Welcome to

Biochemistry I: Proteins, Lipids and Metabolism

Tutorial #1

Sept 7th, 2018

Welcome to BCH210

Chloe Mitchell

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- **Tutorial notes, discussion board**

  Blackboard via Portal

  Tutorial notes will be posted by 4:00 pm day before

- **Course information**

  http://biochemistry.utoronto.ca/courses/bch210h-fall-biochem-1-proteins-lipids-metabolism/

Tutorial Goals

Clarification and review of lecture material.

Address any questions.

via tutorials (past and present), emails, discussion board

Practice questions – Need your participation ☺

Keep on top of material (there's a lot!).

Important Dates

Term Test 1: October 4th @ 6 – 8pm (31%)

Term Test 2: November 1nd @ 6 – 8pm (26%)

Weekly Quizzes: Sun 12pm – Mon 12pm (6%)

Assignment: November 24th – December 4th (2%)

Tutorial Etiquette

Feel free to ask questions (raise your hand).

Include the course name (BCH210) in the title of any emails.

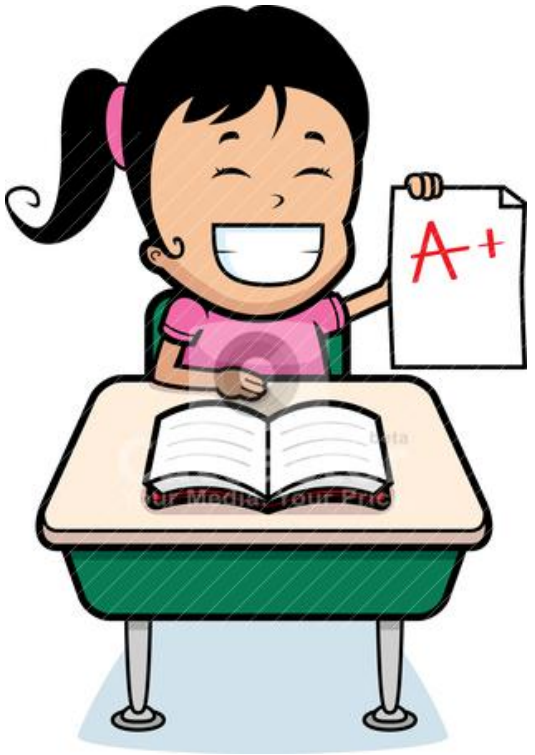
Use the discussion board! Odds are someone else has the same question as you.

Send questions you'd like me to go over in tutorial by email.

Do not distract those around you!

Success tips

1) Go to lecture.
2) Practice problems (actually do them).
3) Review lecture material.
4) Go to tutorial.
5) Go to lecture.
6) Ask questions!
7) Sleep (But not in class ☺).
8) Go to the lectures!



Take away points for today

- **Driving forces involved in protein stabilization**
  - **Hydrophobic effect, Ionic interactions, Hydrogen bonds, Van der Waals**
- **AMINO ACIDS**
  - **Name, single and triple letter code, side groups, properties**
- **Determine protonation state of amino acids in different environments**
  - **pH and pKa**

Why do we study biochemistry?

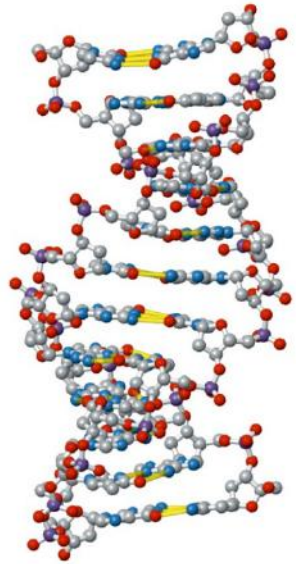


Figure 1-10 Principles of Biochemistry, 4/e
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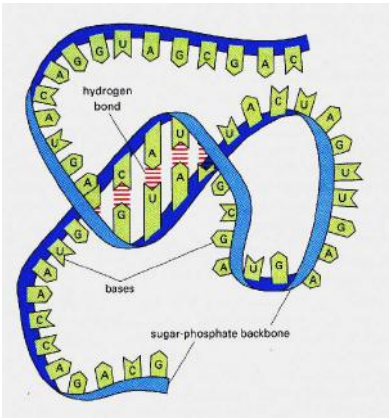
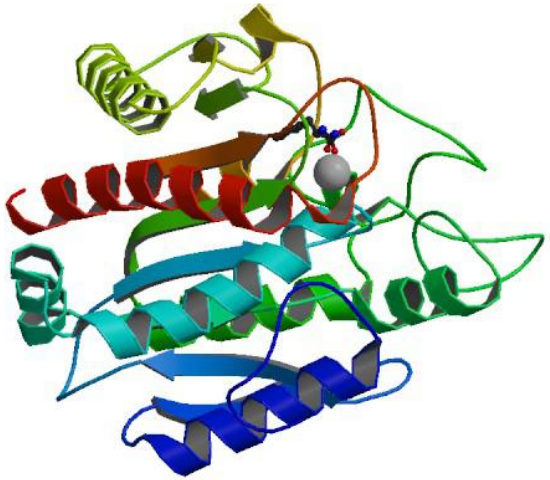




http://www.uic.edu/classes/phys/phys461/phys450/ANJUM04/

PDB ID 1HDU – Bovine Carboxypeptidase

DNA → **RNA** → **Protein**

Information

Function

Understanding the building blocks

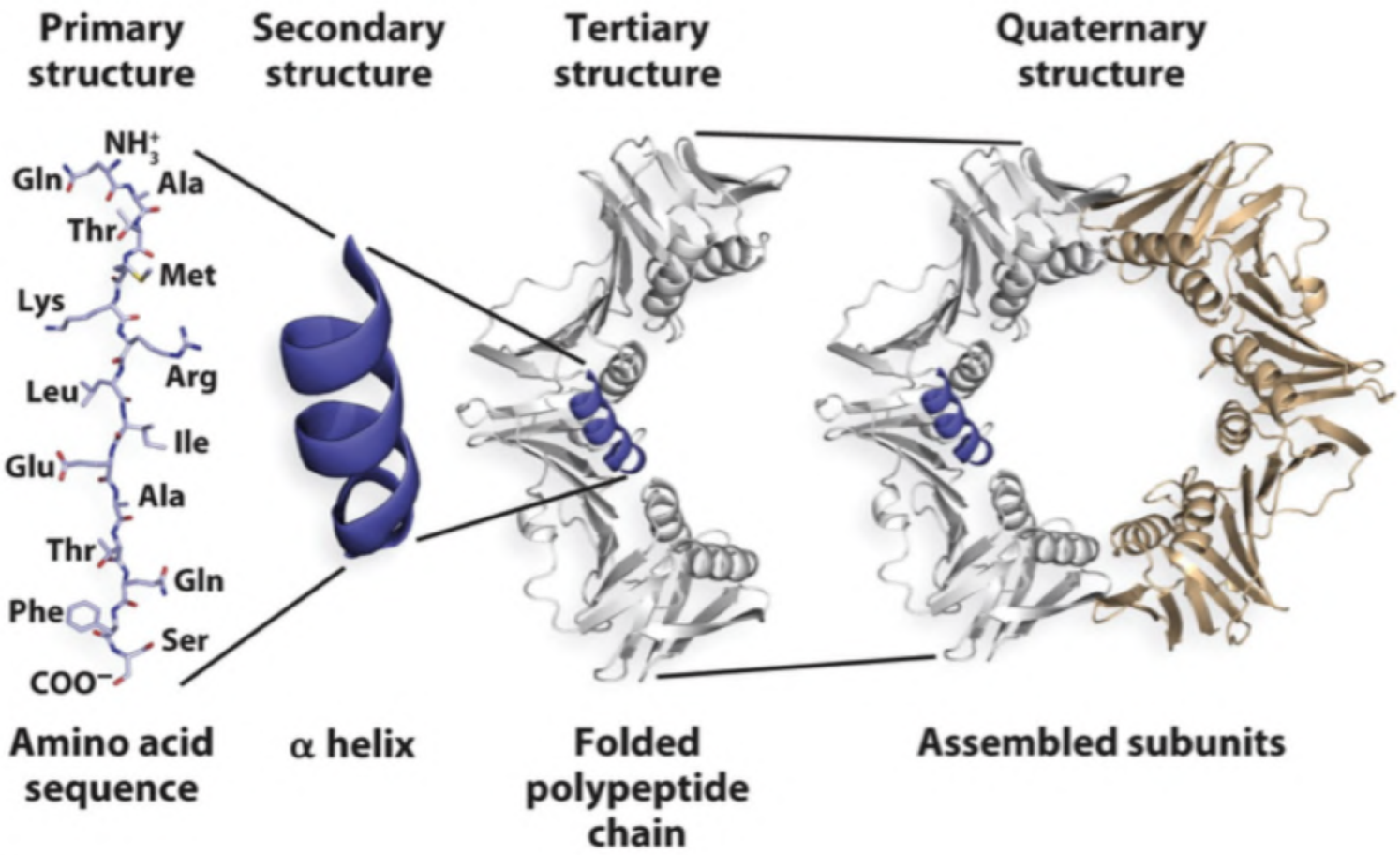
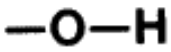


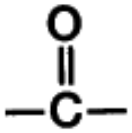
Figure 4-1
Molecular Biology: Principles and Practice

Chemistry Review – Functional Groups

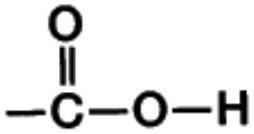
Functional Groups



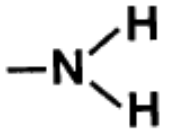
Hydroxyl group



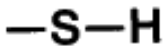
Carbonyl group



Carboxyl group



Amino group



Sulfhydryl group

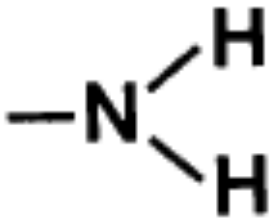
These groups can be:

- Ionized
- Nucleophiles and electron acceptors
- Hydrogen bonding acceptors or donors

H-Bonding occurs between a hydrogen donator (proton bound to an electronegative atom, -OH, -NH, - SH) and a hydrogen acceptor (electronegative atom, lone pairs)

Question

What charge would the following groups have if protonated?



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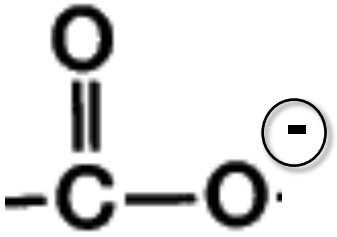
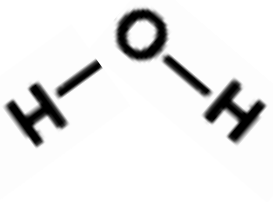


no charge



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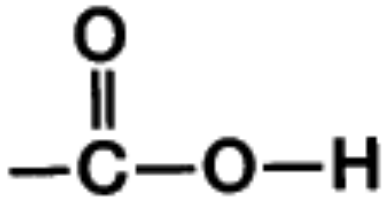
Question

What charge would the following groups have if deprotonated?



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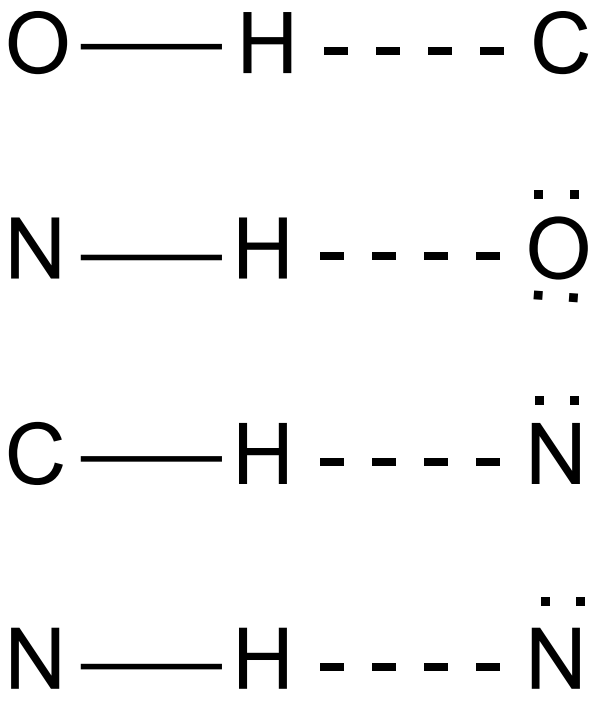
Question

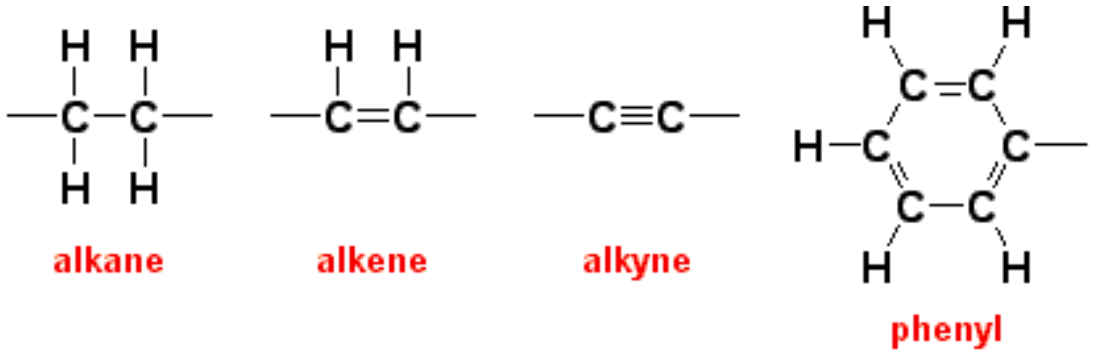
Which of the following is NOT an example of a Hydrogen Bond?



Carbon is not electron withdrawing to be considered a hydrogen donor, nor does it have a lone pair of electrons to accept the proton.

Chemistry Review – Con'd

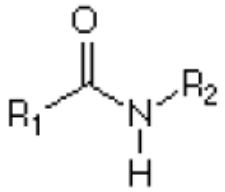
Nomenclature

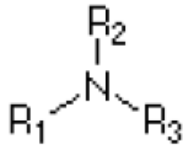


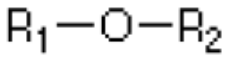
Question

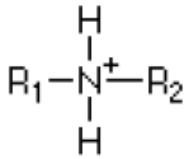
a

Which of the following represents an amide linkage?

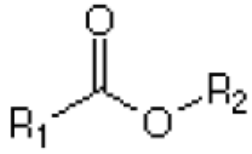
A. 

B. 

C. 

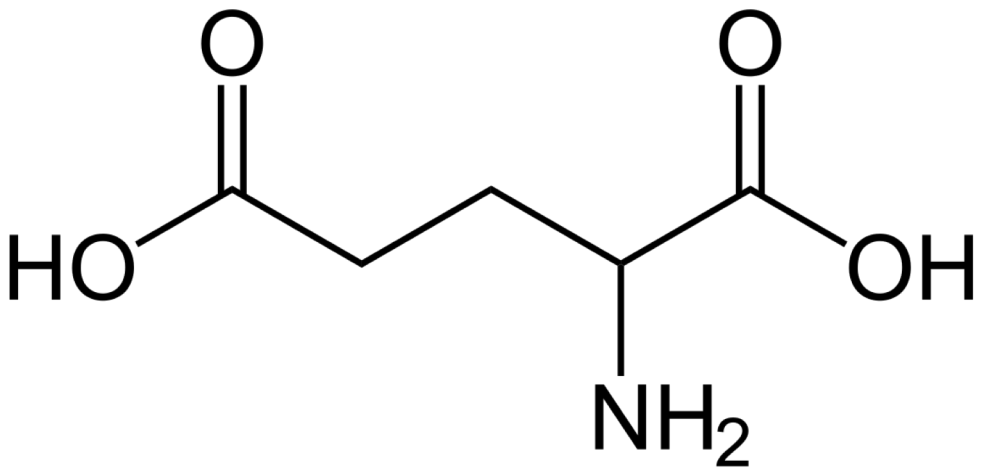
D. 

amine

E. 

Question

What is this molecule?



What functional group(s) are present?

Why do we study biochemistry?

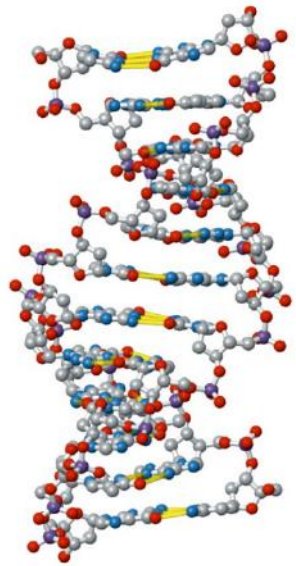


Figure 1-10 Principles of Biochemistry, 4/e
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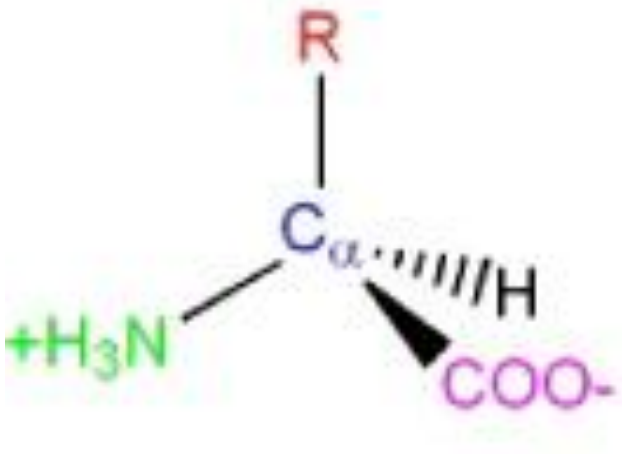
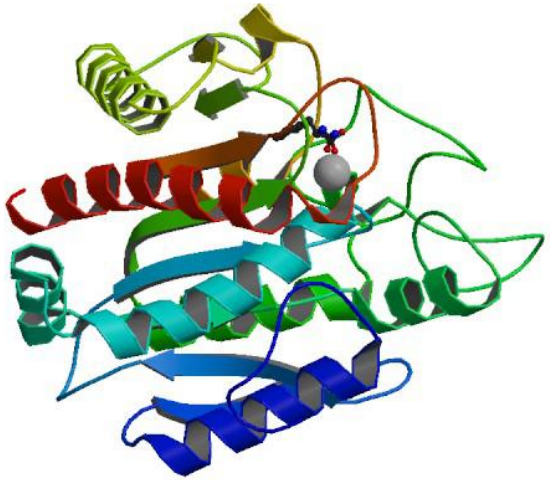


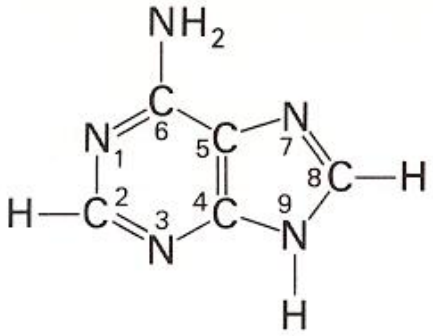


PDB ID 1HDU – Bovine Carboxypeptidase

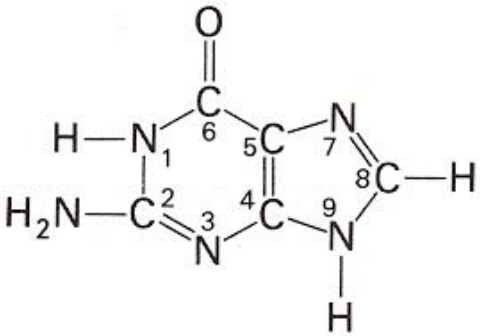
DNA → **Amino Acid** → **Protein**

Information **Function**

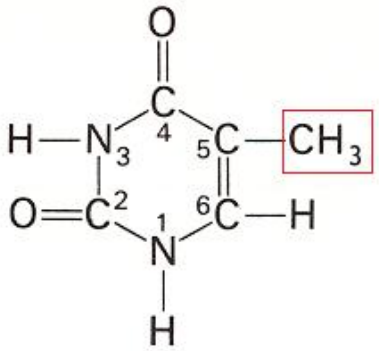
Nucleic Acids - DNA, RNA



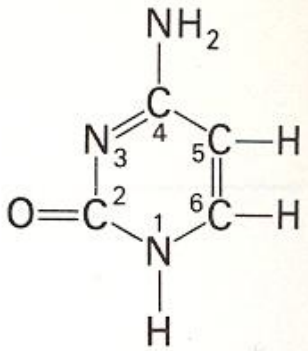
Adenine
(A)



Guanine
(G)



Thymine
(T)

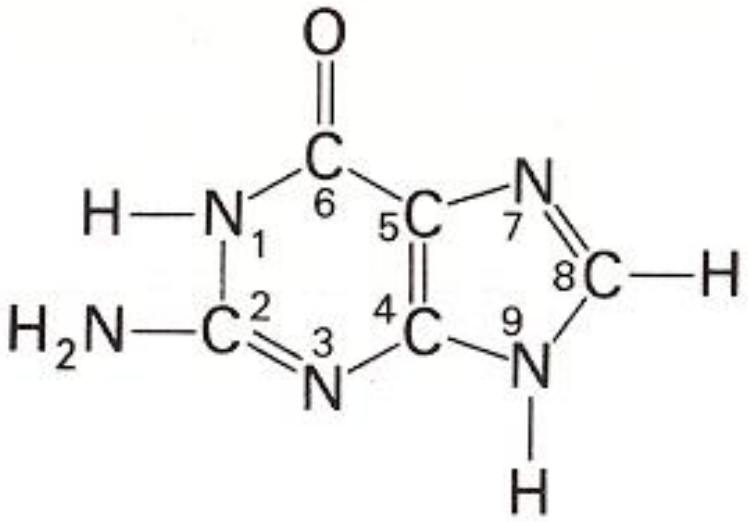


Cytosine
(C)

Which bases are Purines? Pyrimidines?

Question

How many potential H-bonds are present?

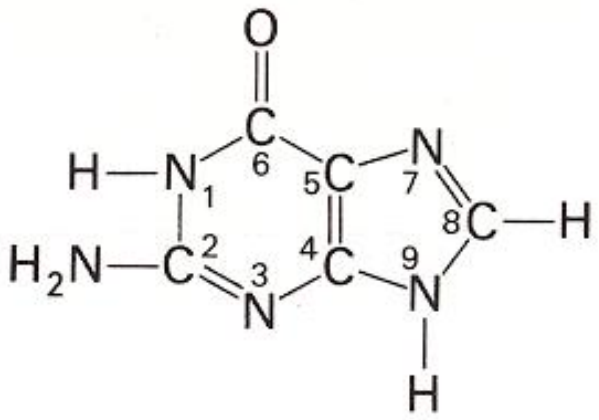


Guanine
(G)

6 total (4 donors and 2 acceptors)

Question

amide
amino (secondary and primary)



Guanine
(G)

How many of the following functional groups are found in guanine?:

ketone, amide, aldehyde, ether, phenyl, or primary, secondary, and tertiary amines

Why do we study biochemistry?

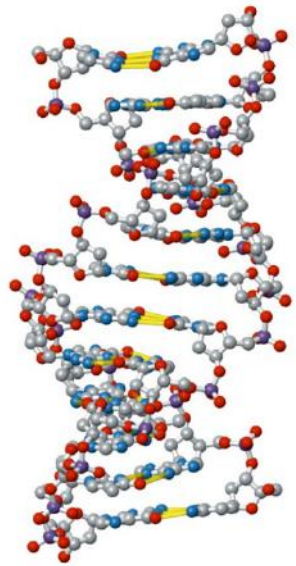


Figure 1-10 Principles of Biochemistry, 4/e
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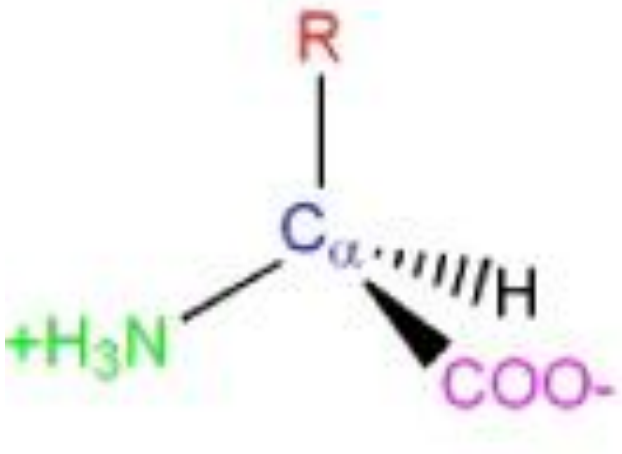
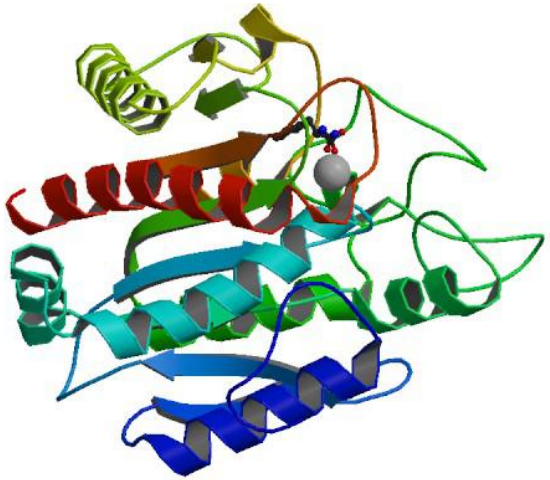




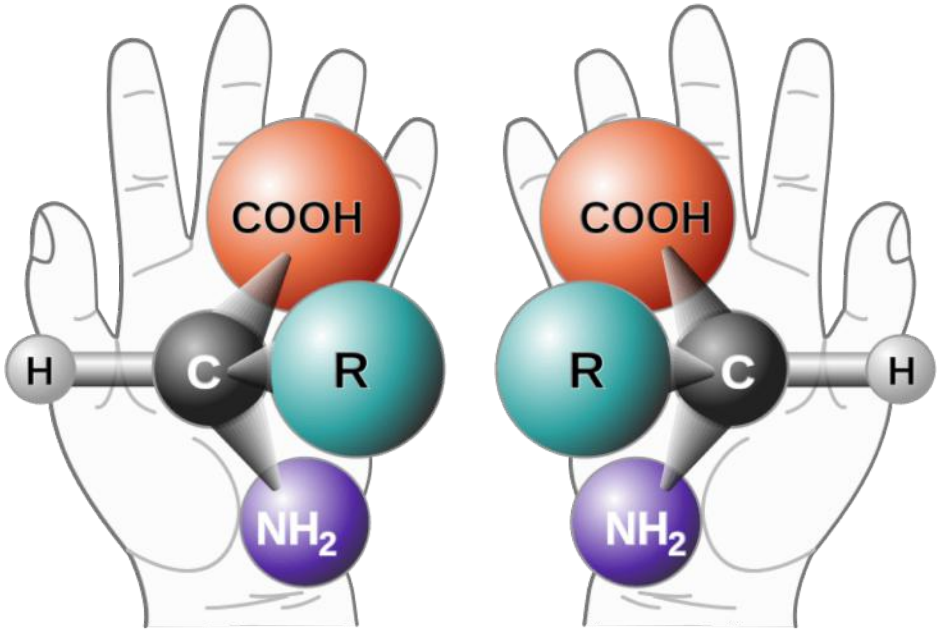
PDB ID 1HDU – Bovine Carboxypeptidase

DNA → **Amino Acid** → **Protein**

Information **Function**

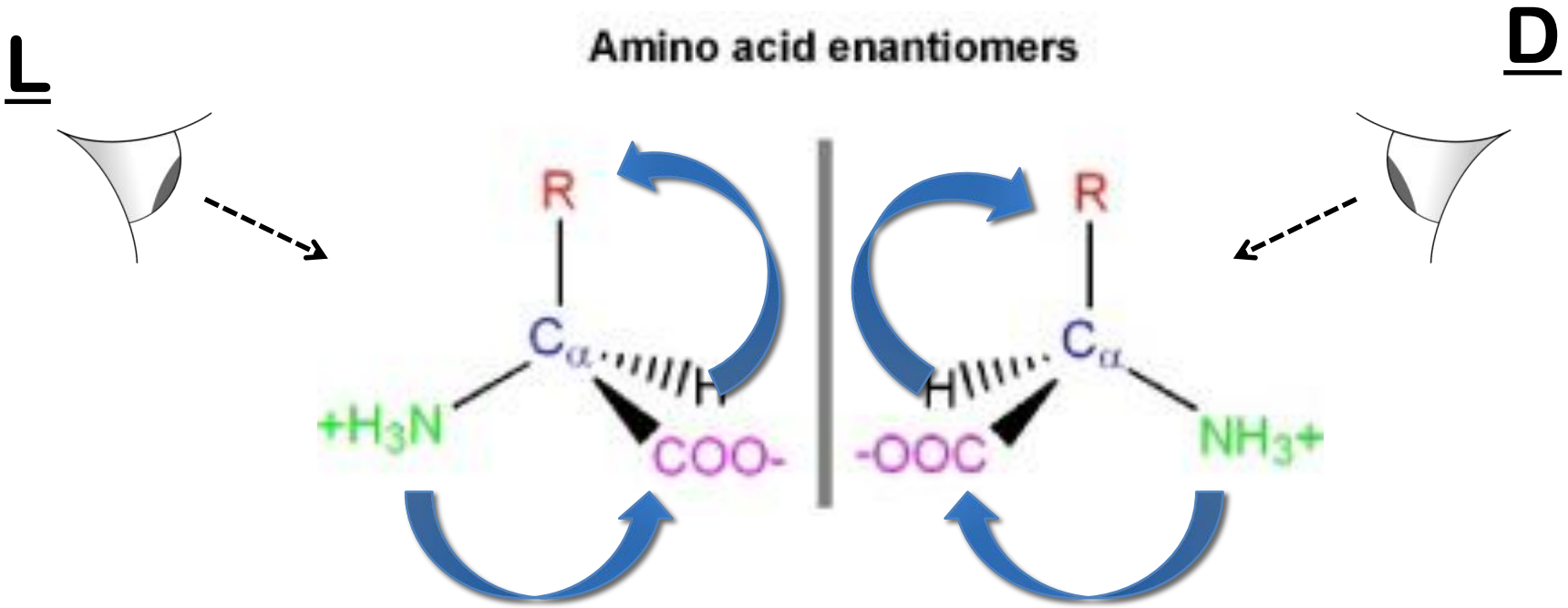
Amino Acids - Stereochemistry

- Cα has 4 different substituents (H, NH_3, CO_2, R), and therefore is chiral.
- L and D enantiomers are not super imposable!
- Many enzymes are enantiospecific.



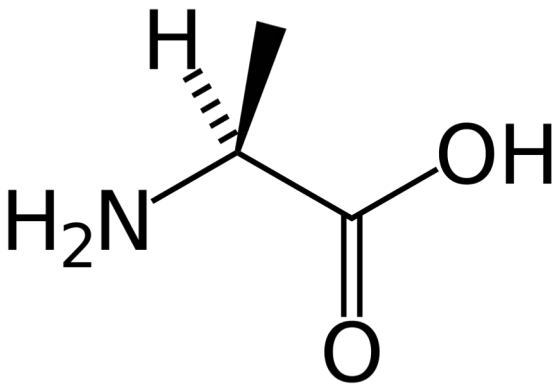
Review – Chirality or asymmetry

- **Enantiomers are non superimposable mirror images that are optically active.**

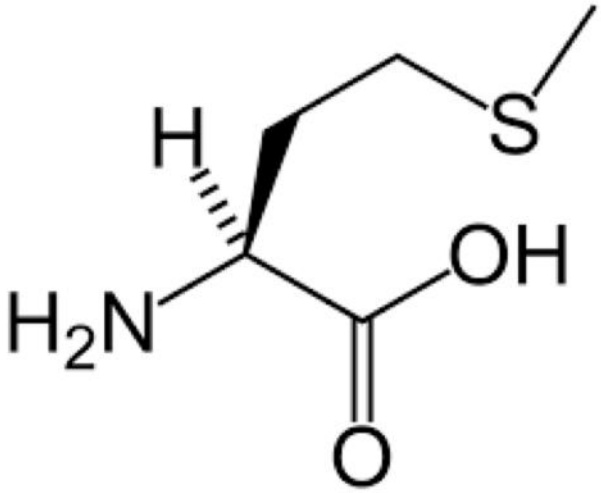


Question

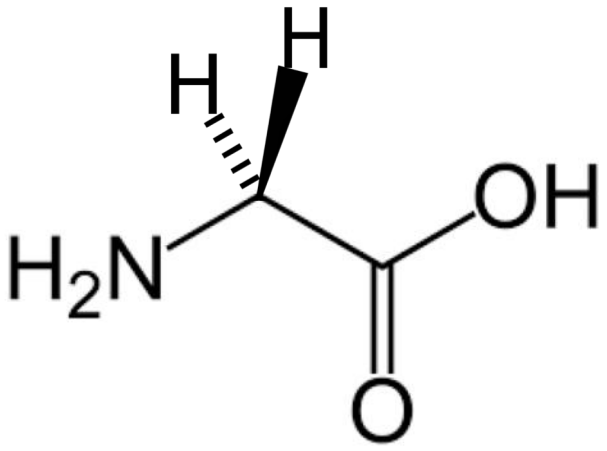
Which amino acid is not chiral?



Alanine



Methionine



Glycine

not chiral

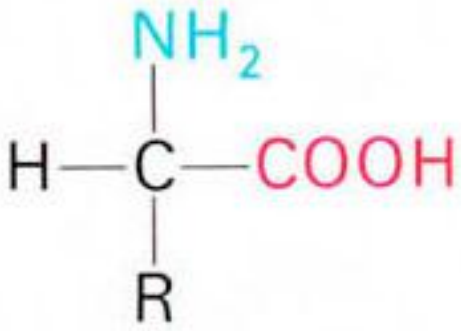
Amino Acids

All 20 amino acids need to be memorized!

Names (Full, three letter and one letter)

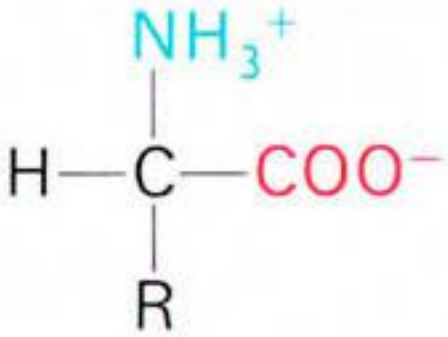
Properties (Charged, Hydrophobic, Hydrophilic?)

Un-ionized



Charge: 0

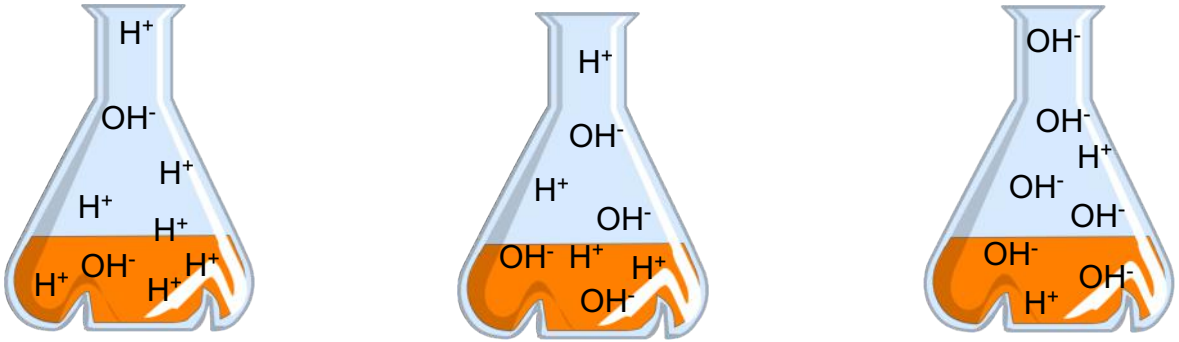
Zwitterionic



Charge: 0

What Factors affect ionization/charge

- **pH of the solution the amino acid or protein is in**



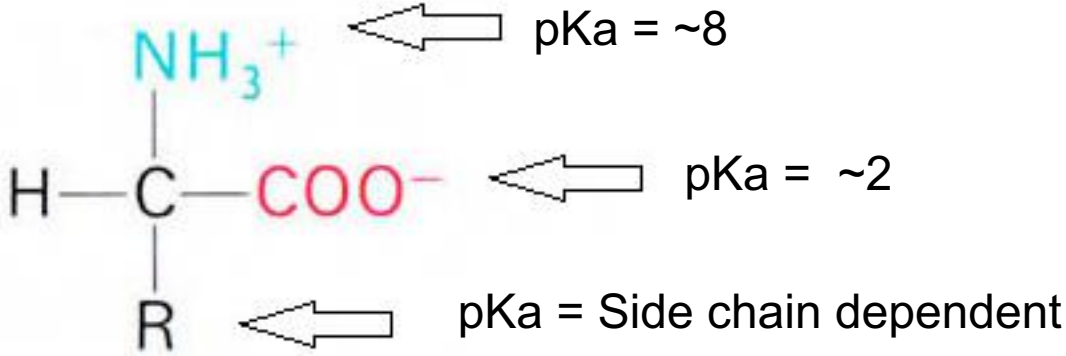
Acidic Neutral Basic

- **pKa: the negative log of the K_a, which is the measure of acid dissociation or how likely the acid is to give up it's proton.**

Strong acids – Lose H^+ readily, Large K_a, thus low pK_a

pKa, pH and Ionization

Amino acid backbone and certain side chains are ionizable



Ionization state of the amino acid is dependent on the pH.

more hydroxyl ions, donates proton

pH < pKa **Protonated**

pH = pKa **Equal amounts protonated and deprotonated**

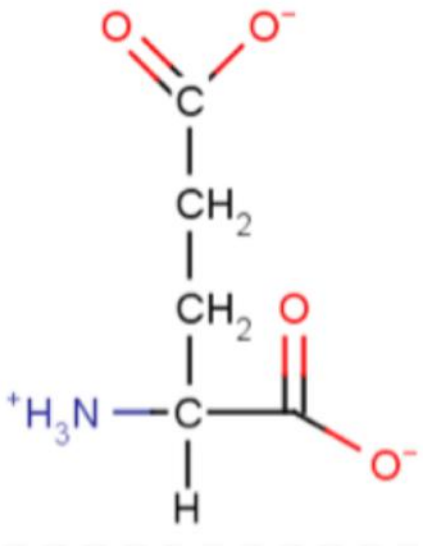
more hydronium ions, pulls hydrogen off and deprotonated

pH > pKa **Deprotonated**

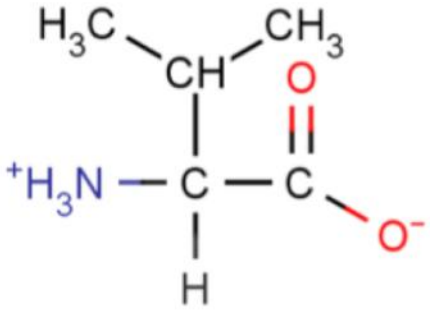
pKa, pH and Ionization

- Zwitterion has separate, oppositely charged ions, so that the overall charge in neutral.
- At physiological pH 7.4 the amine and carboxyl groups are ionized, the overall a.a charge is then dependant on the side chain pKa and it's ionization state.

Glutamate



Valine

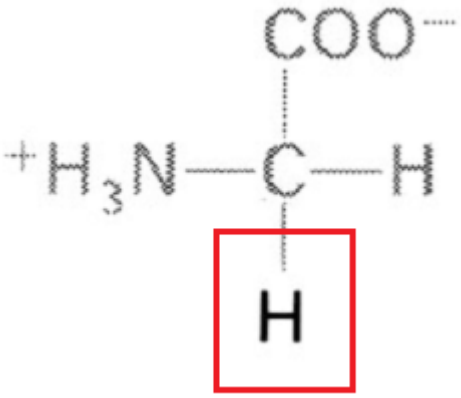


Classifications of Amino Acids

The amino acids can be grouped based on R-group properties, there are several different ways however to group them

- Hydrophobic, Non - Polar
- Polar (Hydrophilic), Uncharged
- Polar (Hydrophilic), Charged Acidic
- Polar (Hydrophilic), Charged Basic
- Amphipathic Aromatic

Non-Polar Hydrophobic Amino Acids

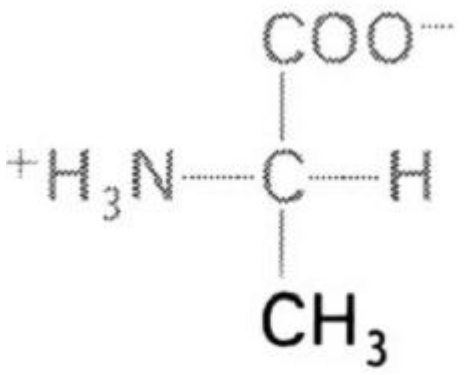


Glycine

Gly, G

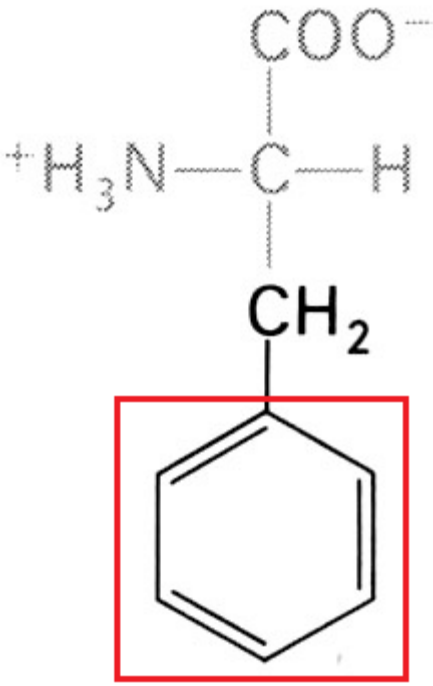
Only amino acid that is not chiral! Why?

Very flexible!



Alanine

Ala, A



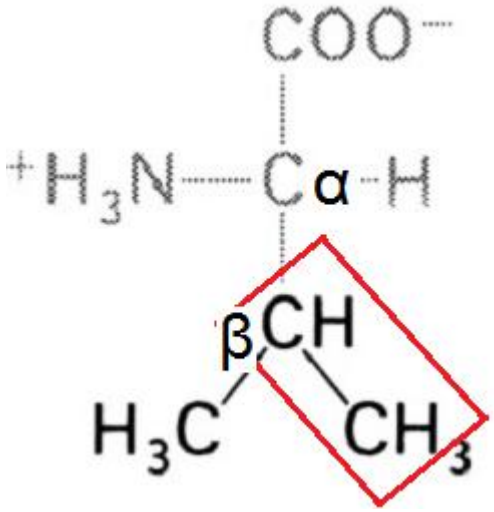
Phenylalanine

Phe, F absorbs around 280nm (?)

(think F-enylalanine)

Aromatic Ring

Non-Polar Hydrophobic Amino Acids

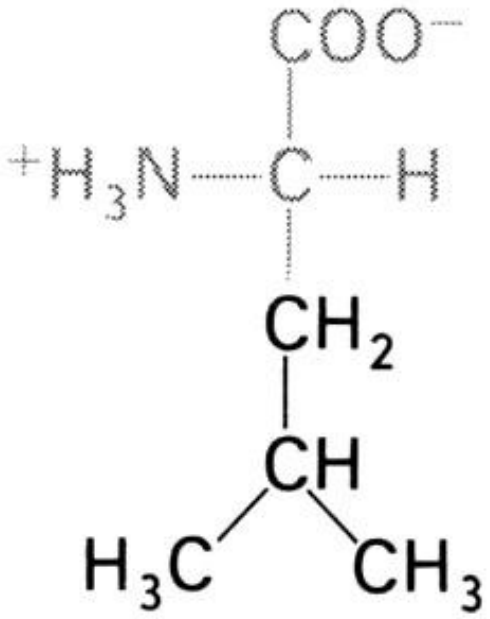


more steric hindrance, since its closer to the backbone

Valine

Val, V

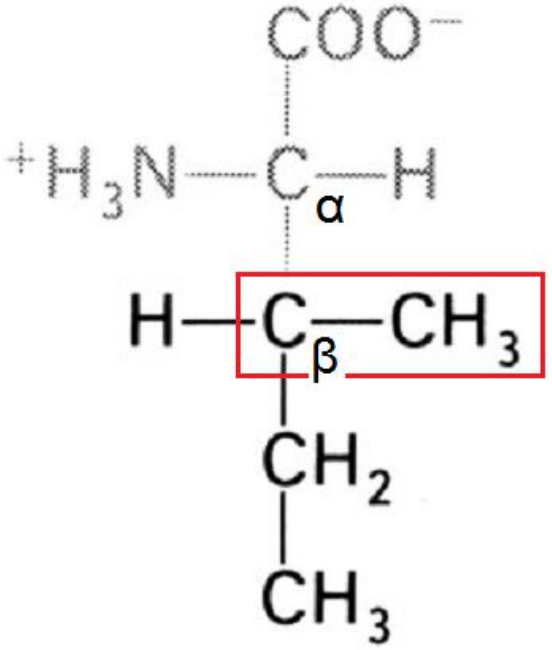
β-branched



gamma beta branched

Leucine

Leu, L

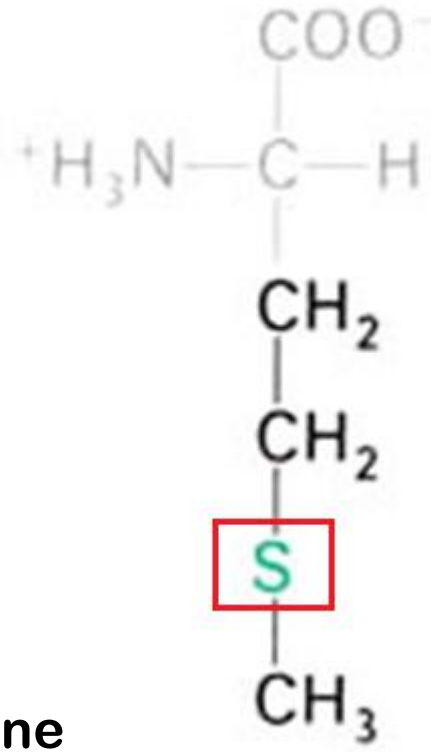


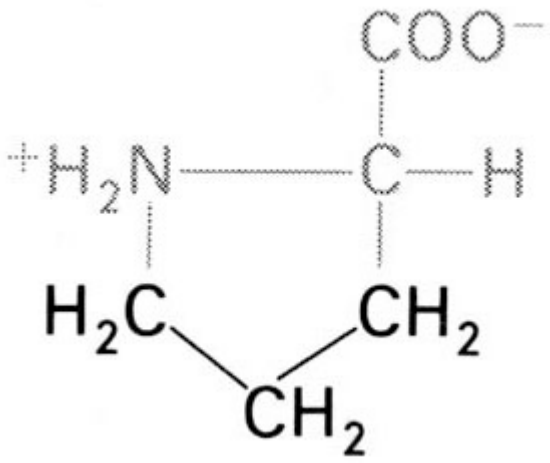
Isoleucine

Ile, I

β-branched!

Non-Polar Hydrophobic Amino Acids





Methionine

Met, M

Contains a Sulfur

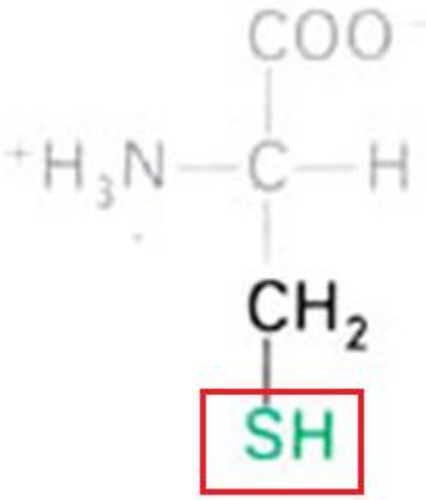
Can NOT form disulfide bonds

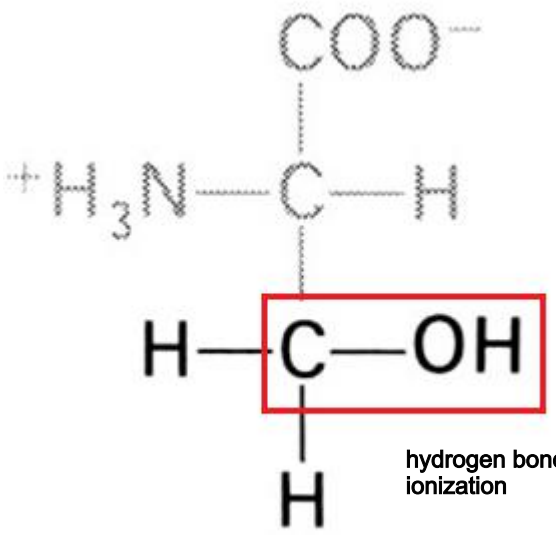
Proline

Pro, P

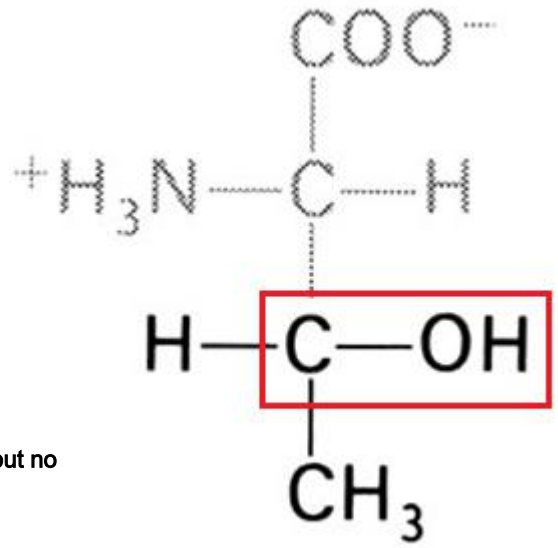
Very rigid!

Polar (Hydrophilic) Amino Acids





hydrogen bonding, but no ionization



Cysteine, Cys, C

Contains a sulfhydryl group

Can form disulfide bonds with other Cys!

S -- S

Side chain pKa ~ 8

Serine

Ser, S

Hydroxyl Group

Can form H-bonds!

Threonine

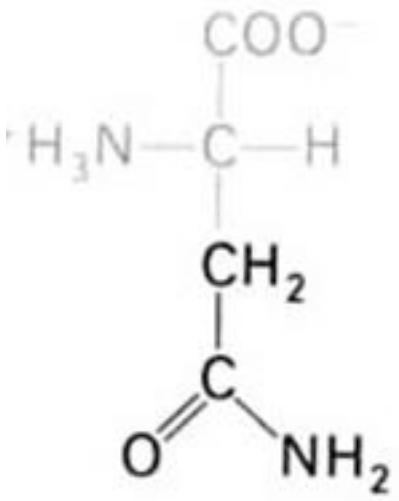
Thr, T

Hydroxyl Group

Beta - branched

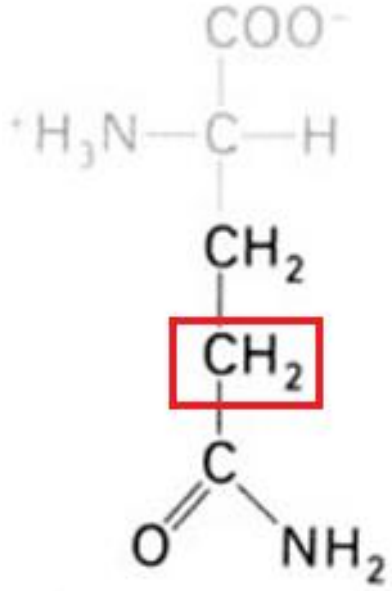
Can form H-bonds!

Polar (Hydrophilic) Amino Acids



Asparagine

AsN, N



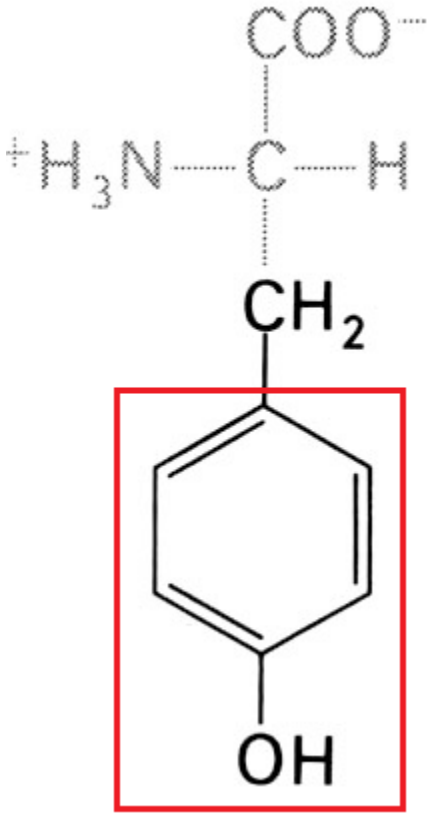
Glutamine

Gln, Q

One extra CH_2 than Asn!

amino acid and residue are interchangeable terms

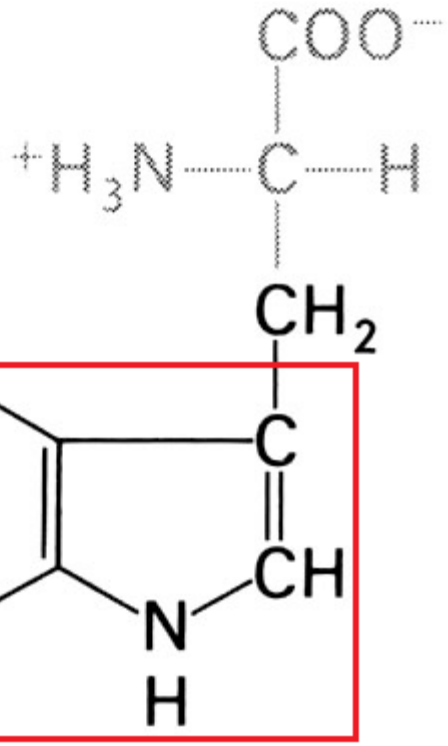
Amphipathic Aromatic Amino Acids



T-Y-rosine, Tyr, Y

Aromatic, hydroxyl group

pKa ~ 10

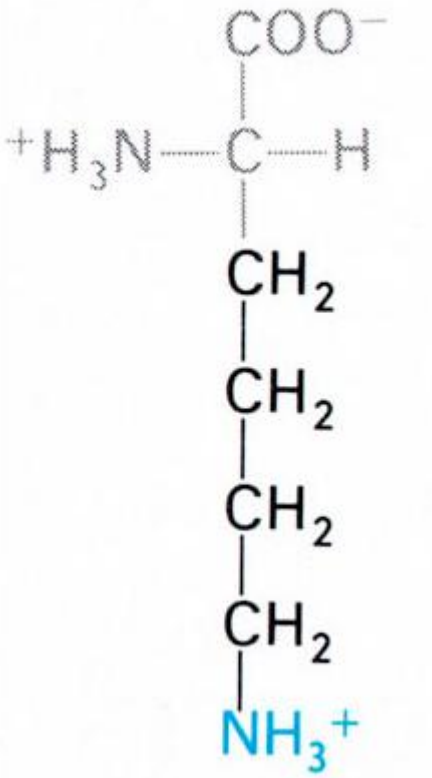


Tryptophan, Trp, W

Aromatic

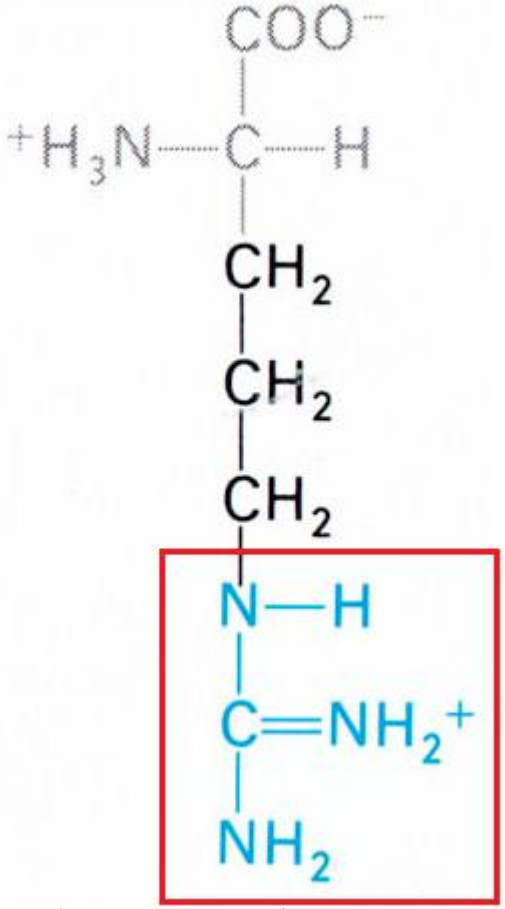
Strong absorbance @ 280nm

Basic Amino Acids



Lysine, Lys, K

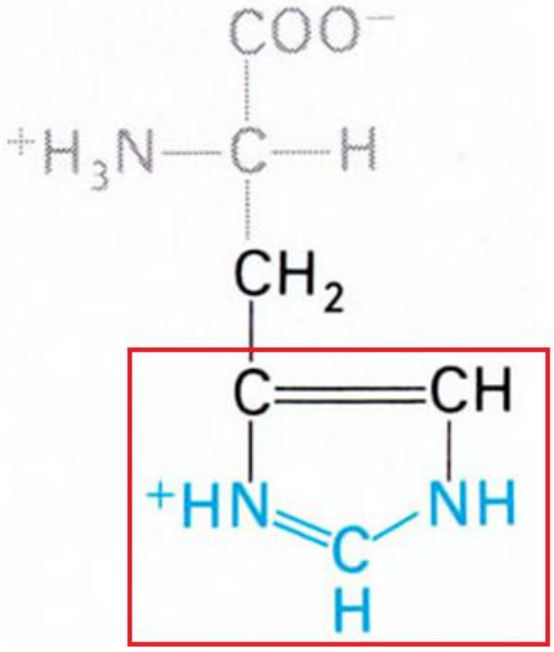
Side chain pKa ~ 10.5



Arginine, Arg, R

Think R-ginine

Guanidinium group, pKa ~ 12.5

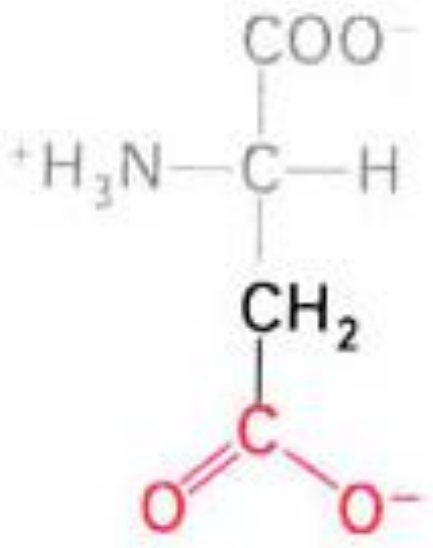


Histidine, His, H

Imidazole ring

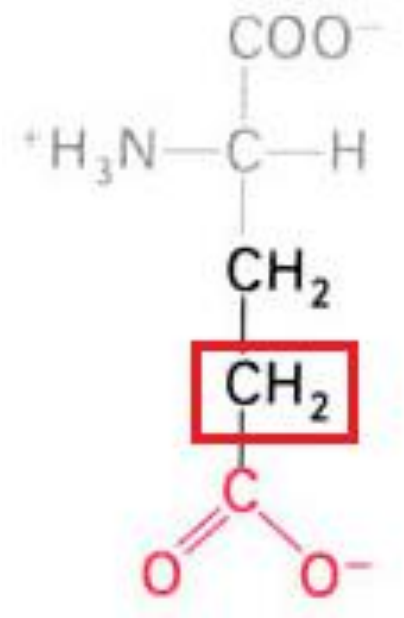
Side chain pKa ~ 6

Acidic Amino Acids



Aspartic acid, Asp, D

Side chain pKa ~ 4



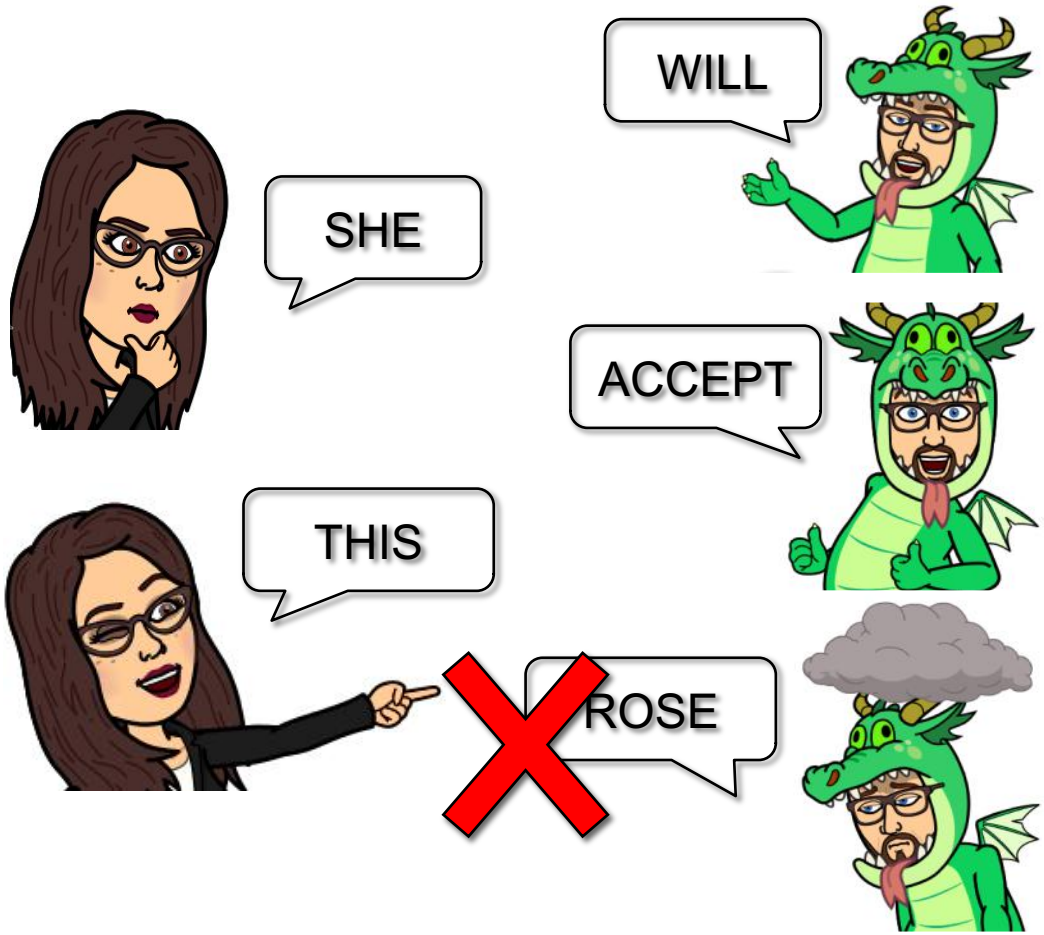
Glutamic acid, Glu, E

One extra CH_2 than Asp!

Side chain pKa ~ 4

GAME!

1. Turn to your Neighbour – Say Hi!
2. Try and form a sentence using only words containing the letters for the amino acids.



Amino Acid Questions

Which amino acid has a pKa near physiological pH?

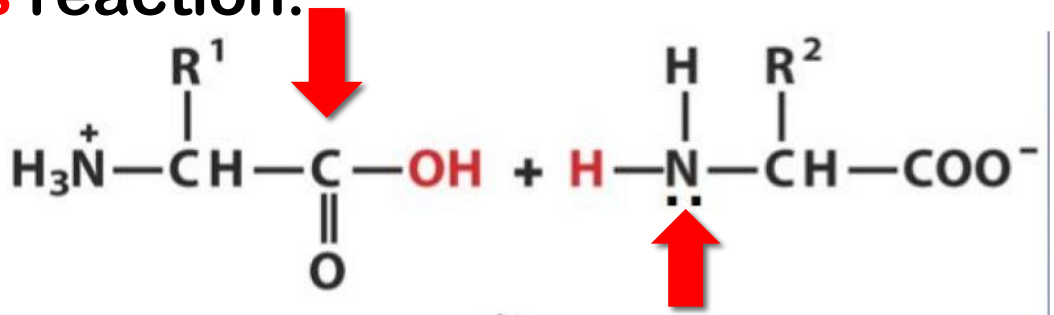
histidine

Which amino acids absorb UV light at 280nm? Which the strongest? tryptophan (strongly), phenylalanine, tyrosine

Which amino acid has three carbons and three oxygens? serine

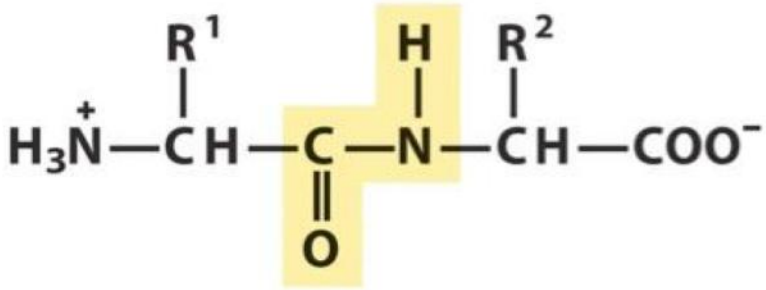
Peptide Bond

Formation of the peptide bond is a condensation reaction. Hydrolysis of the peptide bond involves a hydrolysis reaction.



Hydrolysis **Condensation**

carboxylic acid + amino / amine group



amide bond

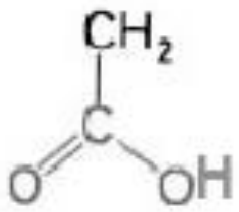
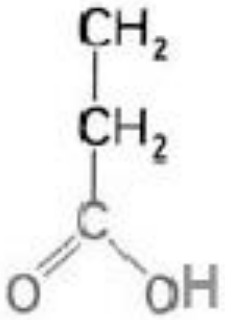
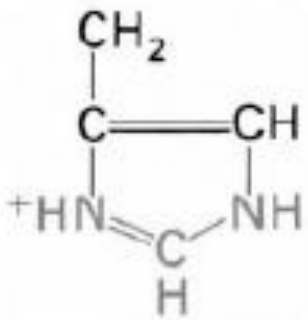
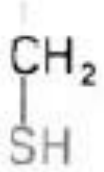
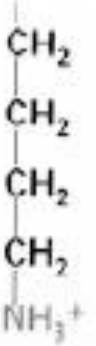
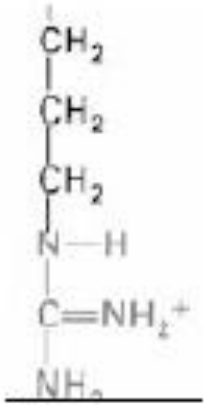
What type of bond is the peptide bond?

Question

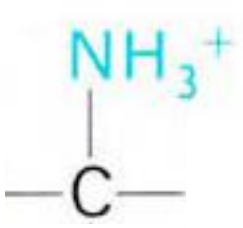
Select the components of the amino acid that participate in peptide bond formation

A. Amide group
B. Amino group
C. Carboxyl group
D. Ketone group

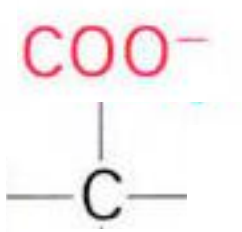
Ionizable amino acid side chains

Asp,	Glu,	His,	Cys,	Tyr,	Lys,	Arg
						
pKa:						
4	**4**	**6**	**8**	**10**	**10.5**	**12.5**

When ionized, N is always +, O and S are always -



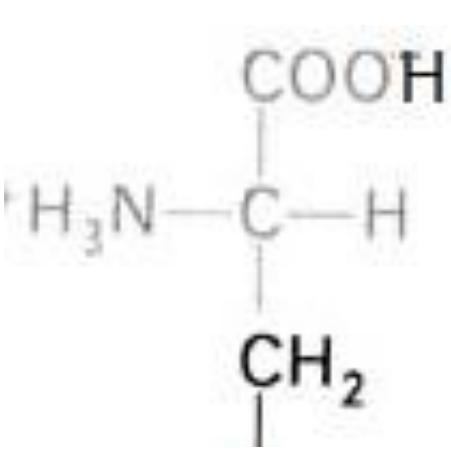
⟸ pKa = ~8



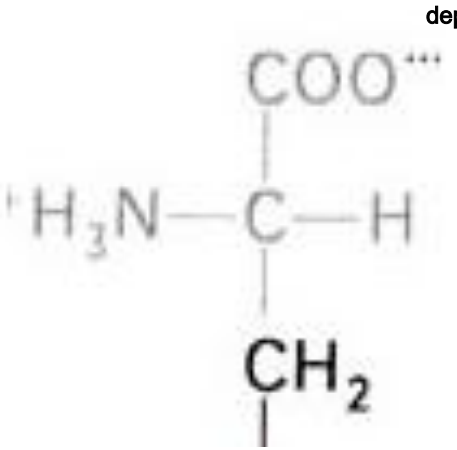
⟸ pKa = ~2

pKa Practice

Draw in the ionization state of the R group of Asp.

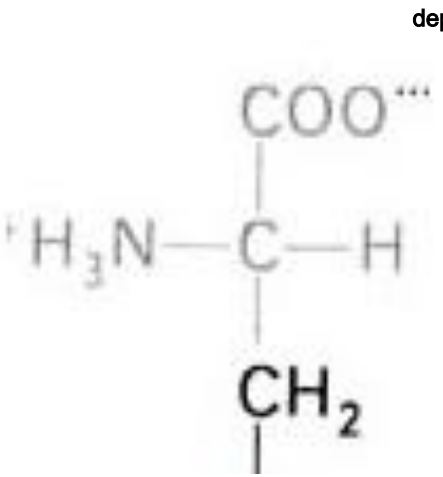


protonated



deprotonated

protonated



deprotonated

pH: 1 3 6

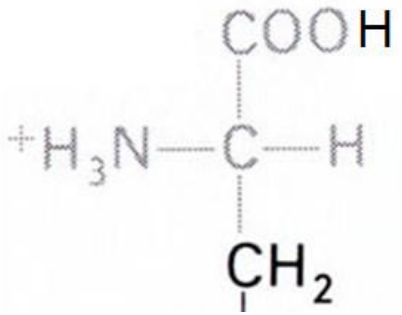
Side chain pKa ~ 4

hemdelson - hassleblock equation to determine amount of protonation/deprotonation

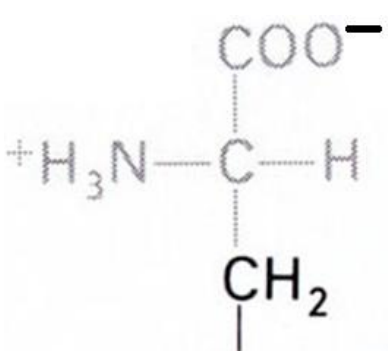
pKa Practice

Draw in the ionization state of the R group and backbone of His. What is the Net Charge?

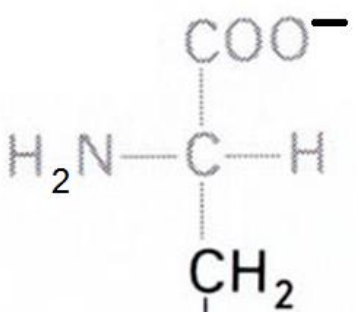
pka 2



protonated



deprotonated



deprotonated

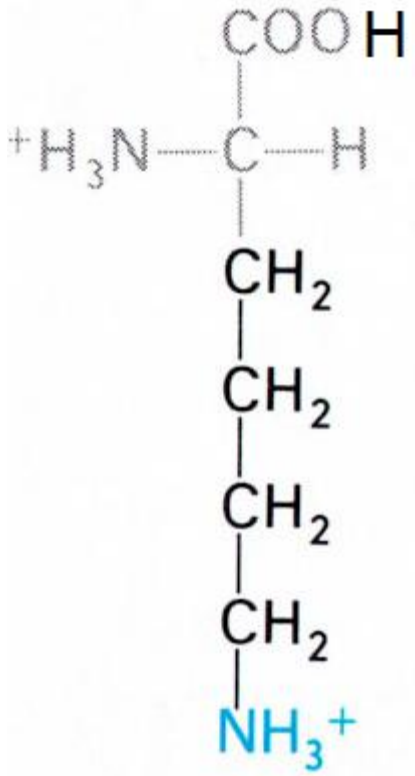
Side chain pKa ~ 6

pH:	**1**	**7**	**9**
Net Charge?	2+	neutral	1-

pKa Practice

What is the pH range? What is the Net Charge?

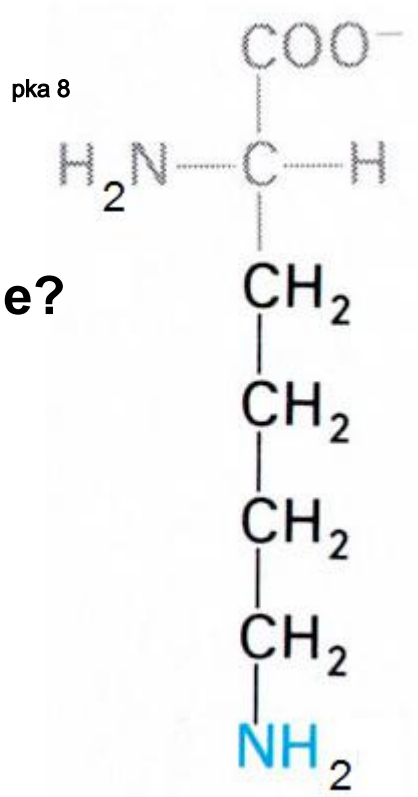
Side chain pKa is 10.5 **Lys**

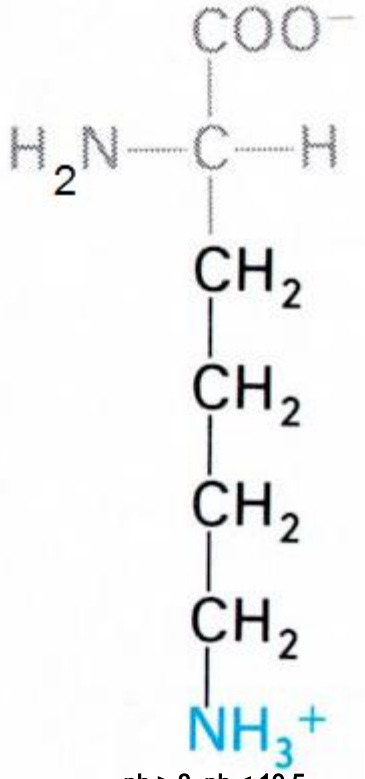


Net Charge?

pka 8

pka 2





pH:

>2

>10.5

ph > 8, ph < 10.5

pKa practice

Consider the following peptide?

Ala-Tyr-Leu-His-Asp-Val-Gly-Arg

How many polar amino acids (including basic and acidic)?

How many hydrophobic amino acids?

How many are Beta-branched?

What is the net charge at physiological pH?

Question

Which of the following statements is true?

A. The most hydrophobic amino acids have side chains with either a negative or positive charge at physiological pH

B. The most hydrophobic amino acids have side chains that are polar but uncharged at physiological pH

C. The most hydrophilic amino acids have no oxygen or nitrogen in their side chains

D. The most hydrophilic amino acids have side chains that are polar but uncharged at physiological pH

E. The most hydrophobic amino acids have side chains that are nonpolar and uncharged at physiological pH

Protein Folding

What forces secondary, tertiary and quaternary structure?

Interactions that stabilize protein structure:

- **Electrostatic**
- **Hydrogen bonds**
- **Hydrophobicity**
- **Van der Waals**

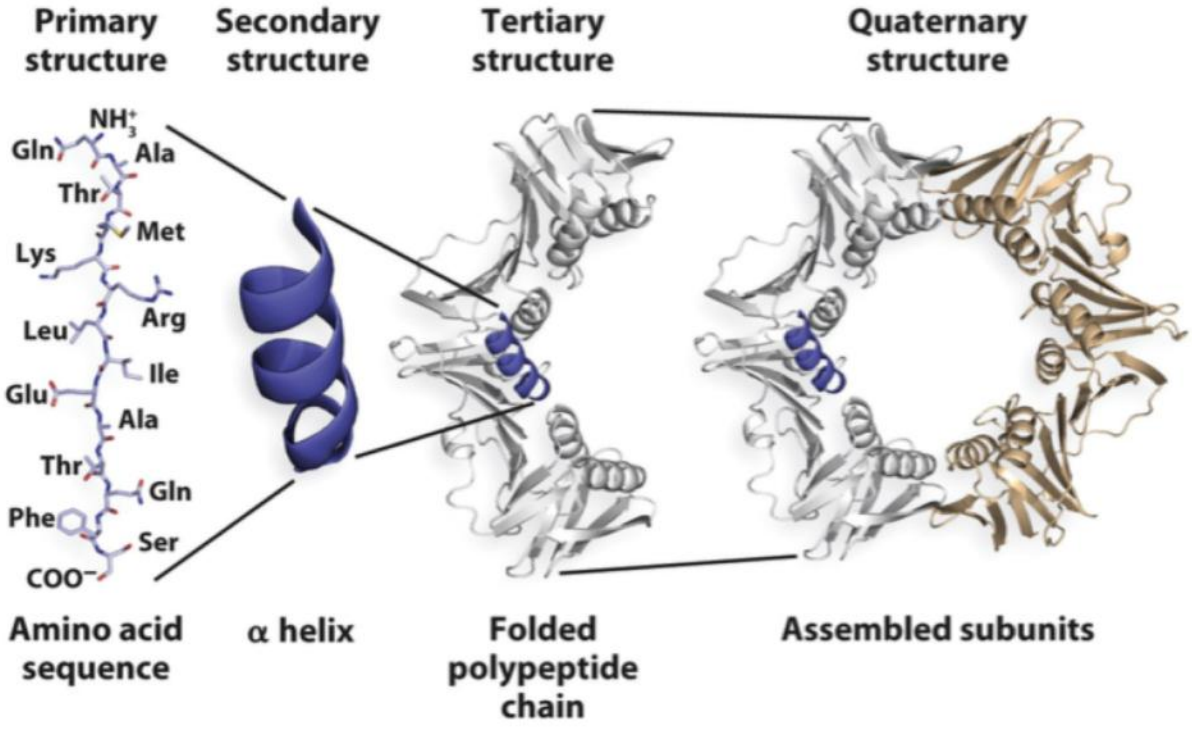
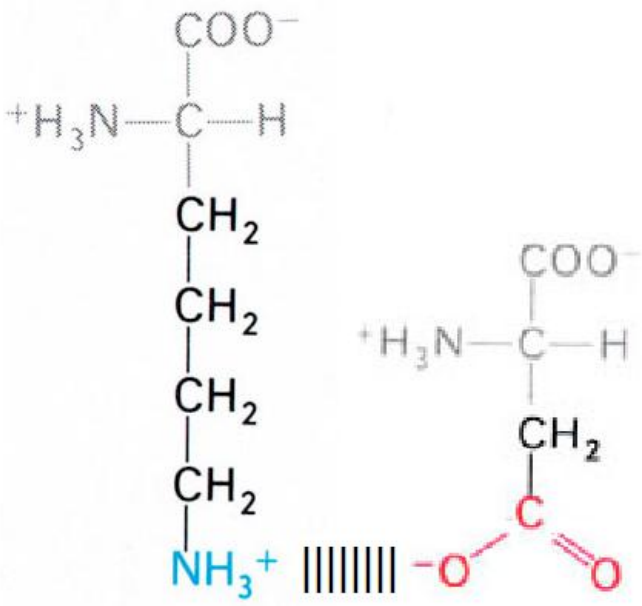


Figure 4-1
Molecular Biology: Principles and Practice

Electrostatic Interactions

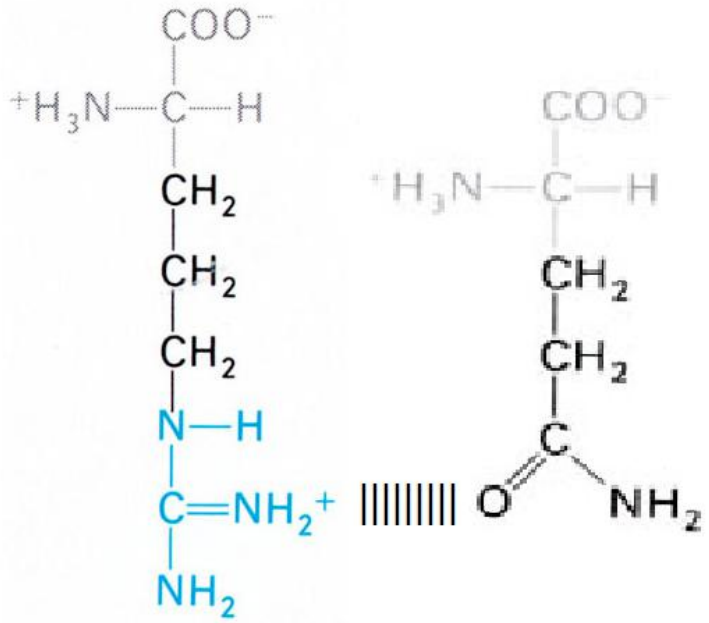
Occurs between positive and negatively charged species.
Opposites attract!

Two Charged Species



Lysine **Aspartic Acid**

Charged and Polar Species



Arginine **Glutamine**

Question

Electrostatic interaction can happen between the R-groups of:

A. Glycine and Aspartate

B. Leucine and Isoleucine

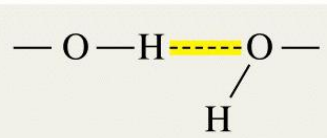
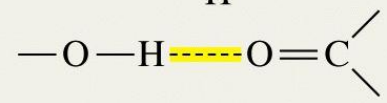
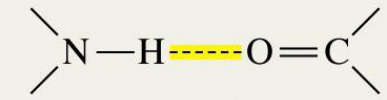
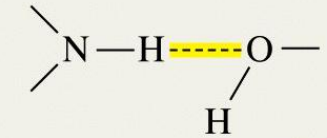
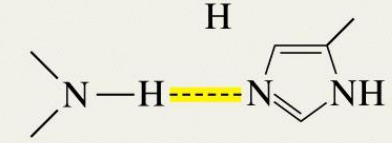
C. Lysine and Aspartate

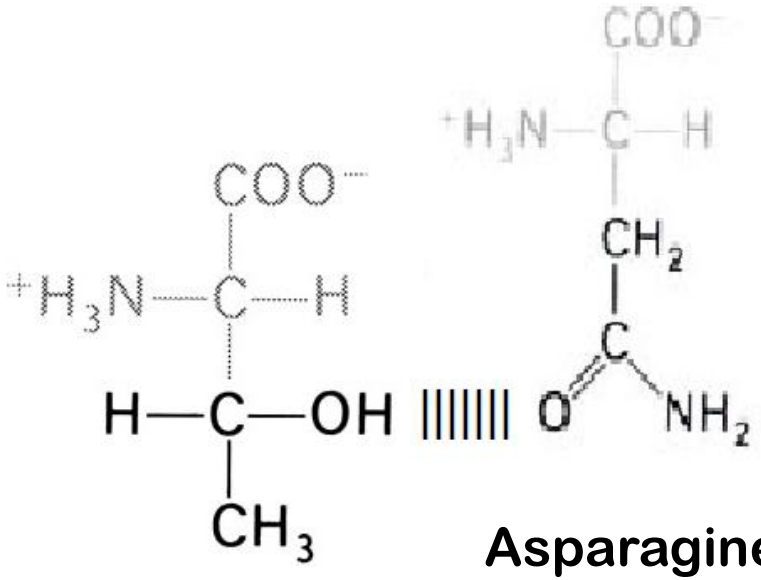
D. Arginine and Lysine

E. Lysine and Lysine

Hydrogen Bonds

Occurs between a proton (-OH, -SH, -NH) and an electron donating species (C=O).

Type of hydrogen bond	
Hydroxyl-hydroxyl	
Hydroxyl-carbonyl	
Amide-carbonyl	
Amide-hydroxyl	
Amide-imidazole nitrogen	



Threonine

Asparagine

Question

Which statement(s) apply to Hydrogen bonds?

A) Non-covalent interaction between electroneutral atoms of different molecules.

B) Non-covalent interaction between two electroneutral atoms of the same molecule.

C) Partially electropositive hydrogen atom of one molecule and partially electronegative atom of another molecule.

D) Partially electropositive hydrogen atom of one molecule and partially electronegative atom of the same molecule.

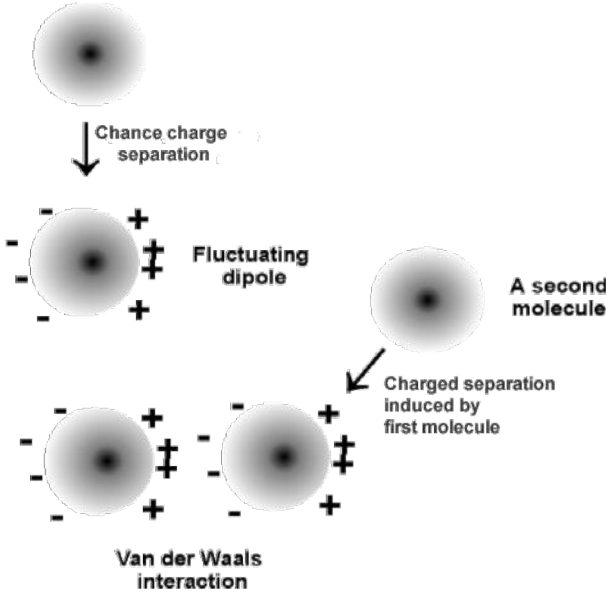
Van der Waals Interactions

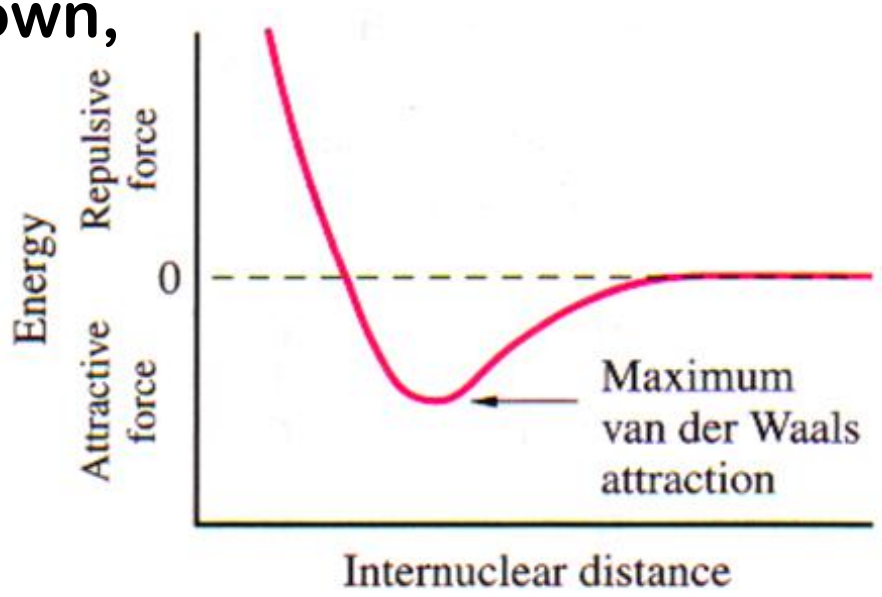
Weak interactions between close molecules.

- **Can not be closer than the van der Waals contact distance (radii) or else positively charged nuclei will repel!**

Weak interactions on their own,

but strength in numbers!



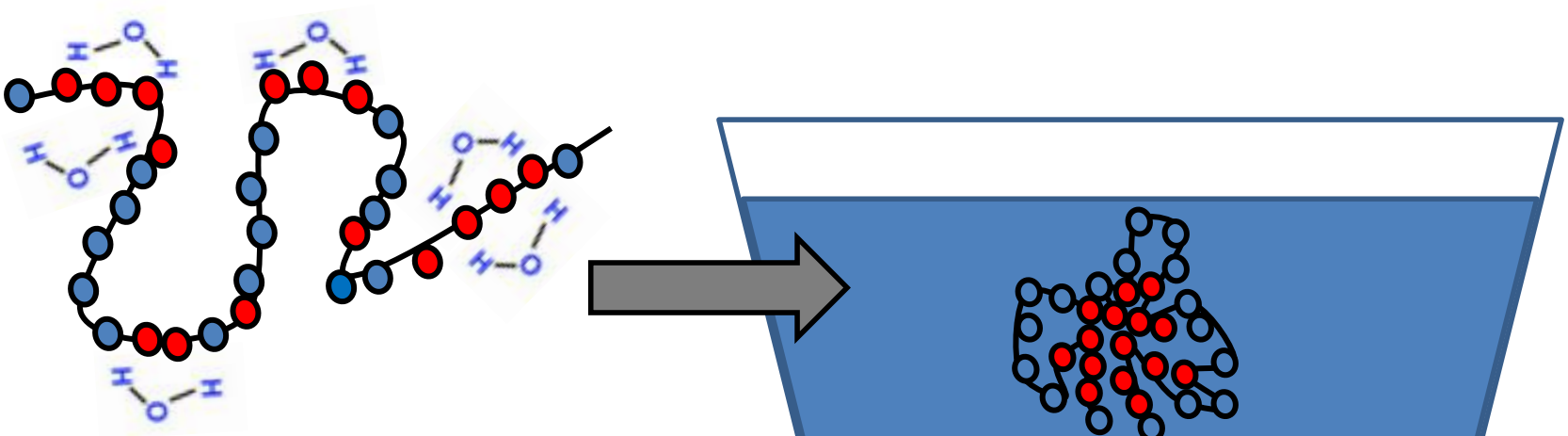


Similar to a temporary electrostatic interaction (induced dipole)

Hydrophobic Interactions

Association of non-polar residues driven by the HYDROPHOBIC EFFECT. Hydrophobic side chain exposure causes unfavourable water molecule 'ordering', reduced entropy! Water also has a high affinity for itself, forming H-Bonds!

The burial of hydrophobic residues is the main driving force for protein folding!



Red = hydrophobic a.a.

Question

Which of the stabilizing forces on a single molecule basics is the weakest?

A. **Hydrogen Bonds**
B. **Electrostatics**
C. **Hydrophobic affect**
D. **Van der Waals**

How would having many interacting molecules affect this force?

Take away points for today

- **Driving forces involved in protein stabilization**
  - **Hydrophobic effect, Ionic interactions, Hydrogen bonds, Van der Waals**
- **AMINO ACIDS**
  - **Name, single and triple letter code, side groups, properties**
- **Determine protonation state of amino acids in different environments**
  - **pH and pKa**