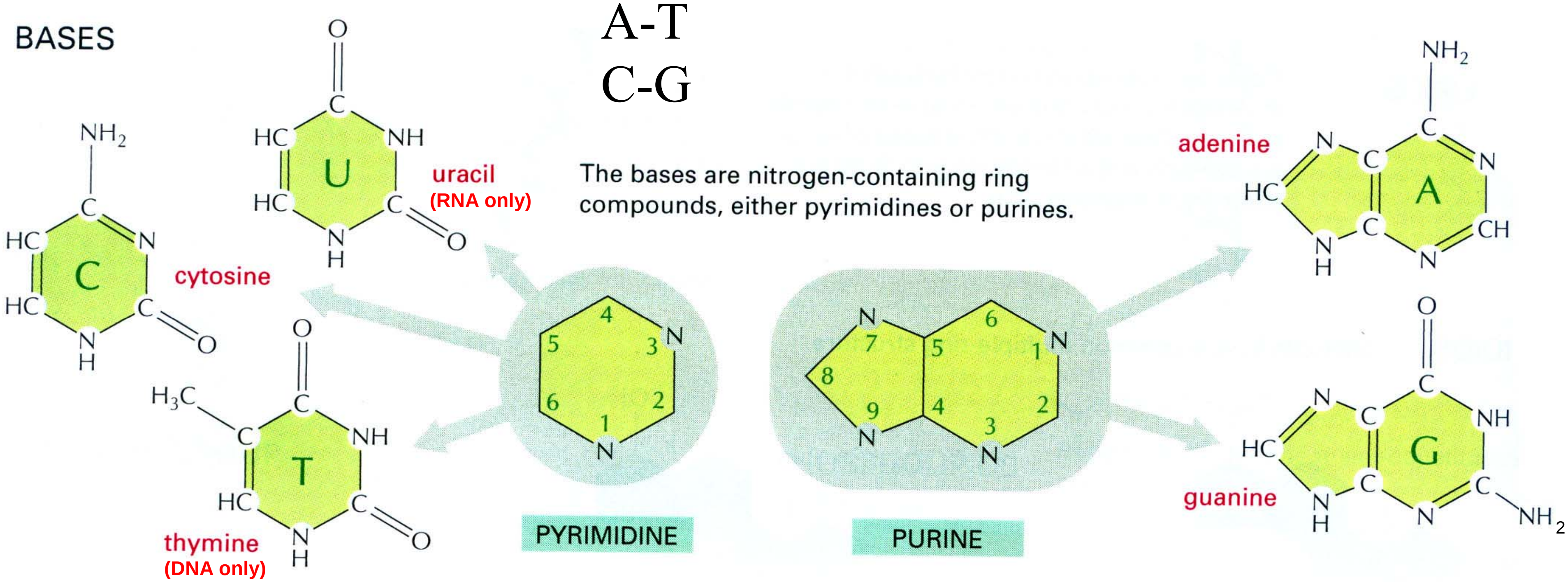


Bases

Pairings (in DNA):

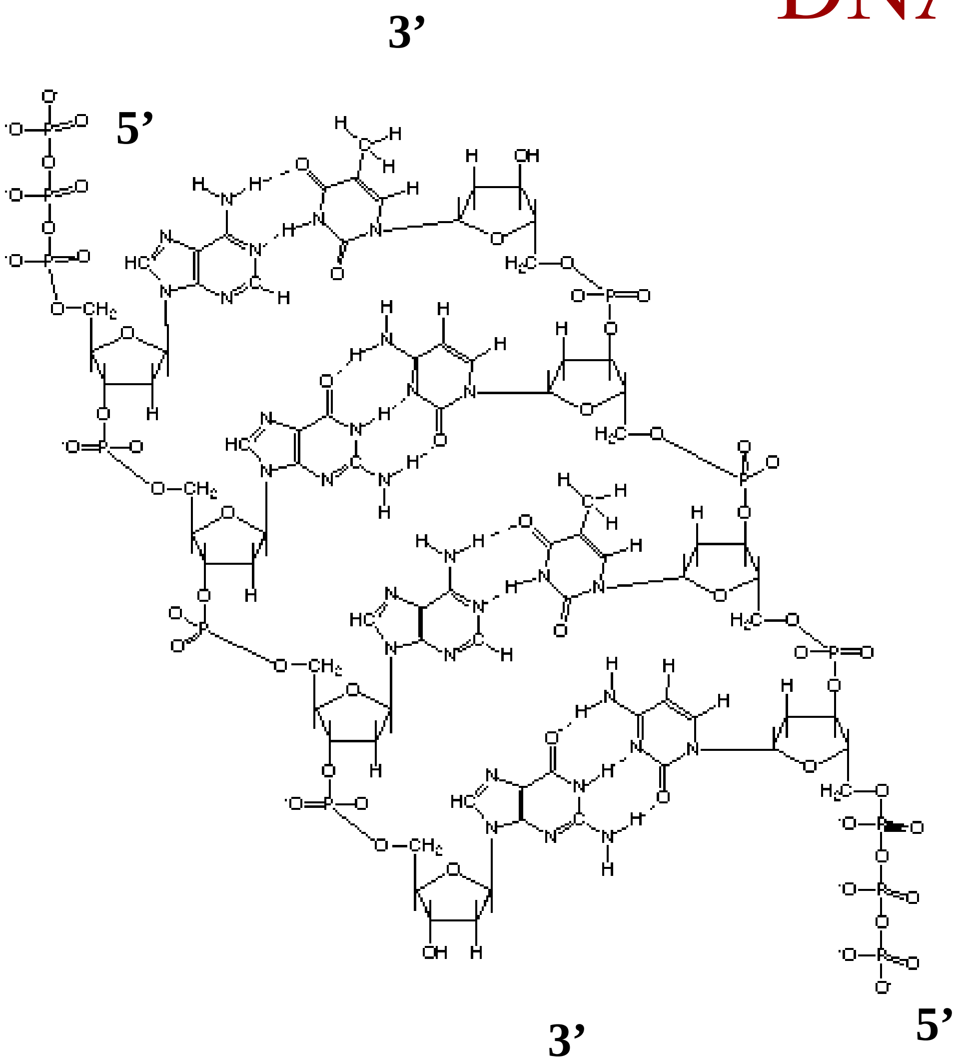
A-T

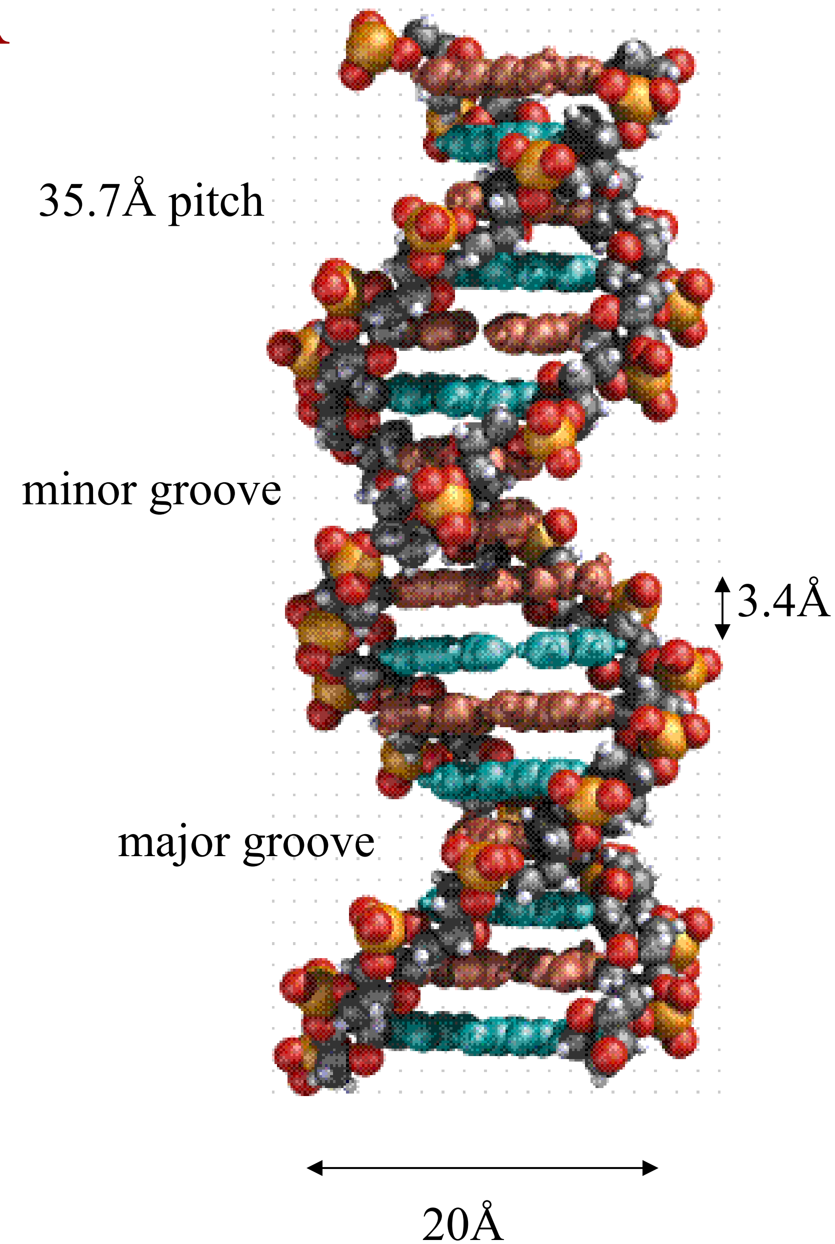
C-G



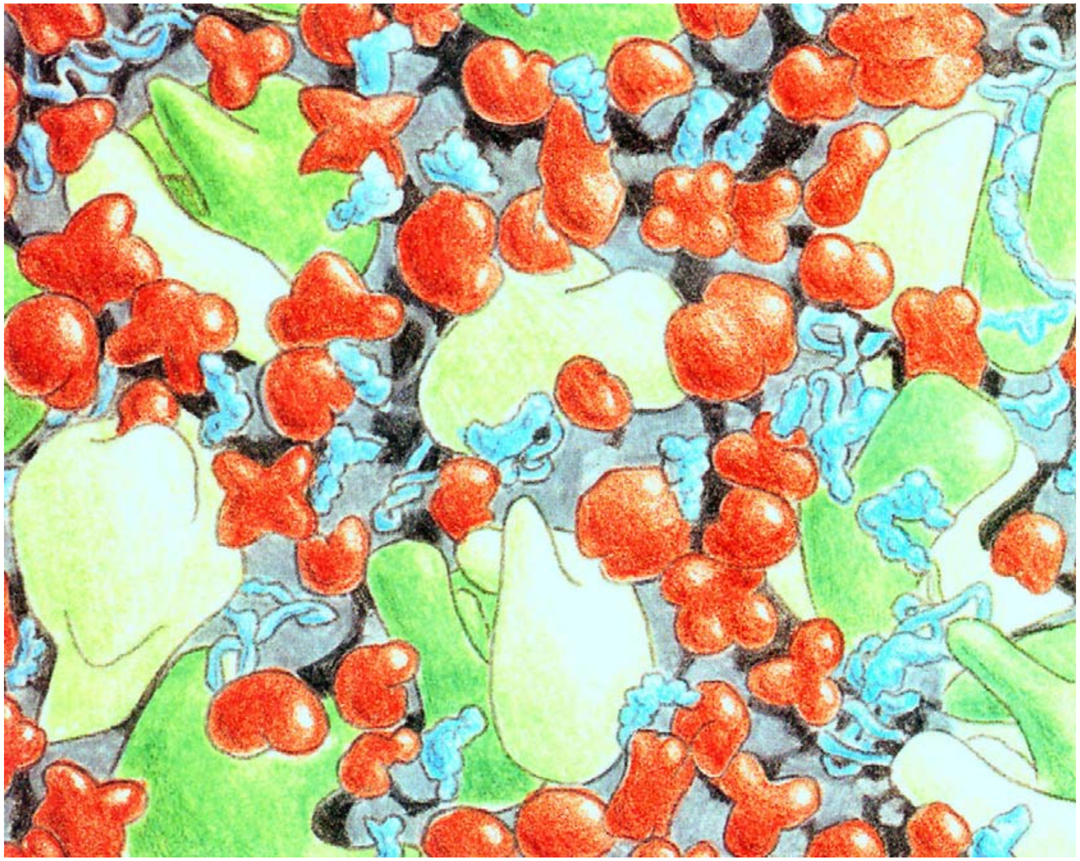
Convention: sequences written 5’ → 3’

DNA



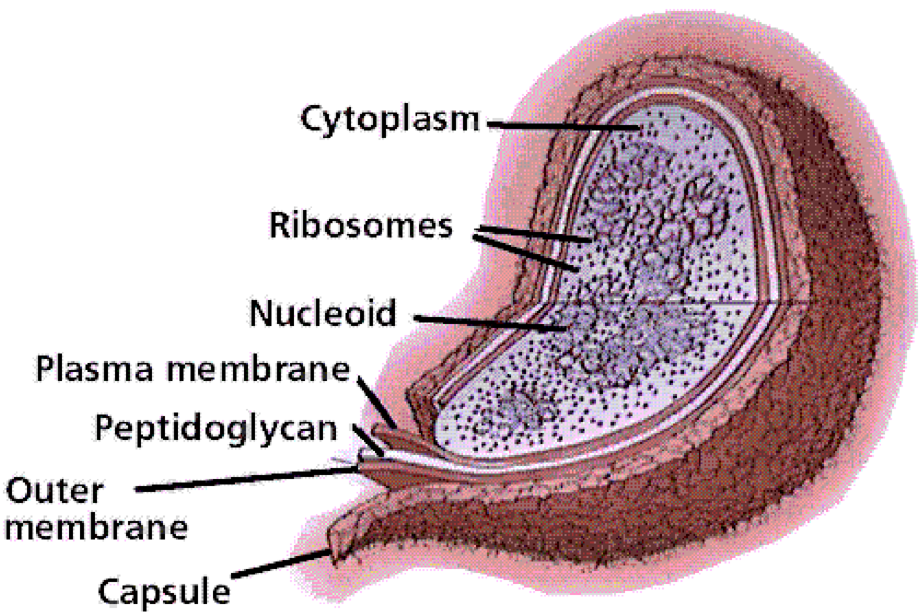


Biomolecules in the Cell Cytoplasm

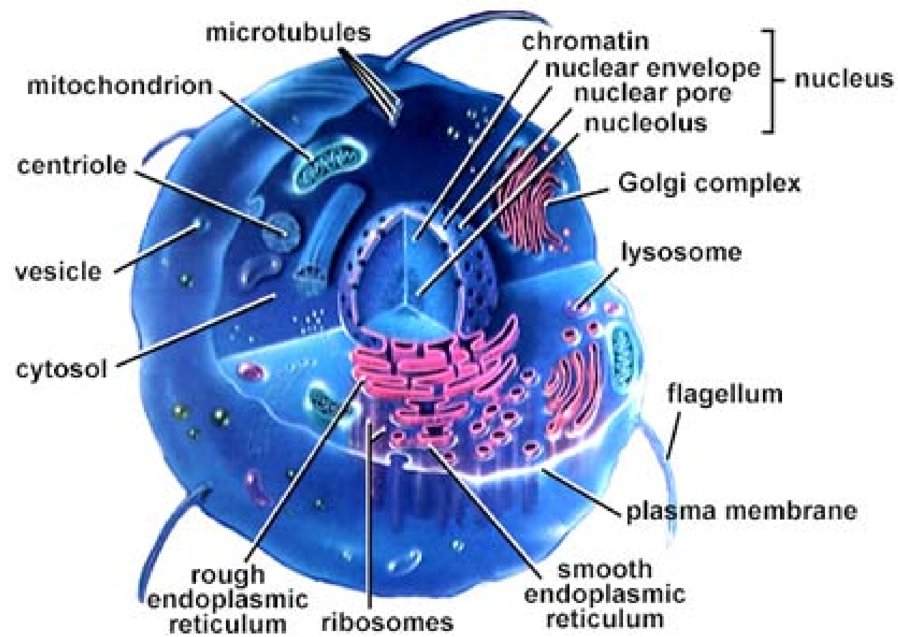


RNAs, ribosomes, and proteins

Cell Structure



Prokaryotic cell



Eukaryotic cell

Purves et al., Life: The Science of Biology

http://www.biosci.uga.edu/almanac/bio_103/notes/may_15.html

Resources and Reading Assignment

WWW:
http://www.emc.maricopa.edu/faculty/farabee/BIOBK/BioBookTOC.html
http://web.mit.edu/esgbio/www
http://users.rcn.com/jkimball.ma.ultranet/BiologyPages

Textbooks:
Schlick, Chapters 1, 3, 4, and 5
Bourne & Weissig, Chapters 2 and 3

Handouts:
P.G. Debrunner, 1993, Proteins and Nucleic Acids