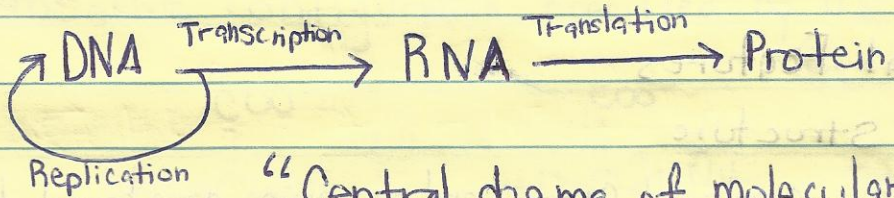
Chapter 3 Lecture 1

Introduction to Proteins and their Building Blocks

1) Fundamental Biology of Life



"Central dogma of molecular biology"

⟹ Slide 2

- Nucleus is the site of transcription
- The ribosome on the rough endoplasmic reticulum is the site of translation.

(For a thorough overview of these biological processes refer to Ch. 24-28).

- Our focus will be on the biochemical processes that proteins and DNA engage in.

2. Overview of Protein

A. Most abundant biological macromolecules
B. Occur in all cells
C. Occur in all parts of cells
D. Widely range in size and ~~function~~ structure
E. Have different specialized functions

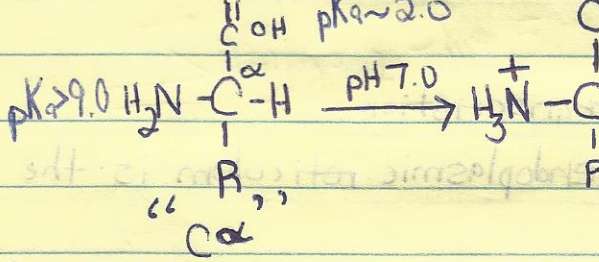
3. Amino acids

- Proteins are polymers of amino acids
- There are 20 main amino acids and their different combinations lead to the rich diversity of proteins

A. Structural Features

I. Basic Structure

- Have a carboxyl group and an amino group bonded to the same carbon but differ in their side group (R group)

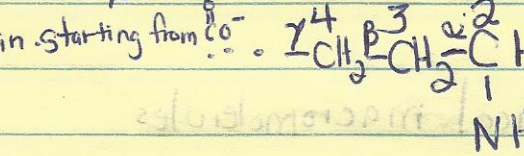


- R group varies in structure, size, and electric charge

⟹ Slide 3 to show all of the amino acids. Pink represents the side group.

II. Label convention

- Number system customary in organic chemistry based on longest chain starting from the COO⁻.



- But in Biochemistry use Greek lettering system

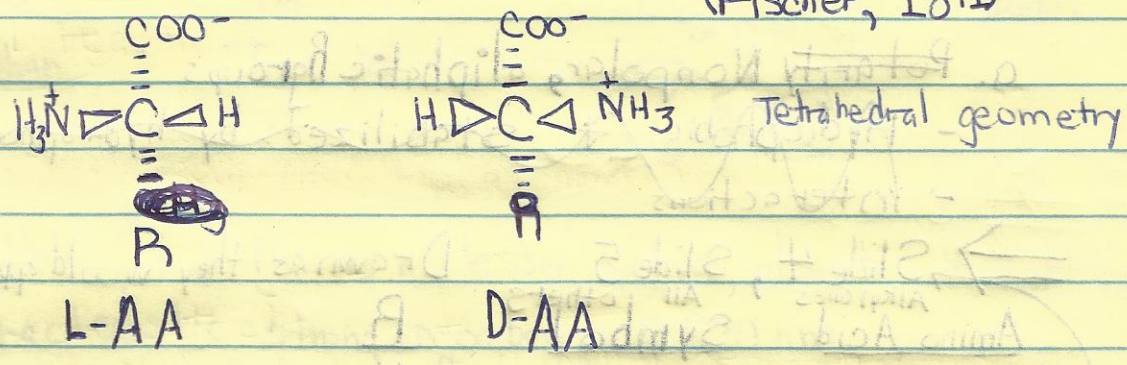
III. Chirality

- For the exception of glycine, the αC is surrounded by four different groups and is chiral

→ optically active
- rotate plane-polarized light

- Two unique spatial arrangements that are not superimposable mirror images of each other called enantiomers

- Absolute configuration specified by D,L system (Fischer, 1891)



When drawn as indicated above with all three C's lined up vertically with the R group below α C

L: represents the α-amino group to the left

D " " " " " to the right

~~Another nomenclature system is the configuration has nothing to do with optical properties of the molecule~~ → R S system

- Another nomenclature for configuration is the RS system (Organic)

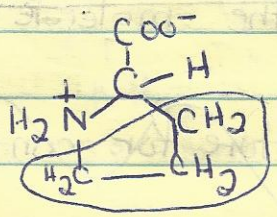
- Typically all amino acids in proteins are L-stereoisomers
  → form because the active sites of enzymes that produce them are asymmetric + catalyze stereospecifically

IV. ~~C~~ Amino Acids classified by R group

- Polarity
- Aromaticity
- Charge

a. ~~Polarity~~ Nonpolar, aliphatic Rgroups
- ~~Hydrophobic~~ ~~stabilized by hydrophobic interactions~~

⇒ Slide 4 (Alkyl ones), Slide 5 (All others) Drawn as they would appear @ pH 7.0

Amino Acid	Symbol		R
Glycine	Gly	G	-H
Alanine	Ala	A	$-CH_3$
Valine	Val	V	$-CH(CH_3)_2$
Leucine	Leu	L	$-CH_2CH(CH_3)_2$
Isoleucine	Ile	I	$-CH(CH_3)-CH_2-CH_3$
Methionine	Met	M	$-CH_2-CH_2-S-CH_3$
Proline	Pro	P	

Cluster together, stabilize protein interactions by hydrophobic interactions

~~Thiol~~ Thioether group

cyclic, rigid conformation, reduces structural flexibility of polypeptide

Oxidizes to yield

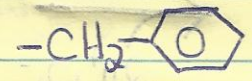
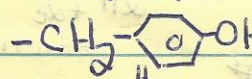
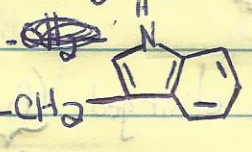
$-CH_2-CH_2-\overset{\overset{O}{\|}}{S}-CH_3$

Oxymethionine

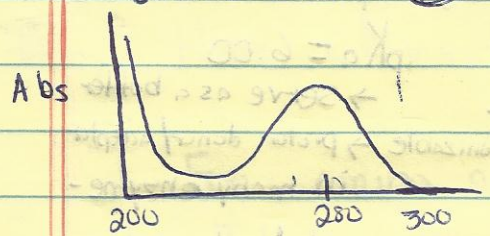
b. Aromatic R groups

- Aromatic side chains, relatively nonpolar

⟹ Slide 6

Amino Acid	Symbol		R
Phenylalanine	Phe	F	
Tyrosine	Tyr	Y	 H-Bonds
Tryptophan	Trp	W	

- All three, but Phe to a lesser extent, absorb ultraviolet light
- Characteristic strong absorbance @ 280 nm
- Can be used to quantify certain proteins by Beer's law $A = \epsilon bc$

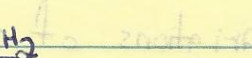


A: absorbance
ε: extinction coefficient
b: pathlength
c: concentration

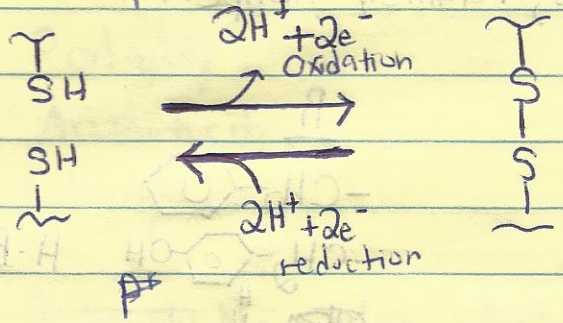
c. Polar, uncharged groups

- Hydrophilic
- Form hydrogen bonds

⟹ Slide 7

AA	Symbol		R
Serine	Ser	S	
Threonine	Thr	T	
Asparagine	Asn	N	
Glutamine	Gln	Q	
Cysteine	Cys	C	

Cys readily oxidizes to form Cystine bonds
proton loss coupled with redox → Help to form protein crosslinks, which stabilizes protein structure



d. Positively charged (Basic) R groups (Accept proton)
⟹ Slide 8

AA	Symbol	R	
Lysine	Lys K	$-CH_2CH_2CH_2CH_2\overset{+}{N}H_3$	$pK_a = 10.53$
Arginine	Arg R	$-CH_2CH_2CH_2NHC(=\overset{+}{N}H_2)-NH_2$	$pK_a = 12.48$
Histidine	His H	$-CH_2$ + imidazole ring	$pK_a = 6.00$

Histidine: ionizable → proton donor/acceptor in many enzyme-catalyzed reactions → serve as a buffer

R group

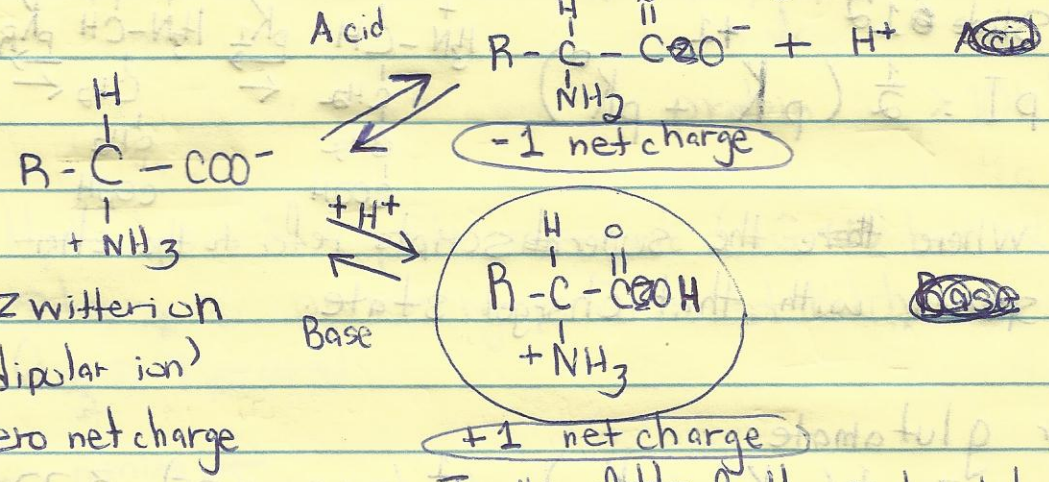
Note if $pK_a > pH\ 7.0$ then, will be protonated.

e. Negatively charged (Acidic) R groups
⟹ Slide 9

AA	Symbol	R	
Aspartate	Asp D	$-CH_2CO^-$	$pK_a = 3.65$
Glutamate	Glu E	$-CH_2CH_2CO^-$	$pK_a = 4.25$

f. There are many uncommon amino acids with important functions
- Are variations of standard amino acids
⟹ Slide #10

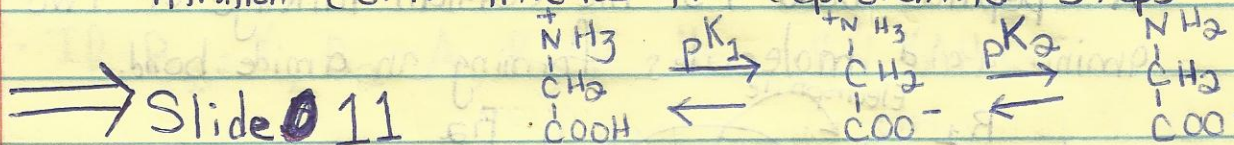
4. Amino Acids are amphoteric
A Can act as an acid or a base, like H_2O



- In this ~~fully~~ fully protonated form, would be a diprotic acid
- Can lose two H^+

~~5~~ B. Have characteristic titration curves

I. For amino acids with no acidic or basic side groups
- Titration curve involves two deprotonation steps



a. First step, deprotonation of the carboxylic acid
b. Second step, deprotonation of the amino group

- The characteristic pH at which the net electric charge is zero is called the isoelectric point or isoelectric pH (pI)

For glycine

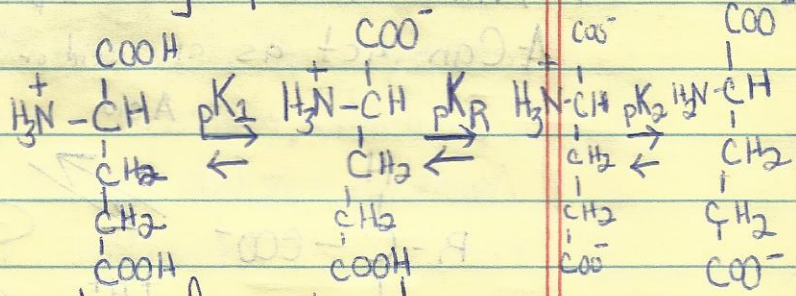
$$pI = \frac{1}{2}(pK_1 + pK_2) = \frac{1}{2}(2.34 + 9.60) = 5.97$$

II. For amino acids with an ionizable R group

- Three deprotonation steps

⟹ Slide 12

- $pI = \frac{1}{2}(pK^{+1} + pK^{0})$



Where ~~there~~ the superscripts refer to the ~~that~~ species with that charged state.

For glutamate

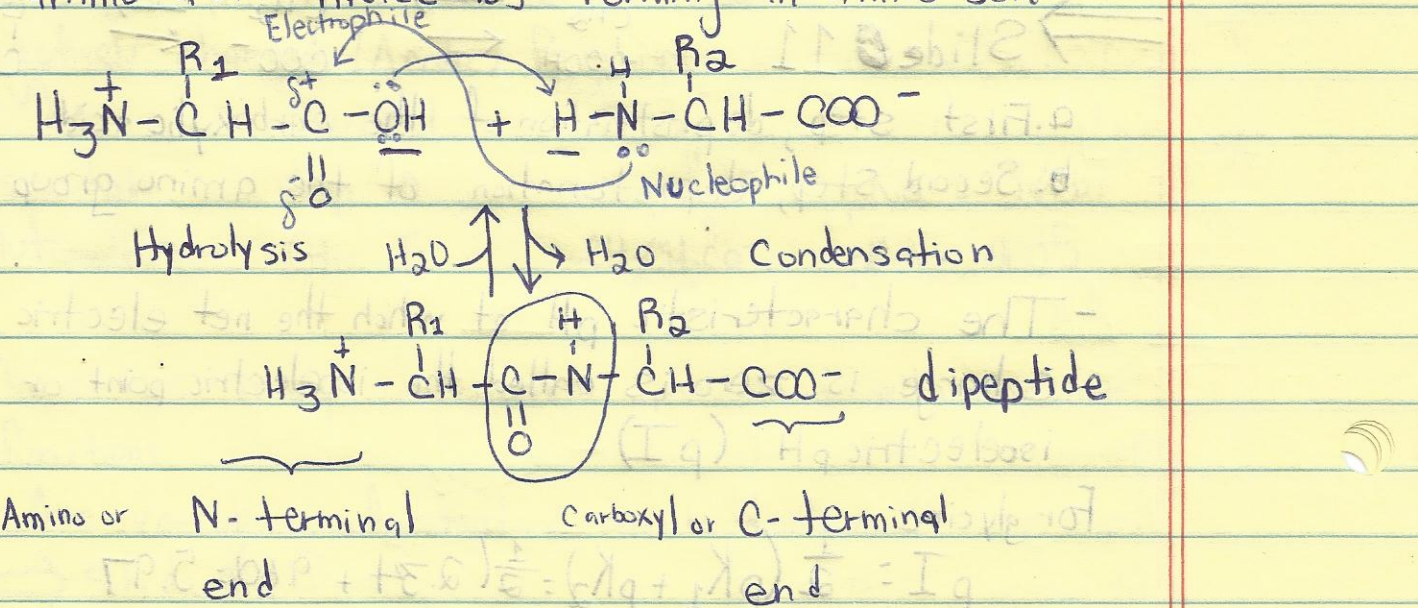
$$pI = \frac{1}{2}(pK_1 + pK_R) = \frac{1}{2}(2.19 + 4.25) = 3.22$$

5. Peptides and proteins

- Polymers of amino acids
- Consist of at least two linked amino acid residues

A. Peptides

- A peptide bond is the covalent linkage of two amino acid molecules forming an amide bond.

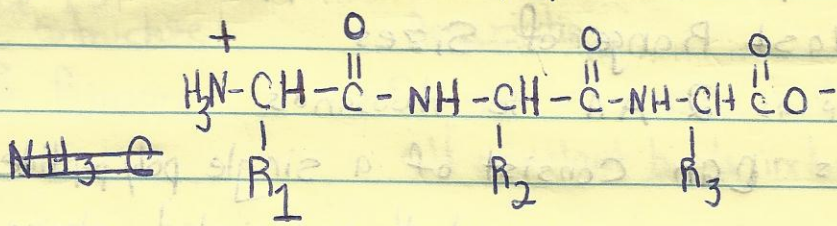


AA-AA-AA

- Three linked ⇒ tripeptide
- A few amino acids linked ⇒ oligopeptide
- Many " " " ⇒ polypeptide < 10 kDa
  ↓
  protein > 10 kDa

- Hydrolysis is quite exergonic ($\Delta G < 0$) but extremely slow ∴ preserving protein stability. ($t_{\frac{1}{2}} \approx 7$ years)

B. The naming ionization of peptides



- Typically represent peptides from N-terminal end to C-terminal end

Tyrosine Alanine Histidine
Tyr Ala His

- If $R_1 = Y$, $R_2 = A$, $R_3 = H$ then $H_3\overset{+}{N}$-YAH-$\overset{O}{\overset{\|}{C}}O^-$

or

simply YAH

- Peptides contain one free α-amino group + one free α-carboxyl group at opposite end of the chain. Ionize @ different ~~constants~~ pKa values when far apart.

- The α amino + α-carboxyl groups of nonterminal amino acids are ~~can~~ covalently joined and do not contribute to the acid-base properties of the peptide.

- However, ionizable R groups of all amino acids do contribute to the acid/base properties
- Peptides have characteristic ~~titratio~~ pH titration curves that depend on the α-amino, α-carboxyl end groups + all ionizable R groups
- Note that the pK_a values for the R groups can change when ~~it~~ in a peptide due to environmental influence.

C. Biologically Active Peptides + Polypeptides occur in a Vast Range of Sizes
- As little as 2 AA to thousands
- Proteins can consist of a single polypeptide chain or two or more noncovalently associated chains called multisubunit proteins
→ If two of the chains are identical then the protein is referred to as oligomeric

D. Polypeptides have characteristic amino acid compositions
- AA composition is unique to a polypeptide
- Acid hydrolysis is generally used to cleave a polypeptide to individual amino acids coupled with other techniques to resolve ambiguous side reactions
Show → Some AAs occur more frequently than others for particular structure-function reasons to discuss later.

E. Proteins

~~A. In addition to amino acids, Some proteins contain non-amino acid group~~

A. Some contain only amino acids

B. others have chemical components conjugated to the amino acids → conjugated proteins.

→ Non amino acid group called prosthetic group

C. The arrangement of the polypeptides of proteins leads to several levels of protein structure

⟹ Slide 13

Structure	Description
~~B.~~ Primary	Sequence of amino acid residues + all covalent bonds including disulfide bonds
Secondary	Stable arrangements of amino acid resides leading to recurring structural patterns
Tertiary	3-D folding of a polypeptide
Quaternary	Arrangement in space of ~~two~~ or more polypeptides

~~→ Slide 1~~