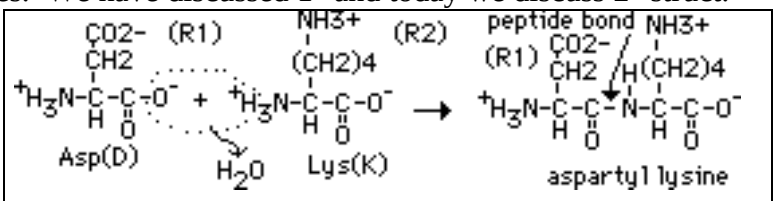
Chem 431A-L14-F'07
admin: Quiz #5 Wednesday (on chapt 3 material since quiz 4 + chapt 4 material covered today)

Last lecture:
We looked at the sequencing of amino acids:

Today: (1) we talk about peptide bond (Chapter 4 material)
(2) 2° structure – α-helix and β-sheet.
(3) Ramachandran plot (Ψ and ϕ)

(1) Recall the levels of structure of a protein:
1°(aa sequence), 2° struc, 3° and 4° structures. We have discussed 1° and today we discuss 2° struct.

How are the monomers bonded to each other? By a *peptide bond*. Consider the reaction of these amino acids when they combine to form peptides by condensation

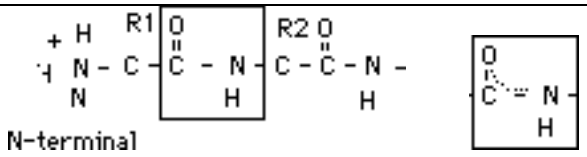


dipeptide "D K "formed by water elimination.

A *metastable* bond is formed called the peptide bond. ΔG is *negative* for its hydrolysis, but actual breakdown of the peptide bond is very slow (but can be speeded up if can be catalyzed by *proteases*). Protein synthesis requires energy in the form of GTP (plays similar role as ATP).

2) Peptide bond has a *partial double bond* character.

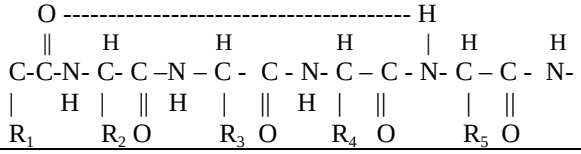
Linus Pauling (and Corey) analyzed the X-ray data from proteins (which indicated what the distances from C=O bonds and C-N are supposed to be and what they were in the peptide bond), Led him to conclude that the C-N bond was not a simple sigma-bond, but a partial pi bond as well. Consequence of this? A double bond character will make the C-N bond hard to rotate (like you can't rotate a double bond). note: C-N bondlength=1.32Å i.e. between 1.27Å(C=N) and 1.49Å(C-N) while C=O =1.24Å ie. between 122Å (C=O) and 143Å (C-O).



resonanace structure: partial double bond character of peptide bond makes it a *planar* structure with a resonance energy of 88kJ/mol; a twist of 10° involves a twist energy of $88\sin^2(10°)$ kJ/mol (NOTE: *trans* vs *cis*)

(3) **Ψ and ϕ :** It means that per residue, there are only 2 degrees of freedom: (1) the rotation between C_α carbon and it's N of the preceding peptide bond and (2) C_α carbon and the C of the next peptide bond. This constraint is important in limiting the possible structures that the polypeptide chain can fold into. The angles are called Ψ and ϕ. Ψ is the angle of rotation about the C_α-CO and ϕ is the angle of	rotation about the C_α-N bond. ** look at the structure of the protein chain: less flexible due to the presence of the peptide bond. ** the *trans* form of the peptide is usually favored. The cis form has bulky R groups of adjacent C_α's start to sterically interfere with each other. Except for case of proline where cis is more allowable (1:4 ratio) with trans still more favored.

4) secondary structure of polypeptide chains: we note that the constraints to the peptide bond don't allow it to rotate so easily. There are two regular structures that allow for the constraints and these are the ***alpha helix*** and the ***beta sheet***. Linus Pauling &Corey (Caltech) proposed the **α-helix**:	The alpha helix is a repeating structure (5.4Å repeat) with the ff parameters: Note: 3.6 residues per turn of the alpha helix. Draw the structure of a poly peptide and show which H-bond to form the α-helix. Note: 13 atoms from the O (H-bond receptor) to the H of the N (H-bond donor) It is ***right-handed***.



note that each peptide carboxyl is H-bonded to the NH group 4 residues up the chain. OK. α-helix is called (3.6_{13}) 3.6 residues per turn, 13 atoms in the H-bonded ring. 1.5Å rise/residue. so (1.5x3.6 = 5.4Å/turn. ignoring sidechains, diam is 6Å. Sidechains extend outward from the core structure of the helix. The α-helix is a right-handed helix.	note that the helix is stabilized by the combined effect of the H-bonds. One thing to be said about the DNA helix is that it is stabilized by many factors. when the base pairs are aligned and H-bonded, the DNA double strand is stabilized. but if you heat it up, it starts to vibrate until some T_m wherein, the first bonds are broken and the thing is quickly unravelled. like a crystal melting.

Here, α helix is also stabilized by the H bonds. between the residues which altho they are not neighbors in the 1° sense, are actually neighbors once the α helix is formed. there is stabilization forward and back. Max Perutz noted x-ray data that indicated α helix is found in α keratin (protein in hair) and is of	fundamental importance in protein structure in general. It is interesting to view the hair as being composed of helical strands of polypeptide chains. hair is mostly stretchable as would be expected. Look at the figures: (pages 121-122). Note that there is a strong dipole moment associated with α-helices.

(5) **Ramachandran Plots:**
Going back to the Ψ and ϕ angles: some of these angles are not favored because of steric crowding. If we could specify these angles for each C_α, we could determine the secondary structure of the polypeptide chain. If the angles are
We note that each of these possible 2° structures is characterized by a Ψ, ϕ. Angles Ψ=-45°to-50°, and ϕ=-60° correspond to α-helical structures. These are shown in the Ramachandran Plots which show allowable values.

Studies with polyamino acids (ie chains containing only one type of amino acid), show that some aa's tend to form α -helices more than others. such as polyA and polyL. These tend to spontaneously form α helices whereas polyE and polyD form random coils (at pHs where it is neg. charged) but at pHs where sidechains are neutral and protonated, they form α -helices. similarly, when poly K is neutral sidechains, the α helices form spontaneously. OK here are some rules of thumb about the tendency of sequences to form helices: (*read p 121-122 discussion*)

dipole moment: each peptide bond has a dipole moment. In a helical structure all the dipole moments point along the axis of the helix and there is a net dipole moment for the a helix itself. with + pole in the N-terminus and - pole in the carboxyl terminus end. Often ligands bind to ahelix structures in protein. negativelhy charged ligands often bind to the N terminal end. (but + ligands rarely bind to the c terminus)

Other less common helices: 3_{10} helix, etc.
Other common structure is the *beta sheet* (pleated sheet). Also proposed by Pauling and Corey in 1951. one can think of the β sheet as if it were a 2-fold helix (helix with only 2 residues/turn). We note that it represents the most extended conformation of the peptide chain. thus proteins with extensive β sheet structure are not very stretchable (like β -keratin in feathers and in silk).

There are actually 2 kinds of β sheet: *parallel* and *antiparallel*. Parallel tends to be more regular than the antiparallel sheet. parallel β sheets typically distribute H-phobic groups on both sides of the sheet while antiparallel tend to distribute H-phobic on one side and H-phillic on the other side.

some proteins have both α helix and β sheet structures within the same chain.
beta turn: (tight turns) -usually forced by Pro.

beta bulges occur between two normal beta structue with 2 residues in 1 strand and only 1 residue in the other.strand.

some general principles describing protein structure: folding of protein in 3 dimensions is called 3° structure. all the info need to fold the protein into its native tertiary structure is contained within the 1° structure of the peptide chain itself.

(denaturat'n of native proteins led to renaturation)
Some principles have become more apparent:

a) 2° struc (α and β struc) form whenever possble (result of extensive H-bond)

b) α -helices and β sheets tend to associate and pack close together in a protein.
c) segments between secondary structures tend to be short and uncomplicated
d) proteins fold to form most stable strucs possible. Stability of proteins arise from: *formation of large no's of intramolec H-bonds, and *reduction in this surface area accesible to solvent.

fibrous proteins: actually α keratin can be quite rigid due to lots of cross linking via Cys-Cys bonds. consists of a helices arranged in coiled coils which are arranged in pairs to form protofilaments which form the filaments (made up of 4 protofilaments).

collagen= triple helix.=rigid inextensible in connective tissue including tendos cartilage, bones, teeth, skin, blood vessels. strength of the collagen allows us to do high impact activities like jogging, running, jumping. Basic structure is tropocollagen, 3ple helix.