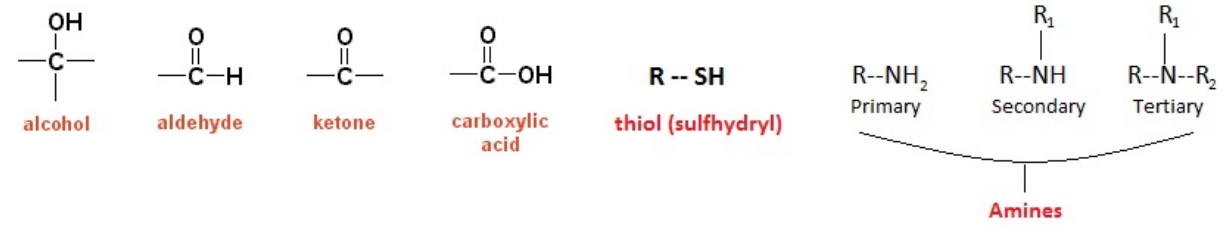
Know Kinds of bonds

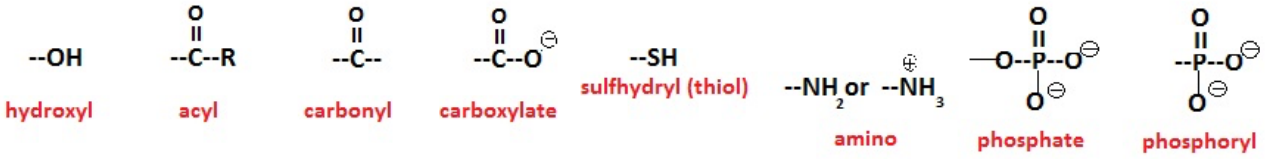
Important Background Material

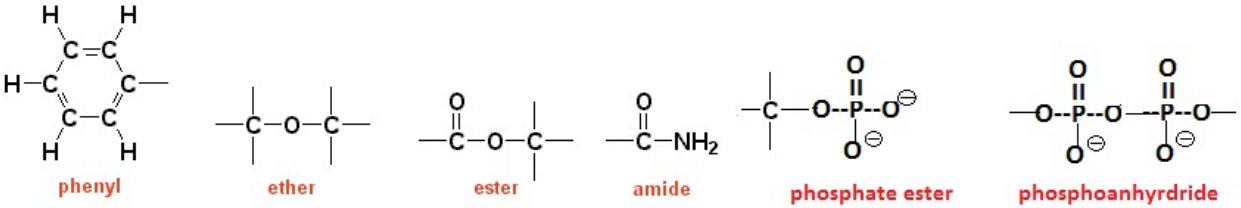
(a) *Organic Compounds*



(b) *Functional groups*

Write them out + draw them reacting w/ condensation





(c) *Linkages in biochemical compounds*

amino acids = amide bonds

Chapter 2
Protein Structure and Function

- It's all in the R groups

structure ↷ function

Protein Functions in Biological Systems

macromolecule

- Enzymes
  - Most enzymes are proteins
    - Act as catalysts to increase rates of reaction
- Transport and Storage
  - Small molecules are often carried by proteins
    - Oxygen by hemoglobin, iron by transferrin
- Movement
  - Proteins are the motors for both large scale (ie muscle) and small scale (ie cytoskeletal) movement.
- Mechanical Support
  - Proteins play major roles in providing structure in multi-cellular organisms

(RNA also)

v diverse in structure why?
↳ 20 diff AA in many combos

accelerate rate (faster)

multicellular organisms need to transport to organs tissues

Movement a meter or more within body

microtubules, actin, myosin all proteins

ECM + basement membrane to bone

connective tissue protiens
= collagen (3 helix rope)

soup stock
denatured collagen

Protein Functions in Biological Systems

- Immune Protection — antibodies, receptors
  - Immune system function is based on the use of proteins as receptors for binding foreign molecules
- Nerve Impulses — animals use nervous system (gpcrs)
  - Gated protein channels serve to initiate and propagate nerve impulses
- Control of Growth and Differentiation
  - Proteins act as receptors for molecules controlling cell development, regulators of metabolic activity and regulators of gene expression.

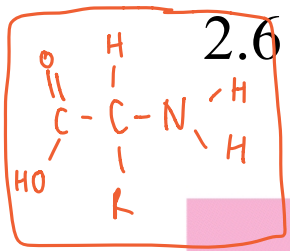
multicellular organisms

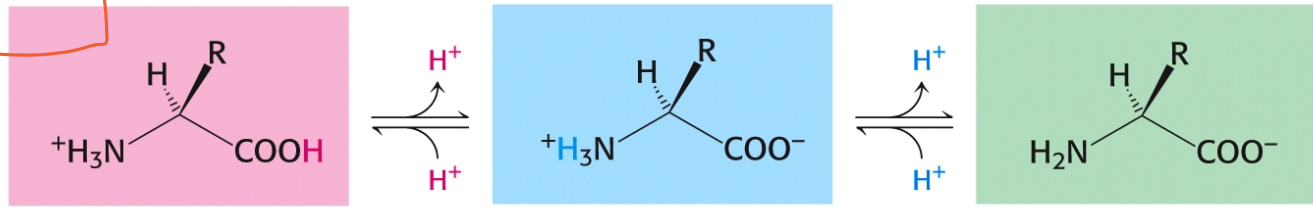
proteins drive gene expression regulation

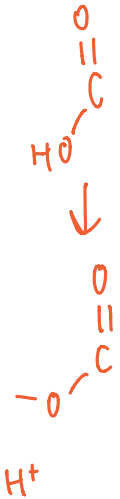
Proteins can do this bc of their diverse structure

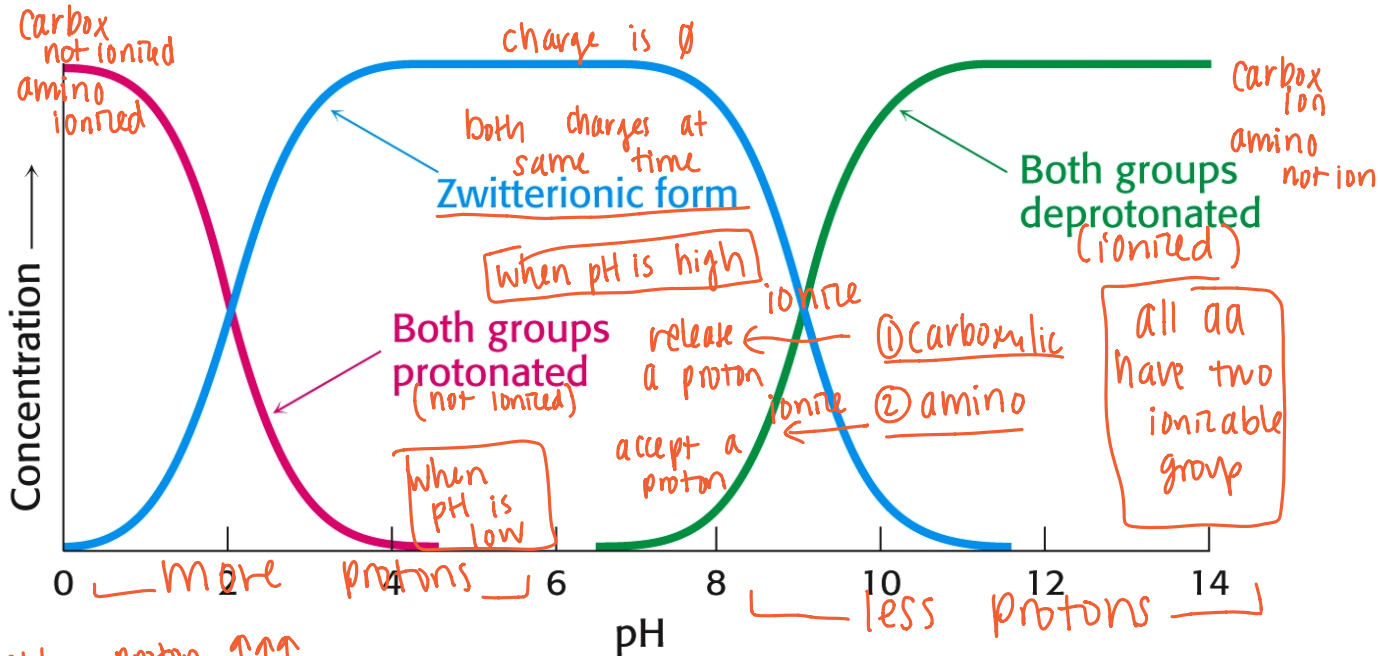
every AA has same structure C, H, amino, carboxyl and an R group

2.6 The α Amino and Carboxylic Acid groups of amino acids can ionize





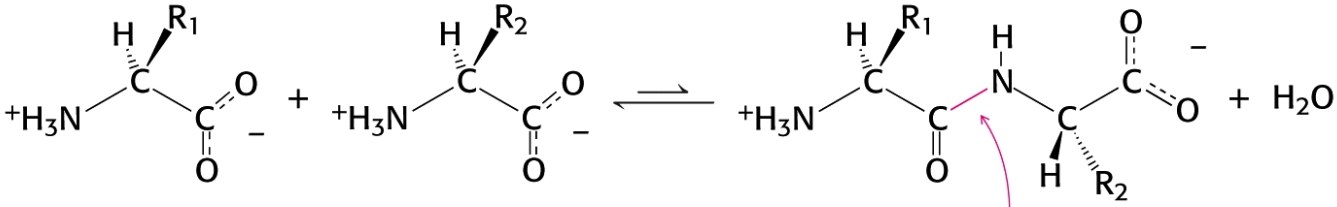




low pH proton ↑↑↑
high pH protons ↓↓↓

Changing of pH to get a reaction to occur

2.18, 2.20 Amino acids are linked via amide linkages known as peptide bonds

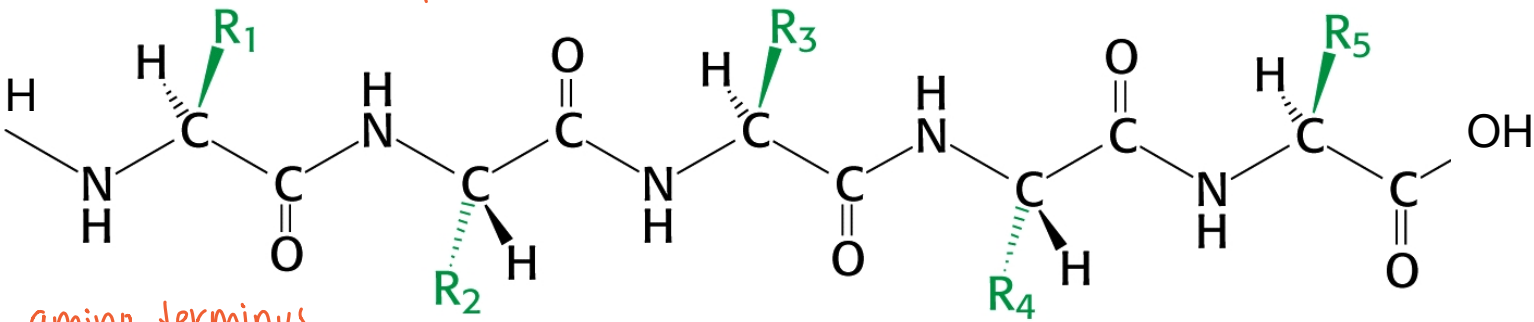


amino - carboxyl condensation reaction

amide bonds

- Amide bonds - reaction of an amino group and a carboxylic acid group.
- Amide between two amino acids - peptide bond.
- Polypeptide has N and C termini

1st → last



amino terminus

"Start" of polypeptide

carboxyl terminus

"End" of polypeptide

polarity = two diff sides not charge

Diversity within R groups

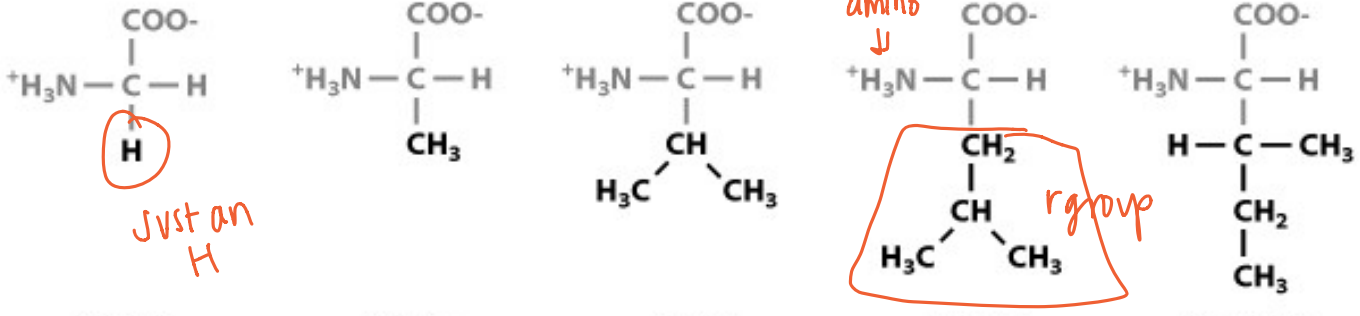
Polypeptide structure controls function

- The sequence of amino acids in the polypeptides controls what shape it folds into.
  - Different AAs have different properties based on their R groups
    - Aliphatics - hydrophobic (carbons + hydrogens)
    - Aromatics - contain phenyl rings, unusual electron properties (benzene rings)
    - Sulfur containing - have S in their side chains
    - Aliphatic hydroxyls - more hydrophilic than the aliphatics (add an OH to it)
    - Basic - side chains with ionizable amine groups
    - Acidic - side chains with carboxyl groups
      - Amide derivatives - the caboxyl has an amine attached to it
      - Cannot ionize but still hydrophillic

Aliphatic Amino Acids

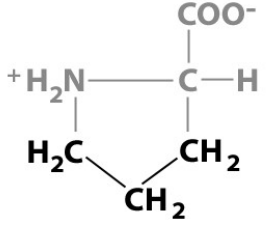
very hydrophobic

don't need to memorize side chain structures



Glycine (Gly, G) | **Alanine (Ala, A)** | **Valine (Val, V)** | **Leucine (Leu, L)** | **Isoleucine (Ile, I)**

- Glycine is the smallest amino acid
- Proline has its side chain linked back to its a amino group.
- a secondary amine or an imine.
- limits folding of polypeptide at that point



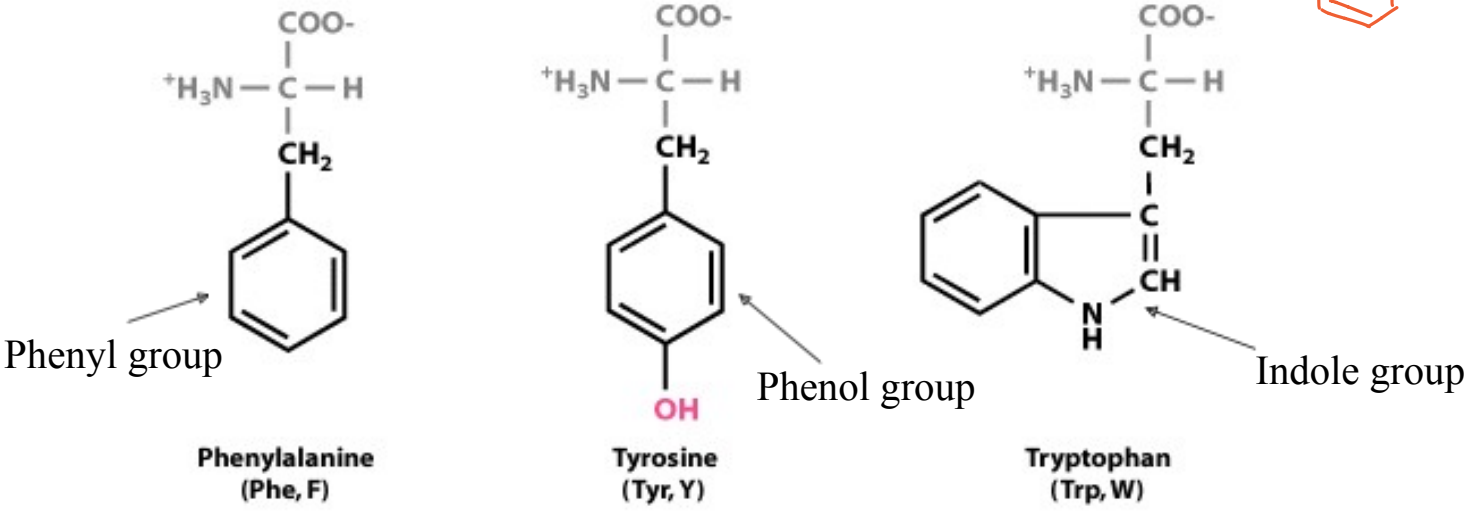
Proline (Pro, P)

2° amine

pretty hydrophobic

2.10 Aromatic Amino Acids

have a benzene ring



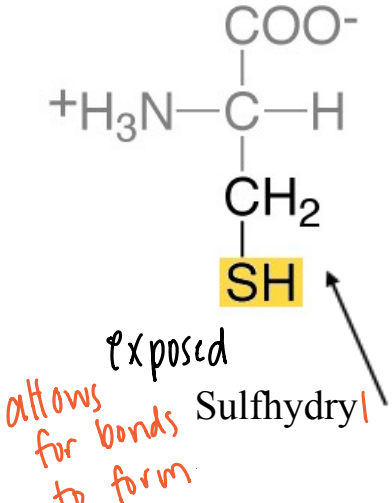
hydroxyl derivative

-A phenyl ring has delocalized π electrons. This allows for certain types of electron transfer reactions and non-covalent bond formation with other

π electron systems.

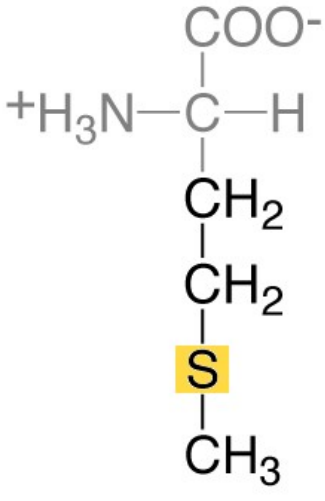
Sulfur Containing Amino Acids

- Somewhat hydrophobic
- Sulfur in methionine not highly reactive
- Sulfhydryl group in cysteine can be reactive



Cysteine
(Cys, C)

important structure

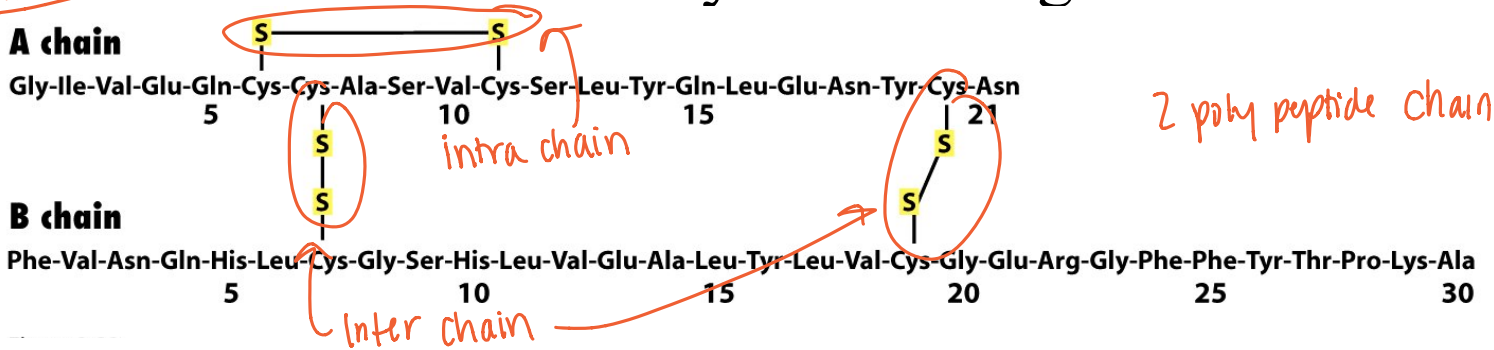


Methionine
(Met, M)

2.21, 2.22 Cysteines can interact to form a covalent cystine linkage

insulin

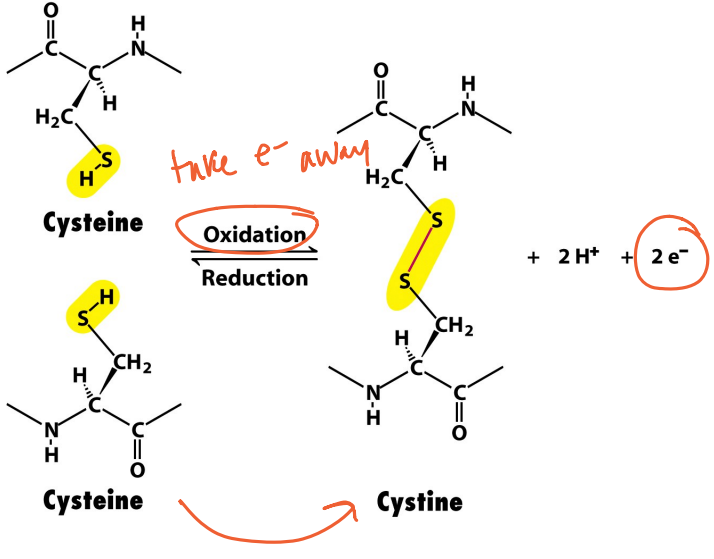
ox-reduct rxn



disulfides

SH

- Two cysteines can be oxidized to form a cystine covalent linkage
- Important in polypeptide structure
- Typically found in extra-cellular proteins

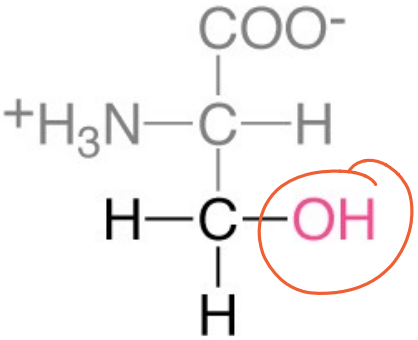


not inside cells because they think its damage

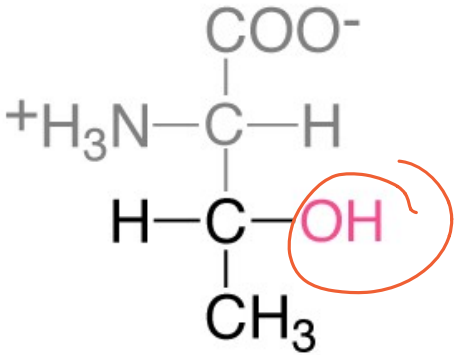
2.11 Aliphatic Hydroxyl Amino Acids

- Have hydroxyl groups
- Hydrophilic, but not acidic at physiological pH, side chains

ionization point is high for these



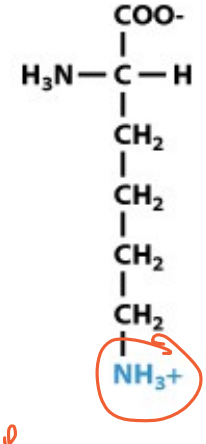
Serine (Ser, S)



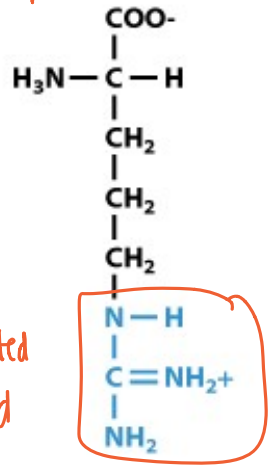
Threonine (Thr, T)

add a hydroxyl group

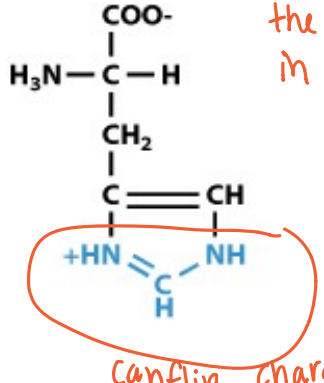
2.14 Basic Amino Acids



Lysine
(Lys, K)



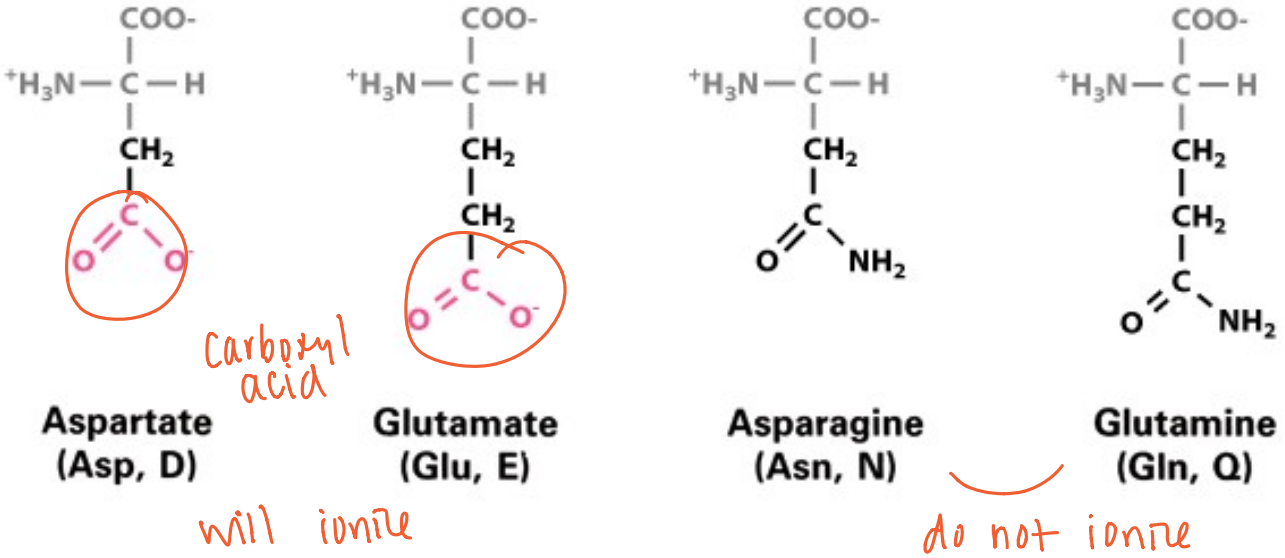
Arginine
(Arg, R)



Histidine
(His, H)

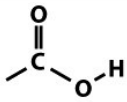
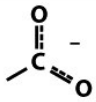
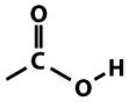
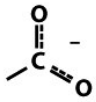
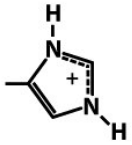
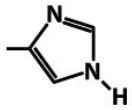
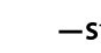
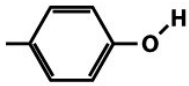
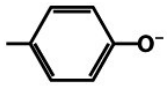
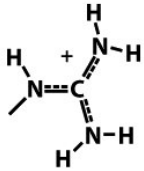
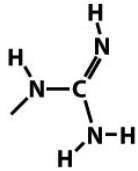
- Basic amino acids all have ionizable groups
- (amino for lysine, guanidinium for arginine and an imidazole group for histidine)
- highly hydrophilic

2.12, 2.16 Acidic Amino Acids And Derivatives



- Aspartate and glutamate have ionizable carboxyl acid groups
- There are two amide derivatives of these amino acids, asparagine and glutamine.
  - These are carboxamide groups
    - Carboxylic acid and an amino group
  - Carboxamide groups are not ionizable

TABLE 2.1 Typical pK_a values of ionizable groups in proteins

Group	Acid	⇌	Base	Typical pK_a*
Terminal α-carboxyl group		⇌		3.1
Aspartic acid Glutamic acid		⇌		4.1
Histidine		⇌		6.0
Terminal α-amino group		⇌		8.0
Cysteine		⇌		8.3
Tyrosine		⇌		10.9
Lysine		⇌		10.8
Arginine		⇌		12.5

*pK_a values depend on temperature, ionic strength, and the microenvironment of the ionizable group.

Know how to use it + what it means

Aspartic acid / Glutamic acid — acid

Histidine

Lysine — base

Terminal α-amino group

Cysteine

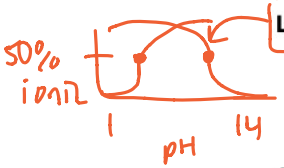
Tyrosine

Arginine

Ionize

acids → release proton

bases → accept protons



more protons
bases = ionized
acid = deionized

less protons
bases = unionized
acid = ionized

pK = pH @ when 50% were ionized

Why do we care?

enzymes manip pH @ active site to make groups change + cause catalysis

epsilon amino group

deprot based = unionized

deprot acid = ionized

partial or full charges

Noncovalent bonds in polypeptide folding

(no sharing of electrons)

all weaker than covalent

- Amino acids can form a variety of non-covalent bonds that influence how polypeptides fold
  - Van der Waals — weakest
    - Weak interaction
    - Caused by momentary dipole on atoms when more electrons happen to be on one or the other side of the nucleus

unequal moment

fleeting charges

in numbers collectively can be strong

  - Hydrophobic Effect — not a force
    - Not really a bond in that it is not an attraction but a repulsion
    - Hydrophobic groups clump together to get away from polar solvents.
  - Electrostatic — can it interact with water
    - Ionized groups have full positive or negative charges. Oppositely charged groups will attract while like charges repel. This is the strongest type of non-covalent bond

$O^{\ominus}$

partial/full charges

permanent charges

fully pos + fully negative

$(Na^{+}Cl^{-})$

ionic bond

protein hydrophobic R groups

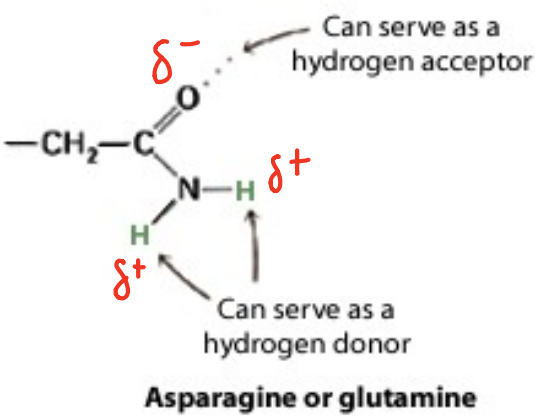
- hydrogen bond are electrostatic but ⊕ is H with a δ+ is attracted to δ- or ⊖ bond

Noncovalent bonds in polypeptide folding

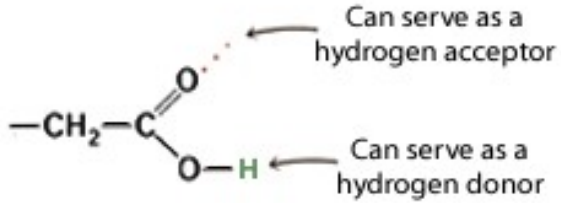
polypeptide bonds have hydrogen bonds

- Hydrogen bonds
  - A type of electrostatic bond in which the groups are not ionized but instead have dipole moments
  - An electronegative atom, N or O, draws electrons away from an electropositive atom (C or H) creating a partial charge.
    - partial charge denoted as d+ or d-
  - Partially positive H is attracted to partially or fully negative O
    - The d+ H is the Hydrogen bond donor and the d- O is the Hydrogen bond acceptor

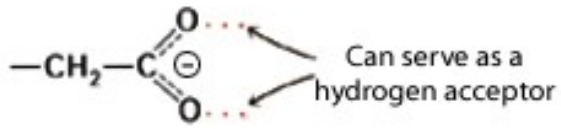
Hydrogen Bonding in Amino Acids



Asparagine or glutamine



Protonated form of aspartic or glutamic acid



Ionized form of aspartic or glutamic acid

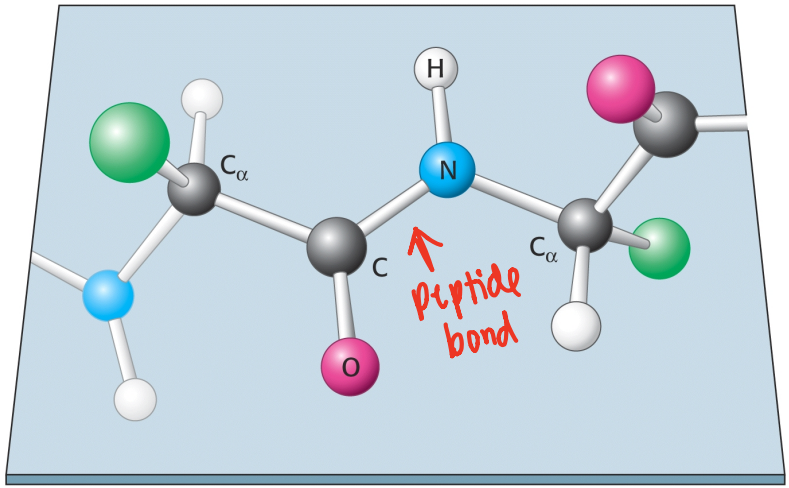
δ^+ = hydrogen donor

δ^- or ⊖ = hydrogen bond acceptor

fully ionized

2.23 Peptide bonds have special properties

doesn't act as a single bond but not a double bond either

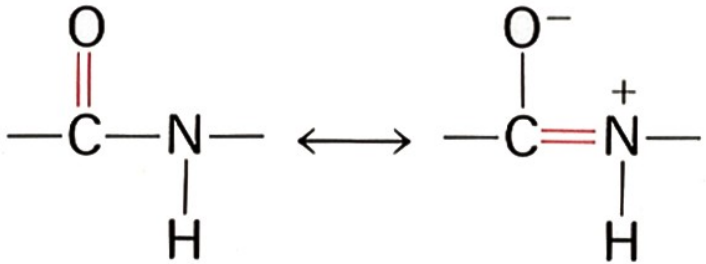


-Peptide bond is rigid and planar
- Rigid in that bond between C and N does not allow for rotation
- Planar in that C O N H atoms are all in one 2-D plane

-Rigid nature due to resonance
- Provides a partial double-bond character
- Prevents rotation

-This limits the number of 3-D configurations a polypeptide can fold into.

what does that mean?



amides = C + N is shorter than C + N single bond but longer than double bond

flip back n forth

resonance state can't rotate

limits number of confia polypeptide

can fold into

The four levels of protein structure

- Primary — every polypeptide/protein has a primary structure
  - This is the amino acid sequence from the N to the C terminus — order aa are put together
- Secondary (optional)
  - Folding of the polypeptide chain that only involved hydrogen bonds between main chain groups — H + backbone
    - a helix
    - b sheet
- Tertiary — every polypepide folds into tertiary structure
  - Folding the polypeptide into its final 3-D form
  - This involves R-groups as well as main chain groups
  - If this is the functional form then the polypeptide is the protein — H + backbone + R groups + ect.

protein = functional at this point

The four levels of protein structure

- Quarternary

Primary or tertiary?

Subunits dont work individually

– Some proteins consist of two or more polypeptides together as one unit

– This is quarternary structure

  - The polypeptides are thus subunits of the protein
  - The subunits may be held together by non-covalent or by covalent bonds or both

– If all the polypeptides in the protein are identical it is then homomeric (ie homo-dimer, etc).

all same subunits

– If there are 2 or more kinds of different subunits in one protein then it is heteromeric (ie heterotrimer)

more than one subunit

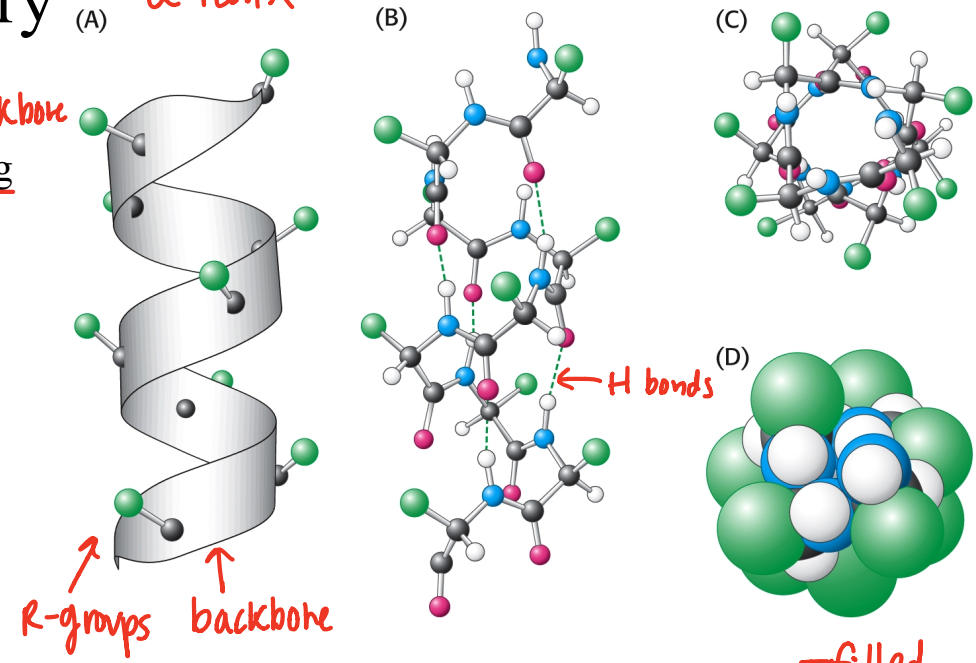
one polypeptide chain on itself

2.29, 2.30 Secondary structure

α-helix of backbone

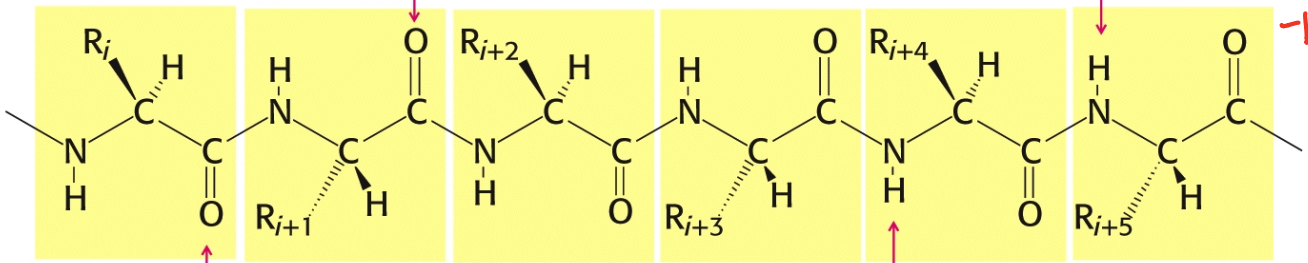
-Alpha helices form by H-bonding
- H of peptide bond group interacts with O of another group 4 amino acids away

-Proline does not fit into the helix well
- often found at start or end of alpha helices but not always



right hand helix

-filled
-not tubes
-rods



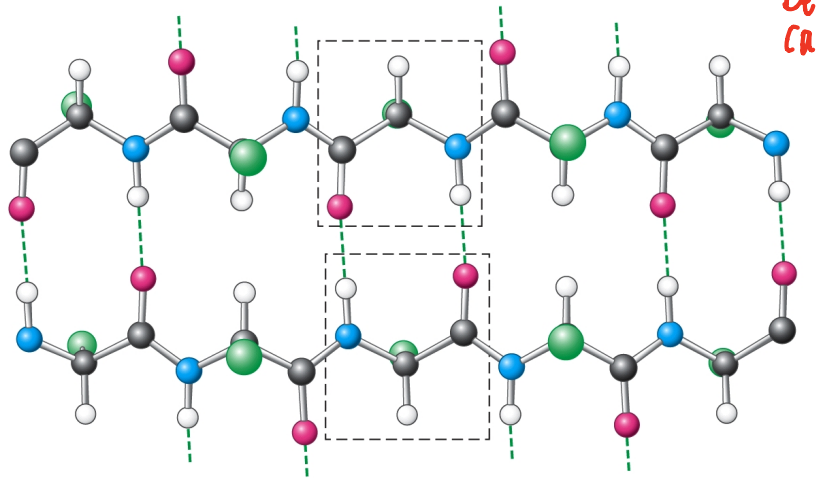
R groups (hydrophil/phob) if a section of polypeptide chain

will fold into this form

2.36,2.37 b-sheet

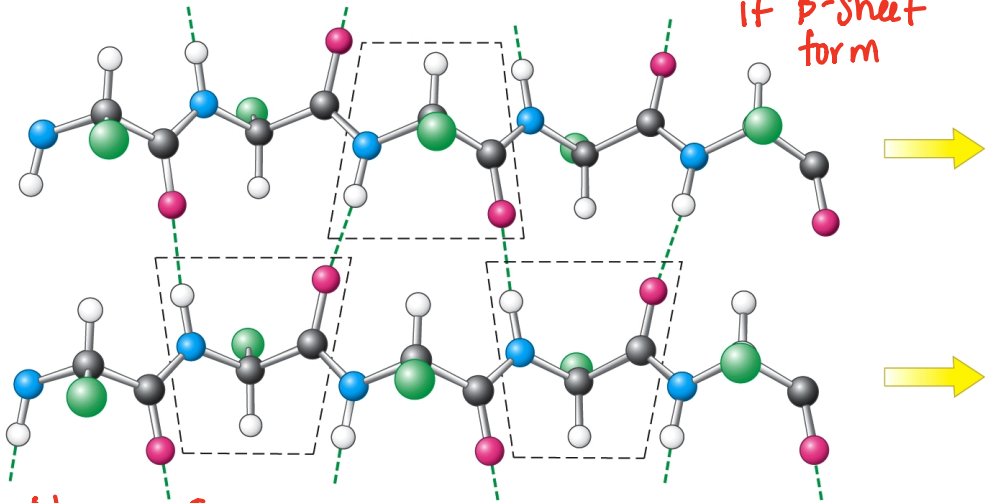
Can be two polypeptides

b-sheets are a very open type of secondary structure.
-Held together by H-bonds between main chain groups far apart in primary sequence.
- Can be parallel or anti-parallel



beta barrels can be formed

N→C C→N



nature of R g if B-sheet form

h-bonds hold together B sheet

- flat structures

- multiple ways

(beta turn) intra → N ||| C

N C ← inter

not rigid flexible

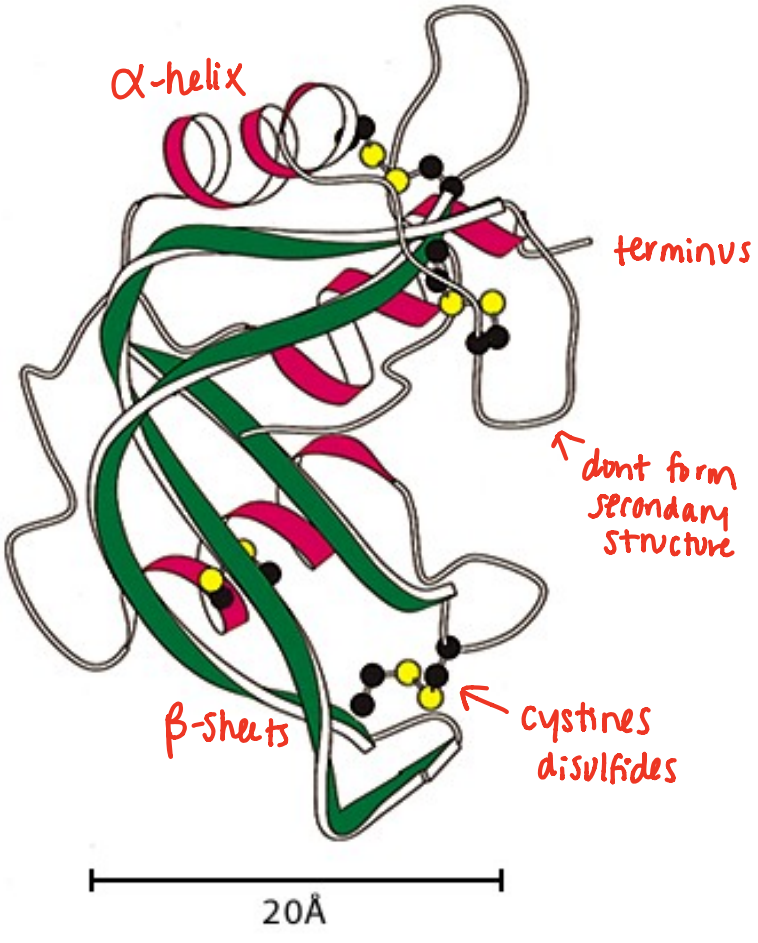
anti-parallel

parallel

can shift
can be folded

Tertiary Structure

- Final folded 3-D form of polpeptide
- If this is functional form, then the protein
-This is RNase A, degrades RNA
-Has both alpha-helix (red) and beta-sheet (green)
-Also has some regions without secondary structure.



Quarternary Structure

-Many proteins consist of multiple polypeptides
-Such proteins have quarternary structure
-Each polypeptide is a subunit
-This is hemoglobin, which consists of four subunits
-Subunits have limited or no function by theselves

cannot stand alone