***** Physical Methods of Biochemistry - Fall 2010 *****

Instructor for the first 2 classes - David Hoffman

Office hours Monday & Thursday 11 am to 1 pm, 5.266C Welch.

Instructor for the remainder of the semester - Prof. Marv Hackert.

Attend class!

Although some slides from class will usually be posted on the class web page, do not expect that every word said in class will be posted.

Bring a notebook to class and take some of your own notes.

It would be extremely difficult to learn the course material simply by viewing the posted slides without the context of your own notes.

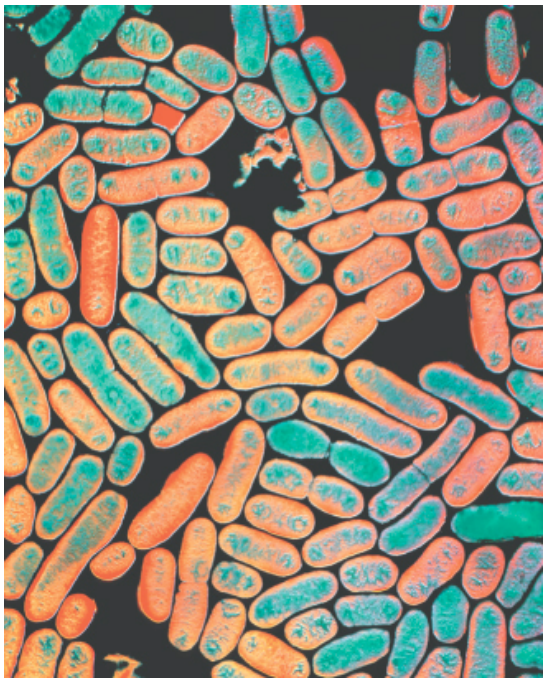
Class attendance is expected.

I guess it is time to get started. :-)

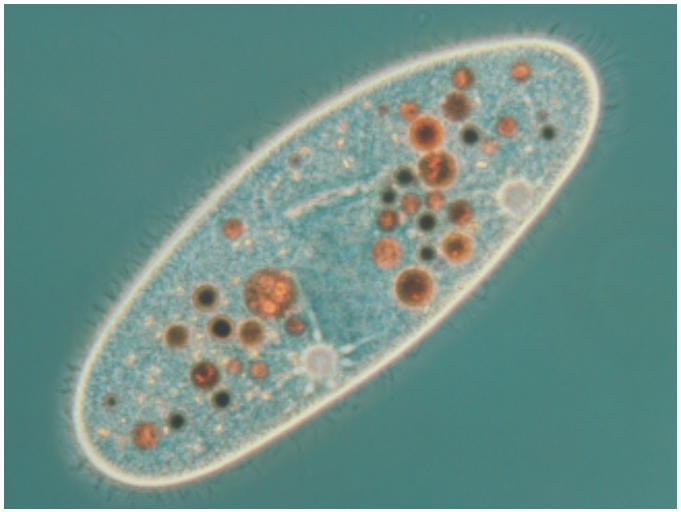
Size scale of the biochemical world.

How big is an atom? Length of chemical bond?

Size of a typical bacterial cell? Eukaryotic cell?



Prokaryotic cells

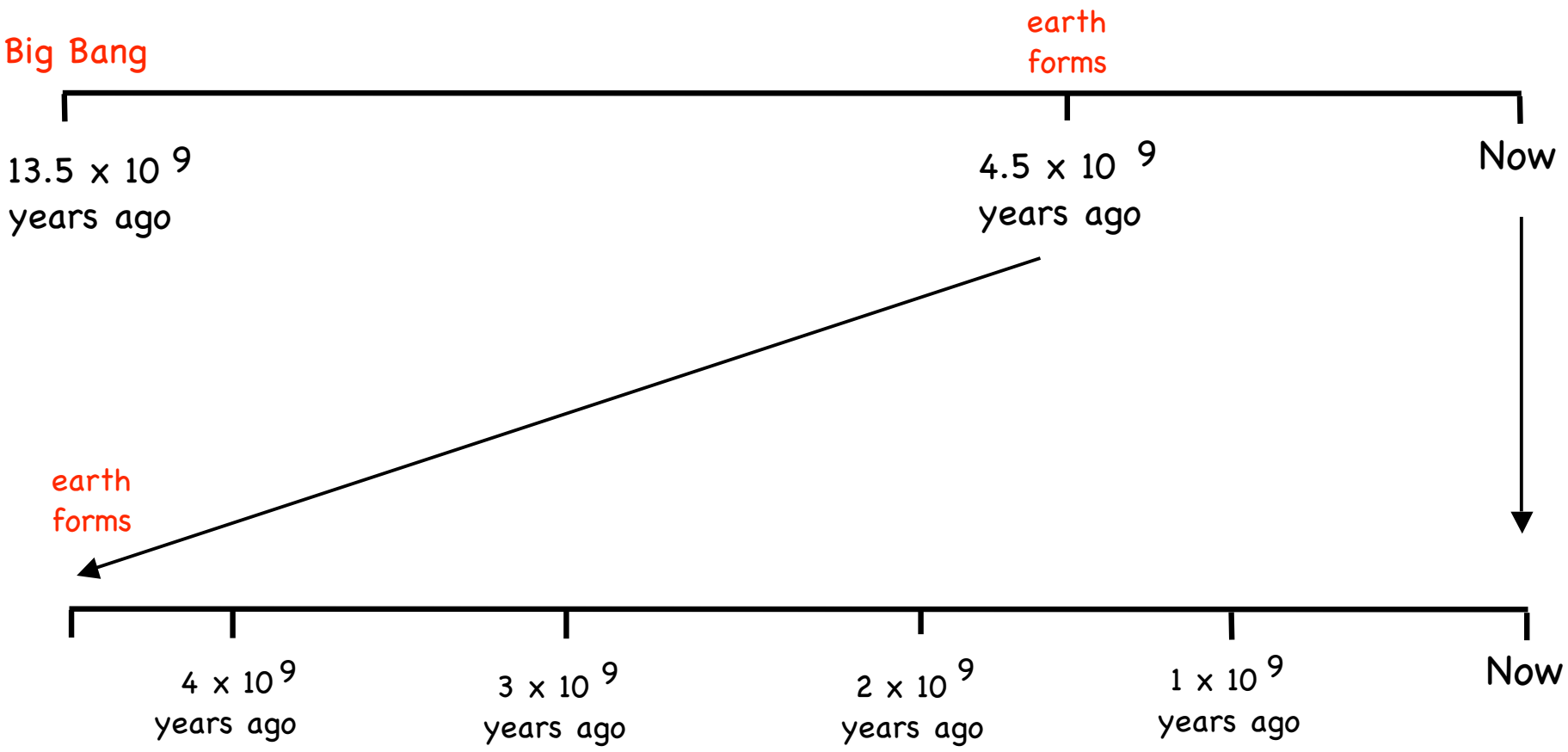


Eukaryotic cells have cell nuclei, other intracellular compartments, many other biological differences from prokaryotes.

What is the wavelength of visible light?

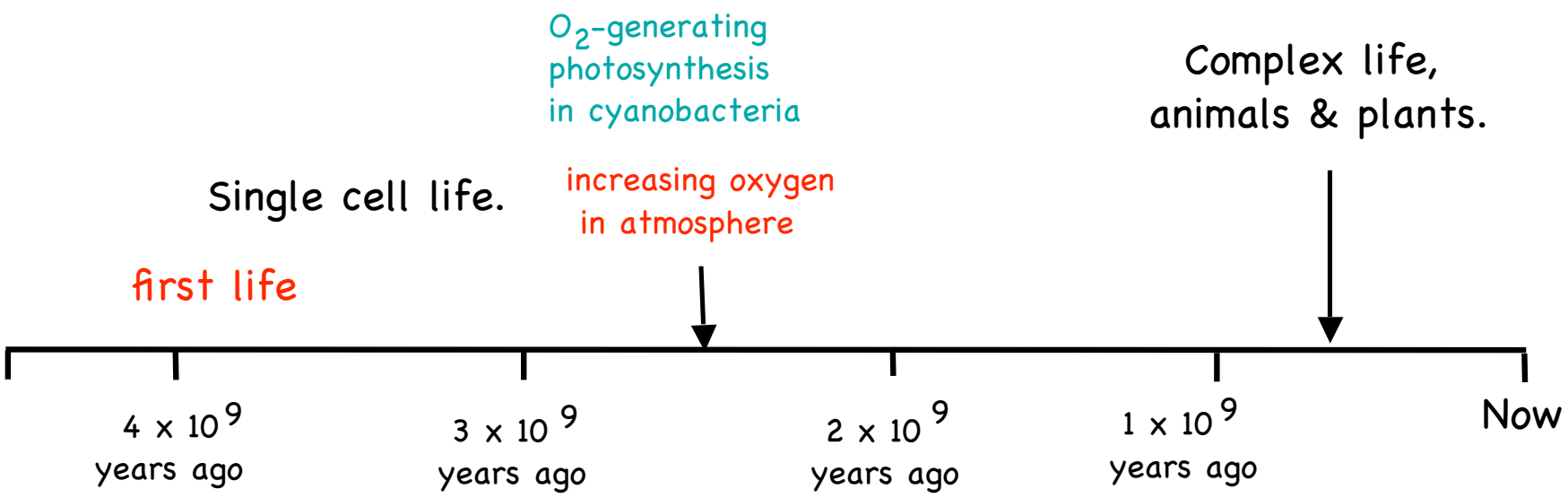
Wavelengths of different waves in the EM spectrum?

Scale of time.



Focus on the part after the earth forms.

Time line for life on earth.



How do we know the age of the earth?

One way is from radioactive decay products in rocks.

When zircon crystals ($ZrSiO_4$) form, they include Uranium-238 as an impurity, but exclude Pb. So any Pb within zircon crystals must be from the decay of uranium.

So, uranium / lead ratio in zircon crystals can tell us how long ago the crystal was formed.

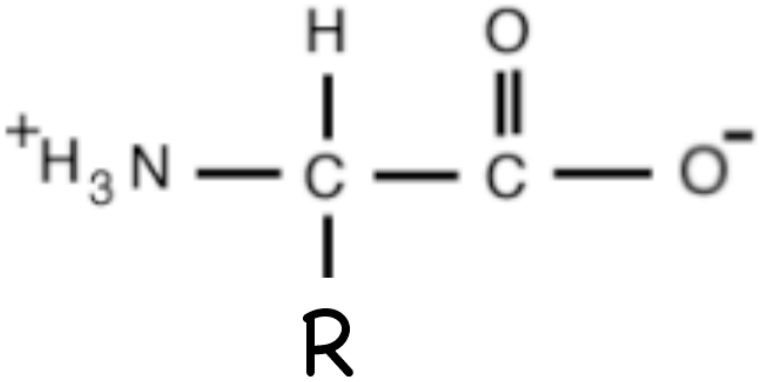
Half-life of Uranium-238 is 4.47 billion years (U decays to Pb).

Oldest earth rocks are about 4.0×10^9 years.

First regular course topic:

"Our friends the amino acids".

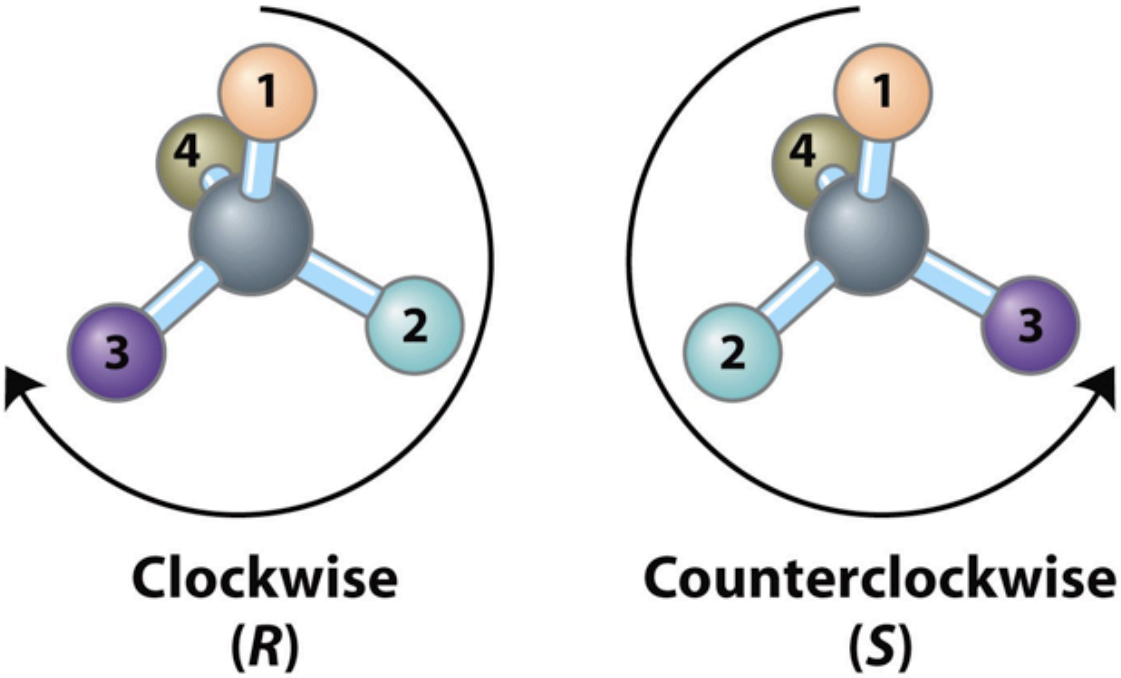
One letter abbreviation, 3 letter abbreviation, properties, structure.



"R" group is different, depending on a.a. type.

Amino acids are chiral.

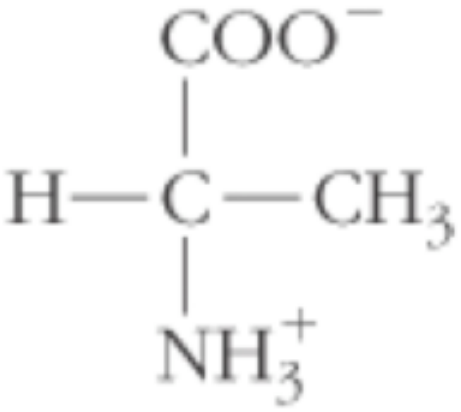
RS system of classifying enantiomers (Cahn-Ingold Prelog, or CIP system, established in 1960's).

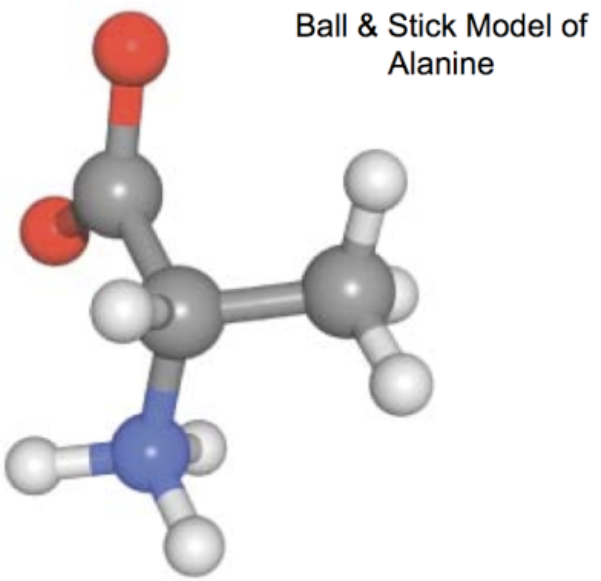


1 = highest priority group (based on atomic # of attached substituents)

With lowest priority group pointing away from observer, decreasing priority of other 3 substituents goes in clockwise direction for R enantiomer.

Example: Alanine found in proteins is the S enantiomer.



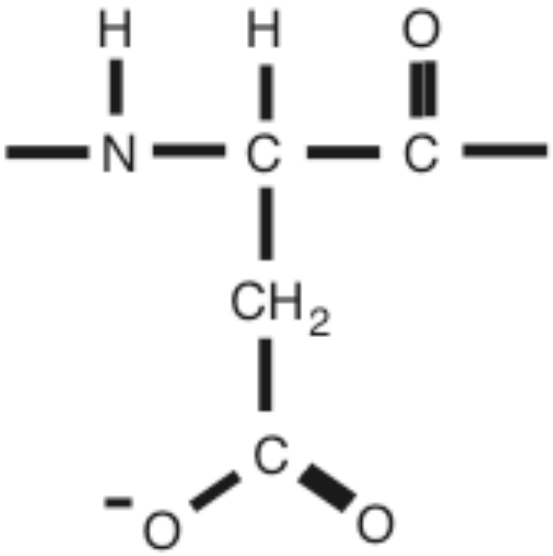


Note: Amino acid enantiomers are often classified by the "DL" system, from the 1890's. The amino acids normally found in proteins are "L-amino acids". For example, "L-alanine".

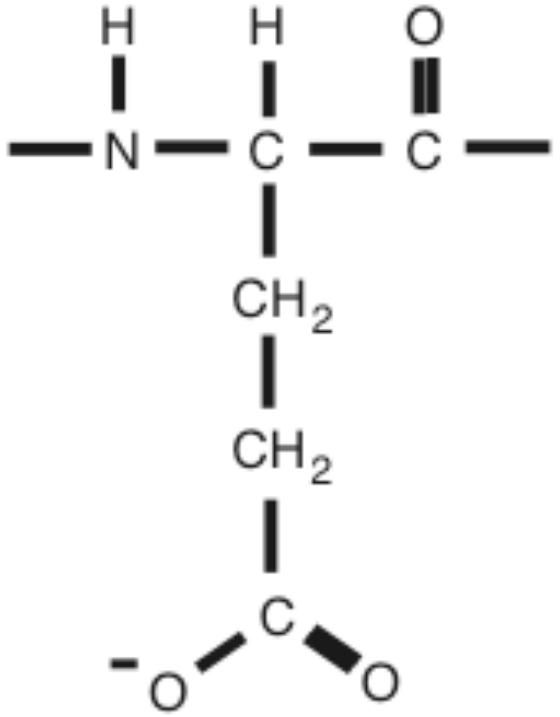
A few words about each of the 20 common amino acids.

Charged amino acids - Negative

Aspartic acid (Asp, D)

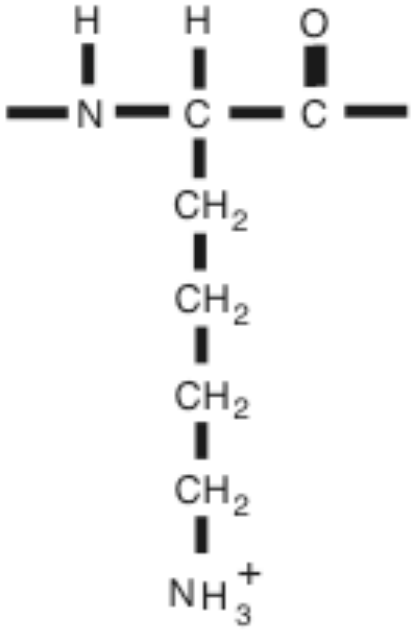


Glutamic acid (Glu, E)

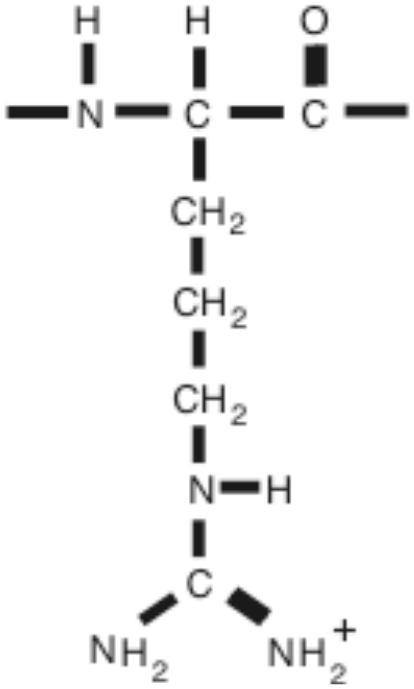


Charged amino acids - Positive

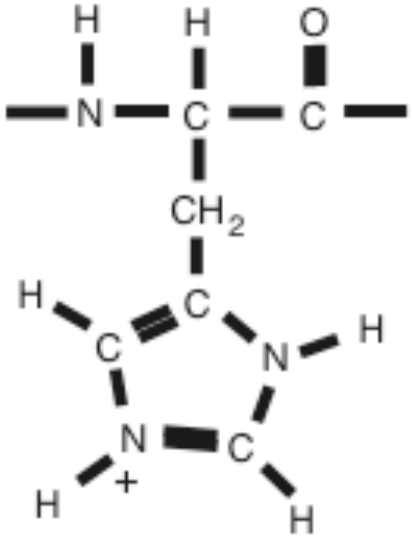
Lysine (Lys, K)



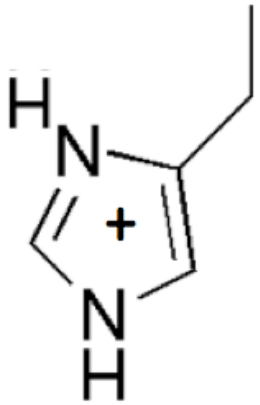
Arginine (Arg, R)



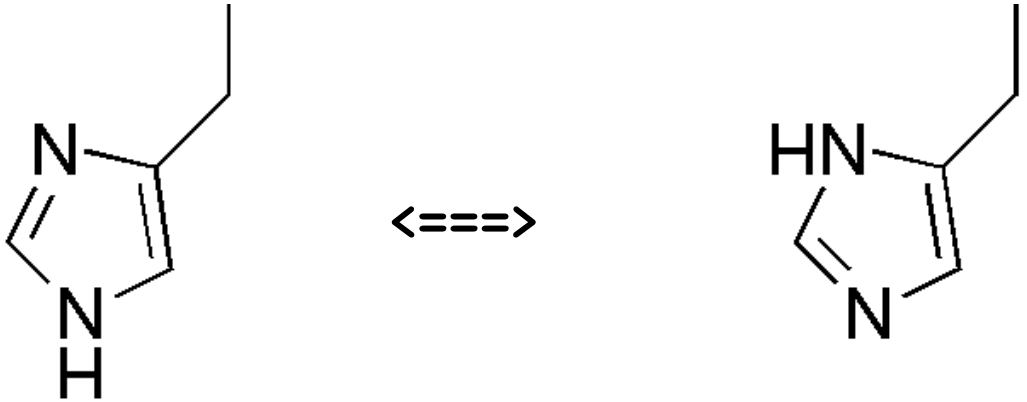
Histidine (His, H)



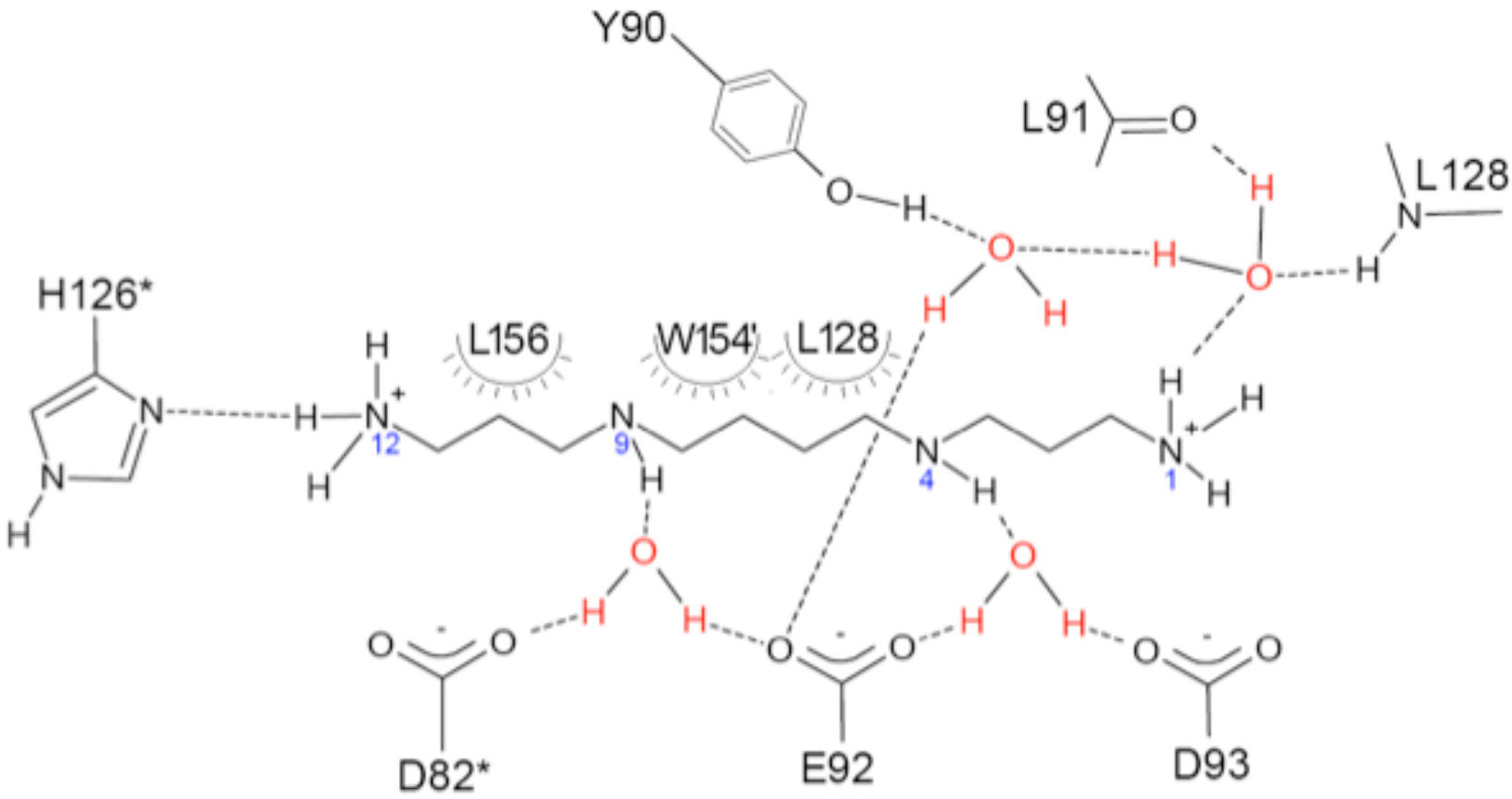
Histidine side chain
at pH < 6.



Histidine side chain at pH > 7.



Tautomer of histidine can be identified from hydrogen bonding network in well-ordered crystal structures.

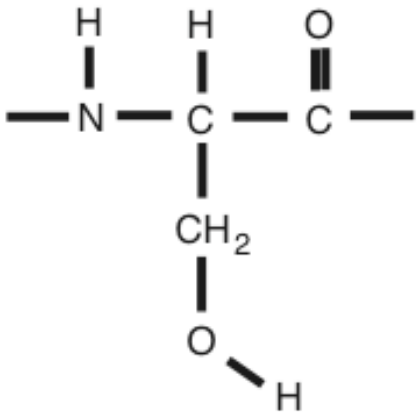


Both histidine tautomers have been observed in crystal structures.

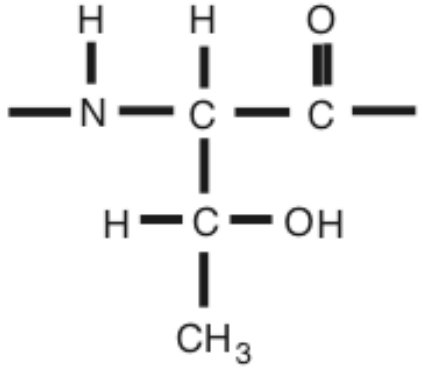
Amino acids - Hydrophilic

Serine, threonine, glutamine, asparagine - can form H-bonds with water.

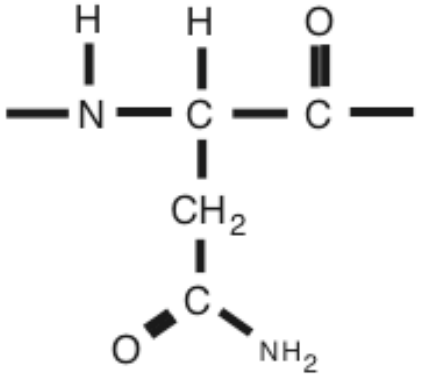
serine (Ser, S)



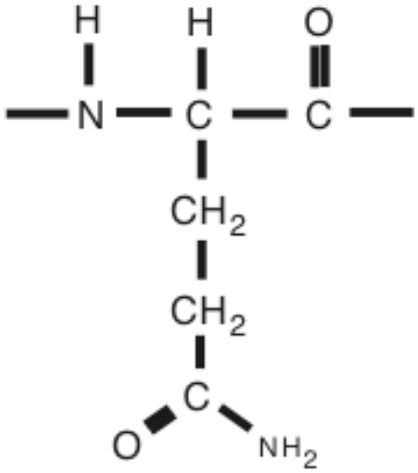
threonine (Thr, T)



asparagine (Asn, N)

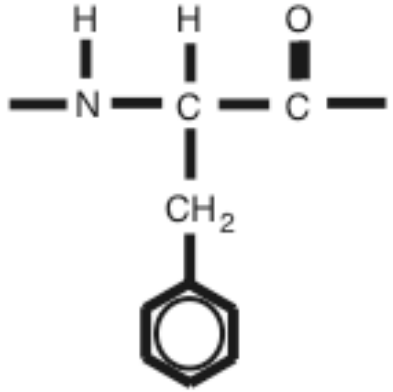


glutamine (Gln, Q)

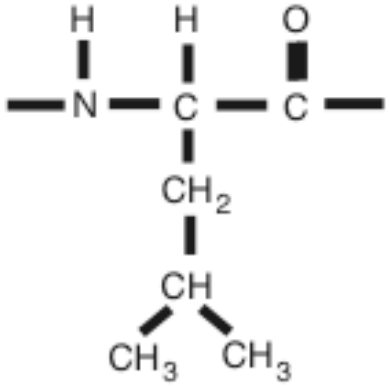


Amino acids - Very hydrophobic

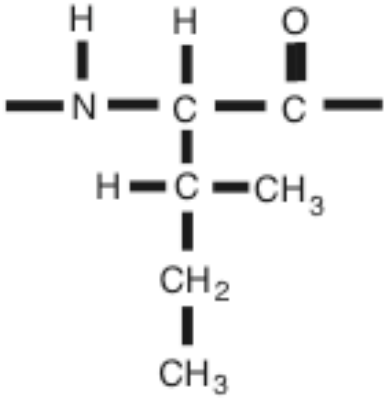
phenylalanine (Phe, F)



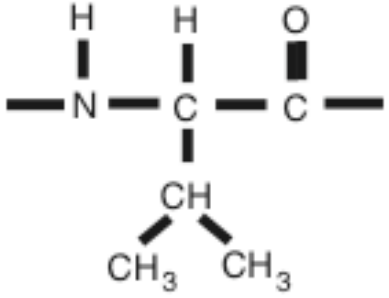
Leucine (Leu, L)



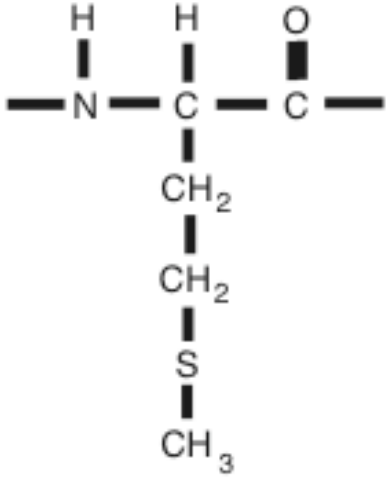
Isoleucine (Ile, I)



Valine (Val, V)

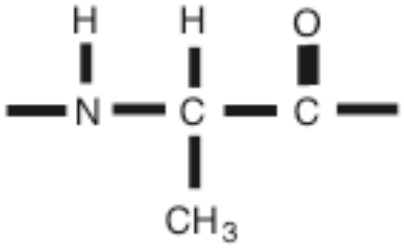


Methionine (Met, M)

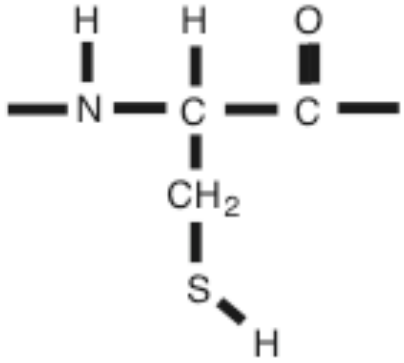


Other (moderately) hydrophobic amino acids

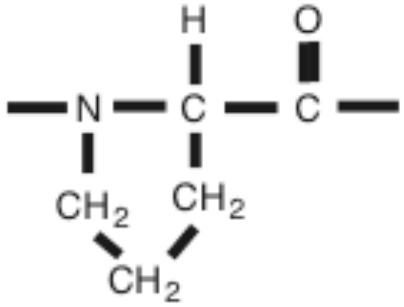
Alanine (Ala, A)



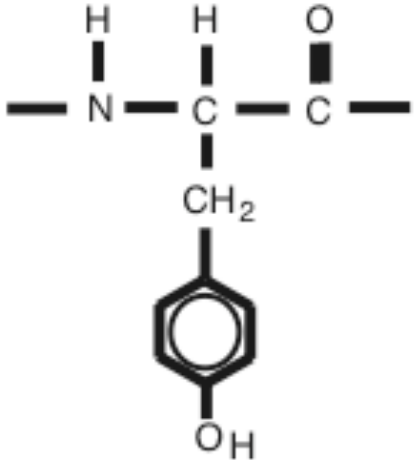
Cysteine (Cys, C)



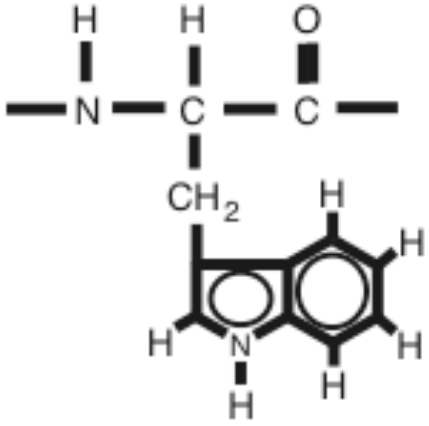
Proline (Pro, P)



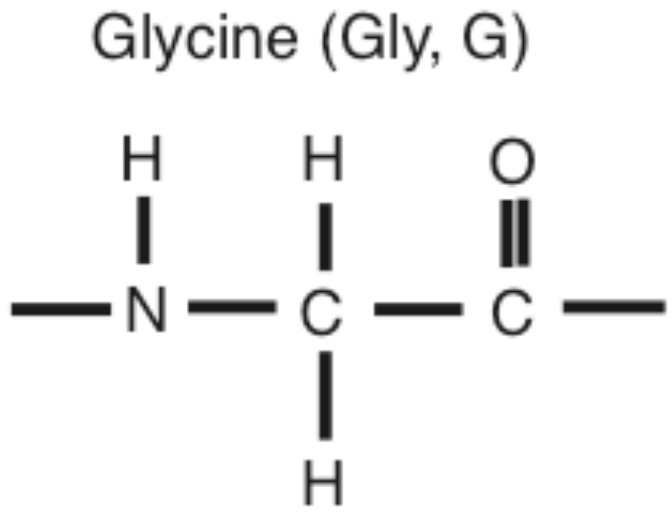
Tyrosine (Tyr, Y)



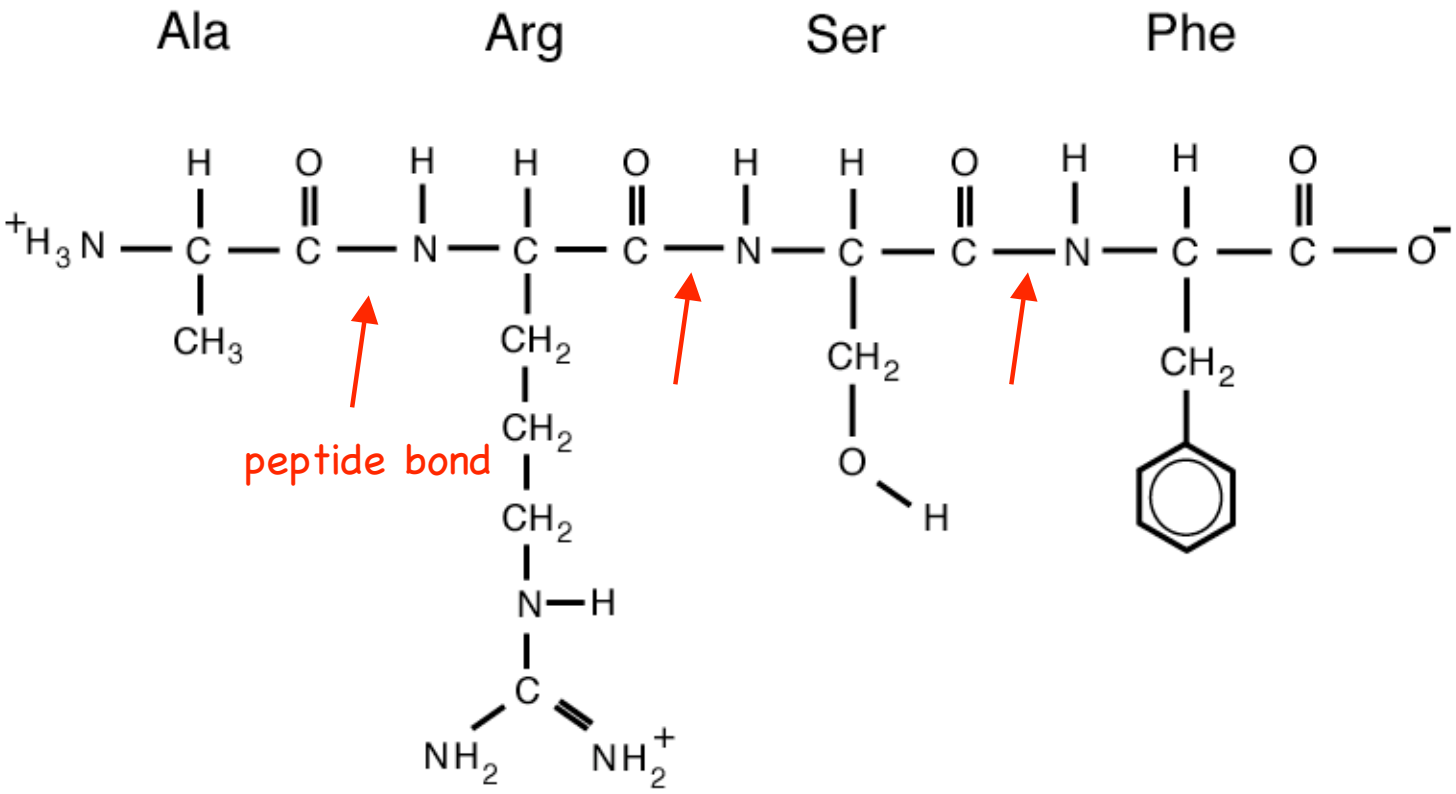
Tryptophan (Trp, W)



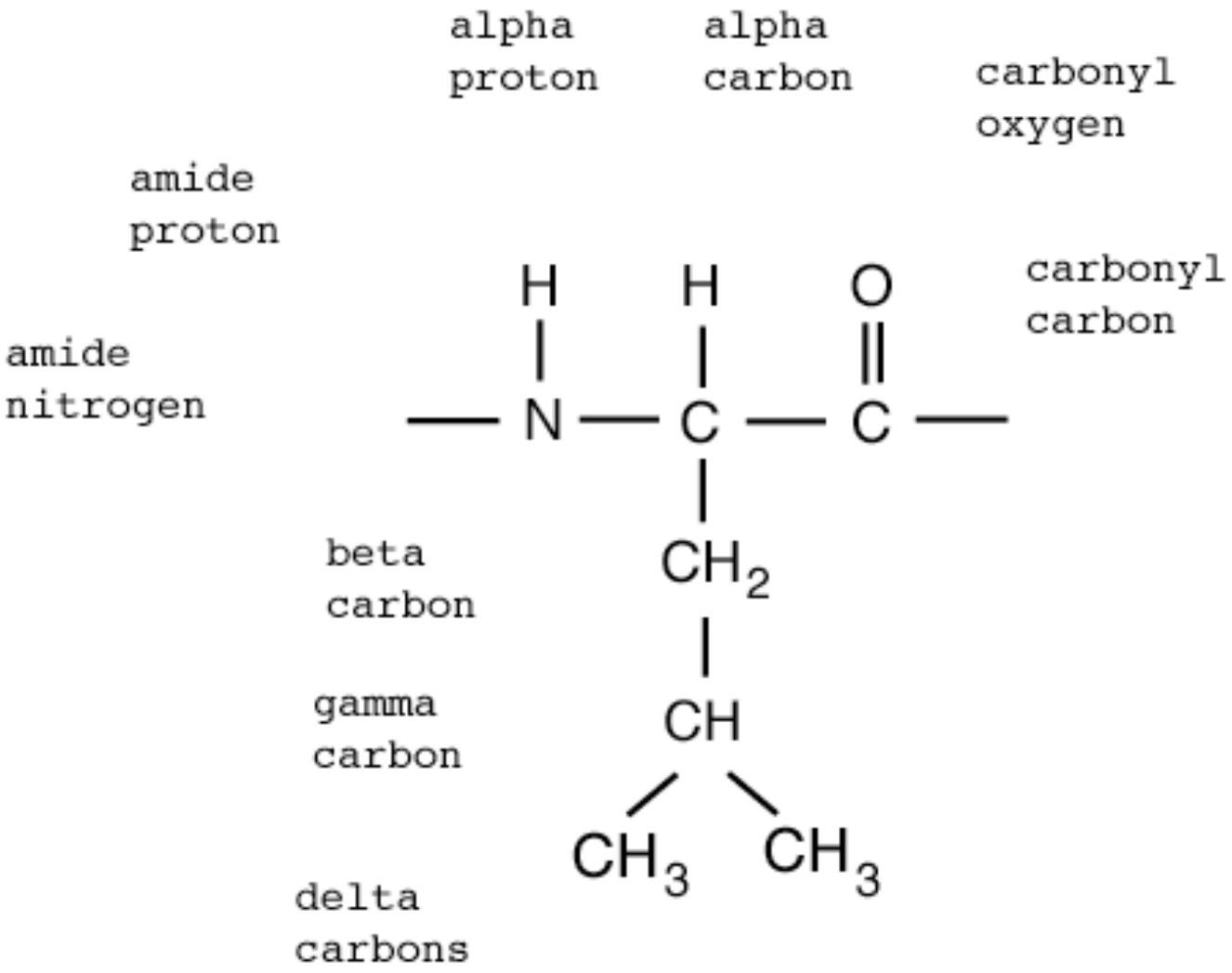
.... and glycine



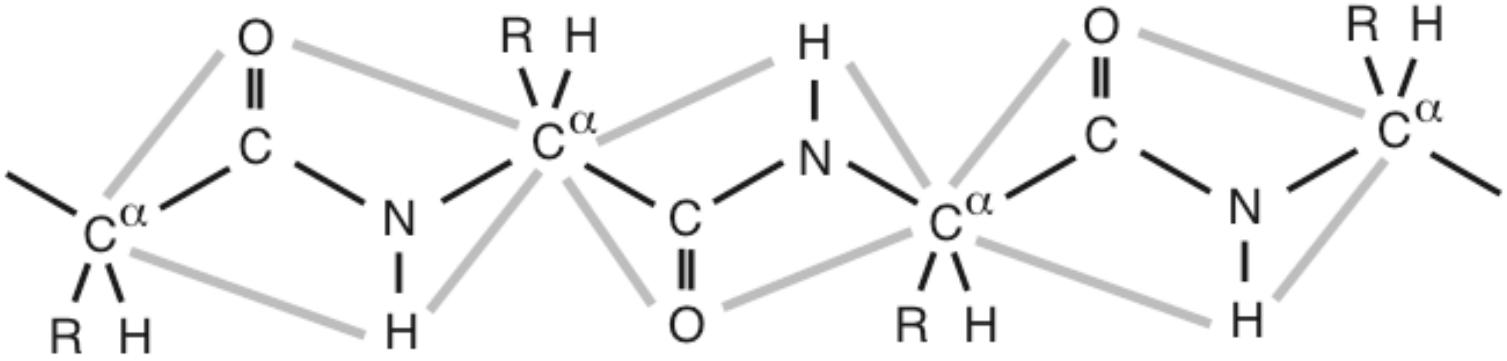
Linkage of amino acids in a protein.



Nomenclature

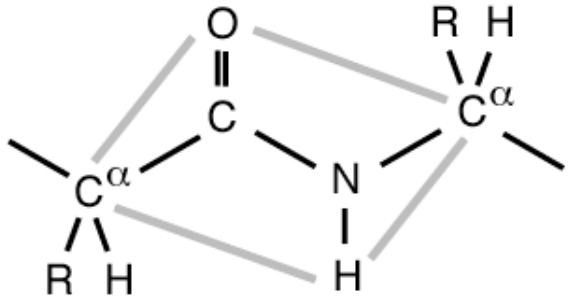


Planar units within peptides are relatively rigid due to partial double bond character of C - N bond.

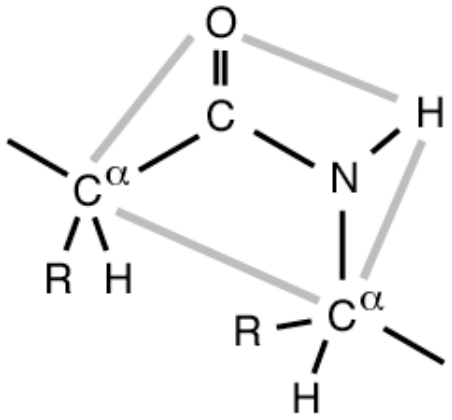


Peptide bonds can be cis or trans,
but within proteins are almost always trans.

trans



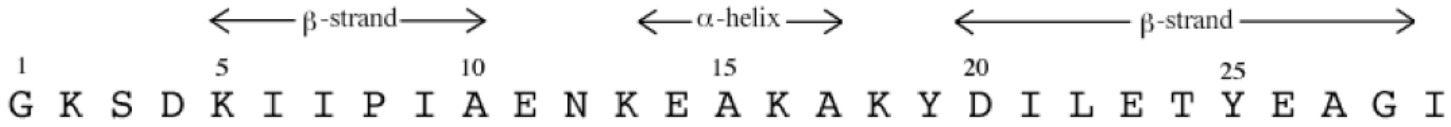
cis



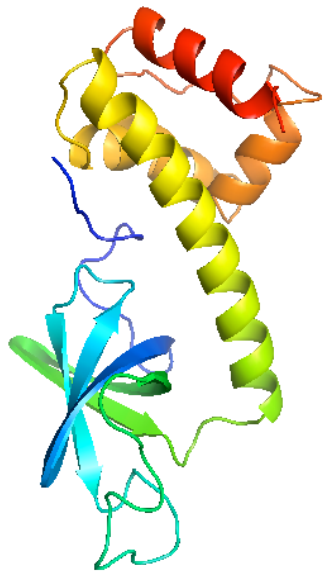
Primary, secondary, tertiary structure of proteins.

Primary structure is just the a.a. sequence.

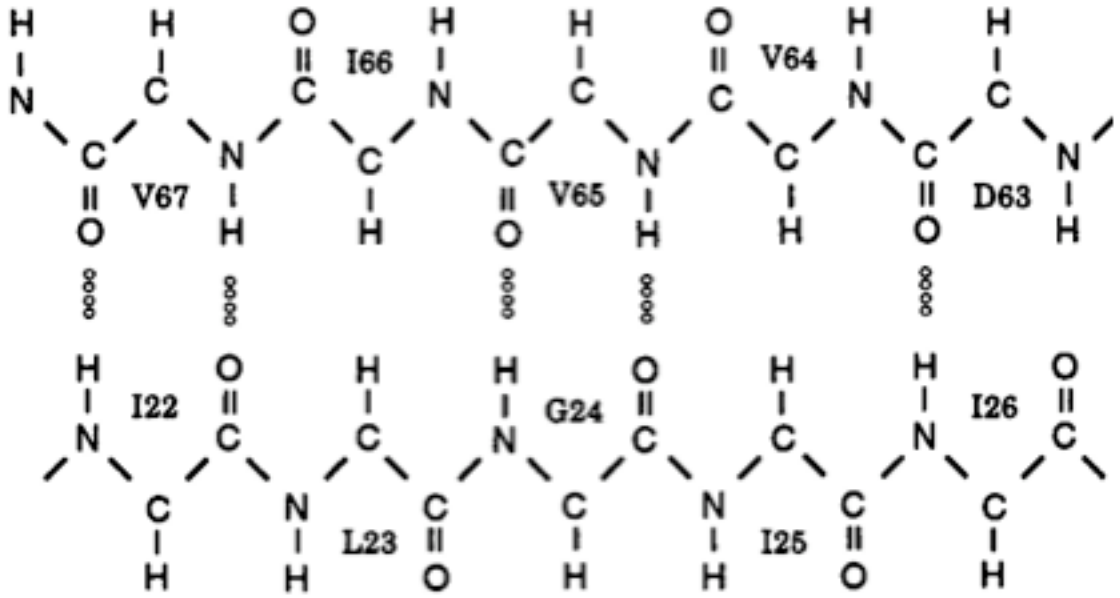
Secondary structure describes which parts of the protein are helices, beta strands, turns.

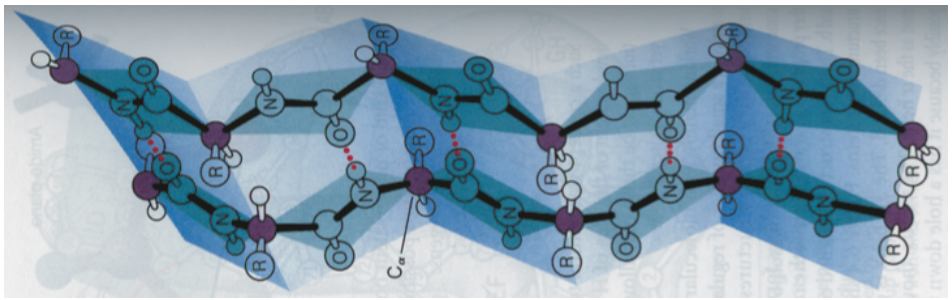


Tertiary structure describes 3-D fold.

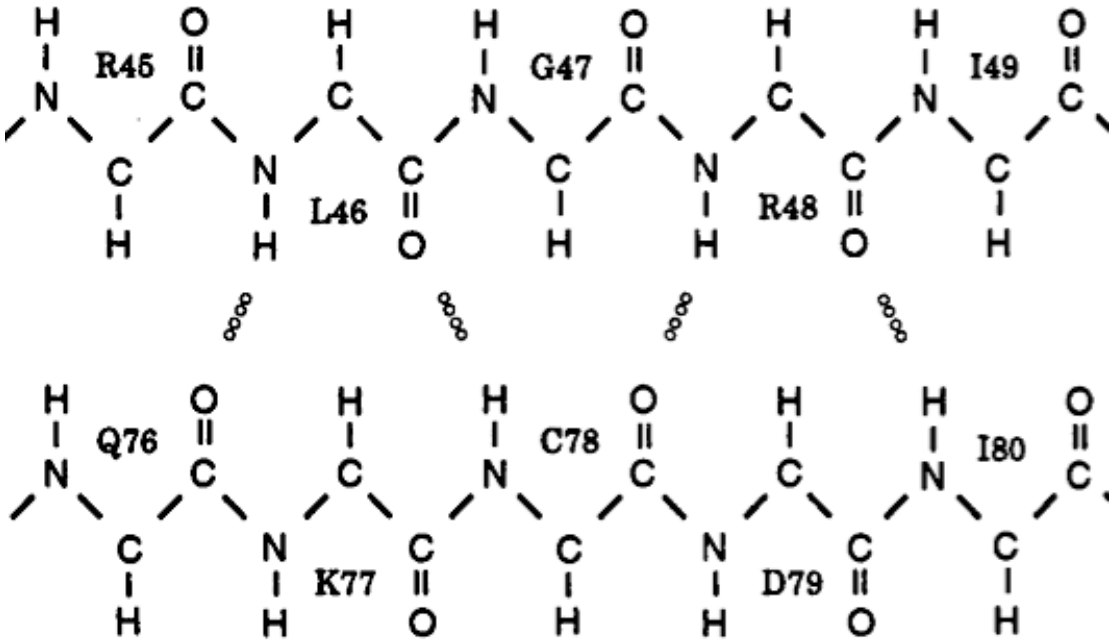


Anti-parallel beta strands





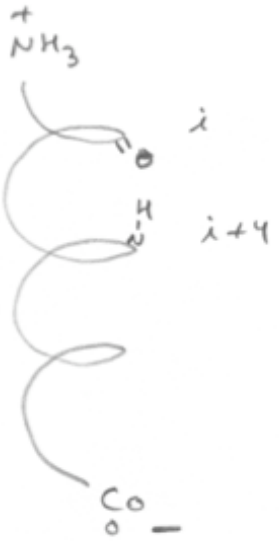
parallel beta strands

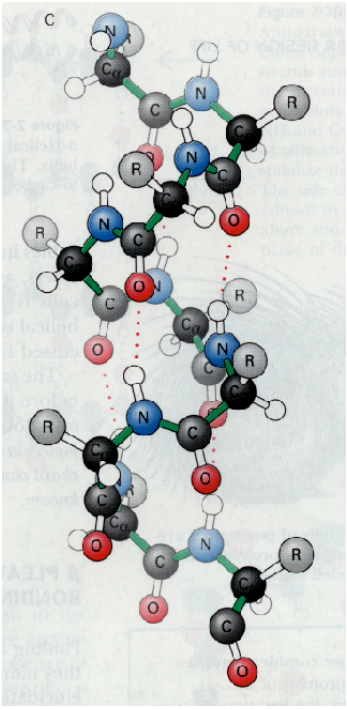


A quick look at α-helix:

a) stabilized by h-bonds between residue i & residue $i+4$

b) 3.6 residues per turn





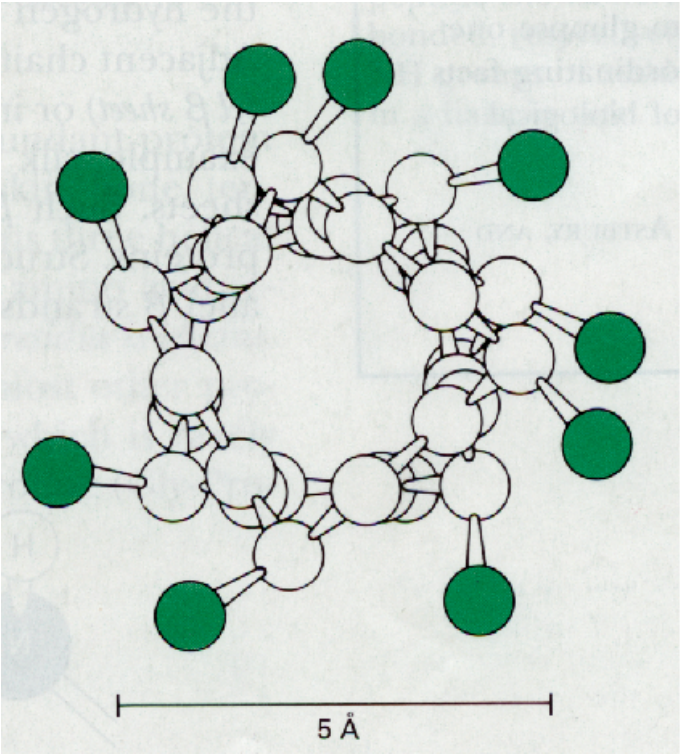
3_{10}-helix : h-bonds between residues

i & $i+3$

π-helix : h-bonds between residues

i & $i+5$

side chains are excluded from the interior of the helix.



"Helical wheel representations"

Consider a 20 a.a. peptide, which is assumed to be helical :

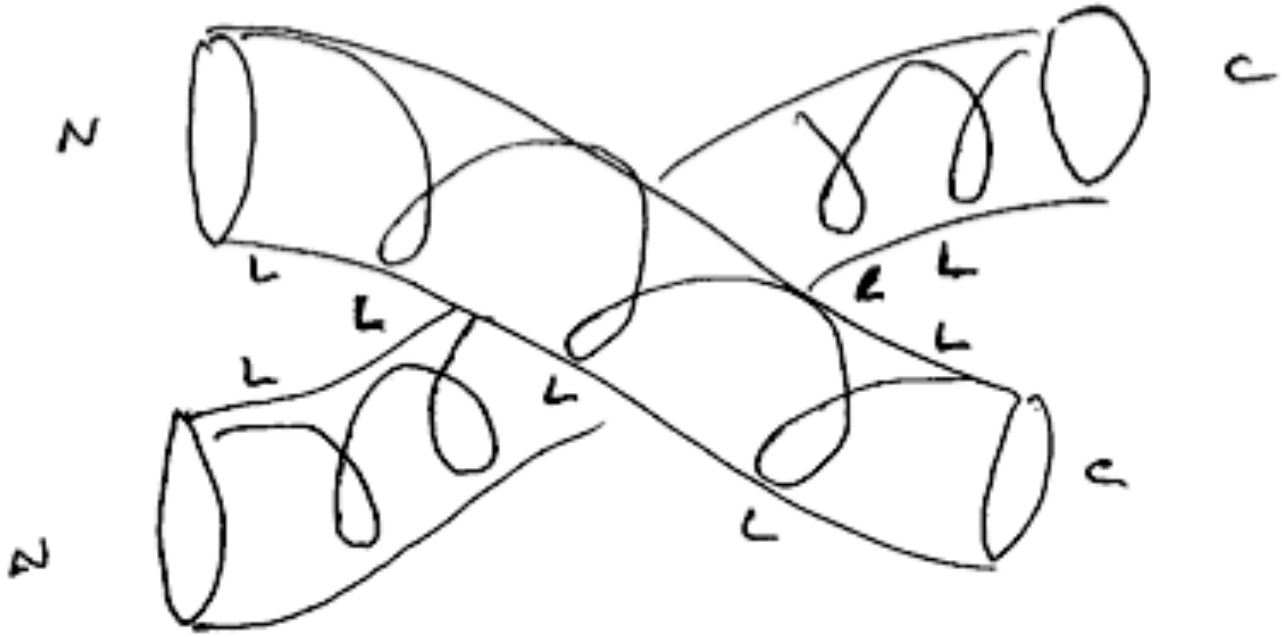
1 20

ELENF VRRLE TMNKQ LKSVI

Which a.a. are on the same side of the helix?

To answer this question, a "helical wheel diagram" can be helpful.

A “leucine zipper” is a fairly common structural motif formed by two helices:



Leucines are on one face of each helix. The “zipper” is stabilized by hydrophobic interactions between the leucines.