Chapter 2 continued

no-sharing of electrons

Noncovalent Bonds in polypeptide folding

- amino acids can form a variety of non-covalent bonds that influence how polypeptides fold all weaker than covalent

- **Van der Waals:**
  - weak weakest
  - caused by momentary dipole moments, fleeting charges that unequally move
  - collectively can be strong

fleeting

weakest

- **Hydrophobic Effect:**
  - not really a bond as in attraction, but a repulsion repulsion from water
  - hydrophobic, water fearing, groups clump together to get away from polar solvents

H_2O

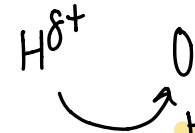
- **Electrostatic:** polar-covalent partial or full charges
  - strongest non-covalent bond
  - ionized groups will have full positive or negative charges permanent charges, not changing
  - opposites attract + likes repel

permanent

ex Na^+ Cl^-
ionic bond

strongest

- **Hydrogen Bonds:**
  - type of electrostatic bond where groups are not ionized but have dipole moments
  - an electronegative (N, O) draws electrons away from an electropositive atom (C, H) to create a partial charge δ^+ δ^-
  - partially positive H is attracted to partially or fully negative O



Hydrogen Bond Donor (N-H group)

Hydrogen Bond Acceptor (C=O group)

all peptides = amides
not all amides = peptides

2.23 Special Properties of Peptide Bonds

- peptide bonds are rigid + planar (type of amide bond)
  - bond between C + N no rotation
  - planar in C, O, H, N all 2D

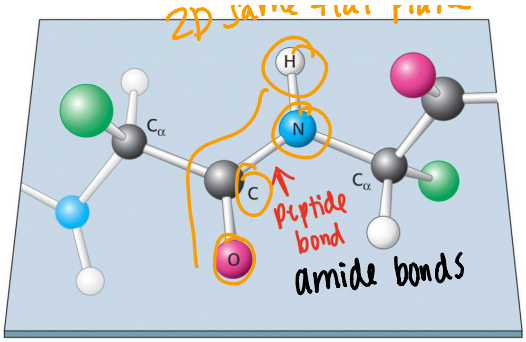
not a single but not double bond
↳ can rotate ↳ cannot rotate

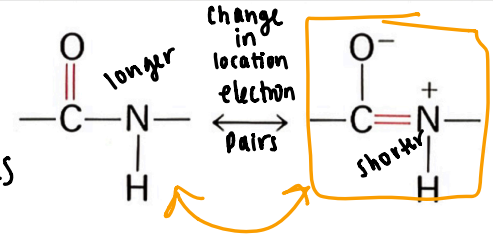
- rigid nature due to resonance double bond character

same flat plane

- provides partial single/double bond character
- this prevents rotation
- limits # of 3D configurations the polypeptide can fold into
- the peptide bond is shorter than single bond but longer than double
- resonance state = locked in rigid
  - flips back and forth

all aa linked by peptide bonds





The Four Levels of Protein Structure

Primary — all polypep

- every polypeptide / protein has a primary structure
- simply the amino acid sequence in order from N → C terminus
  - positive + negative ends
  - each AA = residue

Secondary (only H bonds)

- optional structure, doesn't always form
- folding of the polypeptide chain only by hydrogen bonds between main chain groups (H + backbone)
  - two types = α helix, β sheets — only backbone

Tertiary — backbone + R groups — all polypep

- every polypeptide folds into tertiary
- folding the polypeptide into its final 3D form
- this also involves the R groups as well as the main chain
- if it is functional here, then it is the final form + a functional protein

Quartenary

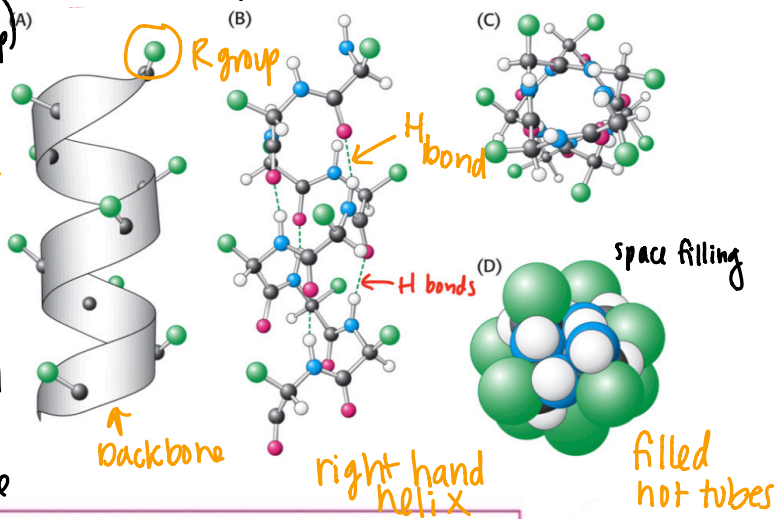
- two or more tertiary peptides together as one unit
- individual polypeptides are the subunits of the protein — don't work alone
- subunits can be held together by covalent or non-covalent bonds
- homomeric (homodimer) = same 2 all polypeptide subunits are the same
- heteromeric (heterodimer) = diff 2 if there are two or more kinds of polypep subunits in the functional protein

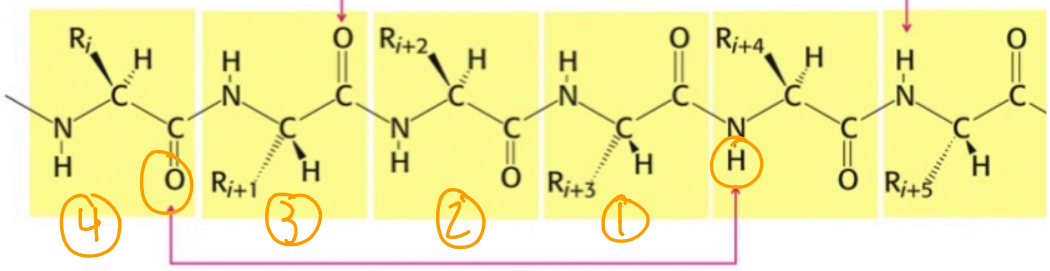
(only H-bonds)

2.29 + 2.30 Secondary Structure α helix

Alpha Helicies (only 1 polypep)

- α-helicies form by hydrogen bonds at backbone
  - H of peptide bond group interacts with O of another group 4 amino acids away
- proline does not fit in well (could be at start or end)
- α helix is one polypeptide chain on itself





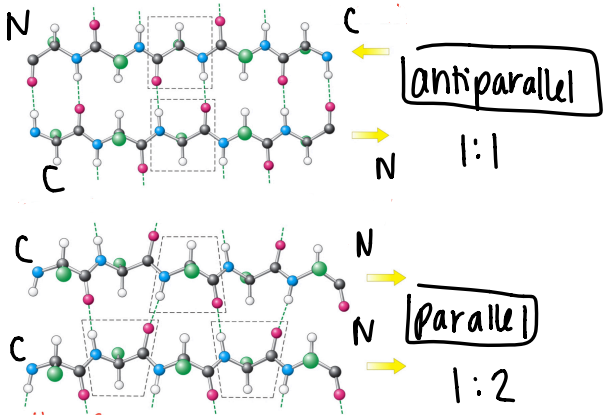
- R groups either hydrophobic/hydrophillic on a section of the polypeptide chain determine if it will fold into this form or not

2.36 + 2.37 β-Sheets

primary structure determines if it will form or not

Beta sheets

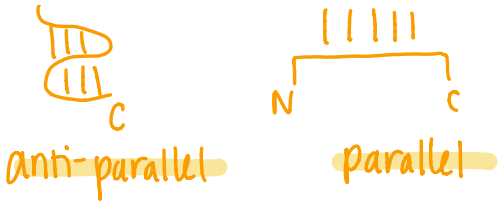
- β-sheets are a very open type of secondary structure
- held together by Hydrogen Bonds between the main chain groups that are far apart in primary sequence
- can be two polypeptides or one
- can be parallel or antiparallel C–N or N–C
- flat structures, not rigid, flexible



Intra

Inter

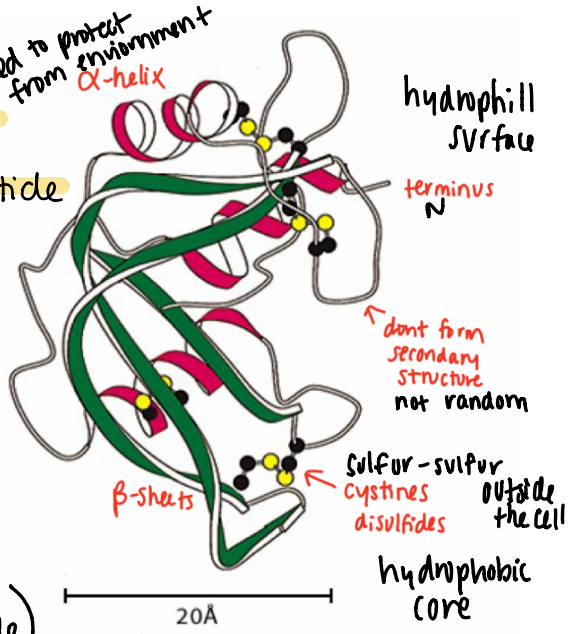
- R groups determine if β-sheet will form or not
  - bonds between H-donors + H-acceptors
  - β turns = twists in sheets stabalized by H-bonds



Tertiary Structure

driving force is hydrophobic interactions

- Final folded 3-D form of polypeptide
- If it is the functional form then it is a protein
- this example is RNase A that degrades RNA
- has both α-helix + β-sheet
- some regions without secondary structure

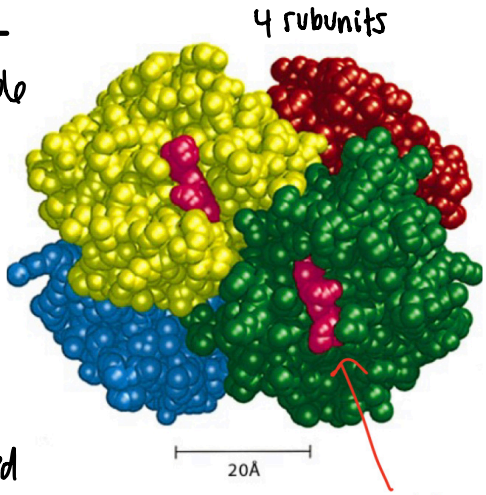


(van der waals interactions inside)

(Hbonds, Ionic Bonds)

Quarternary Structure

- many proteins consist of multiple polypeptides
- such proteins have quarternary structure
- each polypeptide is a subunit
- this example is hemoglobin which consits of four subunits
- the individual subunits have limited or no function by themselves
- held together by Van der Waals disulfide ionic bonds



a non-protein group forming part of or combined with a protein

Chapter 1 Portrait of Allosteric Proteins

- Allosteric: different shapes have different functions
- building a molecular computer with a few billion years of evolution
  - ↳ all random mutations through evolution (physiological need for biochemistry) needs to vary
- In response to physiological changes / needs in the body
  - ↳ how does change in hemoglobins structure change its affinity for oxygen

lungs
hemoglobins affinity for O_2 is highest

peripherial tissues
hemoglobins affinity for O_2 is lowered

Hemoglobin + Myoglobin

carry / storage

- Hemoglobin = transporter protein in RBCs carries oxygen
  also involved in transport of CO_2 + protons
  - can vary its affinity
  - red protein
  - not an enzyme
- Myoglobin = stores oxygen in fast twitch muscle tissue
  keeps it available for quick sprint activity
  - does not vary its affinity, fast twitch muscle

Why are they good model allosteric proteins?

① both complete 3-D tertiary structures that are known
- 1st proteins whose atoms positions have been determined

② Myoglobin is structurally a subunit of hemoglobin
- hemoglobin is an allosterically regulated heterotetramer (different subunits)

(↗ has extra stuff)

Allosteric Regulation

- allosteric regulation = binding of one ligand at one site influences the binding of another ligand at another site

→ one molecule binding to a protein at site A controlls the affinity

of another site B⁰ on the same protein

- the second site may bind the same ligand or a different one, in this way the protein can vary its binding of molecules based off of different parameters

evolutionary driven

- substrate connection
- product concentration
- pH

} binding influences function later

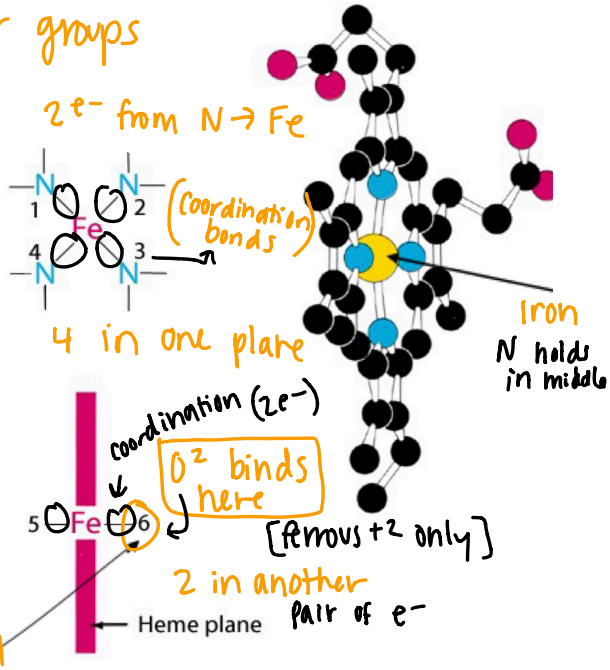
example: hemoglobin

- ↑ BPG binding → drop affinity for O_2 binding
- ↑ CO_2 binding → drop affinity for O_2
- ↑ ionization (H^+) → drop affinity for O_2

Heme Groups

helper groups

- heme: a prostetic group a non-protein segment needed for function
  - protein w/out a prosthetic group is apoprotein



- heme contains Fe ion
  - +2 (ferrous) can bind O_2
  - +3 (ferric) cannot bind O_2
  - Fe has 6 coordination sites
    - O_2 binds in 6th

6 e⁻ can be put into orbitals

- contains preforin ring = holds metal ions in the middle

6 coordination bonds

iron w/ partially filled orbitals have coordination bonds = both e⁻ from one atom (N)

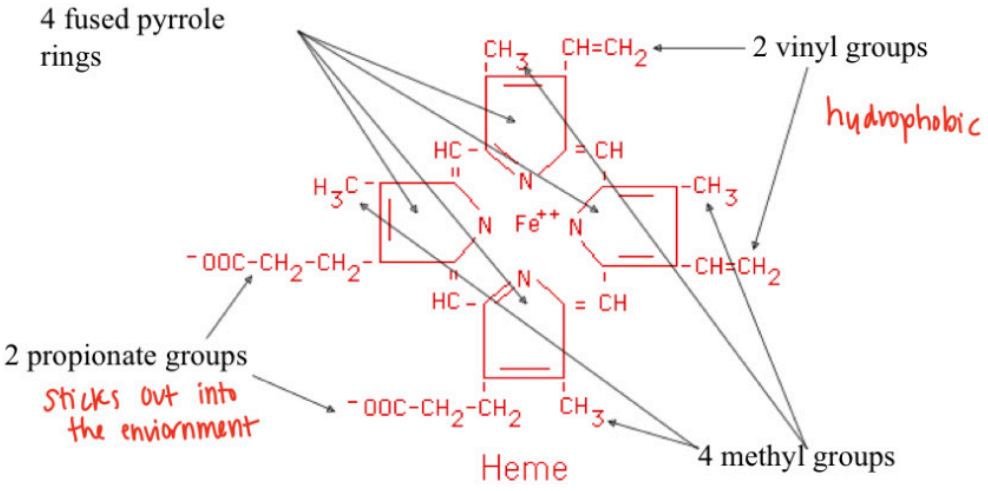
covalent = sharing e⁻
coordination = share 2e⁻

Heme Structure:

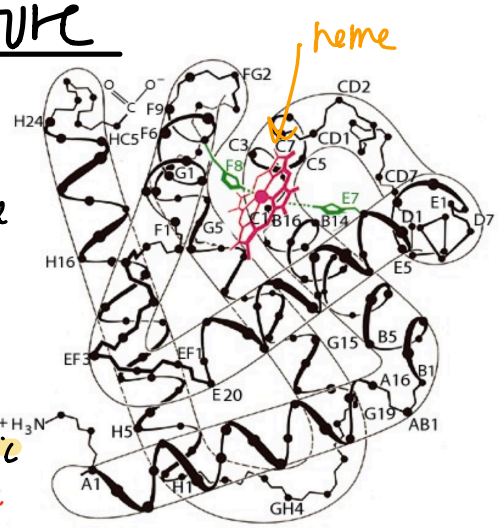
- dont memorize

toaster analogy

preforin ring = toast
myoglobin = slot



Myoglobin 3-D Structure



- Single polypeptide chain in tertiary structure
- very compact, little empty space
- 75% is folded into α helicies 8 total (A-H)
- 4 helicies broken by prolines
- all interior residues are hydrophobic
  - except 2 histidines that are hydrophillic
- the heme is oriented so 2 propionate groups stick out of the top of the cleft
- outside is polar/non mixed hydrophob/phil

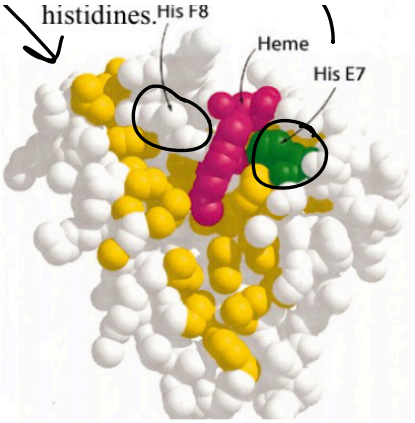
The internal Histidines create a "hindered heme"

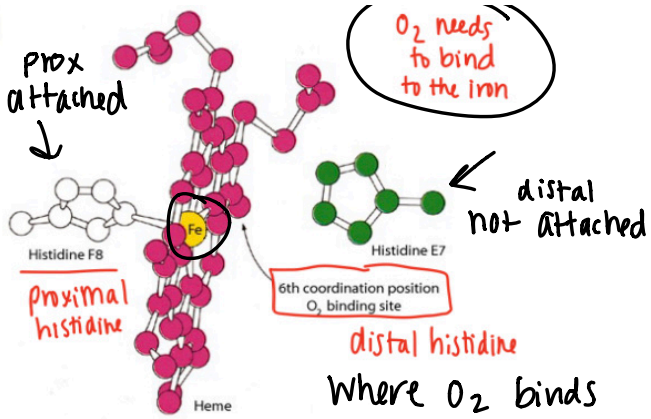
- The cleft in which the heme group sits is lined w/ non-polar residues except the two histidines

non-polar hydrophobic residues

Polar hydrophillic histidines

- One his (F8 proximal) is coordinated to the 5th site on the iron ion. The other is (E7 distal) is near 6th position but not bonded





AK Lectures: Biochem

#18, 19, 20, 21, 22