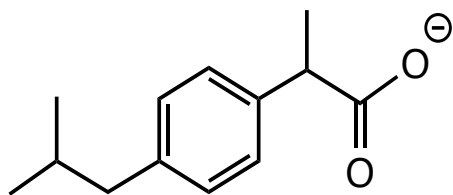


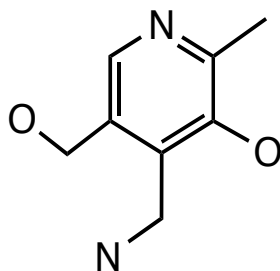
7.016 Problem Set 1

Question 1

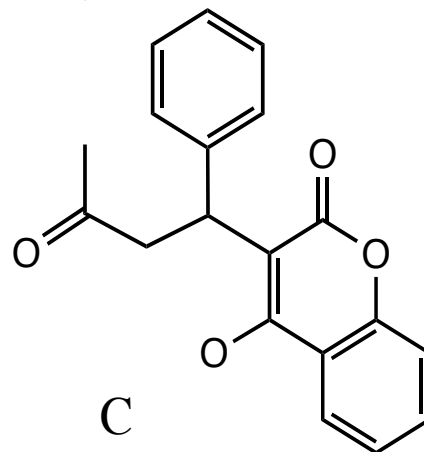
The following "line-angle" drawings represent three chemical structures. On each drawing, the hydrogen atoms that should be bonded to the NON-carbon atoms are missing.



A



B



C

a) For each structure, show the position of **All** carbon (C) and all hydrogen (H) atoms. **Note:** If there is a charge present make sure you take it into account.

b) Give the **chemical formula** of each of the structures shown by the line angle drawings.

A:

B:

C:

c) Circle a **nonpolar** functional group for each of the above structures.

d) Box a **polar functional group** for each of the above structures.

e) Which of the above structures is most soluble in water? **Explain** why you selected this option.

f) Which of the above "line-angle" drawings represent a chemical structure that is amphiphilic? **Explain** why you selected this option(s).

Question 2

a) The biological macromolecules present in the cells of all living organisms are proteins, nucleic acids, carbohydrates and lipids.

- i. Which **three** elements (*choose from C, H, O, N, S, P*) are found in **all** biological macromolecules?
- ii. Which radioactive element (*choose from C, H, O, N, S, P*) is the **best option** to detect the **nucleic acids** in a cell? **Explain** why you selected this element.
- iii. Which radioactive element (*choose from C, H, O, N, S, P*) is the **best option** to detect the **proteins** in a cell? **Explain** why you selected this element.

b) Which of the following represent a condensation reaction? Place an X next to all that apply.

-----The formation of covalent disulfide bonds between two cysteines.

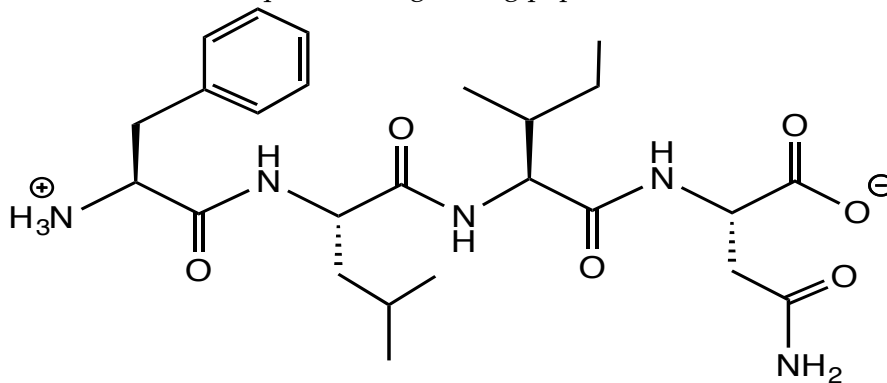
-----The formation of a peptide bond.

-----The formation of a glycosidic linkage to form a disaccharide.

-----The formation of glucose from lactose.

-----The cleavage of double-stranded DNA by an enzyme into small DNA fragments.

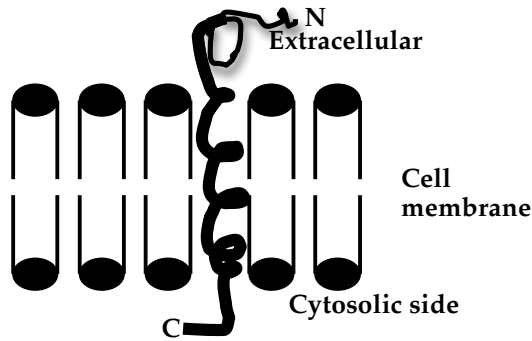
c) The following is the amino acid sequence of a growing peptide in a cell.



- i. Add the amino acid **glycine** to the growing end of the peptide drawn above.
- ii. What level of protein structure does the amino acid sequence in the schematic above represent (*choose from primary, secondary, tertiary and quaternary*)?

Question 2 continued

d) Drawn below is a schematic of a transmembrane protein.



- i. When this transmembrane protein is embedded in the lipid bilayer, what is the highest order of structure (choose from *primary, secondary, tertiary and quaternary*) of this protein? **Explain** why you selected this option.

- ii. From the list below, circle the amino acid(s) that might be more common in the **extracellular domain** of this membrane protein and whose side-chain can form hydrogen bonds with the surrounding water molecules. **Explain** why you selected this option(s).

Lysine

Serine

Phenylalanine

Methionine

- iii. From the list below, circle the amino acid(s) that would likely be found in the **transmembrane/membrane spanning domain** of this protein and whose side-chain interacts with the lipid bilayer.

Lysine

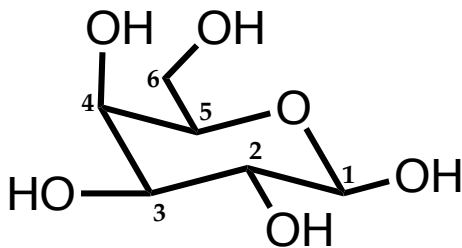
Serine

Leucine

Methionine

Question 3

a) Consider the following structure that represents a galactose molecule ($C_6H_{12}O_6$).



- i. Draw a disaccharide composed of two galactose monomers that are linked between C1 of one monomer and C3 of the other monomer.

- ii. The molecular formula for galactose is $C_6H_{12}O_6$. Which of the following options represents an oligosaccharide composed of five galactose monomers?

$C_{30}H_{60}O_{30}$

$C_{48}H_{50}O_{22}$

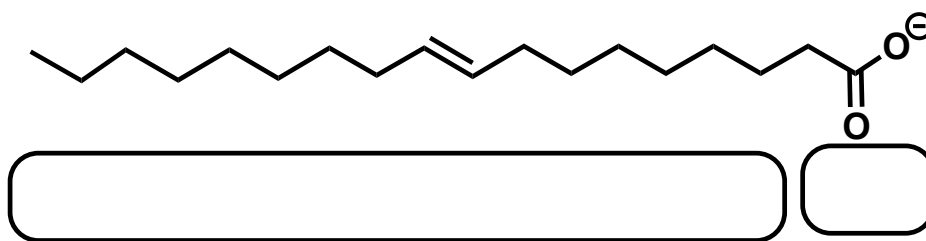
$C_{30}H_{52}O_{26}$

$C_{36}H_{56}O_{30}$

- iii. What types of **non-covalent bonds** or forces (*choose from hydrogen bonds, ionic bonds, hydrophobic interactions, vanDer Waals (VDW) forces*) **most likely** occur between the two oligomers of galactose? **Explain** your answer.

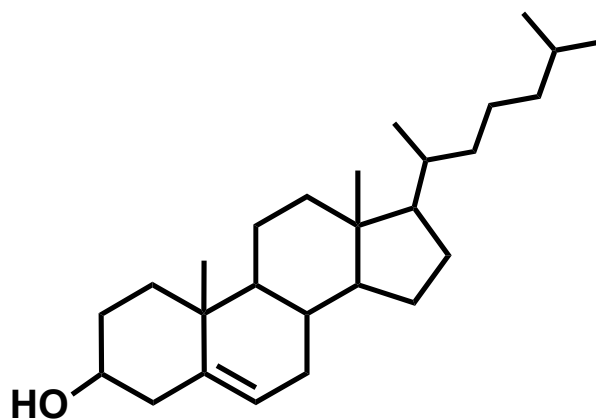
Question 3 continued

b) Consider the structure of the fatty acid below to answer the following questions.



- i. Classify the above fatty acid as saturated or unsaturated? **Explain** your choice.
- ii. Identify whether the boxed regions of the molecule are polar and non-polar (**fill in the boxes**).
- iii. This fatty acid can undergo a condensation reaction with glycerol to form mono-, di- or triglycerides. In the schematic above, **circle the group** that participates in the condensation reaction.
- iv. The fatty acid chains are an integral part of a lipid bilayer. Which bonds or interactions (*choose from ionic, hydrogen, covalent, hydrophobic, VDW*) stabilize the lipid bilayer?

c) Below is the structure of an important component of the plasma membrane, cholesterol, which is also a precursor for the steroid hormones and vitamin D.



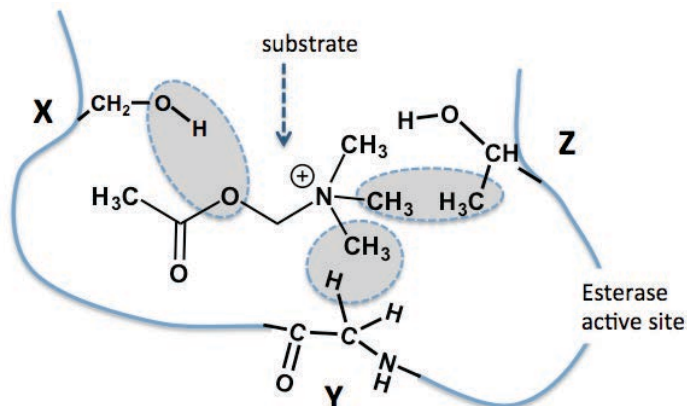
On the diagram above...

- i. **Box the entire hydrophilic region** of this molecule.
- ii. **Circle the entire hydrophobic region** of this molecule.

Question 4

The following schematic represents a substrate that is bound to the active site of an esterase enzyme.

Esterases hydrolyze ester bonds. For simplicity, only the amino acids whose side-chains interact with the substrate are shown. Each circled interaction is important for the binding of the substrate to the enzyme.



a) In the table below, give the **strongest interaction** that can occur between the substrate and the side-chains of amino acids X, Y and Z at the active site of the enzyme.

Amino acid	Hydrogen-bond/Ionic bond/Hydrophobic bond/ VDW forces?
X	
Y	
Z	

b) Which of the above amino acids, (X, Y or Z) is **closest to the N terminus** of the primary sequence of the enzyme?

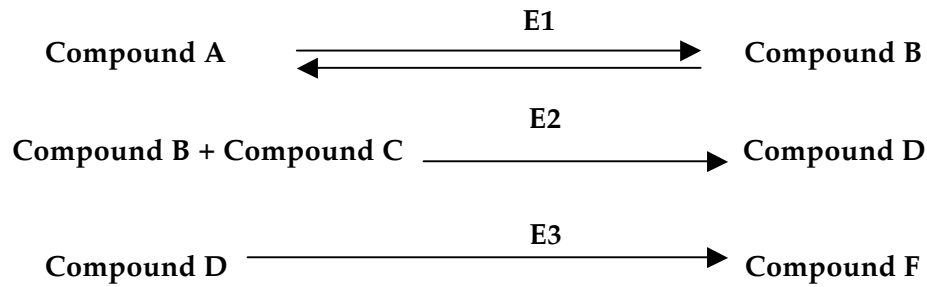
c) You create two mutants (1 & 2) of the enzyme, each of which has two amino acid substitutions at the active (substrate-binding) site. You observe that one mutant can bind to the substrate similarly to the wild-type version of the enzyme, whereas the other cannot. Which of the two mutant versions (1 or 2) will probably **not** bind to the substrate? **Explain, in terms of the characteristics of amino acids**, why you selected this version. *Note: A table showing the structures of amino acids is given on the last page of this problem set.*

Enzyme	Amino acids at the active site		
Wild-type	X	Y	Z
Mutant 1	Asp	Y	Tyr
Mutant 2	X	Ala	Ser

d) Full activity of esterase is observed at 37°C and a pH of 7.4. You isolate the **active form of esterase**, subject it to a **high salt (high sodium chloride) concentration** and show that it cannot bind the substrate. You then return the sample to the original conditions and measure the substrate binding ability of the esterase again. Would the esterase bind to its substrate when returned to the pre-treatment conditions (Yes/No)? **Explain.**

Question 5

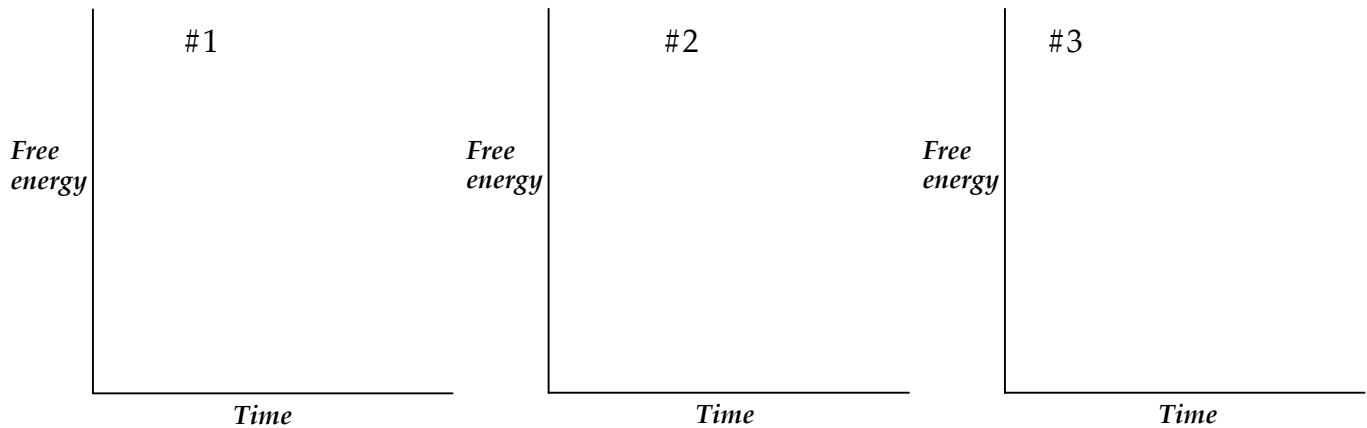
You are looking at the following biological reactions that are catalyzed by specific enzymes (E1, E2, E3).



Note:

- **In Reaction#1**, Enzyme **E1** catalyzes the conversion of Compound A to Compound B. This reaction is **truly reversible** and the reverse reaction is as likely as the forward reaction.
- **In Reaction#2**, Enzyme **E2** catalyzes an **energy requiring reaction** that uses Compounds B and C as substrates to produce Compound D.
- **In Reaction#3**, Enzyme **E3** catalyzes an **energy producing reaction** that converts Compound D to Compound F.

a) Draw the energy profiles of reactions #1, #2 and #3 on the axes given below. On the diagram, please label the reactants and the products.



b) Summarize the effect of each of these enzymes on the following reaction parameters. **Note:** Your choices are increases/decreases/remains unchanged.

Parameters	Enzyme E1	Enzyme E2	Enzyme E3
Reaction equilibrium			
Reaction rate			
Activation energy			
Free energy change (ΔG)			

c) You are told that **Enzyme E1 is the product of a gene** that encodes a protein of molecular weight 50kD. However, this enzyme in its **active form** has a molecular weight of 250KD. Why might the **active form** of Enzyme E1 be **heavier** than the product encoded by its corresponding gene?

Question 5 continued

d) You identify a cell line that **cannot** produce Compound F. You measure the concentration of each metabolite and observe that this cell line shows an excess concentration of Compounds B and C. Based

on this observation, which of the three enzymes is **most likely** non-functional in this cell line? **Explain** your choice.

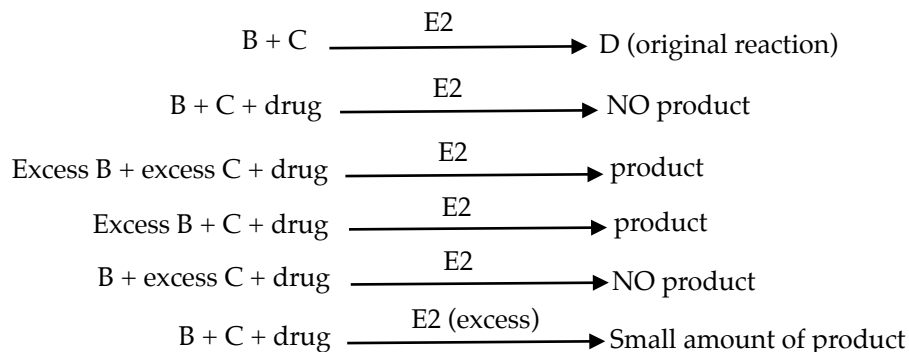
You decide to reproduce Reaction #2 in three test tubes. You may assume that this biological reaction occurs at **37°C** and **pH of 7.4** under **normal conditions**.

- **Test tube #1:** You perform the reaction at **70°C** and **pH 7.4** and observe that no Compound D is produced. When the temperature is brought to **37°C**, Compound D is produced at a rate similar to normal condition.
- **Test tube #2:** You perform the reaction at **37°C** and **pH 10.4** and observe that no Compound D is produced. When the pH is brought to **7.4**, Compound D is produced at a rate similar to normal condition.
- **Test tube #3:** You perform the reaction at **37°C** and **pH 7.4** in the **presence of proteases** and observe that no Compound D is produced. The effect of protease treatment persists even after its removal from reaction mixture.

e) Explain the effect of the changed reaction parameters in each of the above test tubes on **structure** and **function** of Enzyme E2.

Reaction parameters	Effect on Enzyme E2	Is the effect reversible/ irreversible?
<i>70°C in test tube #1</i>		
<i>pH 10.4 in test tube #2</i>		
<i>Protease in test tube #3</i>		

During an experiment, by mistake, you add a drug to the original Reaction #2 mixture and find that the reaction is completely inhibited. You then try to make the reaction work by increasing the concentration of Compounds B and C. You find that the reaction now works. However as indicated below, if you add an excess of Compound B and a normal amount of Compound C together with drug the reaction works, but if you have a normal amount of Compound B and an excess of Compound C the reaction does not work. The reaction is partially restored if you increase the concentration of Enzyme E2. These results are summarized schematically below.



f) Based on this information, briefly **explain** how does the drug most likely inhibit this enzymatic reaction.

Question 6

Hemoglobin (Hb) is a protein present in red blood cells; this protein is responsible for carrying oxygen from the lungs to the tissues and for returning carbon dioxide from the tissues to the lungs. A single amino acid substitution in hemoglobin may distort normal red blood cells into sickle shaped cells. These cells can clog the blood vessels resulting in sickle cell anemia, a genetically inherited disorder.

In this exercise, you will use StarBiochem, a protein 3D viewer, to explore the structure of functional Hb and the abnormal Hb that accounts for sickle cell anemia. To begin using StarBiochem, please navigate to: <http://web.mit.edu/star/biochem>. Click on the Start to launch the application. Click on "Samples-> Select from Samples-> 1A3N". This file represents the PDB structure of normal hemoglobin. Instructions for changing the view of structure can be found in the top menu, under View -> Structure viewing instruction.

a) How would you best classify 1A3N: monomer, dimer, tetramer of two homodimers?

- In the default view (Structure -> Protein tab) click on Quaternary.
- Show the quaternary surfaces by moving the translucency slider in the surface window to the right.
- Each polypeptide chain/monomer is colored differently.
- Alternatively, scroll down the Chain ID [Amino Acid] sequence in the sequence window. Each polypeptide chain/monomer is labeled alphabetically, i.e. chain A, chain B etc.

b) Based on the primary structure of 1A3N, what is the length, in terms of amino acids, of each polypeptide chain of normal Hb?

- Reset the structure by clicking on View-> Reset structure in the top toolbar.
- Click on Structure->Protein -> Primary.
- Scroll down the amino acids sequence shown within the [Amino Acid] sequence window to see the number of amino acids in each polypeptide chain/ monomer.

c) In addition to amino acids, each protein chain in Hb also contains heme groups, which bind to oxygen. How many heme groups do you see in each molecule of Hb?

- Reset the structure. (Reset -> Reset structure).
- Click on View -> View specific regions/ Set center of Rotation.
- In the new window that opens up, click on Non- peptide -> select all non- peptides->bring the VDW radius scale to 1 to distinctly see each heme group in normal Hb.

d) What are the different secondary structures you see in 1A3N?

- Reset the structure. (Reset -> Reset structure).
- Click on Structure -> Protein -> Secondary.
- Explore the different secondary structures by clicking on the check box beside the Helices, Sheets or Coils either individually or in combination.

Question 6 continued

We will now compare the structure of 1A3N with 2HBS, which represents the PDB structure of sickle cell Hb. Note: In the top menu, click on "Samples-> Select from Samples-> 2HbS". You can now view the PDB structure of sickle cell Hb. A single amino acid substitution at position 6 in two of hemoglobin protein chains to the amino acid valine results in sickle cell anemia.

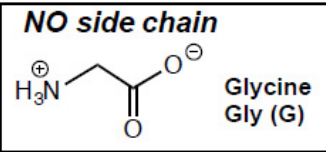
e) Identify the protein chains (A, B, C, etc) in 2HBS with the above amino acid substitution.

f) Name the amino acid present in 1A3N that is substituted to Val⁶ in 2HBS. How does the nature of the side-chain of this amino acid differ from Val?

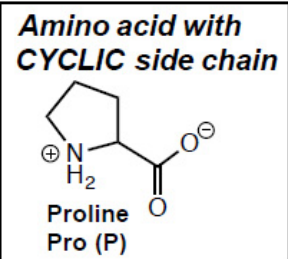
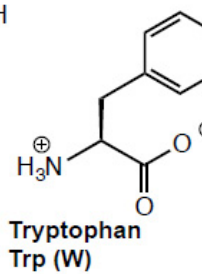
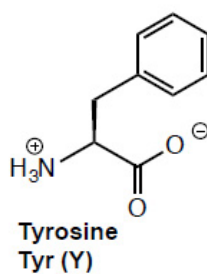
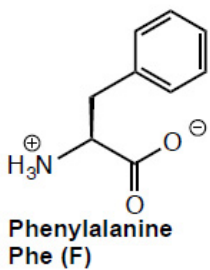
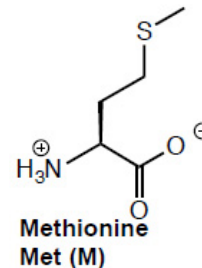
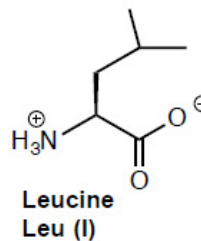
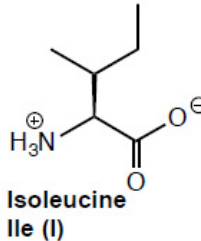
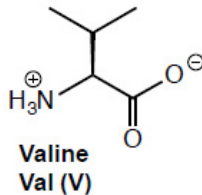
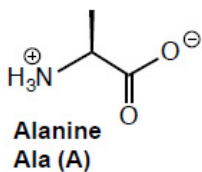
g) In the 2HBS, Val⁶ in one Hb molecule interacts with Phe⁸⁵ and Leu⁸⁸ in another molecule of Hb. What is the most likely type of interaction between the side-chain of Val⁶ with the side-chains of Phe⁸⁵ and Leu⁸⁸? Why is this interaction not observed in 1A3N?

h) Based on what you have learned, briefly explain why the Hb molecules aggregate together in sickle cell anemia patients.

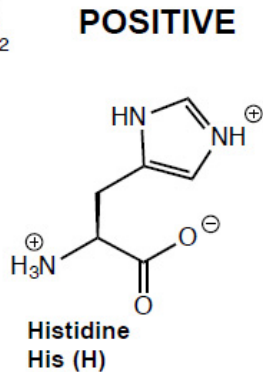
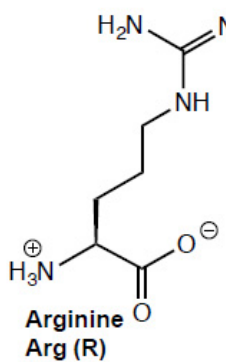
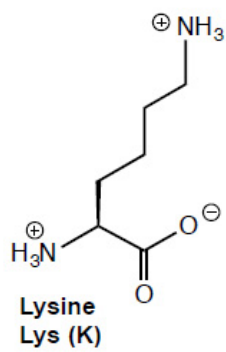
**TWENTY ENCODED
α-AMINO ACIDS
at pH 7**



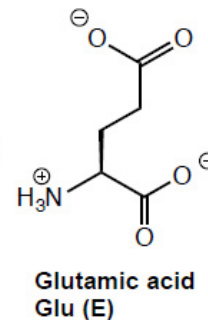
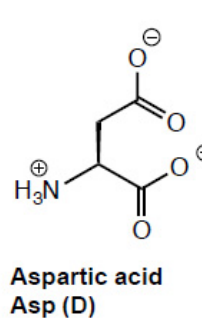
Amino acids with HYDROPHOBIC side chains



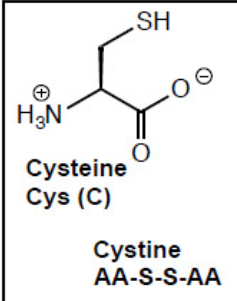
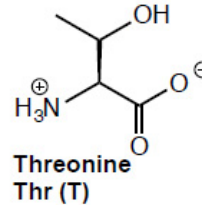
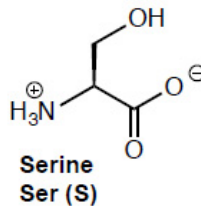
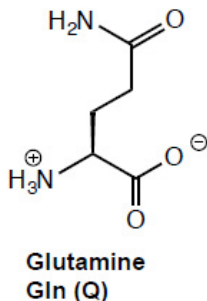
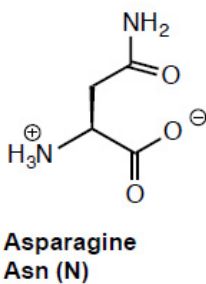
Amino acids with CHARGED side chains



NEGATIVE



Amino acids with POLAR UNCHARGED side chains



MIT OpenCourseWare
<http://ocw.mit.edu>

7.016 Introductory Biology
Fall 2014

For information about citing these materials or our Terms of Use, visit: <http://ocw.mit.edu/terms>.