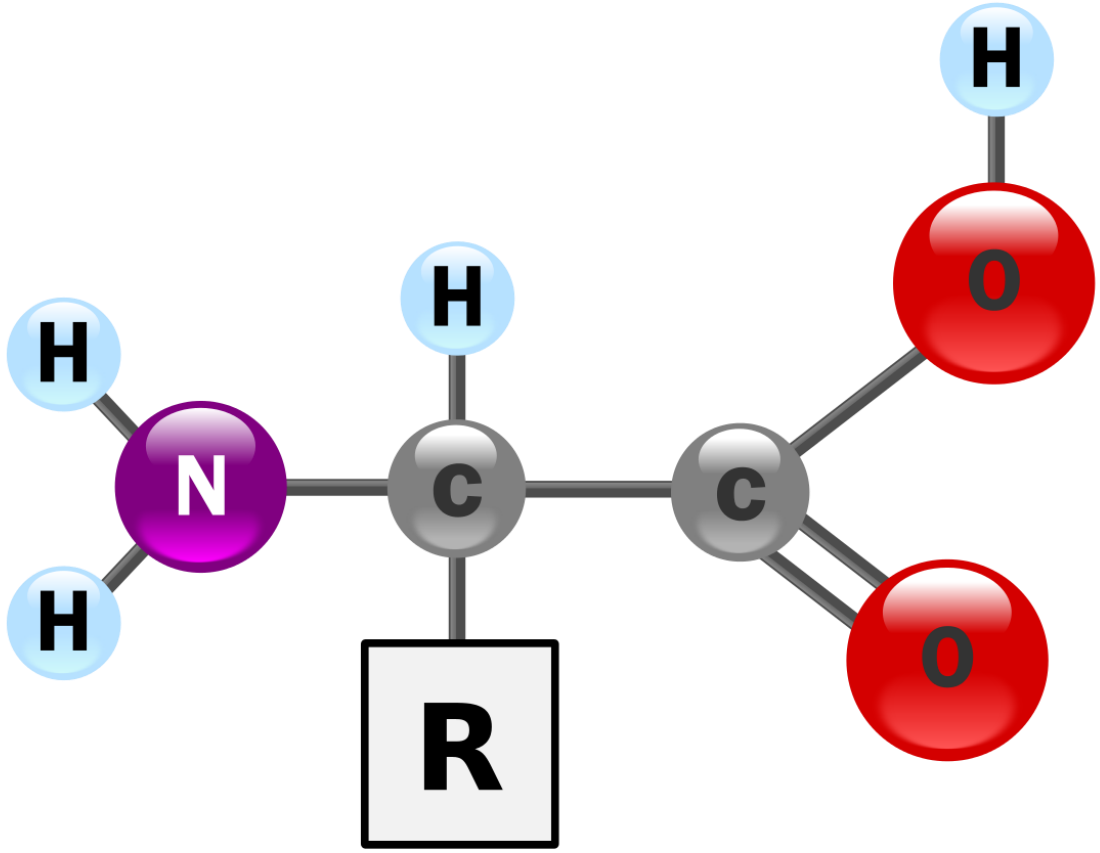
Next Step MCAT Super Review: Amino Acids

- Welcome to Super Review!
- Introduction
- AA Study Strategies
- AA Content Review
- Peptide Bond
- AA Separation & Purification
- MCAT Passage
- What Next? How Can Next Step Help?



Introduction to Super Review

- **Thanks for coming to Next Step Super Review!**
- **Here's how it works…**
- **These sessions are meant to be:**
  - **Interactive**
  - **Problem-focused**
  - **Specific to your needs (*so ask questions!*)**
- **Today's focus: review of amino acids**
- **This is NOT a lecture! You can benefit most by:**
  - **Raising your hand and speaking**
  - **Commenting in the Question/Chat box**
  - **Participating!**

Before Getting Started

1. **If you have a microphone, make sure it is turned on and easily available.**
2. **Locate the hand-raise button on the toolbar on your screen.**
3. **Locate the Question box on the toolbar.**
4. **Let me know if you're having any technical issues!**

If on wireless connection:

- **Close any other internet resource-heavy processes**
- **Ask other users on network to do same**
- **Sit as close to router as possible**

We will have some great free resources and discounts available for you at the end of the presentation. Stick around and give us some feedback on our short survey as well!

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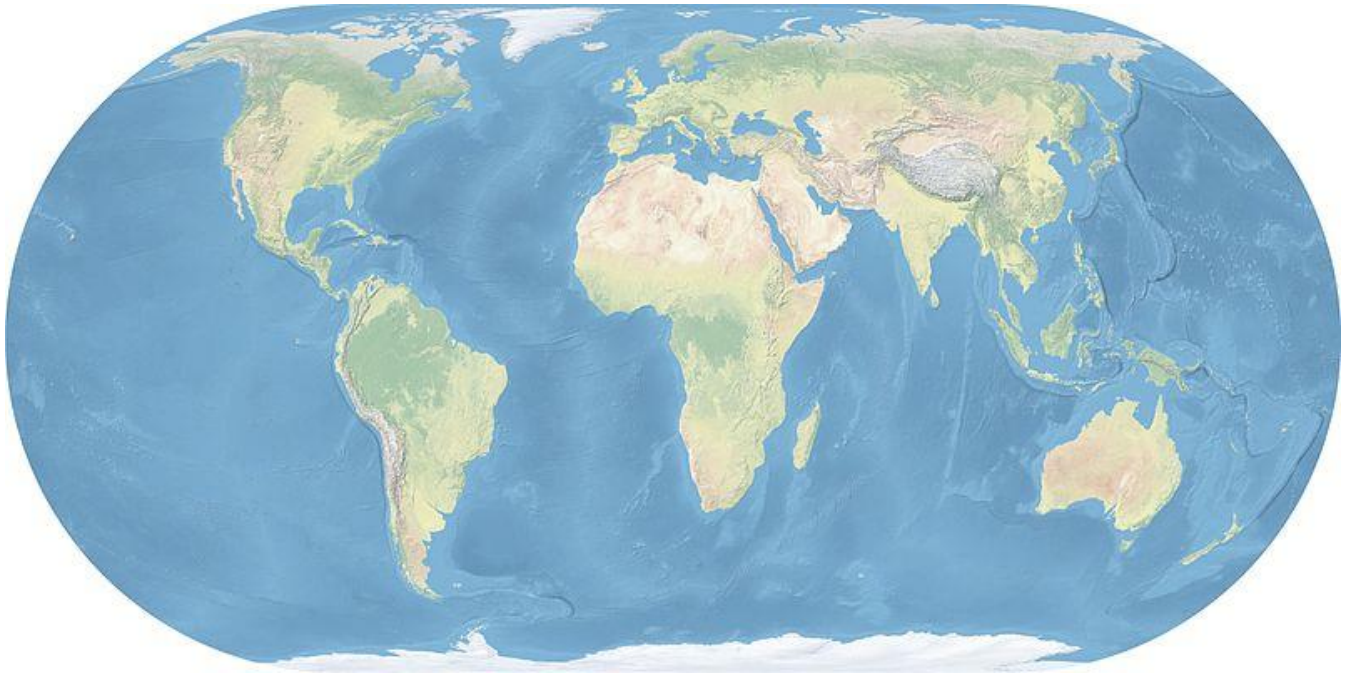
In General: Biochem Study Strategies

A big-picture approach to biochem…

How is biochem tested on the MCAT? How do you get the most bang for your buck in terms of studying?

Focus on:

- Principles
- Physiological function
- Interconnections with other subject matter
  - Amino acids & acid-base chemistry
  - Carbohydrates & stereochemistry
  - Metabolism & physiology



What have your biochem experiences been like? What strategies work for you?

Amino Acid Study Strategies

You may have heard that amino acids are among the most high-yield MCAT topics! Today, let's start learning what you need to know.

- **High-yield topics**
  - Chemical properties
  - Electrical charge properties / acid-base behavior
  - Biological location on proteins
  - Biochemical lab techniques (isoelectric focusing, etc.)
  - Abbreviations!

Amino Acid Study Strategies

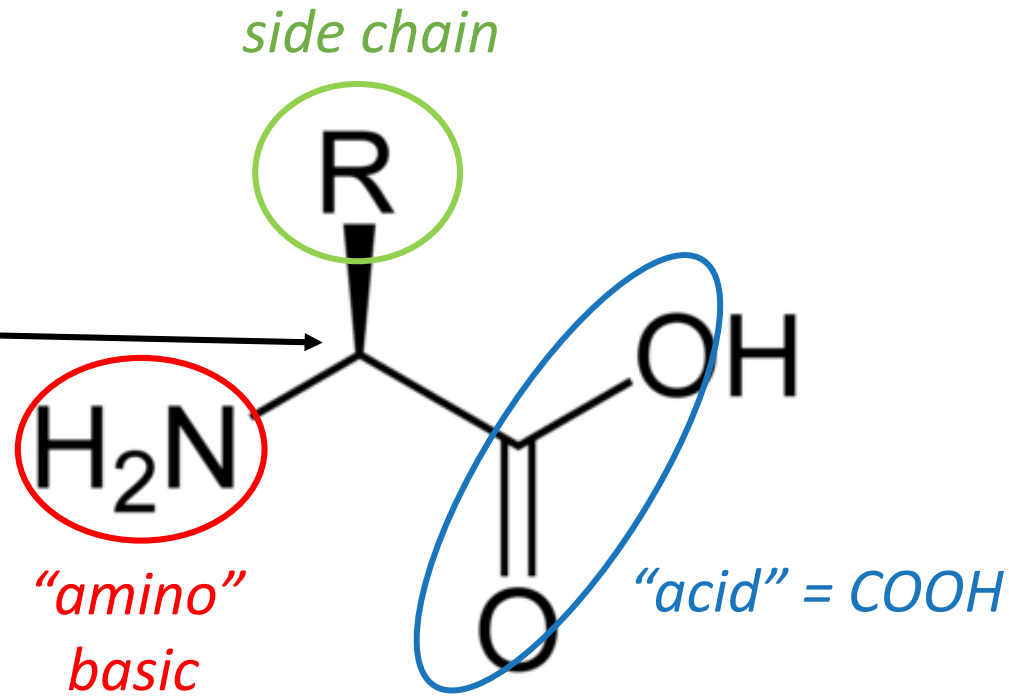
When studying, ask yourself …

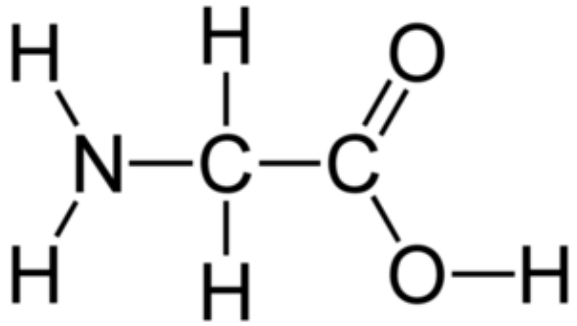
- Why does this matter physiologically?
  - Biomolecules: how does AA identity connect to biological function?
  - What pathways may relate to AA metabolism?
- Are there any neurological or endocrine uses for this AA?

Do not lose the forest for the trees!

General Structure

- AAs only differ in their R groups
- 20 standard AAs = α-amino acids
- Is this structure chiral?
  - Yes, EXCEPT…

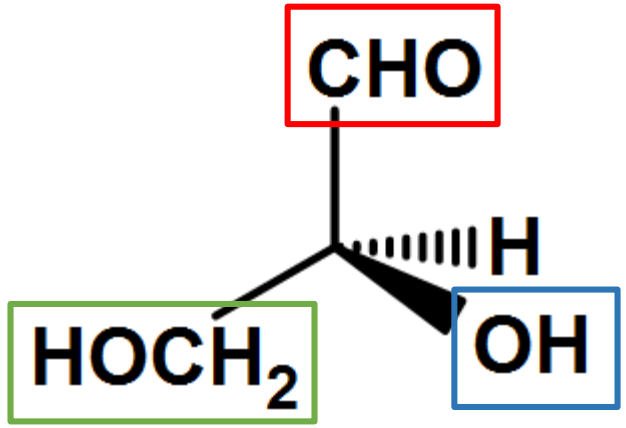




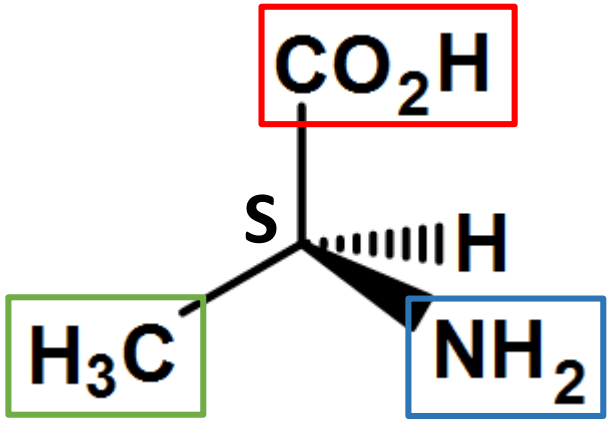
glycine

Amino Acid Configuration – D or L?

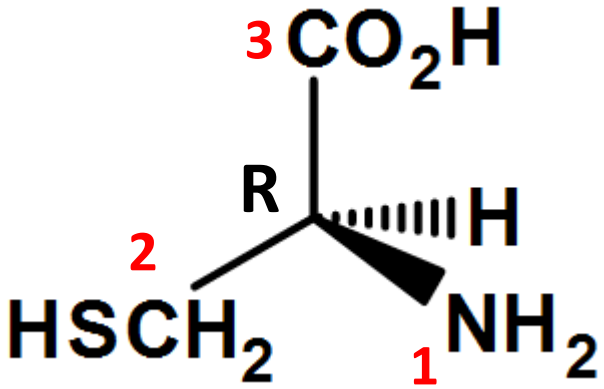
- Misconception: D = R, L = S
- In reality, D/L and R/S are separate systems



L-glyceraldehyde



L-alanine



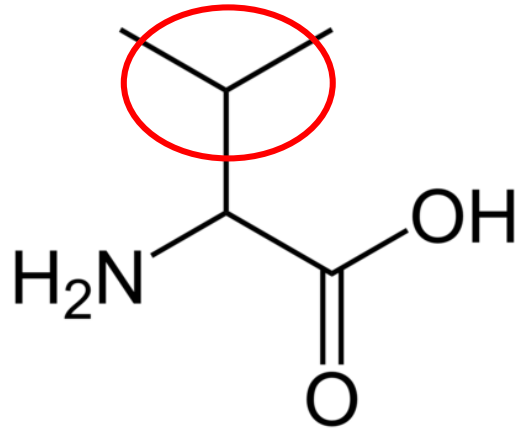
L-cysteine

Classifications – Polar vs Nonpolar

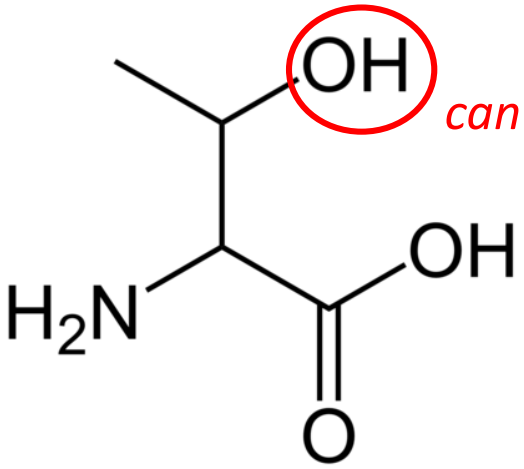
- Note: classifications are based only on side chains
  - Backbone is always the same!
- Nonpolar = hydrophobic
  - Generally have hydrocarbon R groups
  - Location: interior of globular proteins
- Polar = hydrophilic
  - Includes polar uncharged…
  - AND polar charged AAs → *acidic / basic*

charged = very polar

can't H-bond



valine

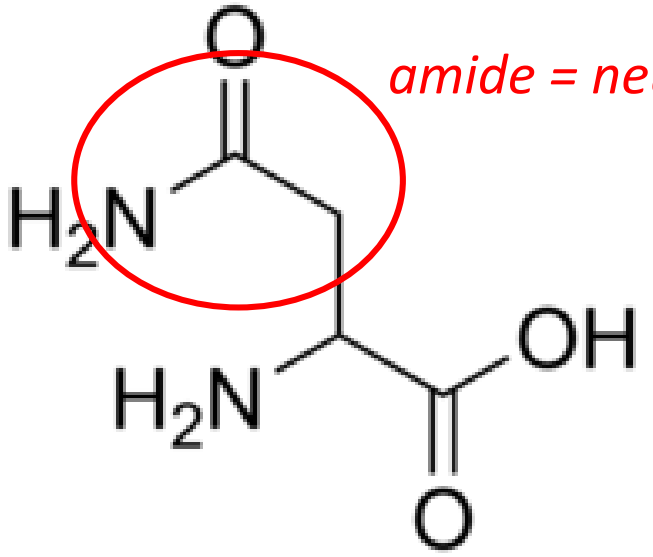


can H-bond

threonine

Classifications – Acidic and Basic

- Acidic side chains = *contain COOH (-OH, -SH)*
- Basic side chains = *contain nitrogen and can become protonated*
  - Lys = amine
  - His = imidazole
  - Arg = guanidinium
  - Be careful: is this a basic side chain?



amide = neutral

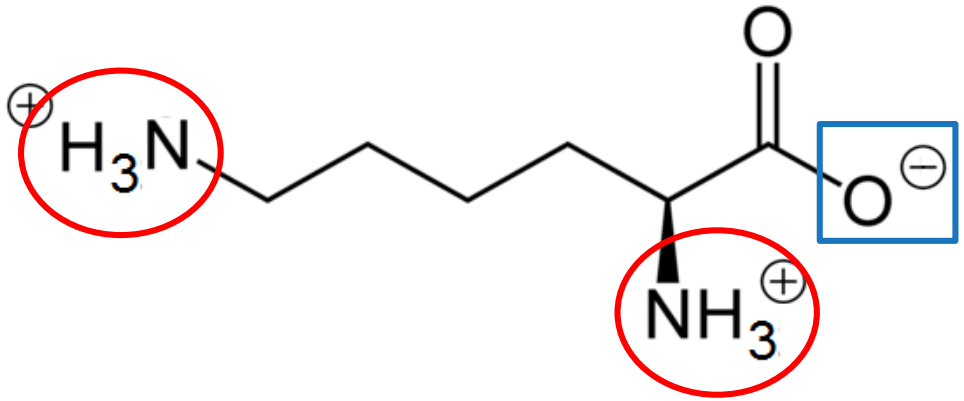
asparagine

Acidic / Basic AAs – Be Careful!

- Lysine exists in a certain 0.5 M solution in the state pictured here. Which group(s) on this molecule can act as bases? *(gain a proton)*
  - Amines? *already protonated!*

    ↓

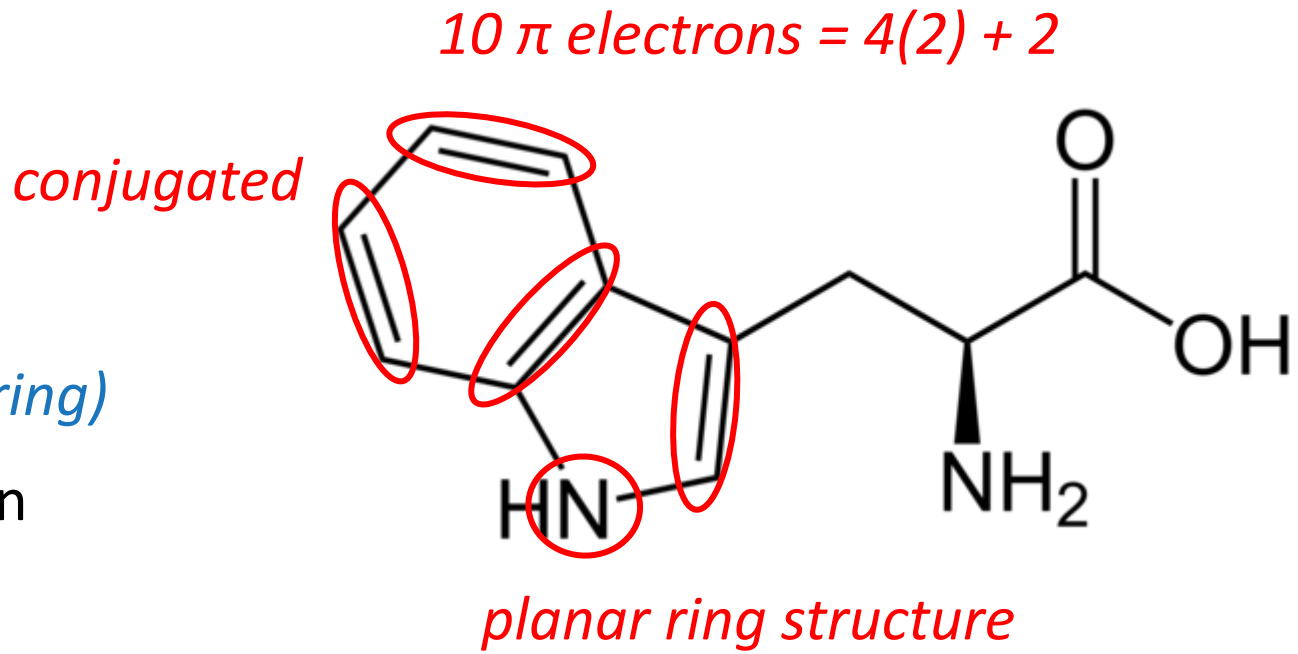
    can act as acids
- Remember: protonation state depends on pH



lysine

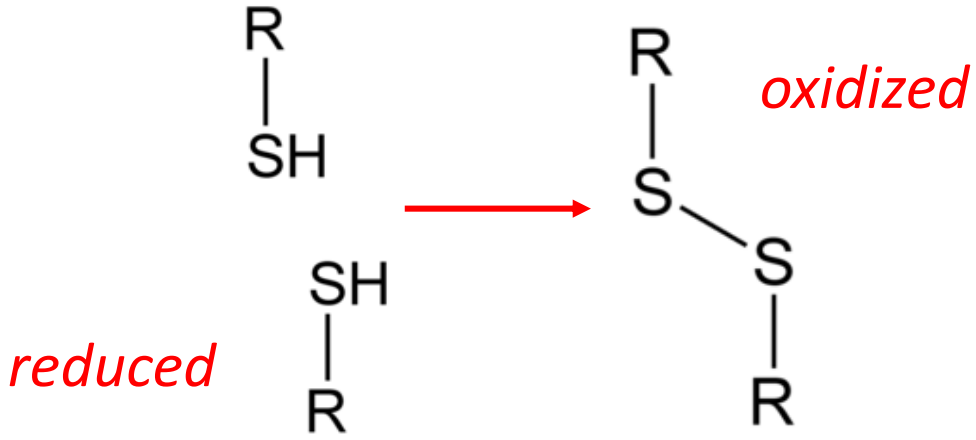
Aromatic Side Chains

- Phenylalanine
- Tyrosine
- Tryptophan
- Histidine* *(contains an aromatic ring)*
- Conjugation → UV light absorption

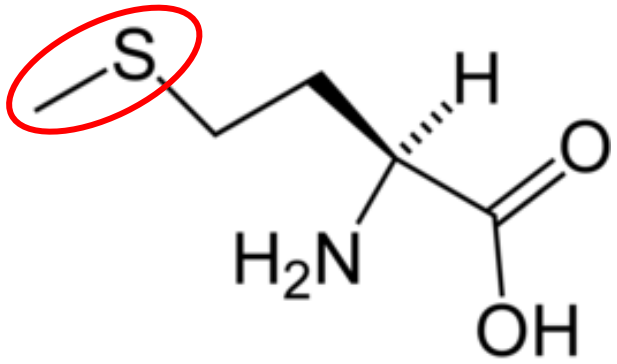


Sulfur-Containing AAs – Why Are They Special?

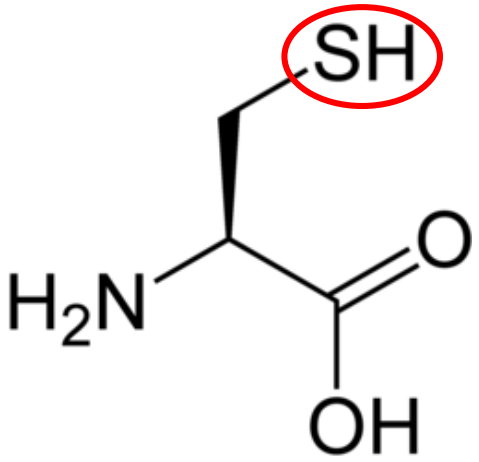
- Disulfide linkages = crucial part of 3° structure



- Cysteine vs cystine



methionine → no S-S bonds

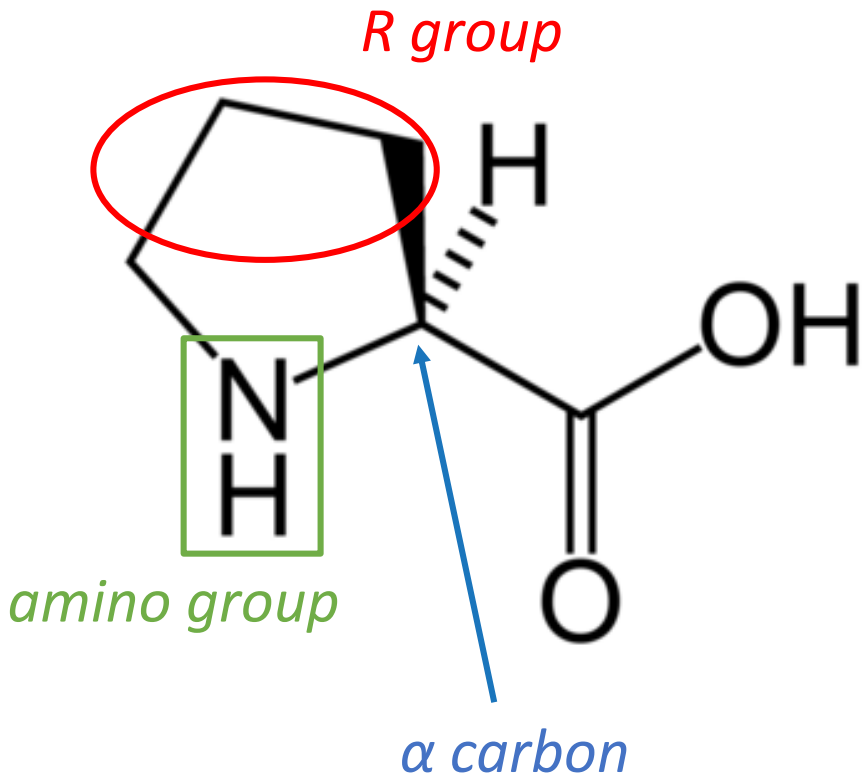


cysteine → S-S bonds

Image adapted from Benjah-bmm27 [Public Domain]

Last But Not Least - Proline

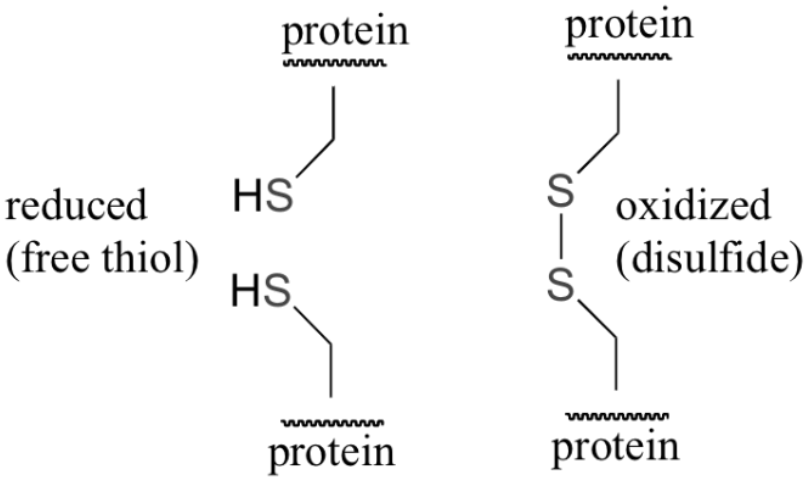
- What's unique about this structure?
- Side chain is connected to α-amino group!
- Introduces "kinks" in 2° protein structure
  - These "kinks" often found on protein surface



MCAT Practice

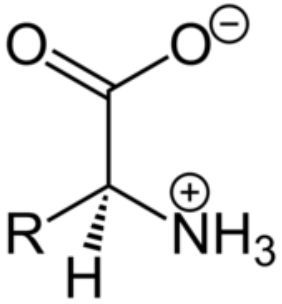
1. In a hair “permanent,” hair is relaxed via alkali agents which act to reduce the disulfide bonds between keratin proteins. What is the most likely function of these reagents?

A) The agents form new disulfide bonds between Thr residues.
B)The agents form new disulfide bonds between Ser residues.
C) The agents break disulfide bonds between Cys residues.
D)The agents break disulfide bonds between Met residues.



Amino Acids and Charge

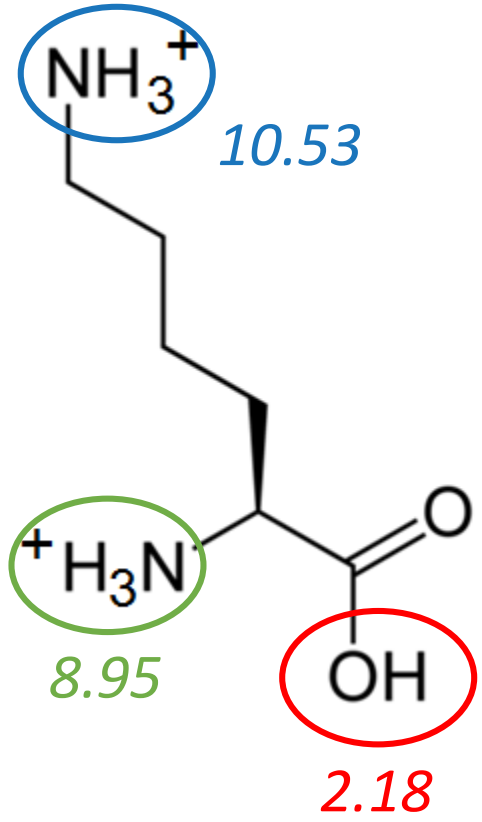
Zwitterion: form where some groups are charged but overall charge of molecule is 0



Glycine (and many others) are zwitterions at physiological pH

- When solution pH > pK_a: *group is deprotonated*
- When solution pH < pK_a: *group is protonated*

pK_a = pH for a given functional group where half of all molecules are protonated



Example: using pK_a to predict net charge

Aspartic acid has three pK_a values: 2.10, 3.86, and 9.82.

- Which pK_a corresponds to which group?
- At pH = 5, net charge = **-1**
- At pH = 11, net charge = **-2**

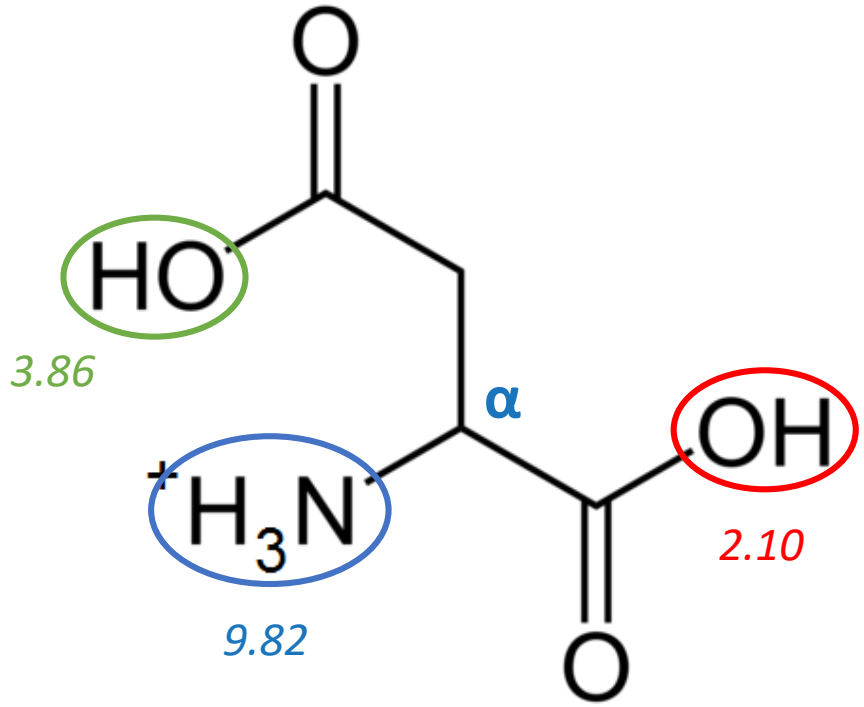


Image adapted from Sten André [Public Domain]

Isoelectric point (pI)

- What is it?
  - The pH at which an entire AA or protein is neutral
- In some ways, like "the pK_a of the entire molecule"
- When pH > pI: *AA is negative*
- When pH < pI: *AA is positive*

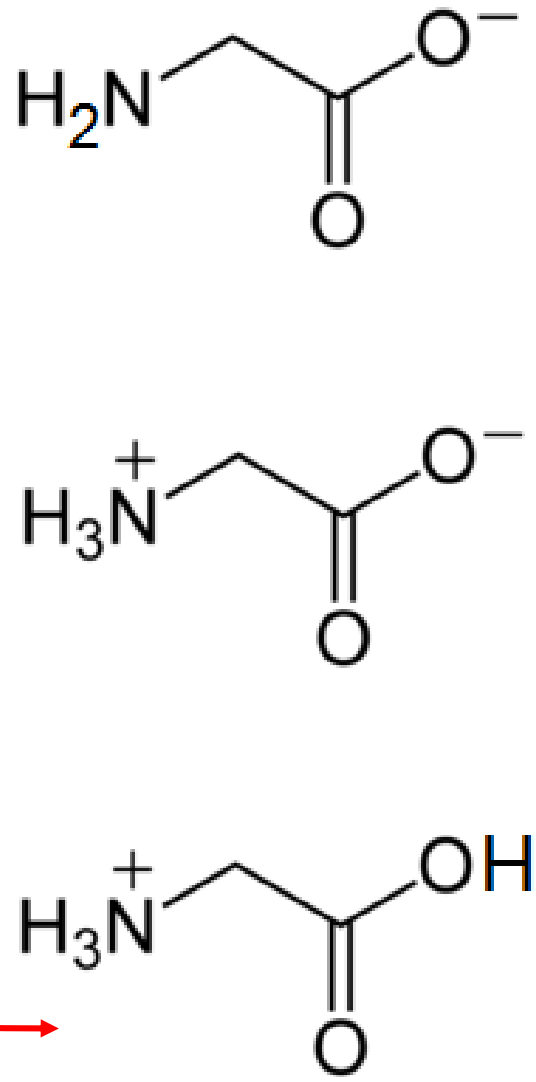
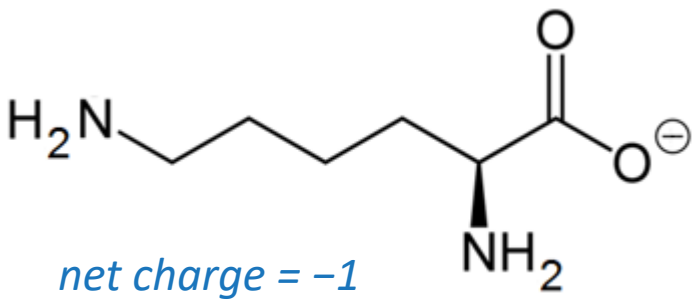


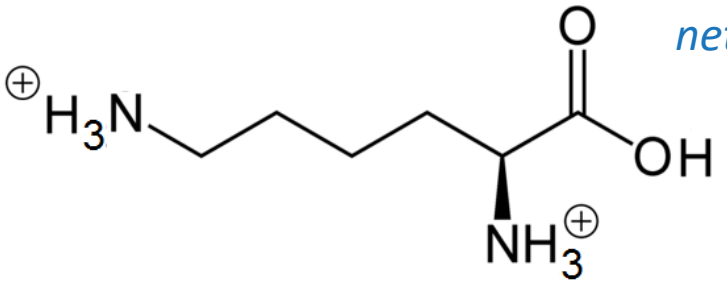
Image adapted from Benjah-bmm27 [Public Domain]

Isoelectric point: how is it calculated?

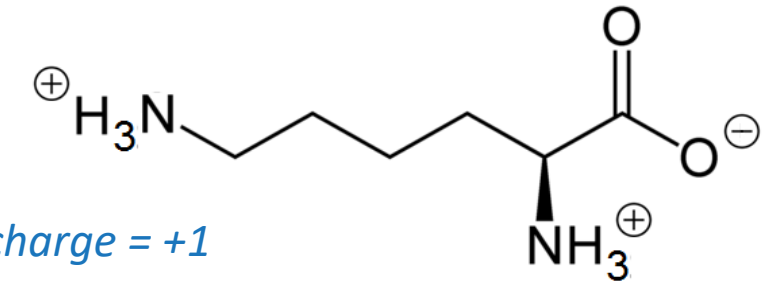
- If AA has two pK_as: just average them!
- If AA has three pK_as: average the **two most relevant**
  - For basic AAs, two most basic
  - For acidic AAs, two most acidic
- Consider lysine →



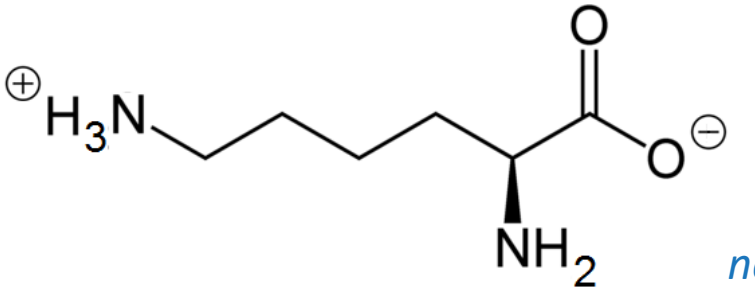
net charge = −1



net charge = +2



net charge = +1



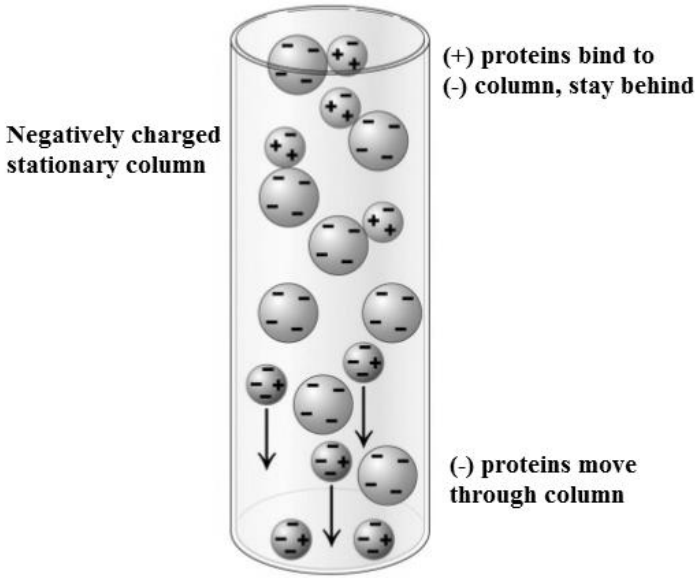
net charge = 0

Images adapted from NEUROtiker [Public Domain]

MCAT Practice

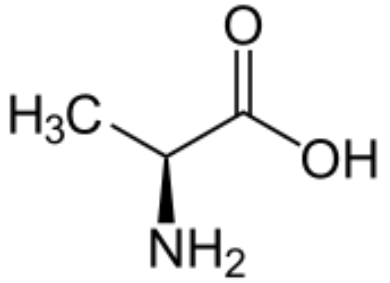
2. Which chromatography technique would most effectively separate Ile from Lys at pH 6.7?

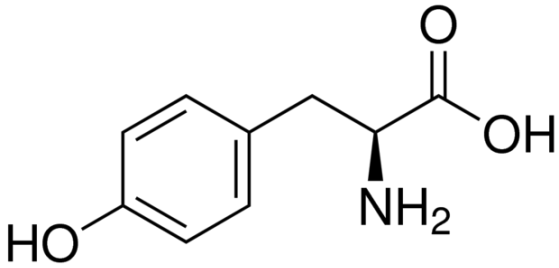
A) Cation-exchange chromatography
B) Anion-exchange chromatography
C) Size-exchange chromatography
D) Nickel affinity chromatography

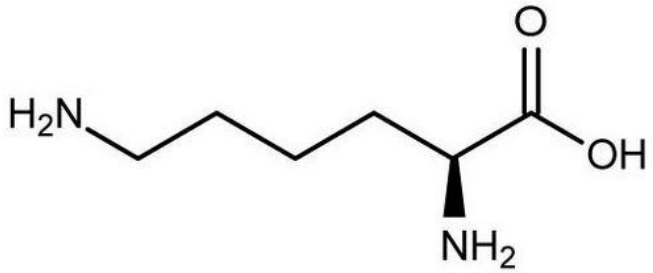


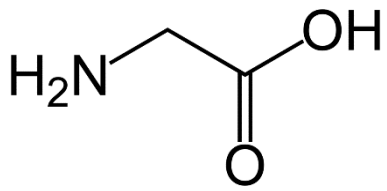
3. Which of the following scenarios is most likely to produce a neutral zwitterion?

A) Alanine at pH 5
B) Tyrosine at pH 12
C) Lysine at pH 4
D) Glycine at pH 1





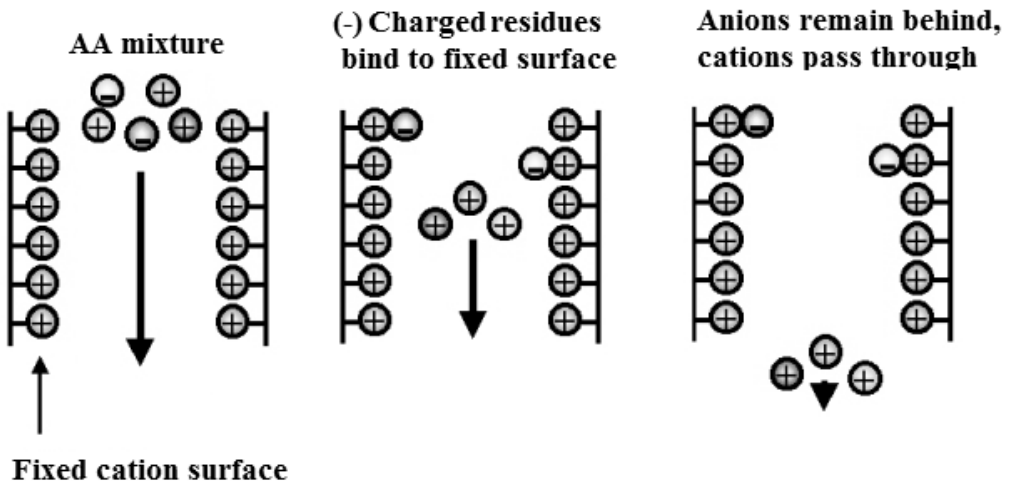




MCAT Practice

4. A professor attempts to purify glycine from a solution using anion-exchange chromatography. At which pH would he observe the largest amount of glycine adhering to the column?

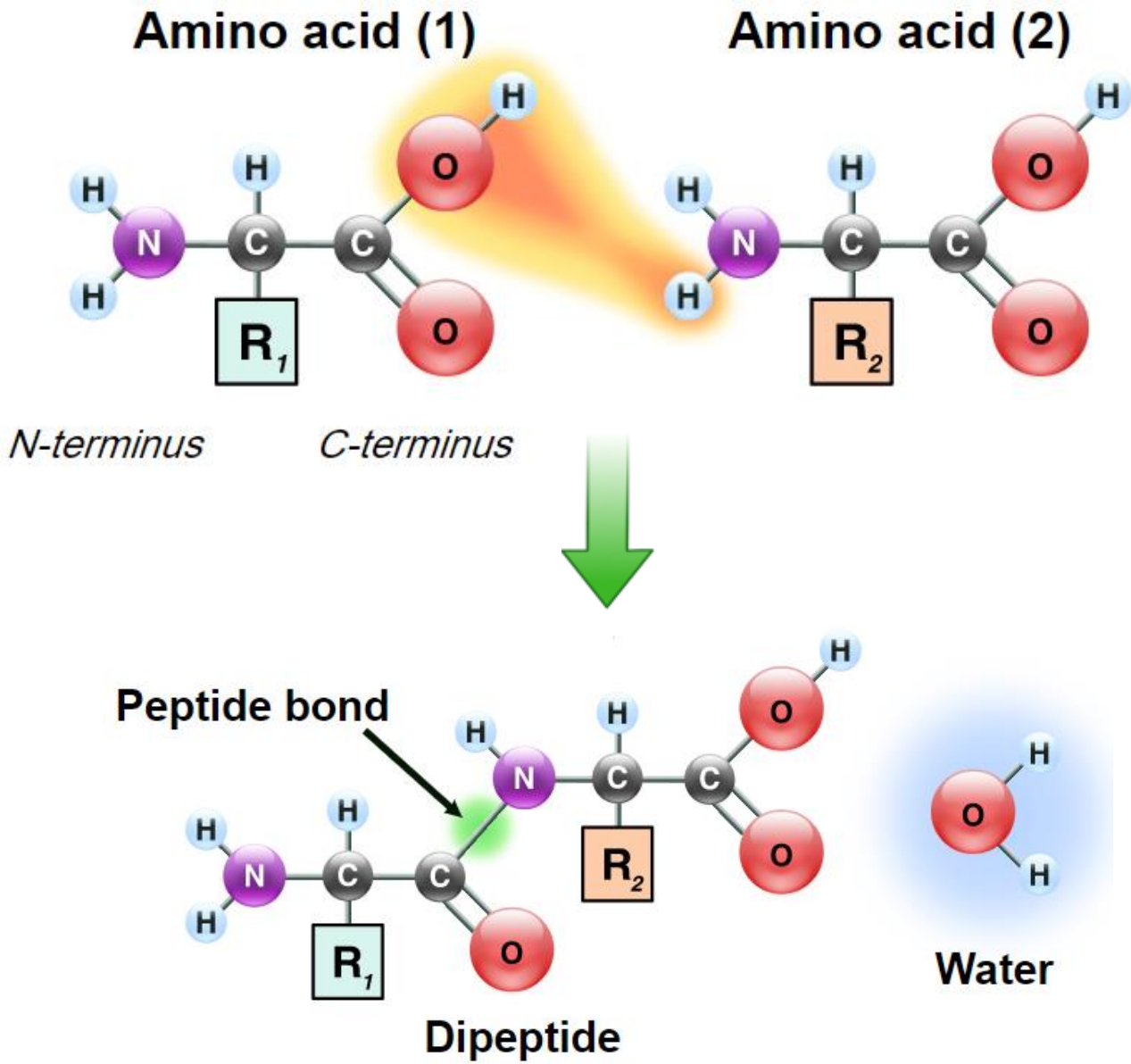
A) 1.5
B) 6.5
C) 8.0
D) 10.0



Anion exchange chromatography

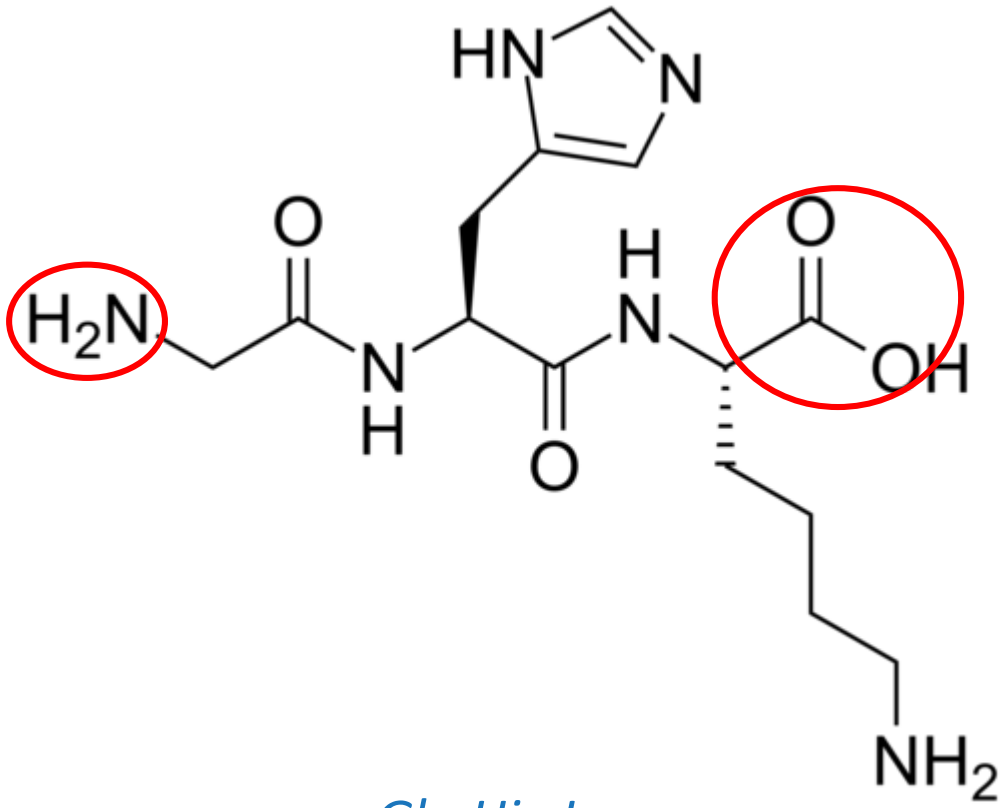
Peptide Bond

- Forms via nucleophilic attack
- Nucleophile = *amino group*
- Nucleophile = *carbonyl C*
- Peptide bond = amide linkage



Primary Protein Structure

- Linear amino acid sequence
- Amino acids now termed: *residues*
- Typically written from N-terminal to C-terminal
- Main type of bond found in 1° structure?
  - Covalent? *(chemical bond)*
  - ~~Hydrogen~~?



Gly-His-Lys

GHK

Image adapted from Ed (Edgar181) [Public Domain]

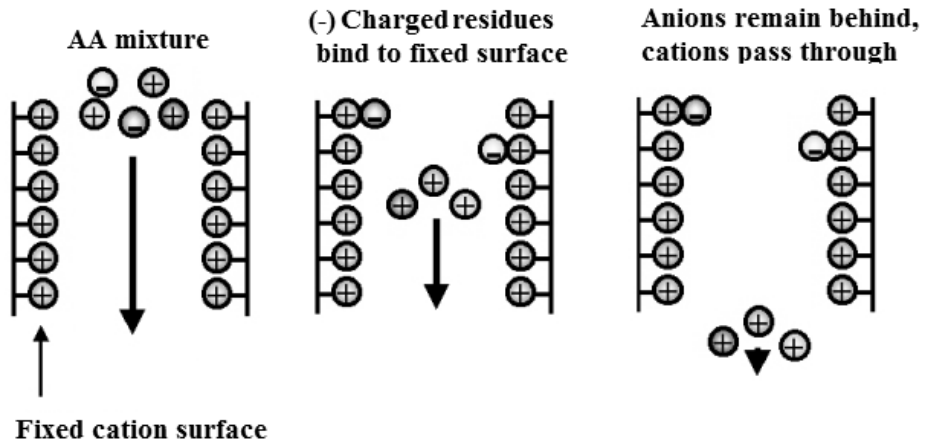
MCAT Practice

5. Due to the planar properties of the peptide bond, proteins can easily assume various organized structures (for example, beta sheets). All of the following are characteristics of the peptide bond EXCEPT:

A) its rotation is restricted.
B) it has multiple resonance forms.
C) it frequently breaks and reforms to allow structural fluidity.
D) it exhibits partial double bond character.

6. Ion-exchange chromatography with a positively-charged stationary phase is used to separate two polypeptides. Which amino acid is LEAST likely to be found in the polypeptide that elutes first?

A) A
B) H
C) P
D) D



Anion exchange chromatography

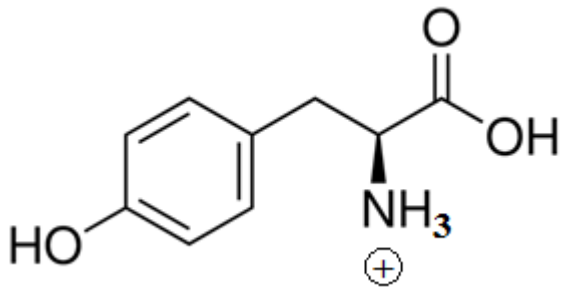
MCAT Practice

7. Which of the following amino acid sequences would incur the *greatest* entropic penalty if it were used to replace Tyr-Cys-Met in the surface region of a protein?

A) His-Gly-Gly
B) Ala-Gly-Ser
C) Leu-Val-Phe
D) Met-Thr-Glu

8. At pH = 1, what will be the net electrical charge on Tyr?

A) -1
B) 0
C) +1
D) +2



MCAT Practice

10. One of the complications in certain forms of schizophrenia is a loss-of-function mutation to peptidyl transferase. What process is most likely to be halted in these patients?

A) Binding of the mRNA template to the ribosome
B) Construction of the cellular ribosome
C) Construction of the primary structure of neuroproteins
D) tRNA recognition of mRNA codons.

Peptidyl transferase catalyzes peptide bond formation on the ribosome.

Enzyme lowers the activation entropy of the reaction due to positioning the two substrates, ordering water in the active site, and providing an electrostatic network that stabilizes the reaction intermediates.

Any issue related to loss of peptide bonding is our best answer.

Peptide bonds comprise the primary structure of proteins.

MCAT Practice

11. Which substitution, of those below, is most likely to cause a change in the tertiary structure of a protein?

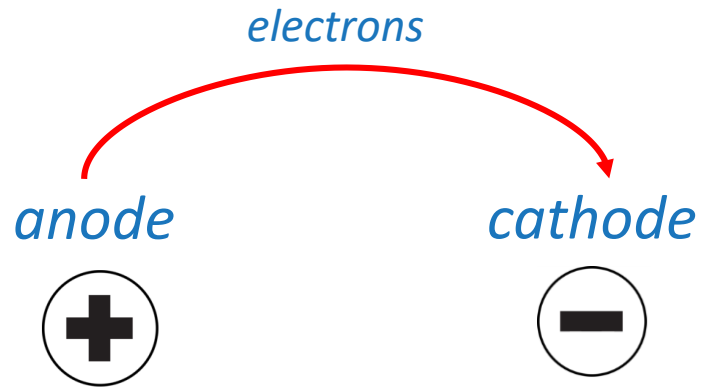
A) Val to Met
B) Lys to Leu
C) Ser to Thr
D) Asp to Glu

12. What structural characteristic marks the side chain of the amino acid N?

A) A four-carbon chain attached to an amine that makes the residue basic overall
B) A sulfur atom in the form of a thioether
C) A simple one-carbon group
D) An amide

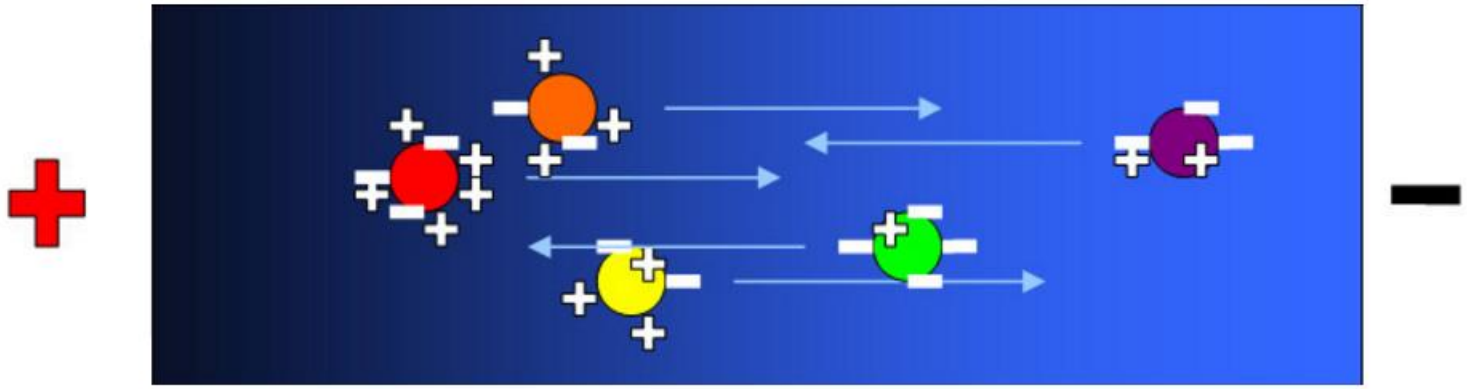
Isoelectric focusing (IEF): the basics

- Separates AAs by pI
- Setup: electrophoresis on an “immobilized pH gradient”
- Acts like an electrolytic / galvanic cell



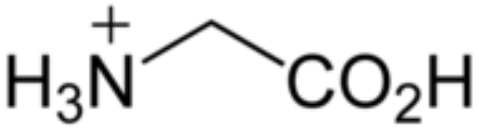
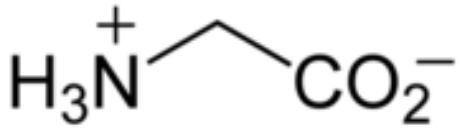
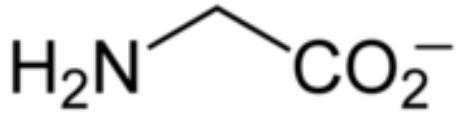
nonspontaneous

spontaneous



IEF: predicting direction of movement

- Net positive AAs will move toward the _*cathode*_
- Net negative AAs will move toward the _*anode*_
- Example: pI of glycine = 5.97

At pH 3	At pH 5.97	At pH 10
		
→ *cathode*	*stationary*	→ *anode*

MCAT Practice Passage

- Now we will take the opportunity to put all of our skills and knowledge to the test with an MCAT-style practice passage.

- Prepare to take notes along with our reading or to think about what you might highlight, just like you would on Test Day.

MCAT Practice Passage

The artificial sweetener aspartame (Figure 1) is the methyl ester of the dipeptide of L-phenylalanine and L-aspartic acid. There are two general approaches to prepare aspartame. The chemical approach involves reacting the methyl ester of phenylalanine with an N-protected anhydride of aspartic acid. The protecting group, either a benzyl or formyl group is then removed by mild acid hydrolysis. In addition to the desired product, a beta structural isomer is also formed due to formation of a peptide bond with the wrong carboxylate group, which must be removed since it produces a bitter taste.

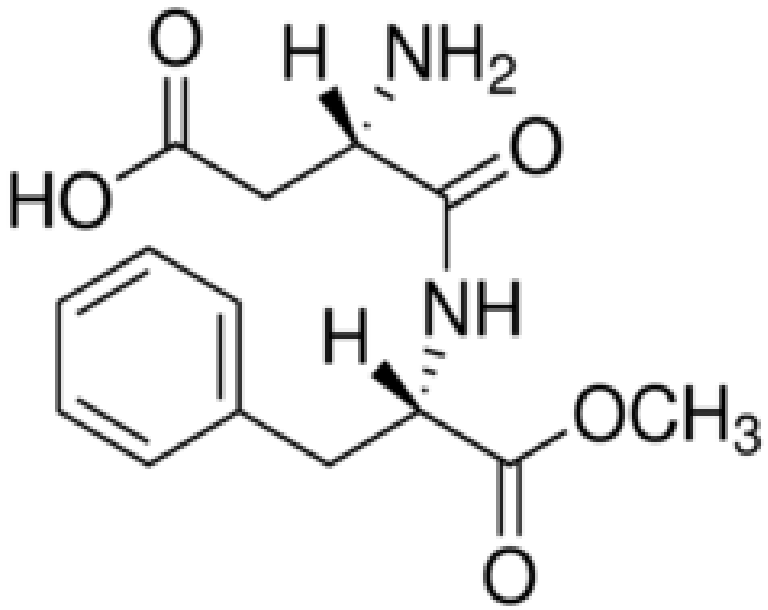


Figure 1 Structure of N-(L-α-Aspartyl)-L-phenylalanine, 1-methyl ester (Note: $pK_{a1} = 3.2$; $pK_{a2} = 7.7$)

A second enzymatic synthesis has been developed in which proteases catalyze the selective peptide bond formation and avoids the formation of the beta isomer.

MCAT Practice Passage

Upon ingestion, aspartame is broken down in the duodenum into its components, aspartic acid, phenylalanine and methanol, with the subsequent formation of metabolites such as formaldehyde and formic acid. Some research has raised concerns that aspartame may lead to the formation of certain cancers as a result of the formation of some of these potentially toxic compounds. A new drug, known as protein AT7 (MW = 5×10^4 amu), has been developed to counter this possibility.

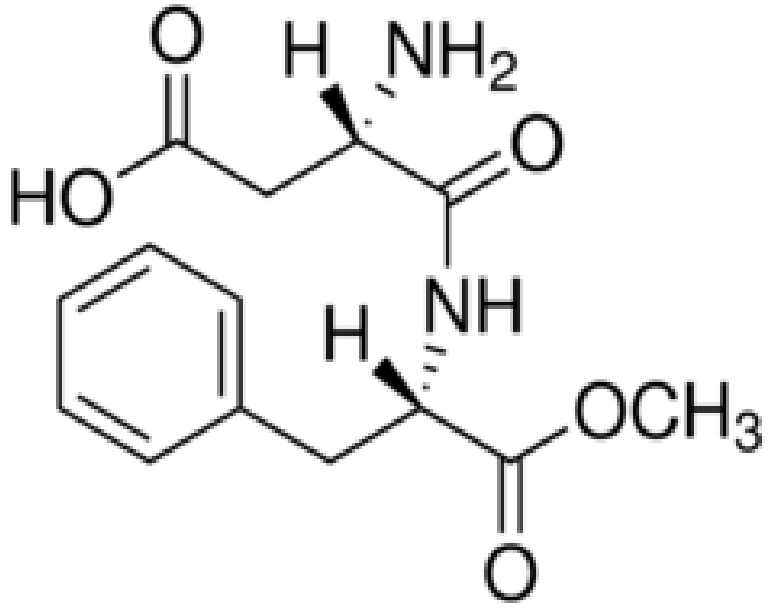
MCAT Passage

1. According to the passage, the pI of aspartame is most nearly:

A. 3.2
B. 5.5
C. 7.0
D. 7.7

2. How many stereocenters are in aspartame?

A. 1
B. 2
C. 3
D. 4



MCAT Passage

3. The two amino acids that form the basis for the dipeptide structure of aspartame, aspartic acid and phenylalanine, are most accurately be classified as:

A. hydrophilic and hydrophilic, respectively.
B. hydrophobic and hydrophilic, respectively.
C. hydrophilic and hydrophobic, respectively.
D. hydrophobic and hydrophobic, respectively.

4. Prior to its digestion in the small intestine, aspartame must pass through the stomach. What is net charge on aspartame while in the stomach?

A. -1
B. 0
C. +1
D. +2

MCAT Passage

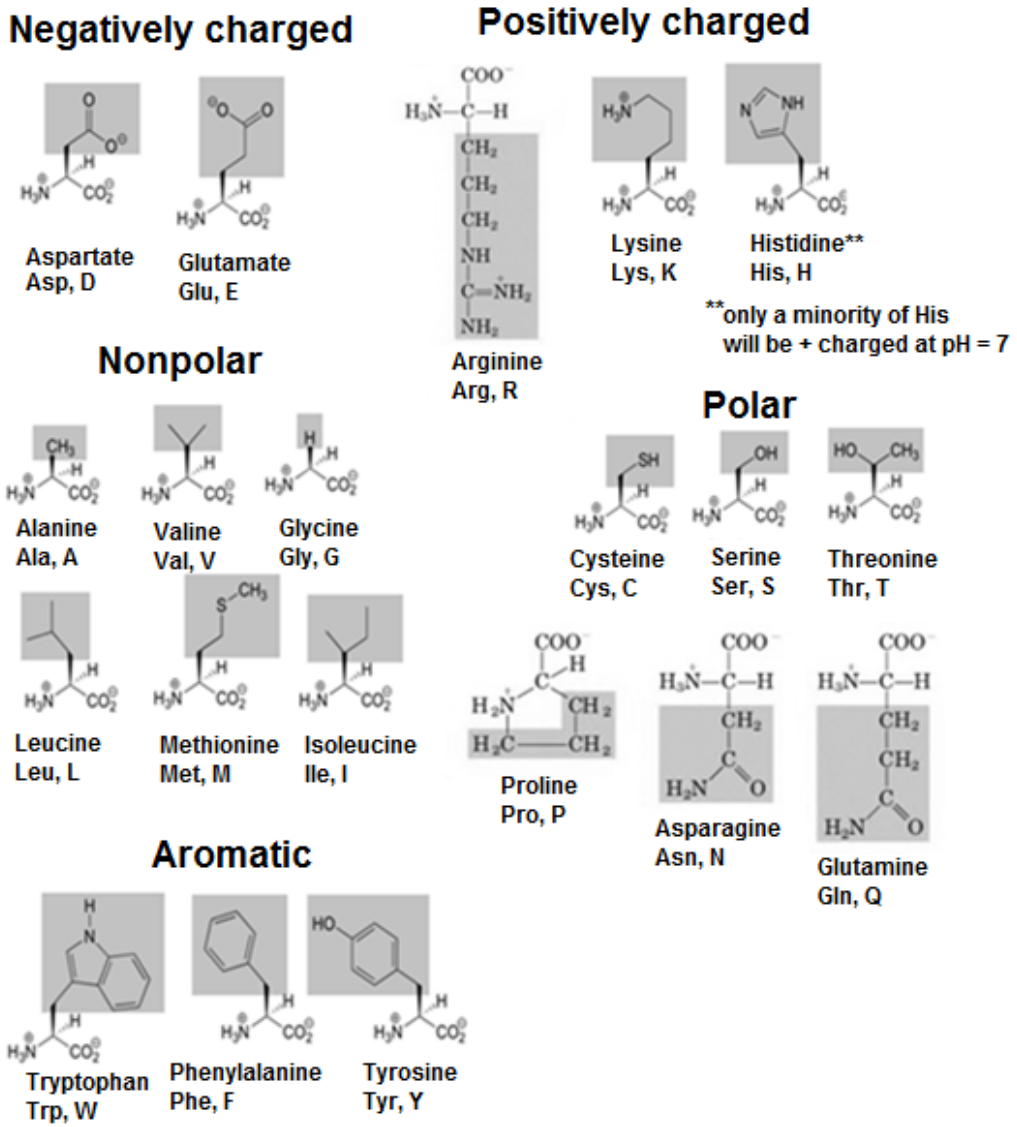
5. How many amino acid residues are in AT7?

A. 2
B. 50
C. 450
D. 900

6. Peptides are stable in water because:

A) peptide bonds cannot be cleaved by hydrolysis.
B) electron sharing between the carbonyl and amino groups allows amide bond resonance.
C) the breakdown of peptides into individual amino acids is entropically unfavorable.
D) peptides hydrogen bond with free-floating proline residues to promote stabilization.

What Next?



You should prioritize your AA studying as follows in order to maximize efficiency and points:

1. Characteristics of each “type” of AA
2. Full name and side group chemical behavior
3. 3-letter abbreviation
4. 1-letter abbreviation
5. Exact side chain structure
6. pK_as of side chains

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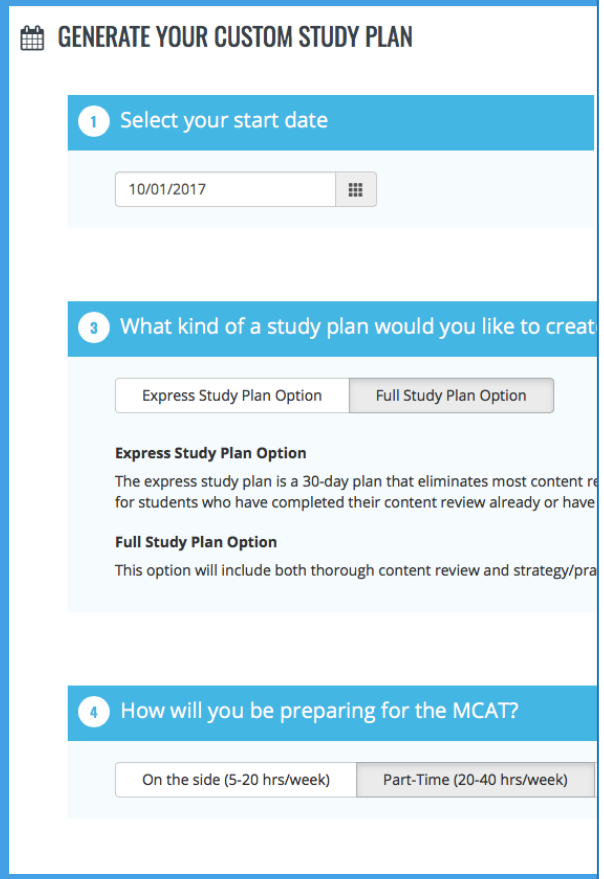

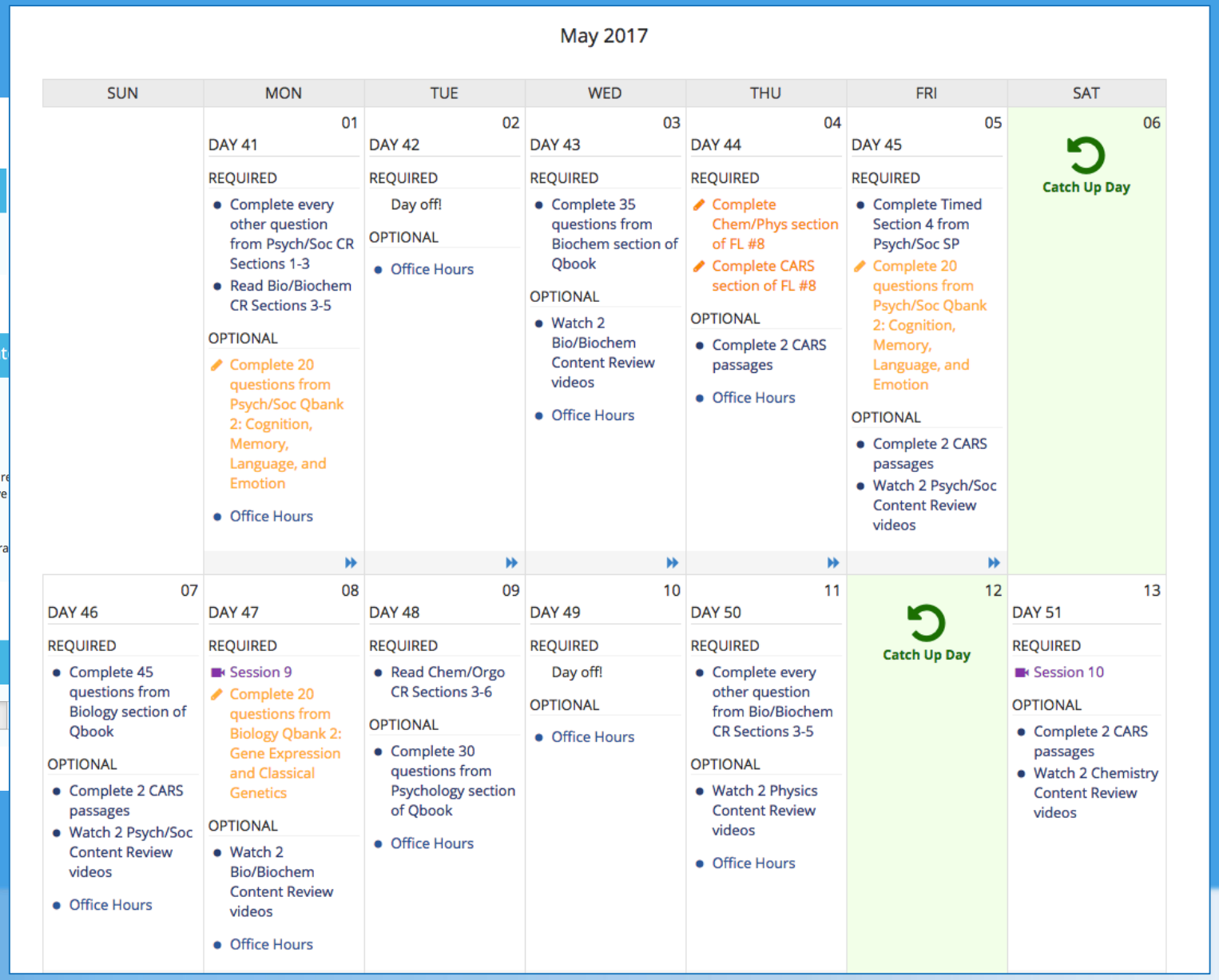

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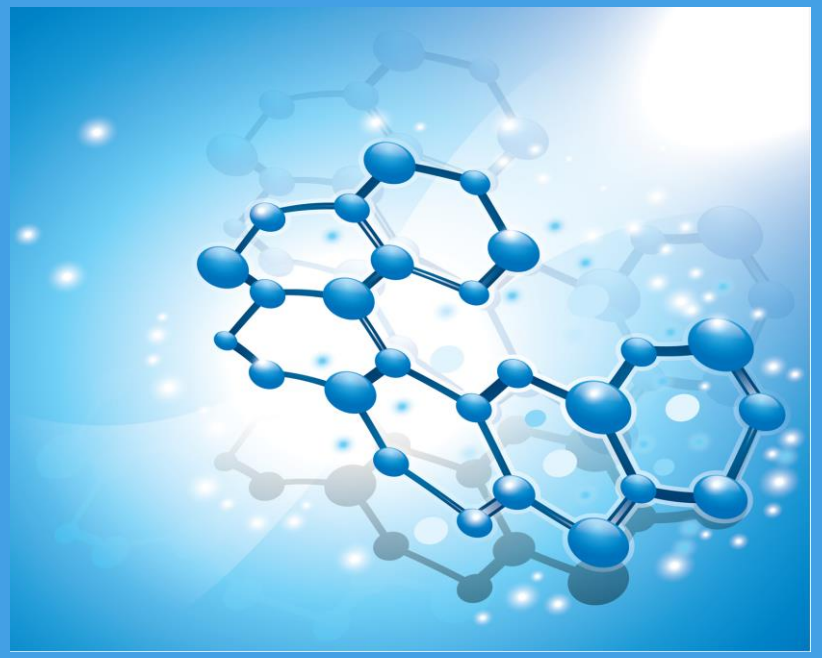

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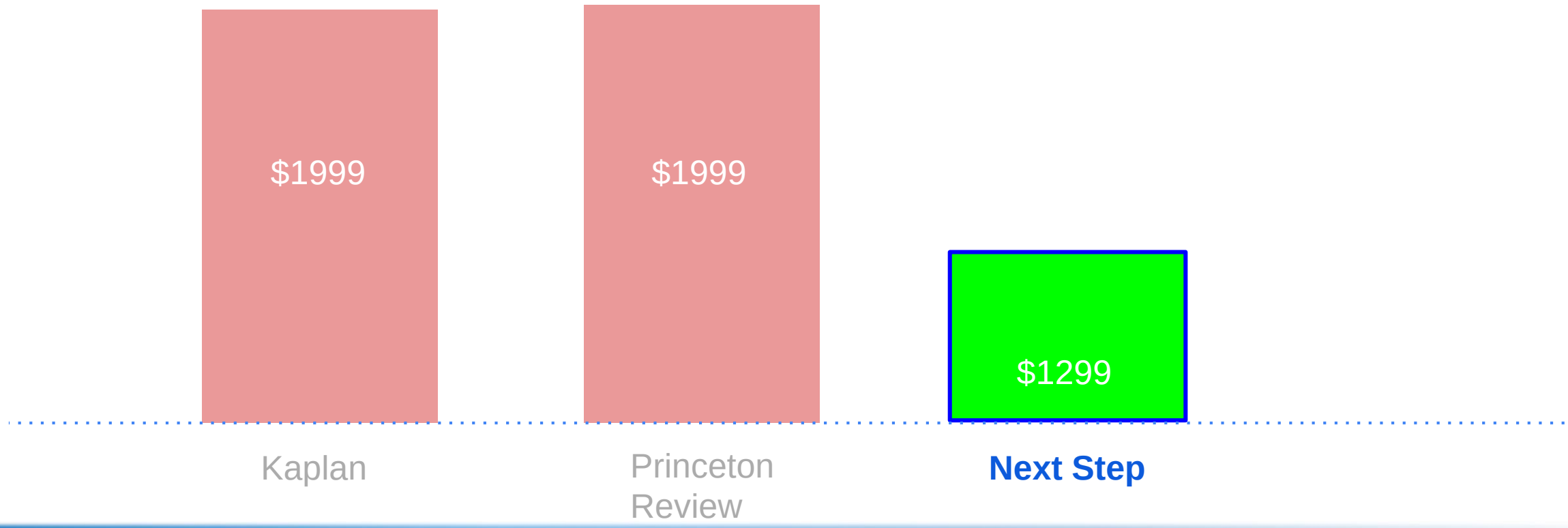

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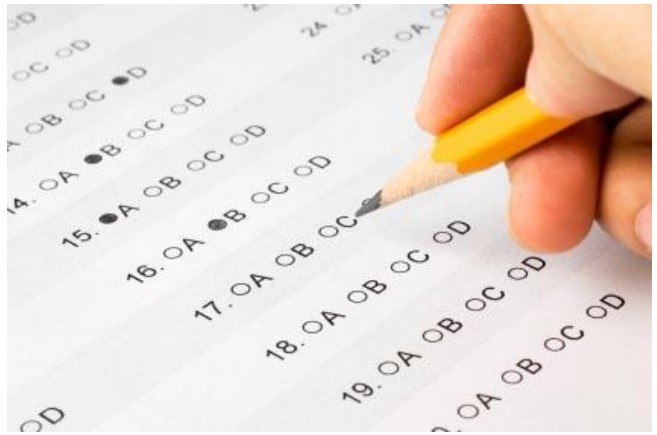

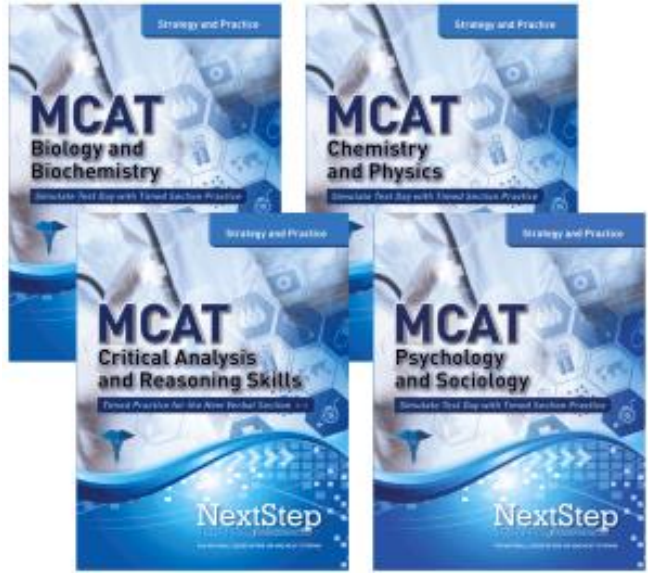

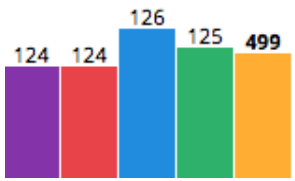

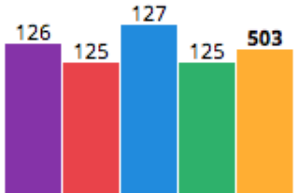

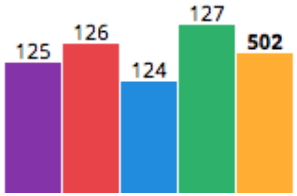

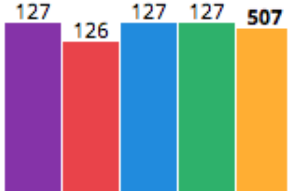

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When I initially took the MCAT, I got a 495. I was destroyed and thought all was lost. To prepare I had taken a once a week Kaplan course which gave me false confidence and an empty bank account. After **tutoring with NextStep I took the MCAT again with much more confidence and a better idea of what to expect** and got a 510. Two points higher than my goal score of a 508! My tutor was honest with me about what was realistic, yet encouraging. He showed me areas I needed to buckle down and improve on and helped me learn strategies to use my knowledge to its full potential. **I am so thankful for NextStep tutoring. They helped me conquer a test I had always feared. I recommend their services to anyone who is preparing for the MCAT.** I am now interviewing at various medical schools and get to go in confident about my score! Thank you Nextstep! - Talitha Sept 8, 2017

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