Amino Acids
General

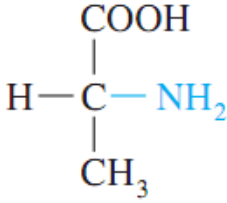
Amino Acids:

- Building blocks for peptides, proteins
- Some individually important (or converted to important molecules)
    - Gly, Glu, Tyr → neurotransmitters
    - Tyr → parent/precursor for epinephrine (adrenaline)
    - His → stomach secretes HCl, symptoms for inflammation, colds.
- Essential (10)
    - needed for normal health
    - not synthesized by the body
    - must be supplied by diet
- Complete (animal) vs. Incomplete (vegetable) protein

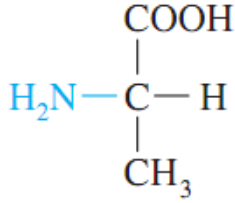
Amino Acids Structure

Amino Acid Structure:

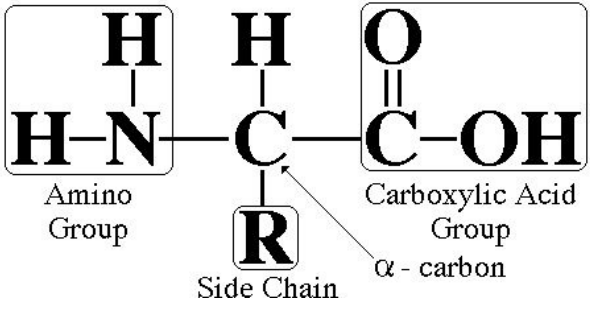
- Amide, CA, R-group (variable)
- D/L Isomers



D-(−)-alanine



L-(+)-alanine



Amino Acids
Side Chains

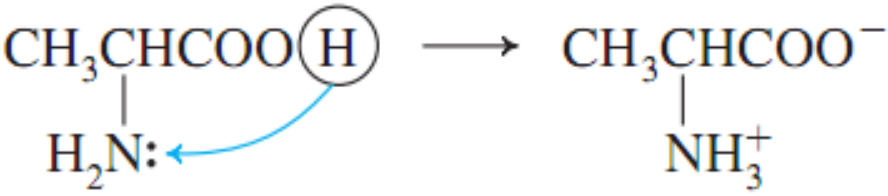
AA – Side Chains:

- Side chains determine the functionality of the AA b/c the –COOH and $–NH_2$ groups react to form the backbone
- 3 letter abbreviations (given on cheat sheet)

Classification	Functional Group	Property
Nonpolar	-R (aliphatic or aromatic)	Hydrophobic
Polar	-COOH, $-NH_2$, -OH	Hydrophilic
Acidic	-COOH (extra)	Lose H_2 → anion → Salt Bridges
Basic	$-NH_2$ (extra)	Gain H_2 → cation → Salt Bridges

Zwitterion

Zwitterion: dipolar form of AA, found at biological pH's (internal acid/base Rxn)

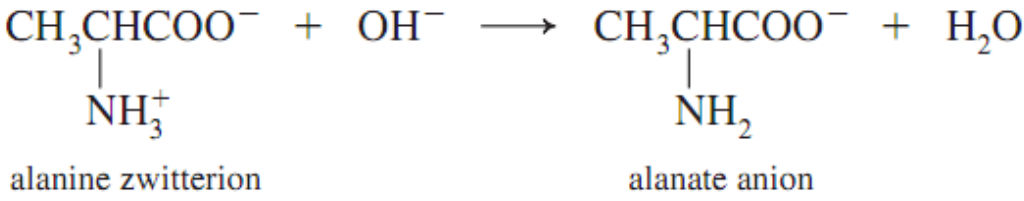


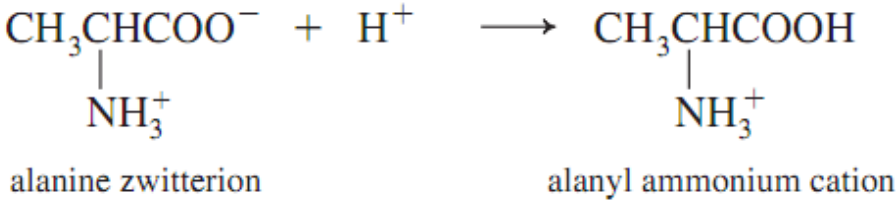
alanine molecule

alanine zwitterion

Amphoteric

Amphoteric: molecules with properties of both acid and base

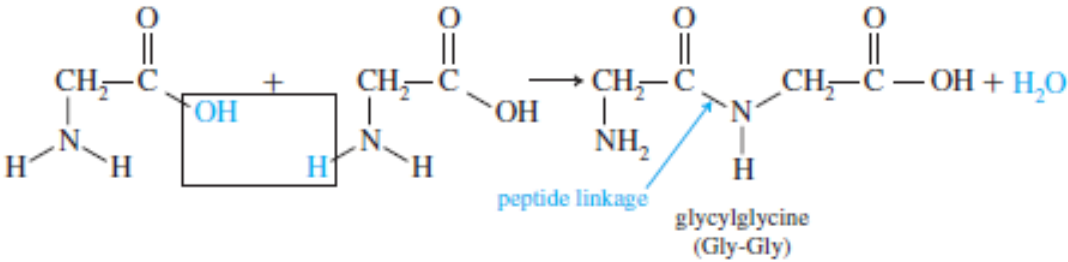




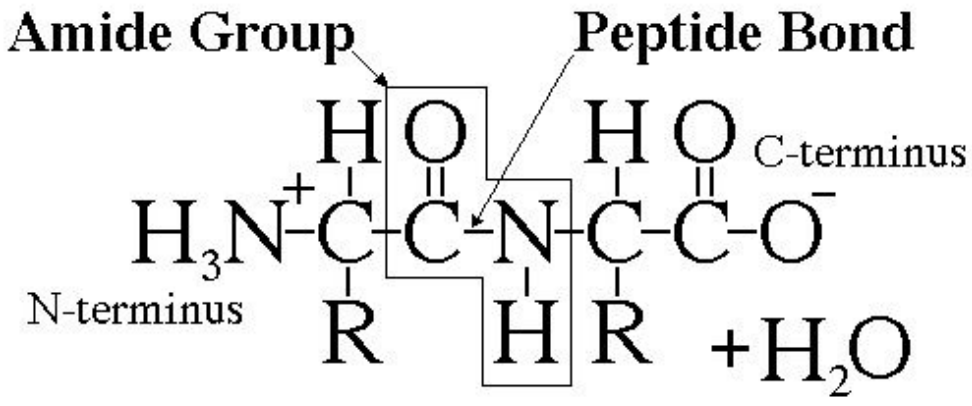
Formation of Polypeptides

Formation Reaction:

- Dehydration reaction
- CA + Amine → Amide
- Amide structure/Peptide bond/Peptide linkage



Amide/Peptide Bonds


Amide Group
Peptide Bond
C-terminus
N-terminus
+H2O

Polypeptides

Polypeptides:

- Small chains of AA (40-50 units)
- Many ways to connect together (N!)
- ~30 biologically relevant ones
- Hormones or Nerve transmitters
- Small changes structure → HUGE changes in functionality

Name	Primary structure	General biological function
Substance P	Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu-Met-NH_2	Is a pain-producing agent
Bradykinin	Arg-Pro-Pro-Gly-Phe-Ser-Pro-Phe-Arg	Affects tissue inflammation and blood pressure
Angiotensin II	Asp-Arg-Val-Tyr-Val-His-Pro-Phe	Maintains water balance and blood pressure
Leu-enkephalin Met-enkephalin	Tyr-Gly-Gly-Phe-Leu Tyr-Gly-Gly-Phe-Met	Relieves pain, produces sense of well-being
Vasopressin	S—S Cys-Tyr-Phe-Gln-Asn-Cys-Pro-Arg-Gly-NH_2	Increases blood pressure, decreases kidney water excretion
Oxytocin	S—S Cys-Tyr-Ile-Gln-Asn-Cys-Pro-Leu-Gly-NH_2	Initiates childbirth labor, causes mammary gland milk release, affects kidney excretion of water and sodium
Thyrotropin-releasing hormone	Glu-His-Pro	Stimulates release of hormones from the pituitary
Orexin	33 amino acids long	Causes wakefulness
Neuropeptide FF	Phe-Leu-Phe-Gln-Pro-Gln-Arg-Phe-NH_2	Modulates pain sensations
Neurotensin	Glu-Leu-Tyr-Glu-Asn-Lys-Pro-Arg-Arg-Pro-Tyr-Ile-Leu	Involved in brain memory functions
Neuropeptide Y	36 amino acids long	Stimulates eating
Endomorphin	Tyr-Pro-Trp-Phe-NH_2	Acts as a morphine-like analgesic

Protein Structure

Proteins – General:

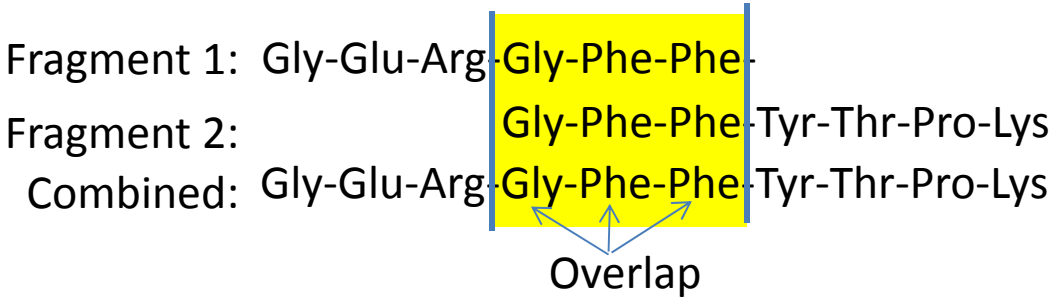
- > 50 AA
- Linus Pauling – 1954 Nobel Prize → α-helix and β-pleated sheet
- Fredrick Sanger – 1958 → Primary structure of beef insulin

Classification	Description	Examples
Primary	#, kind, type and sequence of AA	
Secondary	Regular 3D structure, held together by H-bonds in backbone	α-helix β-pleated sheet triple helix
Tertiary	Distinct 3D structure due to interactions between R-groups	H-bonds Ionic bonds (Salt Bridges) Disulfide bonds Hydrophobic Hydrophilic
Quaternary	Complex proteins	Multiple units Non-protein parts Metal ions

Primary Structure

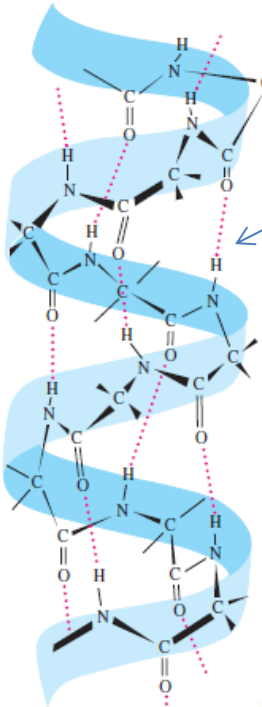
Primary Structure:

- #, kind, type, and sequence of AA
- Fredrick Sanger (1958 Nobel Prize) Beef Insulin
- Several years of work to sequence 51 AA
- Hydrolyzed proteins into smaller fragments to analyze



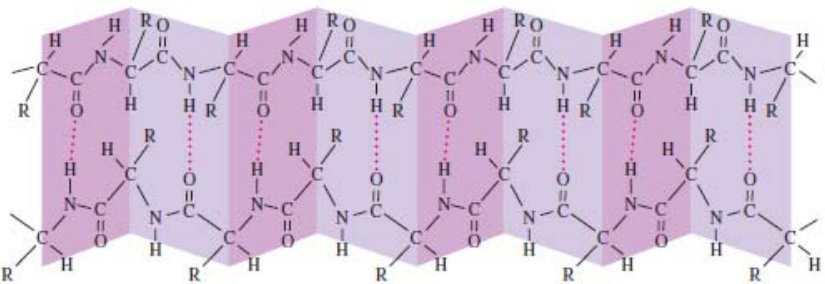
- Edman Degradation – split AA at N-Terminal End

Secondary Structure



Secondary Structure:

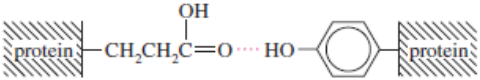
- Determined by <u>H-bonds</u> between AA-backbone
- α-helix → AA 4 residues apart, R-groups towards outside
- β-pleated sheet → AA far apart, R-groups face outwards



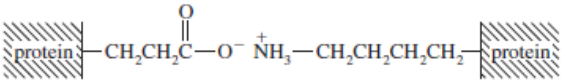
Tertiary Structure

Tertiary Structure:

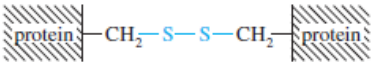
- Determined by interactions between R-groups
- H-bonds: -COOH and –OH



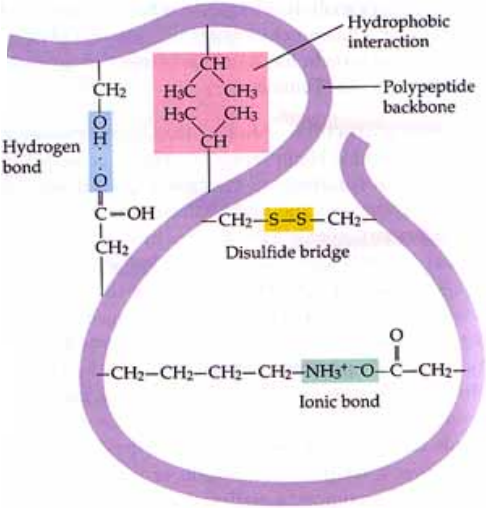
- Ionic/Salt Bridges



- Disulfide Bonds



- Hydrophobic (form core of protein)



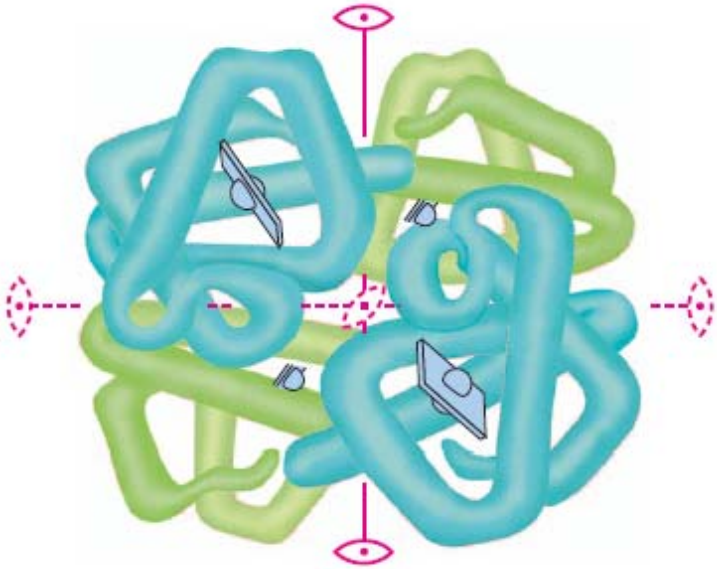
- Hydrophilic (face outwards to interact with water)

Quaternary Structure

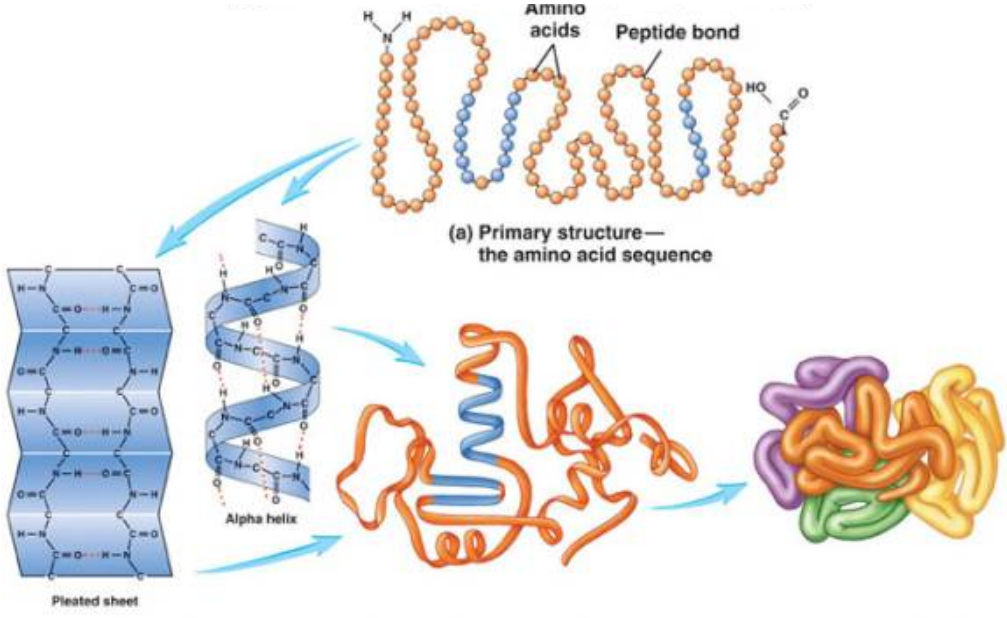
Quaternary Structure:

- Multiple protein units
- Non-protein parts
- Metal ions

- Ex: Hemoglobin
  - 4 subunits
  - Fe atoms



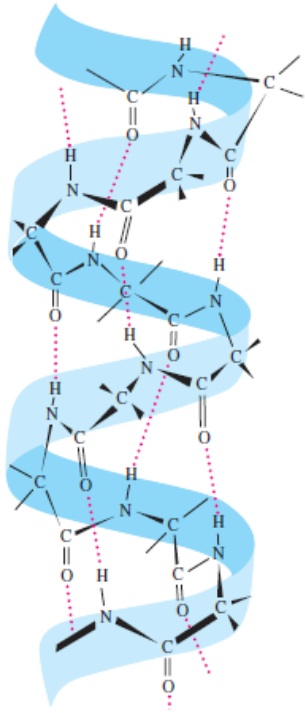
Protein Structure Summary


Amino acids
Peptide bond
(a) Primary structure—
the amino acid sequence
Alpha helix
Pleated sheet
(b) Secondary structure
with folding as a result
of hydrogen bonding
(*dotted red lines*)
(c) Tertiary structure with
secondary folding caused by
interactions within the
polypeptide and its immediate
environment
(d) Quaternary structure
— the relationships
between individual
subunits

α-Helix

α-helix Structure:

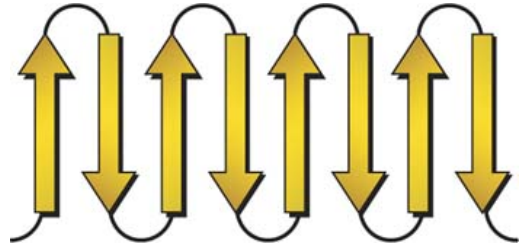
- Secondary
- Determined by H-bonds between AA-backbone
- α-helix → AA 4 residues apart, R-groups towards outside

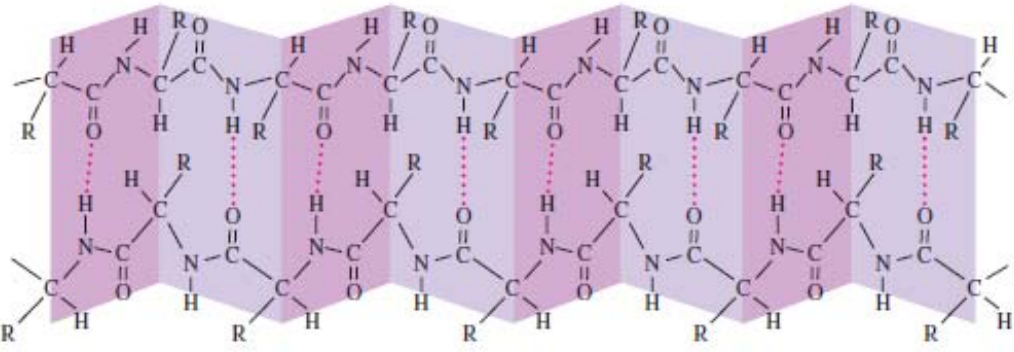


β-Pleated Sheet

β-pleated sheet structure:

- Secondary
- Determined by H-bonds between AA-backbone
- β-pleated sheet → AA far apart, R-groups face outwards

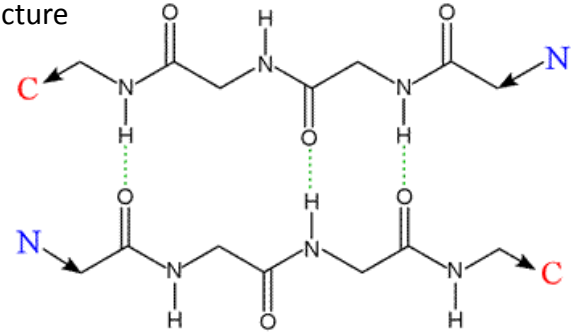




H-bonds

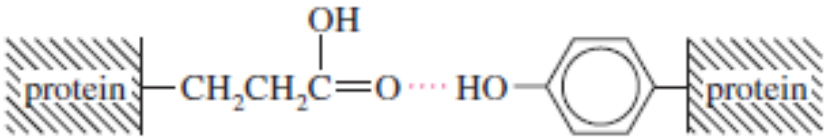
Secondary H-bonds:

- Between the C=O and NH of backbone
- Responsible for secondary structure



Tertiary H-bonds:

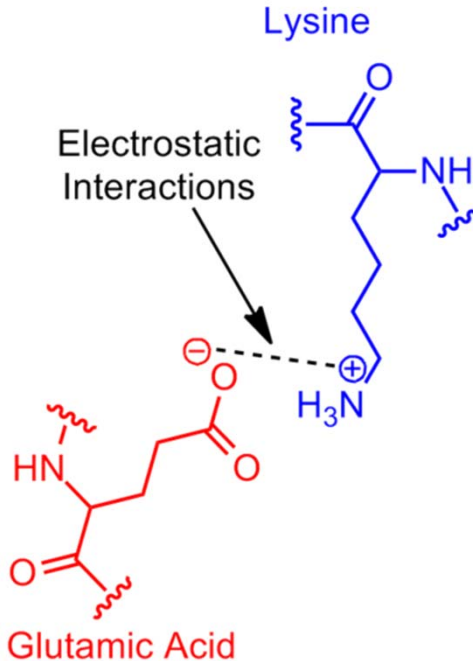
- Between the C=O and -NH or -OH of R-groups
- Responsible for tertiary structure



Salt Bridges

Ionic Bonds/Salt Bridges:

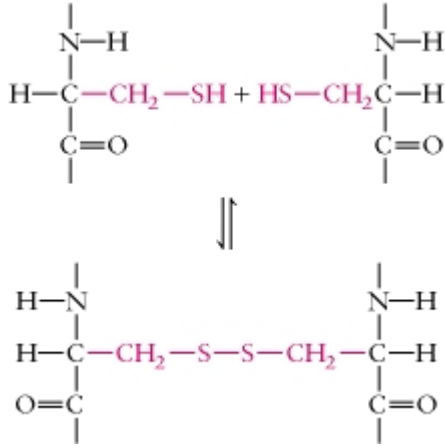
- Tertiary Structure
- Between $-COO^-$ and $-NH3^+$ groups



Disulfide Bonds

Disulfide bonds:

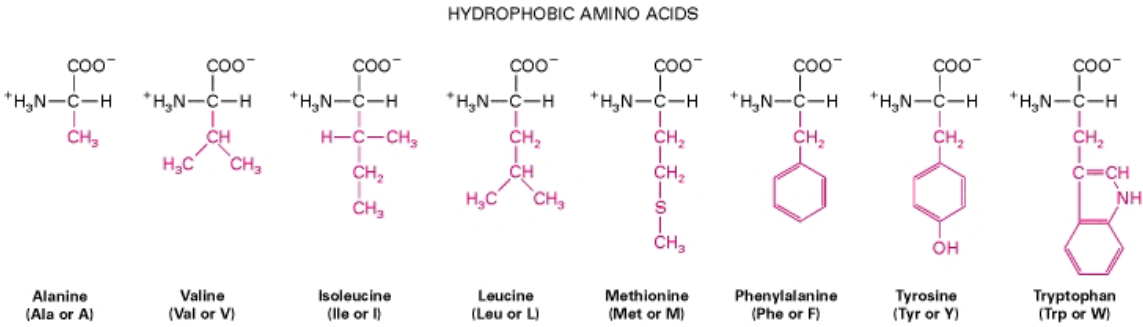
- Tertiary Structure
- Between -SH and –SH groups
- Mainly between Cys-Cys



Hydrophobic Interactions

Hydrophobic Interactions:

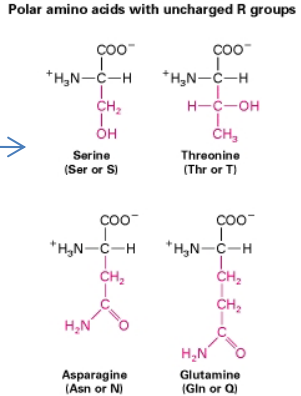
- Tertiary Structure
- Between –R groups (Alkane and Aromatic)
- Interior of proteins to avoid water

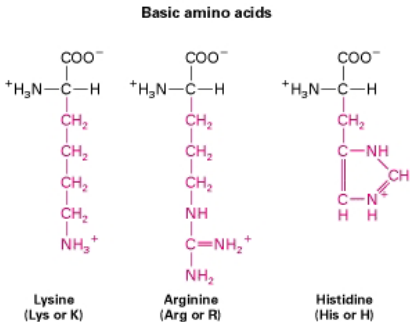


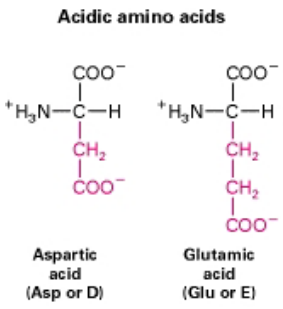
Hydrophilic Interactions

Hydrophilic Interactions:

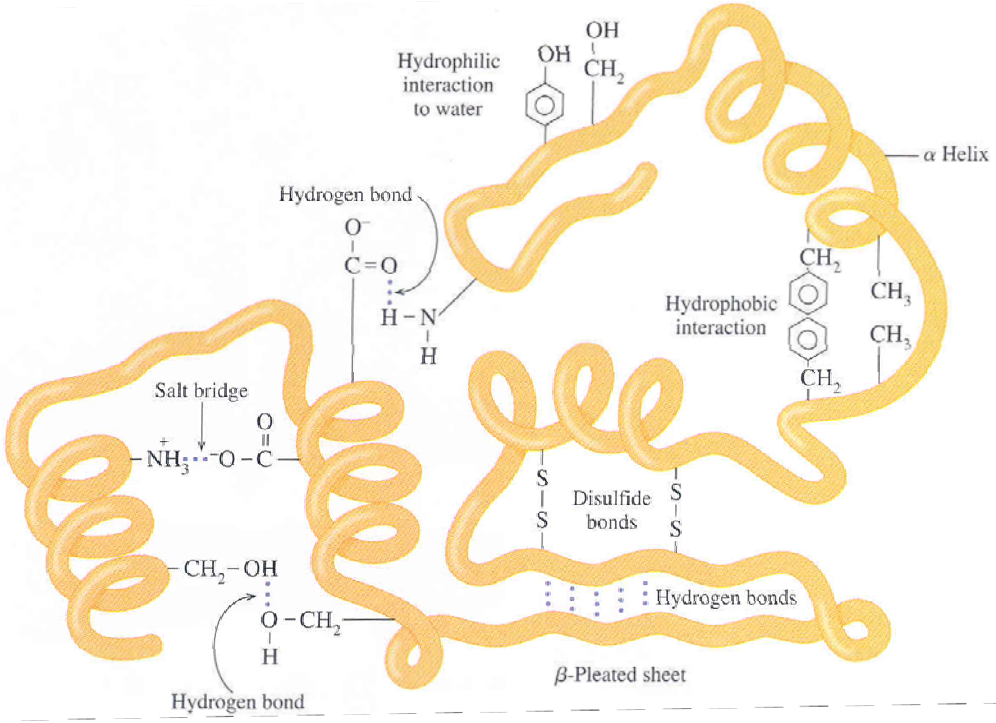
- Tertiary Structure
- Exterior of proteins to interact with water
- Polar groups (OH)
- Acidic groups (COOH)
- Basic groups (NH_2)







Identify 2°/3° Structure


Hydrophilic interaction to water
OH
OH
CH2
α Helix
Hydrogen bond
O⁻
C=O
H–N
H
CH2
CH3
Hydrophobic interaction
CH3
CH2
Salt bridge
+NH3
O
O–C
S
S
Disulfide bonds
S
S
CH2–OH
O–CH2
H
Hydrogen bonds
Hydrogen bond
β-Pleated sheet

Protein Functions

Protein Functions:

- Structural Support – skin, connective tissue
- Storage – Fe in Liver
- Transport – O_2 in Hemoglobin
- Defense – antibodies, venom
- Motion/Movement – muscles
- Regulation – blood/glucose/insulin
- Catalysis – Enzymes (Ch. 30!)

Denaturation

Denaturation: Loss of 3D conformation in a protein

- Disruption of 2°/3°/4° interactions
- Does NOT break 1° structure (hydrolysis)
- Loss of biological activity
- Causes of Denaturation

	Cause	Example
1.	Heat	Cooking
2.	Acids/Base (pH)	Lactic Acid
3.	Organic Molecules	Ethanol/Isopropanol
4.	Heavy Metals	Pb, Hg
5.	Agitation	Stirring
6.	UV Light	
7.	Enzymes	Digestion
8.	Salts	Water purification

Xanthoproteic Test

Xanthoproteic Test:

- Detects Benzene rings
- Yellow color
- Phe, Try, Tyr

Biuret Test

Biuret Test:

- Detects tri-peptides (must have at least 2 peptide bonds)
- Cu_2SO_4
- Violet color

Ninhydrin Test

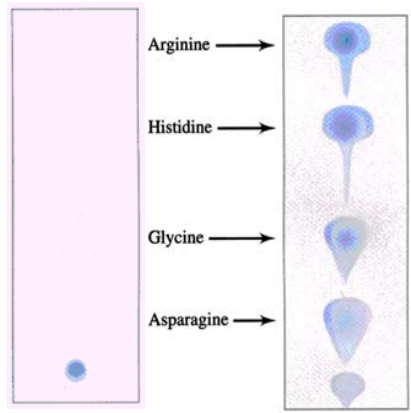
Ninhydrin Test:

- General test for AA
- All AA → blue
- Pro, hydroxyproline → yellow
- Very sensitive 1 µg (10^{-6})

Chromatography

Chromatography: separation technique for AA

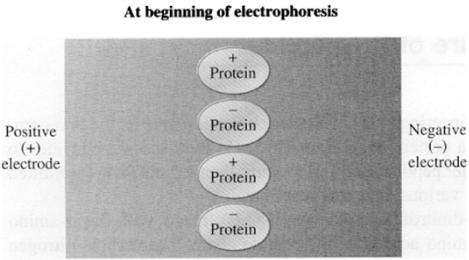
- Difference in distribution between two phases
  - Solubility
  - Charge
- TLC (thin-layer) – solid/liquid phase
  - Solvent Front (rate solvent moves)
  - Differences in solubility cause AA to travel at different rates in the solvent
- Column chromatography (variation of above)

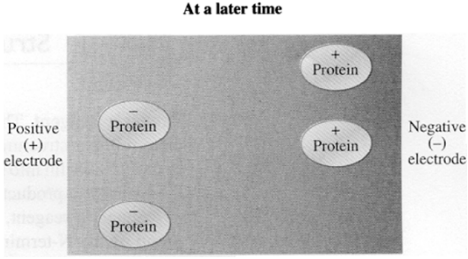


Electrophoresis

Electrophoresis: separation technique for AA

- Charged particles separate in electric field (zwitterions)
- Separation based on
  - Size – friction (sieve)
  - Charge – electric field
- Types
  - SDS – masks charge/separate by mass/size
  - Isoelectric Focusing – AA separated by charge
  - 2D – separate on both.





Fredrick Sanger

Fredrick Sanger:

- Solved structure of beef insulin (1955)
- Nobel prize 1958
- 51 AA in two chains held together by disulfide bonds
- DFNB + N-terminal end + hydrolysis to solve structure
- “Paper shredder”