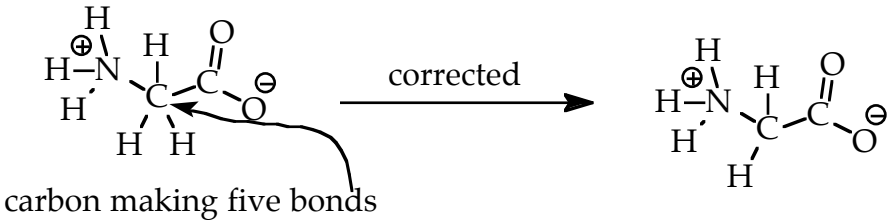
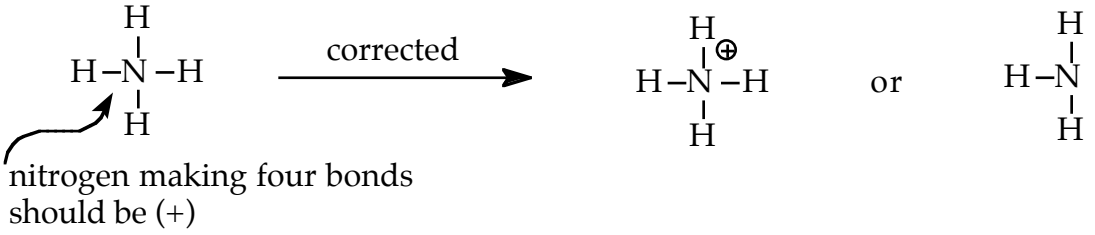
Biochemistry Solutions

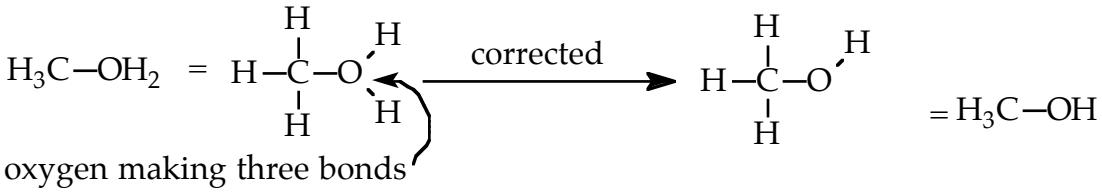
(1) BONDS AND FORCES

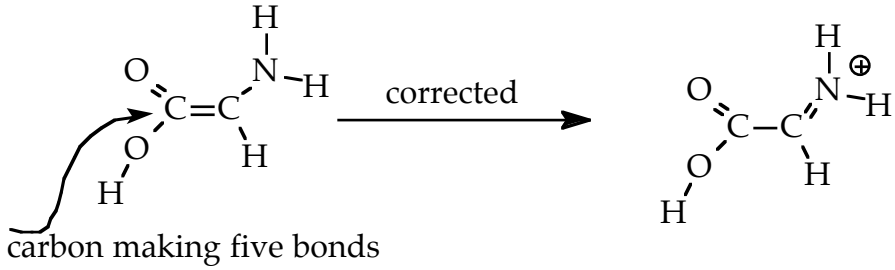
(1.1) Covalent Bonds

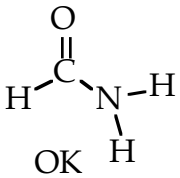
(1.1.1)









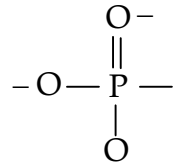


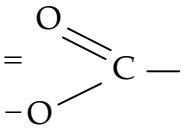
(1.1.2) For each of the functional groups given, draw a structural formula.

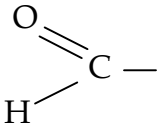
Amino = $^{+}H_3N$ —

Methyl = H_3C —

Hydroxyl = HO —

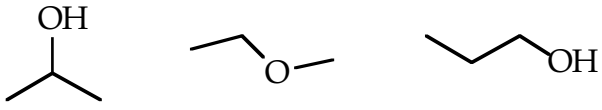
Phosphoryl = 

Carboxyl = 

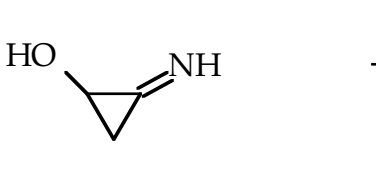
Aldehyde = 

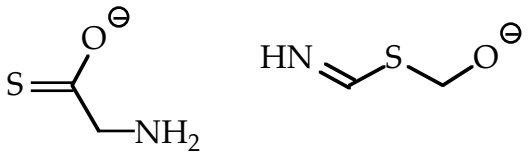
(C1) Computer-Aided Problems 1

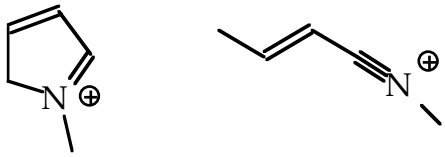
(1.1.3)

a) 

b) 

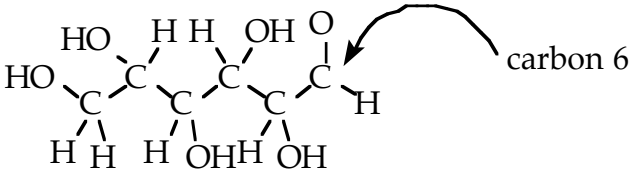
c) 

d) 

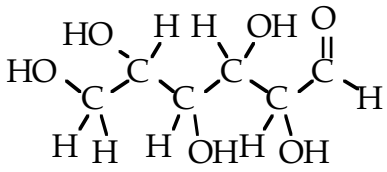
e) 

(C2) Computer-Aided Problems 2

a) The best way to solve these problems is to reproduce what you see on the screen and then go back to fix the single/double/triple bonds. From the screen, you get this:

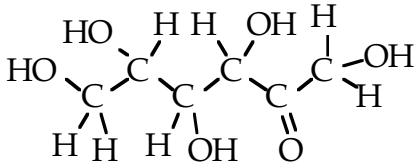


What about carbon 6? The oxygen is shown making only one bond to the carbon. It could be (–) charged or it could be making a double bond with the carbon. If you check the carbon, it is making only three bonds, not four. Therefore, the most reasonable structure is:



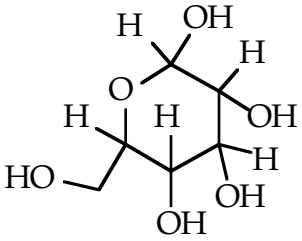
This is the same as the structure shown in most textbooks.

b) Using the same logic as you did with part (a), you get:



This should match the structure in the textbook. Compared with glucose, the C=O is on the second-to-last carbon of fructose but on the last carbon of glucose. The –OHs are also switched.

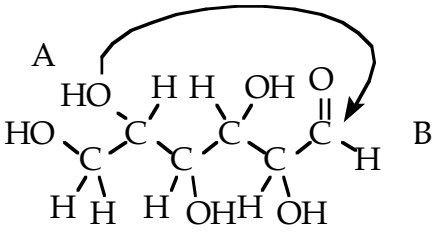
c) The structure looks like this:



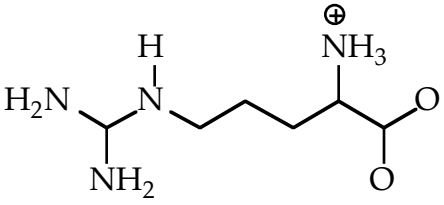
How is this related to the linear form? The key is to compare the carbon atoms. In linear glucose, each carbon has one and only one oxygen atom attached. In the circular form, one carbon atom (the one at the top of the hexagon) has two oxygens attached. This means that one of the oxygen atoms on one carbon is attaching to another carbon atom to form the ring.

This also means that the carbon at the top of the ring must have been at one end of the chain. Therefore, the oxygen marked A in the structure below bonded to the carbon

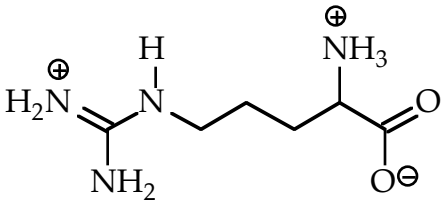
marked B. The H that was attached to A becomes attached to the oxygen that is attached to carbon B. This is shown below:

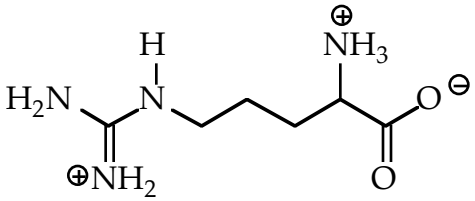


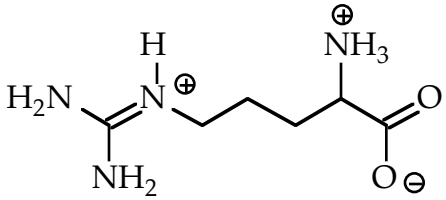
d) The structure shown by the program is:



There are several possible ways the double bonds could be arranged:

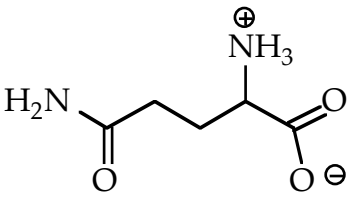




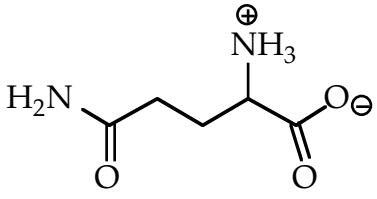


and several other combinations (six total).
In fact, the actual situation is a mixture of all six forms (this is called resonance). For our purposes, it does not matter which one you choose; they are all arginine.

e) The structure is:

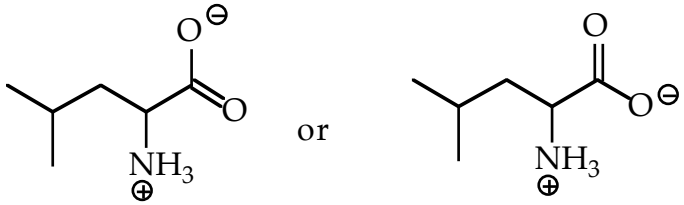


or



Both are glutamine.

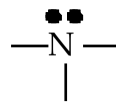
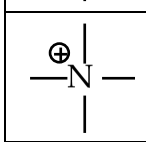
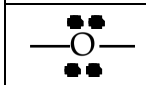
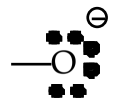
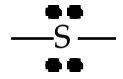
f) The structure is:



Both are leucine.

(1.2) Noncovalent bonds and forces

(1.2.1)

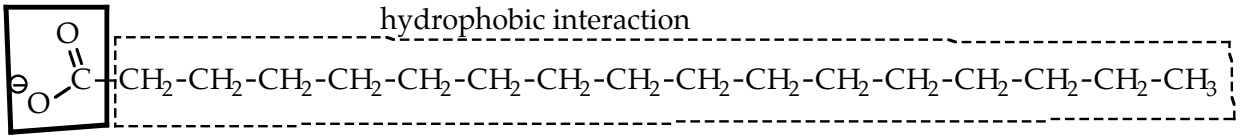
	Is the bond polar or nonpolar?	**Hydrophobic or hydrophilic?**	**Ionic bond?**	**Hydrogen bond?**	**Hydrophobic interactions?**
C–S	nonpolar - roughly equal electronegativities	nonpolar, so hydrophobic	not charged, so NO	no N or O, so NO	hydrophobic, so YES
P–O	polar - different electronegativities	polar, so hydrophilic	if O is charged, YES; otherwise, NO	if O: or O-H, YES; otherwise, NO	hydrophilic, so NO
S–H	nonpolar - similar electronegativities	nonpolar, so hydrophobic	not charged, so NO	no N or O, so NO	hydrophobic, so YES
S–O	polar - different eletronegativities	polar, so hydrophilic	if O is charged, YES; otherwise, NO	if O: or O-H, YES; otherwise, NO	hydrophilic, so NO
	an atom, so neither polar nor nonpolar	can make H bonds, so hydrophilic	not charged, so NO	lone pair on N (N:), so YES (acceptor)	hydrophilic, so NO
	an atom, so neither polar nor nonpolar	charged, so hydrophilic	N is charged, so YES	no N:, so NO (not to the N atom)	hydrophilic, so NO
	an atom, so neither polar nor nonpolar	can make H bonds, so hydrophilic	not charged, so NO	lone pair on O (O:), so YES	hydrophilic, so NO
	an atom, so neither polar nor nonpolar	charged, so hydrophilic	O is charged, so YES	lone pair on O (O:), so YES	hydrophilic, so NO
	an atom, so neither polar nor nonpolar	no charge or H bonds possible, so hydrophobic	not charged, so NO	no N or O, so NO	hydrophobic, so YES

(1.2.2)

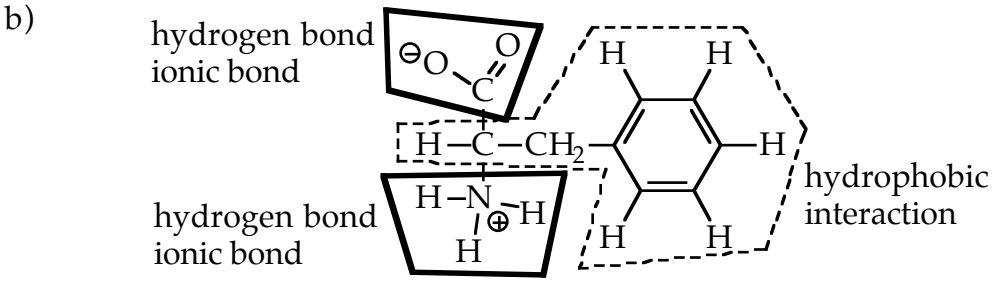
The toes of geckos adhered equally well to neutral, strongly hydrophobic, and strongly hydrophilic surfaces. If ionic or hydrogen bonds were the noncovalent forces involved, then you would not expect a gecko toe to stick to neutral or strongly hydrophobic surfaces. If hydrophobic interactions were the noncovalent forces, then you would not expect a gecko toe to stick to strongly hydrophilic surfaces. The adhesive properties of gecko toes are due to the van der Waals forces between the molecules on the millions of tiny hairs and the molecules of the surface. The millions of tiny hairs on the gecko toe increase the surface area and increase the number of van der Waals forces and increase the adhesive properties.

(1.2.3)

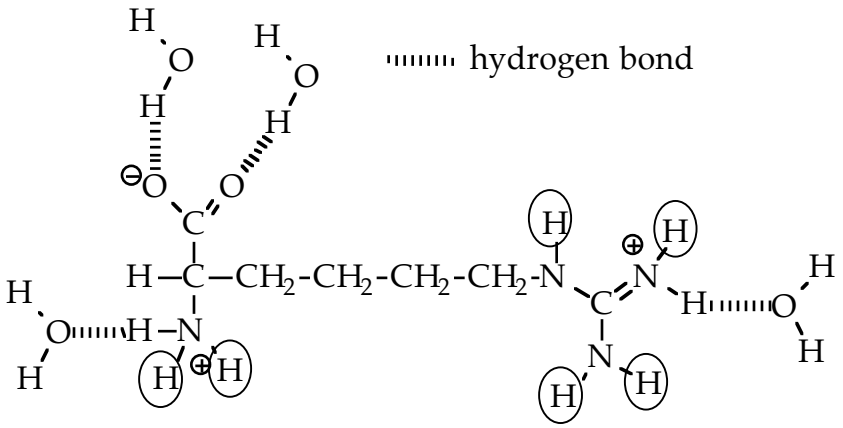
a) soap



b)



(1.2.4)



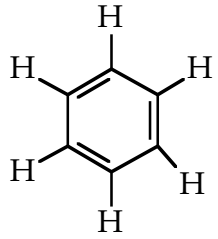
similar for all circled hydrogens

(1.2.5)

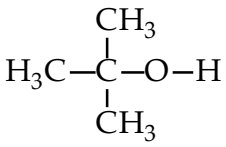
Part	Could this part form **ionic bonds** with another molecule?	Could this part form **hydrogen bonds** with another molecule?	Could this part form a **hydrophobic interaction** with another molecule?
(i)	YES. This is a nitrogen with a positive charge.	YES. It is a hydrogen donor, so it could form an H bond with an H acceptor.	NO. This is a polar hydrophilic part of the molecule
(ii)	NO. This is an oxygen with no charge, so it cannot make ionic bonds.	YES. It has two lone pairs of electrons (hydrogen acceptors), so it could make an H bond with an H donor.	NO. This is a polar hydrophilic part of the molecule
(iii)	NO. There is no charge to this part of the molecule.	NO. This part is exclusively carbon and hydrogen. It is therefore nonpolar and cannot participate in H bonding.	YES. This part is exclusively carbon and hydrogen. It is therefore nonpolar and a hydrophobic interaction is possible with a suitable partner.

(1.2.6)

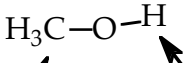
most hydrophobic



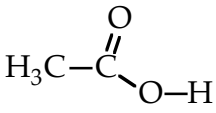
only nonpolar bonds, therefore very hydrophobic



has more hydrophobic parts than



most hydrophilic



has more hydrogen-bonding potential than

(C3) Computer-Aided Problems 3

1)

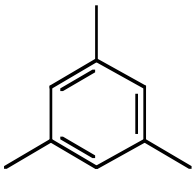
a) The simplest molecule is #2. Compared with #2, #1 has an added CH_2-OH. The added CH_2 is hydrophobic while the -OH is hydrophilic. Since polar groups like -OH contribute more to the hydrophilicity of a molecule on a per-atom basis than small hydrophobic groups, #1 is more hydrophilic than #2. Molecule #3 is more hydrophilic than #1 since it has an added charged group. Therefore, the most hydrophobic is #2, #1 is intermediate, and #3 is the most hydrophilic.

b) Using the Molecular Calculator, you should get:

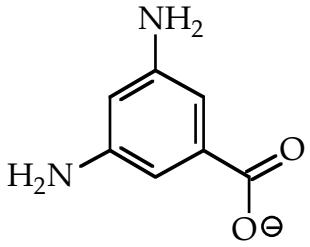
Molecule	**logP**
1	1.211
2	2.022
3	–1.798

Although answers for (c through e) will vary, a possible answer is given for each.

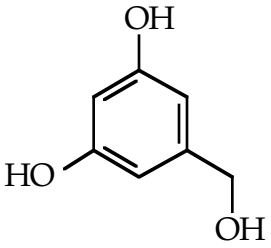
c) The following molecule is more hydrophobic than #2 because it has more hydrophobic CH_3 groups attached. Its logP is 2.7:



d) The following molecule is more hydrophilic than #3 because it has more hydrophilic -NH_2 groups attached. Its logP is –3.432:



e) The following molecule is more hydrophilic than #1 because it has more polar -OH groups; it is less hydrophilic than #3 because it is not charged. Its logP is 0.399:

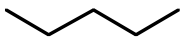


2)

a) This is one of the many possible answers for this question. In this case, R was a butyl group ($CH_3CH_2CH_2CH_2$-); this gives four structures:

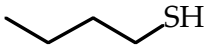
HYDROPHOBIC

R-CH_3 C_5H_{12}



logP = 2.13

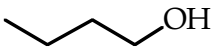
R-SH $C_4H_{10}S$



logP = 2.191

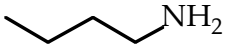
HYDROPHILIC

R-OH $C_4H_{10}O$



logP = 0.64

R-NH_2 $C_4H_{11}N$

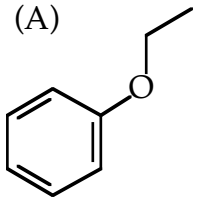


logP = 0.573

b) Since C-C, C-H, C-S, and S-H bonds are nonpolar, adding these to a molecule would make it more hydrophobic. Since O-H and N-H bonds are polar, adding these to a molecule would make it more hydrophilic.

3)
a) There are many possibilities; here is one pair of molecules:

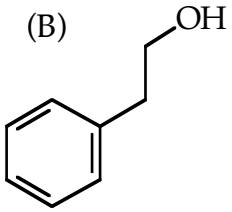
(A)



$C_8H_{10}O$

logP = 2.36

(B)



$C_8H_{10}O$

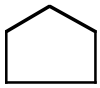
logP = 1.369

b) Both a C-O-C and a C-OH group have two free lone electron pairs on their oxygen atoms that are capable of making hydrogen bonds. However, the H atom of the -OH group can participate in hydrogen bonds that the C-O-C group cannot. Therefore, the alcohol form (B) would be expected to be more hydrophilic than the ether form (A).

c) The logP values agree with the prediction.

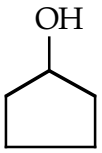
4)
a) through c) There are many possible answers; here is one set of molecules:

Original Molecule



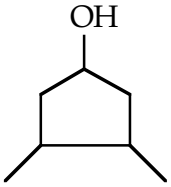
logP = 1.79

Add an -OH



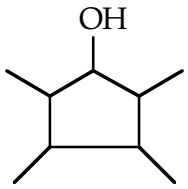
logP = 0.76

Add two -CH_3's



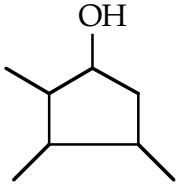
logP = 1.35
not quite enough

Add four -CH_3's



logP = 1.948
a little too much

Add three -CH_3's

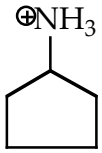
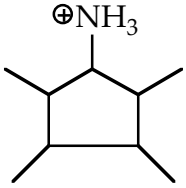
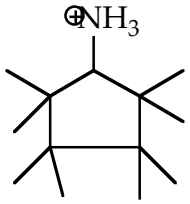
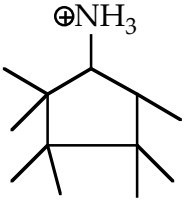


logP = 1.651
pretty close

It took between three and four -CH_3 groups to overcome the effect of the -OH. You should get similar results. This shows that, per atom, hydrophilic groups contribute more than hydrophobic groups.

5)

a) through c) There are many possible answers; here is one set of molecules:

Original Molecule	Add an $-NH_3^+$	Add four $-CH_3$'s	Add eight $-CH_3$'s	Add seven $-CH_3$'s
				
logP = 1.79	logP = -0.0773	logP = 0.415 not quite enough	logP = 1.995 a little too much	logP = 1.6 pretty close

It took about seven $-CH_3$ groups to overcome the effect of the $-NH_3^+$. You should get similar results. This shows that charged groups are more hydrophilic than uncharged polar groups.

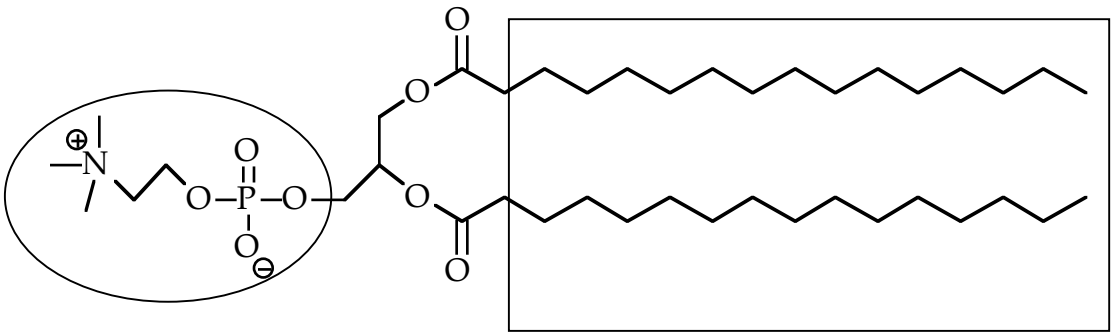
(2) MACROMOLECULES

(2.1) Lipids and phospholipids

(2.1.1)
A saturated fatty acid can form a solid at room temperature. The hydrocarbon chain of a saturated fatty acid contains no C=C bonds, so the molecules can align and pack together in an orderly fashion. The C=C bonds in the hydrocarbon chain of an unsaturated fatty acid prevent this orderly arrangement and result in a lower melting point.

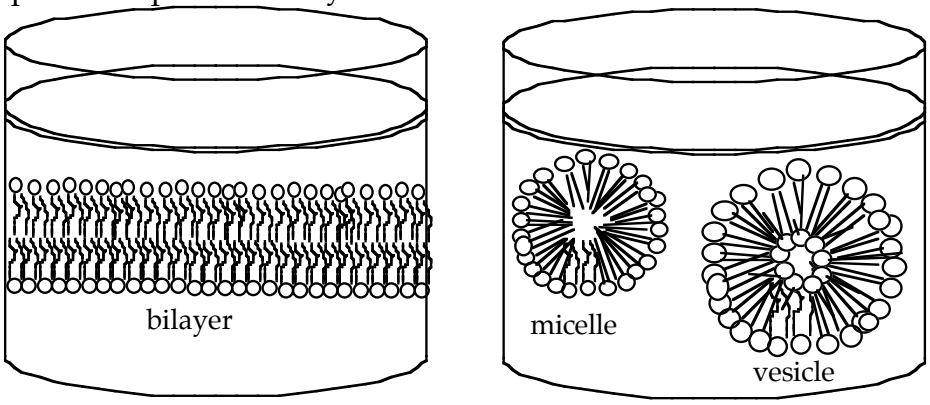
(2.1.2)
Phospholipids are a major component of <u>membranes</u>.

A phospholipid contains both polar and nonpolar domains. Circle the polar domain. Box the nonpolar domain.



The environment within the cell is aqueous and therefore hydrophilic. The arrangement of phospholipids shown had the hydrocarbon tails exposed to this environment. These hydrocarbon tails are extremely hydrophobic.

(2.1.3)
Phospholipids can spontaneously form the three different structures below.



(2.2) Nucleic acids

(2.2.1)
The first molecule is deoxyribonucleic acid (DNA). DNA can be distinguished from ribonucleic acid (RNA) by the absence of an OH group on the 2′ carbon. DNA is the genetic material.

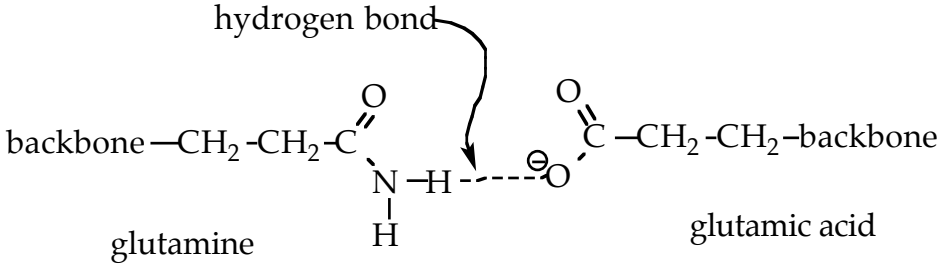
The second molecule is RNA. There are several different types of RNA in the cell.
Messenger RNA (mRNA) is an RNA copy of a gene that is used in protein synthesis.
Ribosomal RNA (rRNA) forms part of the structure of the ribosomes.
Transfer RNA (tRNA) acts as an adaptor molecule. Each tRNA recognizes a codon in the mRNA and carries the appropriate amino acid to the ribosome.

(2.3) Polypeptides and proteins, background

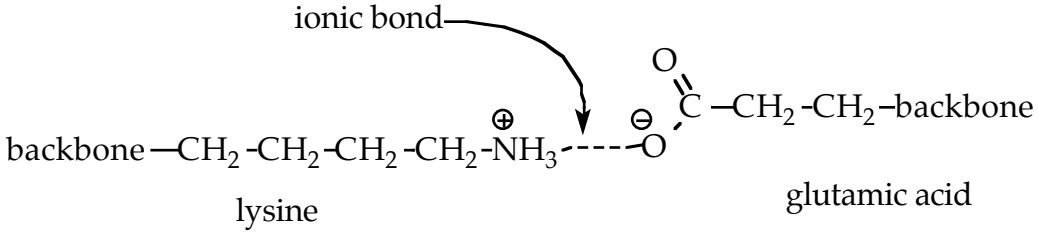
(2.3.1)
Remember that the problem asked only about the side chains, so don't consider the $-NH_3^+$ or $-COO^-$ groups.

a) Glutamine's side chain has both H bond donors (2 N-H's) and H bond acceptors (=O: and N:) so it can form H bonds with any amino acid that has either a hydrogen donor or a hydrogen acceptor.

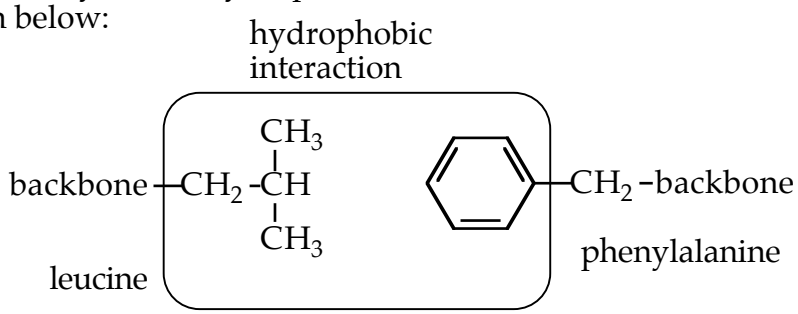
Example: Glutamic acid has only hydrogen bond acceptors on its side chain. It could form many hydrogen bonds with the side chain of glutamine; here is one possibility:



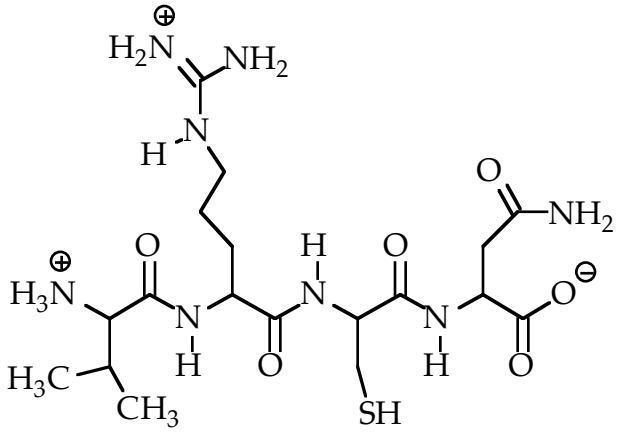
b) Lysine has a (+) charge, so it can only form an ionic bond with a (–) charge. The only amino acids with (–) charged side chains are glutamic acid and aspartic acid. Glutamic acid can form only one ionic bond with the side chain of lysine. This is shown below:



c) Leucine has a hydrophobic side chain. It can form a hydrophobic interaction with any hydrophobic part of a side chain. Phenylalanine has a completely hydrophobic side chain and can easily form a hydrophobic interaction with the side chain of leucine. This is shown below:



(2.3.2)
N-Val-Arg-Cys-Asn-C



(C4) Computer-Aided Problems 4

1) a) The complete secondary structure is:

1 – 2: random coil
3 – 11: alpha helix
12 – 13: random coil
14 – 19: beta sheet
20 – 23: turn
24 – 27: beta sheet
28 – 30: turn
31 – 34: beta sheet
35 – 38: random coil
39 – 50: alpha helix
51 – 53: random coil
54 – 57: turn
58: beta sheet
59: random coil
60 – 80: alpha helix
81: random coil

82 – 90: alpha helix
91 – 92: random coil
93 – 106: alpha helix
107: random coil
108 – 113: alpha helix
114: random coil
115 – 123: alpha helix
124 –125: random coil
126 – 134: alpha helix
135 – 136: random coil
137 – 141: alpha helix
142: random coil (it can sometimes be hard to see this amino acid)
143 – 155: alpha helix
156 – 158: random coil
159 – 162: turn
163: random coil

b) Depending on how you count them, there are approximately three amino acids per turn of the alpha helix. The actual value, as measured from many proteins, is 3.6.

c) The four sections interact as two pairs:
(15-17):(56-58) are antiparallel
(24-27):(31-34) are also antiparallel

(2.4) Polypeptides and proteins, interactions

(2.4.1)

a)

Gln_{57}	hydrophilic and polar		Pro_{48}	hydrophobic
Leu_{60}	hydrophobic		Ile_{46}	hydrophobic
Lys_{67}	hydrophilic and charged		Phe_{83}	hydrophobic
Glu_{71}	hydrophilic and charged		Arg_{34}	hydrophilic and charged

b)

MHC II side chains	Interaction with opposite side chain of TSST
Gln_{57}	van der Waals
Leu_{60}	van der Waals + hydrophobic
Lys_{67}	van der Waals
Glu_{71}	van der Waals + ionic + hydrogen

c) There are a number of different answers for this part. The idea is to make another strong bond. The strongest bond to add would be an ionic bond. For example, if you change Phe_{83} of TSST to an aspartic acid, the Asp_{83} of TSST would now be able to form an ionic bond with Lys_{61} of MHC II.

d) Changing Arg_{34} to Gln prevents the formation of an ionic bond with Glu_{71} of MHC II. The interaction between Gln_{34} of TSST and Glu_{71} of MHC II would be a hydrogen bond. It may be that an H bond at that position is not strong enough to hold the proteins together.

e) A glutamic acid at position 34 instead of an arginine replaces a positively charged amino acid with a negatively charged one. The glutamine at position 71 of MHC II is also negatively charged. The two (–) charges will now repel each other. The remaining van der Waals interactions must not be strong enough to overcome the repulsion.

f) van der Waals interactions occur between any two nonbonded atoms. Replacing an isoleucine with leucine is unlikely to change the strength of the MHC II-TSST interaction, so they should still bind.

g) With these substitutions, one ionic bond and a van der Waals force have been replaced with two H bonds. It must be that the two H bonds are strong enough to hold the two proteins together.

h) One possibility would be to change Glu_{71} to lysine or arginine, thus restoring the ionic bond.

(2.4.2)

a) The interaction between the side chain of valine #6 and the side chains of phenylalanine #85 and leucine #87 is a hydrophobic interaction.

b) The aggregation is driven by an interaction between the side chain of amino acid #6 (valine) of one hemoglobin molecule with a pocket formed by the side chains of amino acids #85 (phenylalanine) and #87 (leucine) of another hemoglobin molecule. The amino acid #6 in Hb^{+} (wild-type) is glutamic acid. Glutamic acid is a charged amino acid and cannot participate in a hydrophobic interaction with amino acids #85 and #87 of another hemoglobin molecule.

c) Phenylalanine is hydrophobic like valine, so it should be able to interact with the side chains of amino acids #85 (phenylalanine) and #87 (leucine) of another hemoglobin molecule. However, phenylalanine is larger than valine.

i) If Hb^{Phe} **<u>does not</u>** form polymers under any circumstances, it is possible that the larger phenylalanine cannot fit into the pocket formed by the side chains of amino acids #85 (phenylalanine) and #87 (leucine) of another hemoglobin molecule.

ii) If Hb^{Phe} **<u>does</u>** form polymers with the same general structure as polymers of Hb^{S}, then it must fit into the pocket formed by the side chains of amino acids #85 (phenylalanine) and #87 (leucine) of another hemoglobin molecule and interacts in the same manner as valine.

(2.4.3)
a) There are two models for why these amino acid changes result in an inactive enzyme: 1) the new amino acid side chain is charged instead of neutral; or 2) the side chain of the new amino acid is larger than that of glycine.

The first data set is ambiguous, because the side chains of the added amino acids are both big and charged. However, the second data set shows that substituting valine, whose side chain is larger than glycine but uncharged, results in an inactive enzyme. This indicates that it is the size of the amino acid side chain at position A that matters, not the charge (model ii). If this is the case, it is possible that the binding pocket can accommodate only an amino acid with a small side chain like glycine. Substituting an amino acid with a larger side chain alters the pocket and changes the conformation of the molecule so that it is no longer able to function.

b) A possible explanation for mutant 6 is that the amino acids at positions A and B interact somehow, so that changes in one can compensate for changes in the other. For example, perhaps when the enzyme is in its active form, side chains of both A and B lie near each other in the pocket within the enzyme. Mutant 1 (Gly ⇒ Glu) is inactive because the Glu side chain is too big to fit in the pocket where Gly normally sits. The effects of this can be partially reversed by changing Tyr ⇒ Cys, which opens up more space in the pocket to accommodate the side chain of Glu.

c) In this case, it appears that reducing the size of a side chain in the pocket (Tyr ⇒ Cys) also results in formation of an inactive enzyme. Therefore, the pocket has to be a certain size for the enzyme to function: Gly ⇒ Val overfills it and Tyr ⇒ Cys underfills it. Given the compact nature of protein structures, these results are not surprising.

(2.4.4)
a) Each subunit is a polypeptide, so eight polypeptides compose the nucleosome complex.

b) Quarternary structure is the association of different polypeptides or subunits. The nucleosome has eight interacting polypeptides so it has quarternary structure.

c) The amino acids in the sequence are hydrophobic. You would expect to find this stretch of amino acids to be buried in the hydrophobic interior of the complex.

d) The regions high in the positively charged amino acids lysine and arginine would likely be on the surface of the complex. Lysine and arginine can form ionic bonds with the negatively charged backbone of the DNA.

e)

Treatment	Effect on nucleosome complexes list appropriate number(s) from above
Disrupt hydrogen bonds	4, 2
Disrupt ionic bonds	2
Disrupt peptide bonds	2, 4, 5

f)

Treatment	Effect on structure of DNA double helices list appropriate number(s) from above
Disrupt hydrogen bonds	2
Disrupt ionic bonds	1
Disrupt peptide bonds	1

(2.4.5)

a)

	Amino acids	Strongest interaction
i)	Ser and Gln	Hydrogen bond
ii)	Ala and Met	van der Waals forces
iii)	Phe and Tyr	van der Waals forces

b) The α-helical structure of each polypeptide is due to a large number of hydrogen bonds. The interaction between the two polypeptides is based on van der Waals forces and a hydrogen bond. Low heat is sufficient to disrupt weak binding between the two α-helices, yet secondary structure is maintained. High heat will disrupt all hydrogen bonds and produce elongated peptides.

c) Under some conditions, changing both of these residues to cysteine will increase the stability of the interaction. Two closely opposed cysteine residues are capable of forming a type of covalent bond called a disulfide bond.

(C5) Computer-Aided Problems 5

1) Hydrophobic/hydrophilic

a) The exterior is mostly hydrophilic. Surprisingly, there are many hydrophobic side chains on the surface. This is likely because, on a per-atom basis, hydrophilic elements make a much greater contribution to the molecule than the hydrophobic parts. To put it another way, the hydrophobic effect is so weak that only a few hydrophilic groups are required to make the protein soluble and stable.

b) The interior of the protein is almost exclusively hydrophobic. This is not surprising as even a little hydrophilic character would prevent a side chain from remaining in the interior.

c) There are nine valines in lysozyme:

Valine	Position of side chain
57	pokes out into water
71	small exposure
75	pokes out into water
87	small exposure
94	pokes out into water
103	very small exposure
111	totally buried
131	pokes out into water
149	totally buried

Thus, only two of nine are totally in the interior of the protein. This is consistent with part (a). The surface of many proteins is a mosaic of hydrophobic and polar amino acids.

d) None of the 13 lysines are completely in the interior of the protein; all of the $-NH_3^+$ groups are exposed to the water. This is exactly as expected.

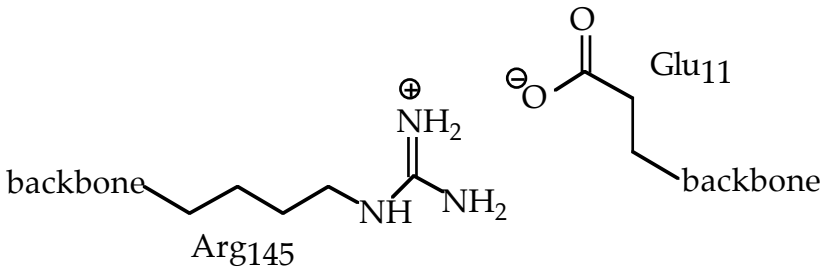
2) Side-chain interactions

a) Glu_{11} and Arg_{145}.

i) Glu has a (–) charge and H-bond acceptors (lone pairs on oxygen atoms); Arg has a (+) charge and H-bond acceptors (lone pairs on nitrogen atoms) as well as H-bond donors (hydrogen atoms covalently bonded to nitrogen atoms). Therefore, ionic bonds, hydrogen bonds, and van der Waals interactions are possible. Since both are highly hydrophilic, a hydrophobic interaction is not possible.

ii) Ionic bond is the strongest.

iii) The structure of the side chains looks like this:



Note that the (+) charge could be on any of the N's in arginine and the (–) charge could be on either of the oxygens in glutamic acid. There is not enough information in the structure to tell which is correct. [In fact, the (+) charge is distributed over the three N's and the C at the end of the arginine and the (–) charge is distributed over the two O's and the C in glutamic acid. This is called resonance, but it is beyond the scope of this book.]

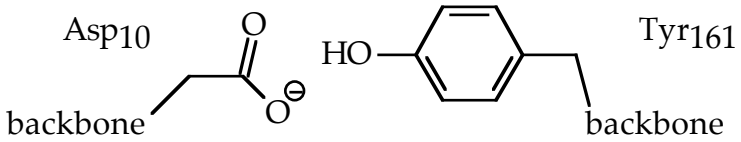
iv) Since the (+) and (–) charges are in close proximity, an ionic bond is the strongest possible interaction between these side chains.

b) Asp_{10} and Tyr_{161}

i) Asp has a (–) charge and H-bond acceptors (lone pairs on oxygen); it has only one CH_2 in its side chain, not enough for a hydrophobic interaction. Tyr has an –OH, which can serve as an H-bond donor and an H-bond acceptor; it also has a large hydrophobic ring. Since only one is charged, there cannot be an ionic bond. Since Tyr has an H-bond donor and Asp has H-bond acceptors, an H bond is possible. Since Asp is not hydrophobic, a hydrophobic interaction is not possible. van der Waals is always possible.

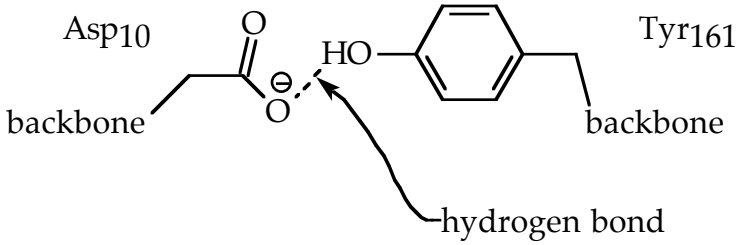
ii) H bond is the strongest possible.

iii) In the protein, the side chains are oriented like this:



Note that the (–) charge could be on either of the oxygens in aspartic acid. For our purposes, it does not matter.

iv) Since the H-bond donor (the H on the OH in Tyr) points toward the H-bond acceptor (the lone pair on the O in Asp), a hydrogen bond is the most likely bond. It would look like this:

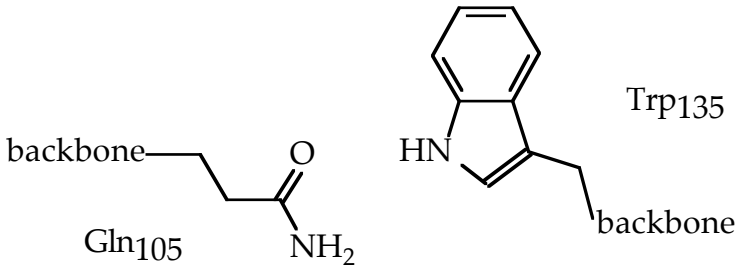


c) Gln_{105} and Trp_{138}

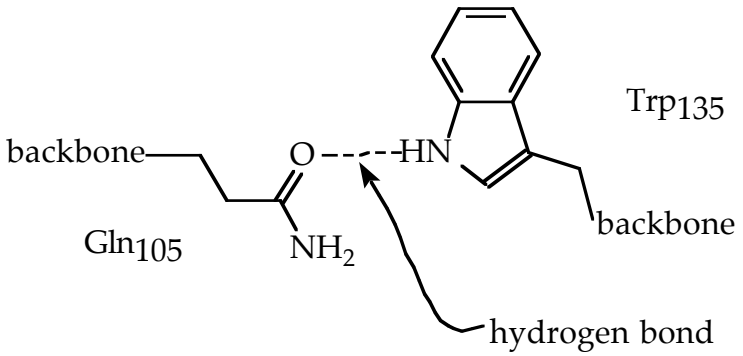
i) Glutamine's side chain has no charge. It has both H-bond donors (H's on N) and H-bond acceptors (lone pairs on N and O). It has a short chain of CH_2's, so a hydrophobic interaction is possible, but VERY unlikely. Tryptophan's side chain has no charge. It has both an H-bond donor (H on N) and an H-bond acceptor (lone pair on N). It also has a highly hydrophobic ring system. Therefore, an ionic bond is impossible; a hydrogen bond is possible; hydrophobic interaction is borderline possible; and van der Waals is possible.

ii) The strongest is H bond; many such bonds are possible.

iii) In the protein, the side chains of the two amino acids are oriented like this:



iv) Since the H-bond donor (the H on the N in Trp) points right at an H-bond acceptor (the lone pair on the O in Gln), an H bond is very likely. It would look like this:

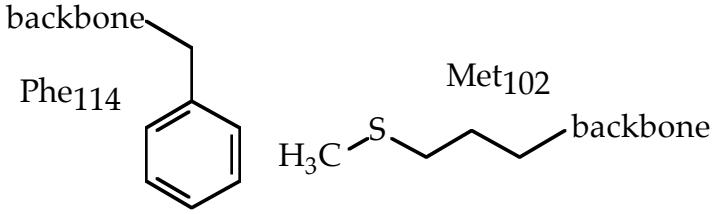


d) Met_{102} and Phe_{114}

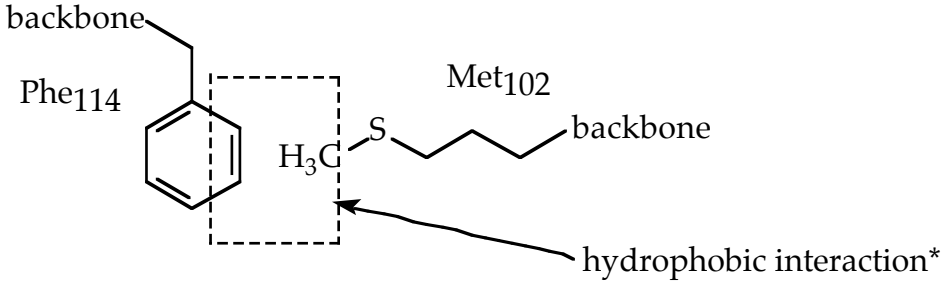
i) Met has no charge or H-bond possibilities; it has a large hydrophobic side chain. Phe has similar properties. Therefore, only a hydrophobic interaction or van der Waals is possible.

ii) The strongest is hydrophobic interaction.

iii) In the protein, the side chains are oriented like this:



iv) Based on the structure, the strongest possible interaction is a hydrophobic interaction. It could be shown like this:



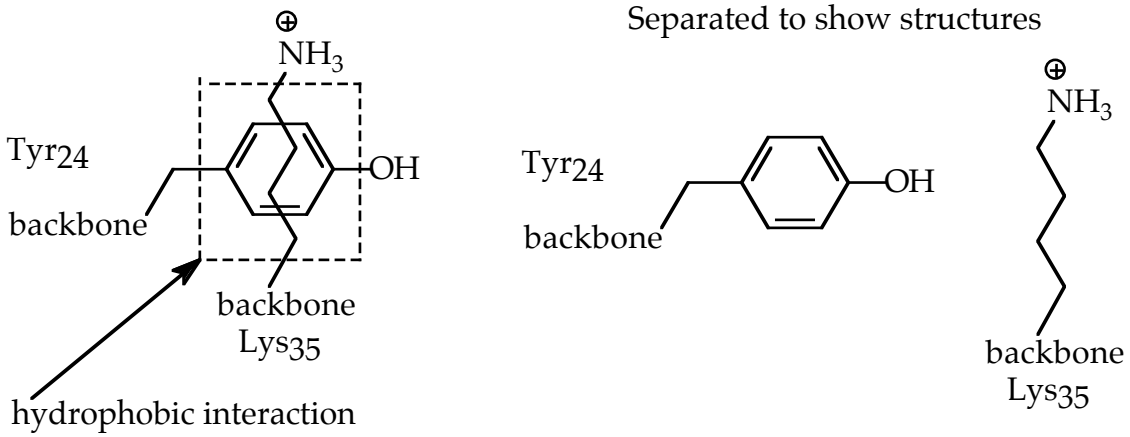
*It is shown as a dashed box rather than a bond because it is not a true bond between a pair of atoms. It is an interaction between these groups and the water surrounding the protein.

e) Tyr_{24} and Lys_{35}

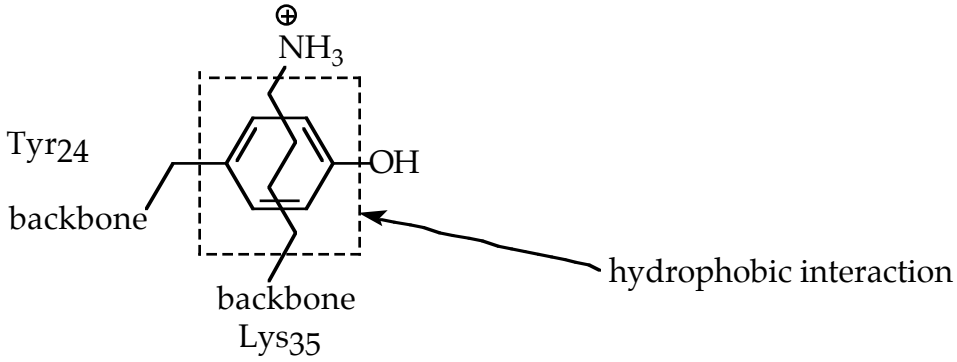
i) Tyrosine's side chain has no charge. It does have an H-bond donor and an H-bond acceptor. It also has a large hydrophobic ring. Lysine's side chain has a (+) charge. It also has H-bond donors (the H's on the N^+) but no H-bond acceptor (no lone pair on the N). It also has a somewhat hydrophobic set of four CH_2's. Therefore, ionic bonds are not possible. A hydrogen bond, (borderline) hydrophobic interaction, or van der Waals is possible.

ii) The strongest is an H bond.

iii) In the protein, the side chains are oriented like this:



iv) Since the H-bond donor (H's on the N^+ of lys) is nowhere near the H-bond acceptor (lone pair on O of Tyr), an H-bond is not possible. However, the hydrophobic parts of the two molecules are very close together. Therefore, a hydrophobic interaction is the most likely interaction in this case. This is why it is important to look at the relative orientation of the side chains, rather than just that they are neighbors. The interaction could be shown like this:



3) Effects of mutations on protein structure

a) Glu_{11} normally makes an ionic bond with Arg_{145}. If Glu_{11} were replaced by Arg, that Arg's (+) charge would be right next to the (+) charge of Arg_{145}. Given that like charges repel, this would destabilize the protein, making it not fully active.

b) Glu_{11} normally makes an ionic bond with Arg_{145}. If Glu_{11} were replaced by Phe, which cannot make ionic bonds because it is not charged, this ionic bond would not be present in the mutant protein. Without this interaction to hold it in the proper shape, the mutant protein is not fully active.

c) Glu_{11} normally makes an ionic bond with Arg_{145}. If Glu_{11} were replaced by Asp, you might expect that this ionic bond would still be possible. However, Asp's side chain is not as long as that of Glu. Looking at the protein's structure, Glu_{11}'s side chain is stretched out very straight as it reaches out to Arg_{145}. If the side chain were shorter, the

(–) charge on Asp would not be close enough to make an ionic bond to Arg_{145}. This weakens the structure enough so that the protein is not fully active.

d) Arg_{145} normally makes an ionic bond with Glu_{11}. If Arg_{145} were replaced by Ser, an ionic bond is no longer possible. Although Ser could possibly form an H bond [although it may be too short – see part (c)], this is weaker than an ionic bond. This weaker bond, if it exists, must not be strong enough to maintain the proper structure of the protein and it is not fully active.

e) Arg_{145} normally makes an ionic bond with Glu_{11}. Since both His and Lys have (+)-charged side chains, you would expect that either substitution would have no effect on the protein's activity. The only relevant difference between His and Lys is that Lys's side chain is substantially longer than that of His. It is likely, then, that although Lys still has a (+) charge, it is too long to make a proper ionic bond with Glu_{11} and so the resulting protein is not fully active. His, on the other hand, is the right size, so the resulting protein is fully active.

f) Tyr_{161} normally forms an H bond with Asp_{10}. If Tyr_{161}were replaced by Ser, an H bond would be possible, based on the structures alone. However, if you look at the structures of the side chains in the protein, the side chain of Tyr_{161} is stretched far out from the backbone. Since the side chain of Ser is much shorter than that of Tyr, the Ser cannot reach to Asp_{10} to make an H bond and, as a result, the protein lacks this crucial H bond and is not fully active.

g) Asp_{10} normally forms an H bond with Tyr_{161}. If Asp_{10} were replaced by Glu, an H bond will still be possible. Although the side chain of Glu is one carbon longer than that of Asp, this does not affect the H bond, and the altered protein is still fully active.

h) Gln_{105} normally makes an H bond with Trp_{138}. If Gln_{105} were replaced by Glu, the H bond could still be formed and the length of the new side chain would be exactly the same as the normal protein. This explains why the altered protein is fully active.

i) Gln_{105} normally makes an H bond with Trp_{138}. If Gln_{105} were replaced by Leu, that H bond would be impossible. Therefore, you'd expect that the mutant protein would not be active. Perhaps, the Leu makes a hydrophobic interaction with Trp_{138} and this is enough to stabilize the protein.

j) Met_{102} normally makes a hydrophobic interaction with Phe_{114}. If Met_{102} were replaced by Glu, Lys, or Arg, this type of interaction would not be possible. In addition, based on the view shown in the CD-ROM for this problem, the side chain of Met_{102} is in the hydrophobic core of the protein. Therefore, a hydrophilic amino acid at this position would be expected to seriously disrupt the protein's structure as it would "prefer" to be on the surface of the protein. The absence of the hydrophobic interaction, or the disruption described, is enough to cause the protein to not be fully functional.

k) Lys_{35} normally makes a hydrophobic interaction with Tyr_{24}. Based on the view shown in the CD-ROM for this problem, the side chain of Lys_{35} is on the surface of the protein. Because Lys_{35} can be replaced by any other amino acid, we must conclude that this hydrophobic interaction is not important for the protein's structure and function.

Furthermore, substitutions to hydrophilic amino acids are tolerated because their side chains will be on the surface of the protein; substitutions to hydrophobic amino acids are also tolerated because a small number of surface hydrophobics are always tolerated.

l) Phe_{67} is in the middle of an alpha-helical section of the protein. Although Pro is hydrophobic like Phe, Pro has a highly constrained backbone that tends to destabilize α-helices. Presumably, changing Phe_{67} to Pro disrupts the α-helix and renders the protein inactive.

(2.5) Polypeptides and proteins, binding sites

(2.5.1)

a) The closest part of Molecule X to Glu_{75} is the $-NH_3^+$. It has a (+) charge and H-bond donors; it is therefore hydrophilic, so it cannot participate in a hydrophobic interaction. The side chain of Glu_{75} is uncharged so an ionic bond between Molecule X and Glu_{75} is not possible. The side chain of Glu_{75} has both H-bond donors and acceptors; the possible interactions are H bonds and van der Waals forces. The strongest of these is the H bond.

b) The closest parts of Molecule X to Ile_{147} are the CH's of the ring. They are hydrophobic and uncharged and cannot make ionic or H bonds. Ile_{147} is uncharged as well. The possible interactions are, therefore, hydrophobic interaction or van der Waals. The strongest is hydrophobic interaction.

c) The closest part of Molecule X to Lys_{302} is the $-COO^-$ group. It is highly charged and cannot participate in hydrophobic interactions. The closest part of Lys_{302} to Molecule X is the $-NH_3^+$. It has a (+) charge and H-bond donors. The possible interactions are, therefore, ionic bond, H bond, and van der Waals. The strongest is ionic bond.

d) Glutamine and asparagine have essentially identical bonding capabilities so that you would expect this change to have no effect on the bonding of Molecule X to the protein. The only difference between the two side chains is that asparagine's side chain is one carbon shorter than glutamine's. Presumably, this shorter side chain cannot reach to Molecule X and form the necessary H bond. As a result, Molecule X no longer binds to the protein.

e) Glutamic acid has a negatively charged side chain; lysine has a positively charged side chain. In the altered protein, there will be two negative charges near each other. Since like charges repel, you would not expect Molecule X to bind the altered protein.

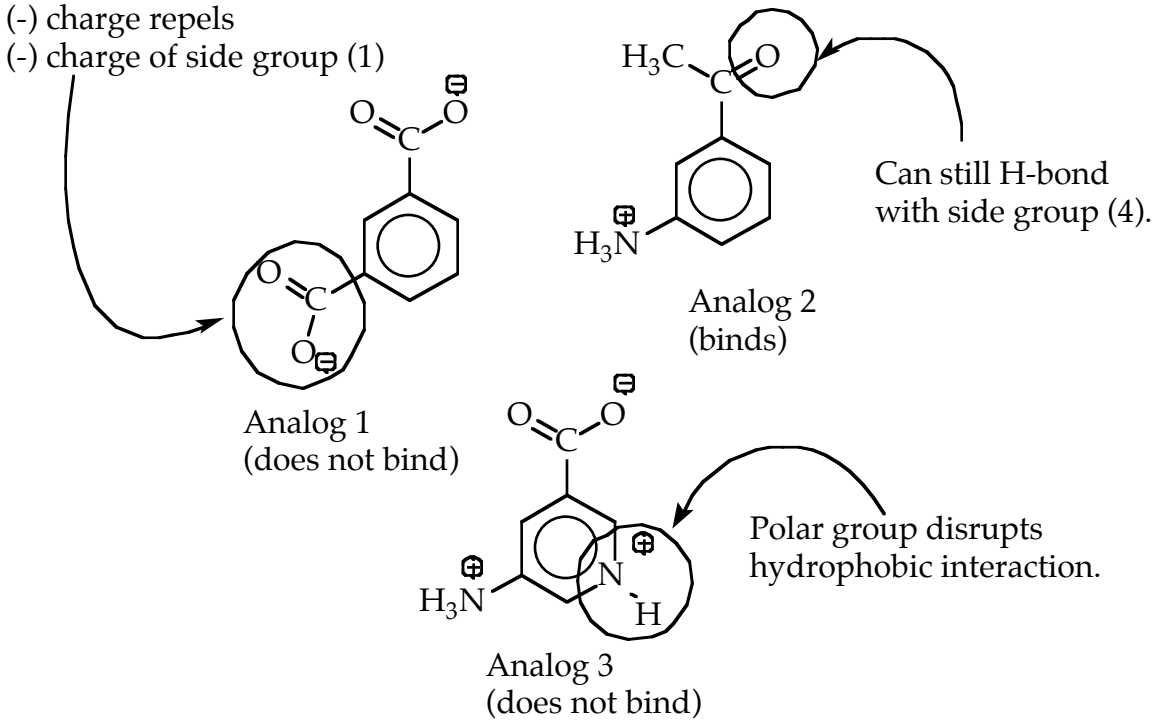
(2.5.2)

a) (1) aspartic acid (2) cysteine (3) valine (4) asparagine

b)

Group	Interaction(s) of Group with Substrate	Classification of Group
(1)	ionic (hydrogen also possible)	hydrophilic, charged
(2)	all nonpolar bonds so hydrophobic interactions or van der Waals forces	hydrophobic
(3)	all nonpolar bonds so hydrophobic interactions or van der Waals forces	hydrophobic
(4)	hydrogen bond	hydrophilic, polar

c)



d) Groups (1), (2), and (3) make the strongest interactions possible given the structure of the substrate. That is:

• Group (1), whatever it is, will be able to interact with the $-NH_4^+$ group of the substrate–this can make H bonds or ionic bonds–the strongest are ionic. The normal enzyme makes an ionic bond, so this cannot be stronger.

• Group (2), whatever it is, will be able to interact with some C-C and C-H parts of the substrate–a very nonpolar region. Therefore, only hydrophobic interactions are possible with that part of the substrate and that is what is already present.

• Group (3), whatever it is, will be able to interact with some C-C and C-H parts of the substrate–a very nonpolar region. Therefore, only hydrophobic interactions are possible with that part of the substrate and that is what is already present.

• Group (4), whatever it is, will be able to interact with the $-COO^-$ region of the substrate, which can make a hydrogen bond or an ionic bond. In the normal protein, it

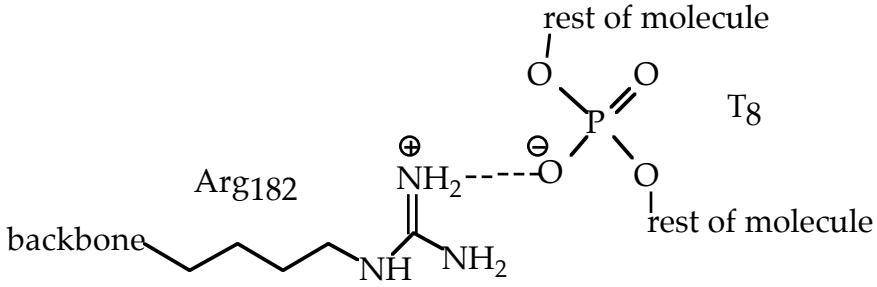
is a hydrogen bond; an ionic bond would be stronger. To make an ionic bond, you'd need a positively charged amino acid at position (4). If the amino acid at position (4) was changed to lysine, arginine, or histidine, the binding could be strengthened.

(C6) Computer-Aided Problems 7
1) Molecules in three dimensions

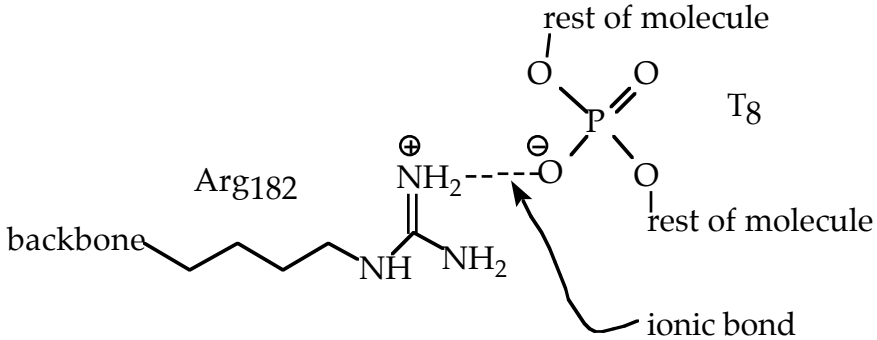
a) There is no answer for this part.

b)

i) Arg_{182} and T_8. The structures of the relevant parts are:

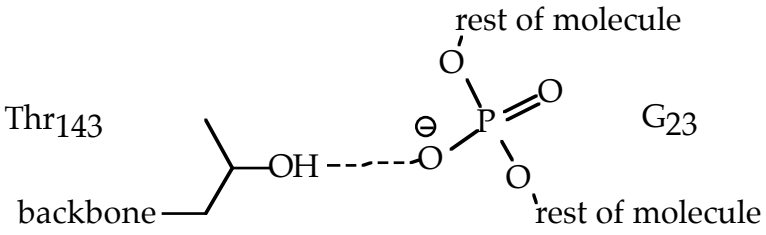


ii) Note that the structure does not make it clear which N has the (+) charge in Arg, nor does it make clear which oxygen in the DNA is (–) charged. However, the strongest bond is achieved if the charges are as shown; thus, this is the most likely configuration. The closest part of the Arg has a (+) charge as well as H-bond donors and acceptors. The closest part of the DNA has a (–) charge and H-bond acceptors. Therefore, ionic bonds, H bonds, and van der Waals interactions are possible. An ionic bond is the strongest of these. It would be shown like this:

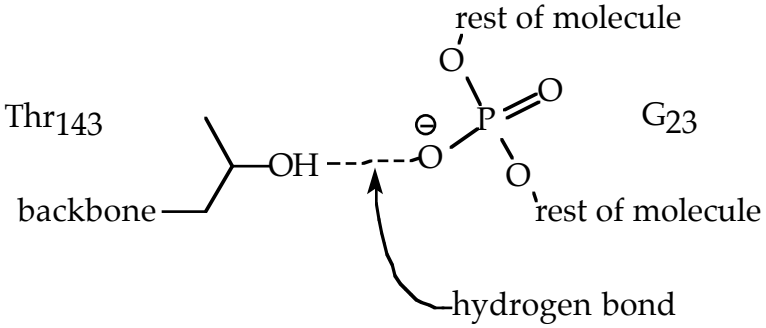


c)

i) Thr_{143} and G_{23}. The structures of the relevant parts are:

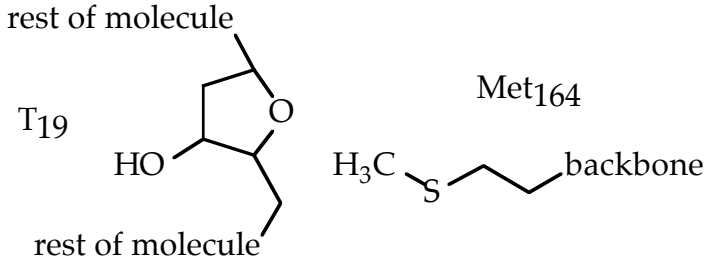


ii) Note that the structure does not make it clear which oxygen atom has the (–) charge. For the purposes of this problem, it does not matter, since either form has a lone pair H-bond acceptor. The closest part of the Thr is the –OH, which is an H-bond donor. Therefore, H bonds and van der Waals interactions are possible. The strongest is an H bond.



d)

i) Met_{164} and T_{19}. The structures of the relevant parts are:

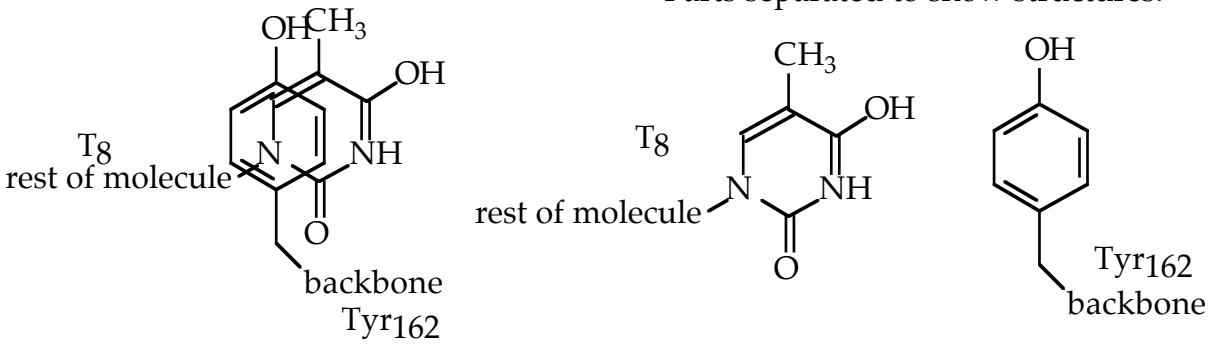


ii) The closest part of T_{19} has H-bond acceptors and some small hydrophobic parts. The closest part of Met_{164} is also hydrophobic. Therefore, a hydrophobic interaction or van der Waals forces are possible. The strongest is a hydrophobic interaction.

e)

i) Tyr_{162} and T_8. The structures of the relevant parts are:

Parts separated to show structures:



ii) Tyr has a large hydrophobic ring as well as H-bond donors and acceptors. Thymine has a hydrophobic ring as well as H-bond donors and acceptors. Looking carefully at the structures, the two –OH groups are not close enough to

form an H bond [see how close they are in part (c), especially using the spacefill view]. Therefore, the only possible bonds are hydrophobic interaction and van der Waals. Hydrophobic interaction is the stronger of the two.

f) Thr_{143} forms an H bond with G_{23}. Gln also has H-bond donors that could form an H bond with this part of G_{23}, resulting in a fully functional protein.

g) Met_{164} forms a hydrophobic interaction with T_{19}. Both Ile and Phe are also hydrophobic, so they could form a hydrophobic interaction with T_{19} as well, resulting in a fully functional protein.

h) Tyr_{162} forms a hydrophobic interaction with T_8. You would the expect that other hydrophobic amino acids (especially he) would be able to form a similar, if not identical, interaction. It must be that Tyr_{162} makes other essential interactions that require this amino acid to be Tyr.

(3) ENERGY, ENZYMES, AND PATHWAYS

(3.1) Energy and enzymes

(3.1.1)

a) When calculating ΔG for reactions, you need consider only the energy states of the reactants and products. Since the ΔG difference between A and B is most negative, A ⇒ B is the more spontaneous of the two reactions.

b) Though reaction 1 is more thermodynamically favorable, it has a huge energy barrier (a very positive ΔG) to overcome before changing to I_1. Having one step in a reaction that is very unfavorable will not change the energy of the overall reaction, but it can slow it down drastically. Reaction 2 has smaller energy barriers to overcome as it converts to I_3 and I_4, so even though its ΔG is less negative, it is likely to be faster than reaction 1.

c) The overall ΔG of the reaction would stay the same, but the energy barrier between A and I_1 would be smaller, so the reaction A ⇒ B would proceed much faster.

(3.1.2)

a) The reaction is spontaneous to the left. Therefore, the hydrolysis of glucose 6-phosphate is the spontaneous reaction (glucose 6-phosphate ⇒ glucose + P_i).

b) Since $\Delta G'_0$ is < 0, the reaction is spontaneous to the right. Therefore, the hydrolysis of ATP is the spontaneous reaction (ATP ⇒ ADP + P_i).

c)

	glucose + P_i ⇒ glucose 6-phosphate + H_2O	$\Delta G'_0$ = +3.3 kcal/mol
+	ATP + H_2O ⇒ ADP + P_i + H^+	$\Delta G'_0$ = –7.3 kcal/mol
	glucose + ATP ⇒ glucose 6-phosphate + ADP + H^+	$\Delta G'_0$ = –4.0 kcal/mol

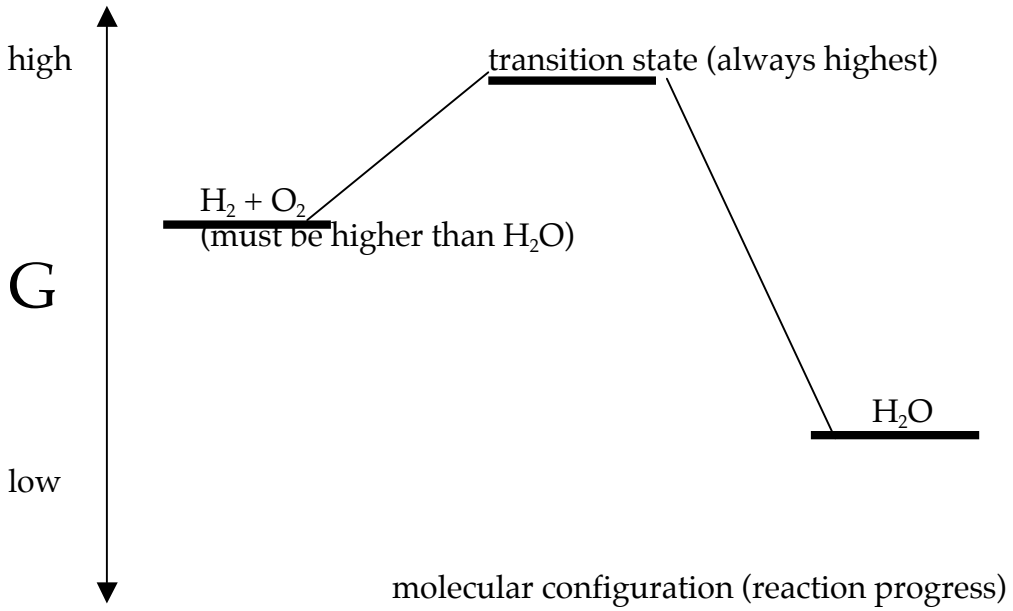
Since $\Delta G'_0$ is < 0, the overall reaction is spontaneous to the right. The nonspontaneous formation of glucose 6-phosphate is coupled to the very spontaneous hydrolysis of ATP, resulting in a net spontaneous formation of glucose 6-phosphate from glucose and ATP.

(3.1.3)

a) The highest energy species are the nonbonded atoms; these are state 2. The two bonded states will have lower energies. Since the reaction from H_2 + O_2 to H_2O is spontaneous, we know that the products (H_2O) will have lower energy than the reactants (H_2 + O_2). Therefore, from highest energy to lowest energy, it will be 2, 3, then 1.

b) Covalent bonds are broken when you go from state 3 to state 2. You are breaking the molecules into atoms (covalent bonds hold atoms together to form molecules).

c) The diagram would look like this (only the relative levels are important here, not the actual values):



(3.1.4)
a) The water slows the rate at which atmospheric O_2 gets to the enzyme, thus slowing the reaction. When the potatoes are again exposed to air, the enzyme and all substrates are present at high levels, so the reaction proceeds rapidly.

b) The cooking destroys the enzyme. The heating causes the enzyme to denature (the three-dimensional structure is lost) and thus to become inactive.

c) The enzyme is not active at the lower pH.

(3.1.5)
a) Penicillin inactivates transpeptidase, making it impossible for the bacteria to synthesize their cell wall. Without a cell wall, the bacterial membrane is not supported, and it can burst, killing the cell.

b) Human cells do not have a cell wall; therefore, they do not need transpeptidase, so penicillin has no effect on them.

c) The β-lactamase must destroy the penicillin before it can inactivate the transpeptidase. β-Lactamase is therefore likely to be located in the cell wall, outside of the cell membrane (in real life, it is).

(3.1.6)
The targets for parathion and paraoxon are virtually identical in insects and humans. Parathion itself is relatively inert, but paraoxon is very reactive toward both the human and insect target molecules. Paraoxon acts by covalently binding to and irreversibly inhibiting a critical enzyme in insects and humans. In the situation we described, humans are exposed only to parathion, which is not very toxic. Insects convert the parathion to paraoxon, which is very toxic. The insect's ability to convert the parathion to paraoxon makes parathion more toxic to insects than humans.

(3.1.7)
a)

i) By inhibiting COX-2, aspirin prevents production of prostaglandin E_2. The resulting lower levels of prostaglandin E_2 cause the pain-sensitive cells to send fewer and weaker pain messages to the brain. This reduces the sensation of pain.

ii) By inhibiting COX-1, aspirin prevents production of prostaglandin E_1. The resulting lower levels of prostaglandin E_1 reduce the production of new stomach lining cells. When these cells are not replaced, the stomach lining can break down, leading to an ulcer.

b) COX-2 inhibitors have all the analgesic properties of aspirin, but since they don't inhibit COX-1, the stomach lining is unaffected and the risk of ulcers is reduced.

(3.2) Biochemical pathways, general

(3.2.1)

$$\text{compound X} \xrightarrow{\text{enzyme 1}} \text{compound Y} \xrightarrow{\text{enzyme 2}} \text{compound Z} \xrightarrow{\text{enzyme 3}} \text{compound A}$$

Bacterial cells with defective enzymes 1, 2, or 3 will grow only if compound A is available (added to the growth media).

a) Each enzyme acts on a substrate to create a new compound. If an enzyme is nonfunctional, then the substrate cannot be used to create a new compound, and the substrate may accumulate. Compound X will accumulate in the cells defective in enzyme 1, compound Y will accumulate in the cells defective in enzyme 2, and compound Z will accumulate in the cells defective in enzyme 3.

b) Assume that for the cell to live it must have a supply of compound A. A cell lacking enzyme 1, 2, or 3 will not survive because compound A is not made. If a cell lacking only enzyme 1 is provided with a usable source of compound Y, then compound Y can be converted to compound Z and compound Z can be converted to compound A and the cell will survive. Likewise, a cell lacking only enzyme 1 can be provided with a usable source of compound Z or compound A and survive. However, if a cell lacking only enzyme 2 is provided with a usable source of compound Y, it will not survive because compound Y cannot be converted to compound Z. If a cell lacking only enzyme 2 is provided with a usable source of compound Z or compound A, it can survive. A cell lacking enzyme 3 must be provided with a usable source of compound A.

c) The compound that is acted on by the first enzyme in the pathway will be the compound that builds up. So in a cell lacking enzyme 1 and enzyme 2, compound X will accumulate. A cell lacking enzyme 2 and enzyme 3 will accumulate compound Y, and a cell lacking enzyme 1 and enzyme 3 will accumulate compound X.

d) Only compound(s) that can be acted on by functional enzymes to make compound A will allow the cells to survive. A cell lacking enzyme 1 and enzyme 2 can survive only if supplied with compound Z or compound A. A cell lacking enzyme 2 and enzyme 3 can survive only if supplied with compound A. Likewise, a cell lacking enzyme 1 and enzyme 3 can survive only if supplied with compound A.

(3.2.2)
Remember that arginine is the ending point and must be produced if the cells are to live. The pathway has at least four enzymes. Therefore, even before examining the data in the table, you can sketch out the pathway:

compound __ $\overset{\text{enzyme}}{\Rightarrow}$ compound __ $\overset{\text{enzyme}}{\Rightarrow}$ compound __ $\overset{\text{enzyme}}{\Rightarrow}$ compound __ $\overset{\text{enzyme}}{\Rightarrow}$ arginine

From the table we know that cells missing enzyme 2 survive only if arginine is added. So we can draw the following:

compounds A, B, C $\overset{\text{enzyme 2}}{\Rightarrow}$ arginine Thus, enzyme 2 is the last enzyme in the pathway.

From the table we know that cells missing enzyme 1 survive (make arginine) if compound B is added. Therefore, compound B must be later in the pathway than compounds A or C. Building on the previous step, we can draw:

compounds A, C $\overset{\text{enzyme 1}}{\Rightarrow}$ compound B $\overset{\text{enzyme 2}}{\Rightarrow}$ arginine

From the table we know that cells missing enzyme 3 survive (make arginine) if compound A or B is added. Therefore, compound A must be later in the pathway than compound C. Building on the previous step, we can draw:

compound C $\overset{\text{enzyme 3}}{\Rightarrow}$ compound A $\overset{\text{enzyme 1}}{\Rightarrow}$ compound B $\overset{\text{enzyme 2}}{\Rightarrow}$ arginine

Thus, the overall pathway is:

$\overset{\text{enzyme 4}}{\Rightarrow}$ compound C $\overset{\text{enzyme 3}}{\Rightarrow}$ compound A $\overset{\text{enzyme 1}}{\Rightarrow}$ compound B $\overset{\text{enzyme 2}}{\Rightarrow}$ arginine

(3.2.3)

Enzyme	**Inhibitors**	**Explanation**
a	chorismate	If this were inhibited by Phe, Trp, or Tyr, high levels of any one could cut off the synthesis of all three, which would be bad for the cell. The only appropriate condition when this enzyme should be inhibited is where ALL three amino acids are in excess. Chorismate will build up only when all three amino acids are in excess [because later steps (**b** and **c**) will be inhibited], so chorismate is the appropriate regulator.
b	prephenate	Similar reasoning as for **a** (this is also product inhibition).
c	tryptophan	It is the final product of the dedicated pathway where Trp is the final product.
d	phenylalanine	Same reasoning as for **c**.
e	tyrosine	Same reasoning as for **c**.

Note: All enzymes are also inhibited by accumulation of their immediate products by mass action (e.g., **d** by phenylpyruvate). This is not allosteric feedback regulation, but product inhibition.

(3.3) Glycolysis, respiration, and photosynthesis

(3.3.1)

a) This is an example of a phosphoryl transfer (phosphorylation) reaction. It is similar to the reaction catalyzed by **hexokinase,** which converts glucose into glucose 6-phosphate. It is also similar to the **phosphofructokinase** reaction, which converts fructose 6-phosphate into fructose 1,6-bisphosphate. Also, it is similar to the **phosphoglycerate kinase** reaction, which converts 1,3-BPG into 3PG, making ATP in the process. (Note that an enzyme can catalyze both the forward and reverse reactions at each step.) It is not similar to the pyruvate kinase reaction, which uses a reactive dehydrated C=C bond to drive the synthesis of ATP in converting PEP to pyruvate.

b) This is an isomerization reaction. It is similar to the one catalyzed by **phosphoglucoisomerase**, which converts glucose 6-phosphate into fructose 6-phosphate. It is also similar to the **triose phosphate isomerase** reaction, which converts dihydroxyacetone phosphate into glyceraldehyde 3-phosphate.

c) Each enzyme specifically recognizes and binds to the correct substrate. Not all of the above substrates would fit correctly in the right orientation in the enzyme's substrate-binding region.

d) Malonate is very similar in structure to the normal substrate, succinate. The most likely possibility is that it is competing with succinate for the enzyme's substrate-binding region.

(3.3.2)

a) In the presence of O_2, pyruvate is no longer converted to lactic acid, but instead is converted to acetyl-CoA, which can enter the citric acid cycle. Thus, glucose is converted to CO_2 and H_2O.

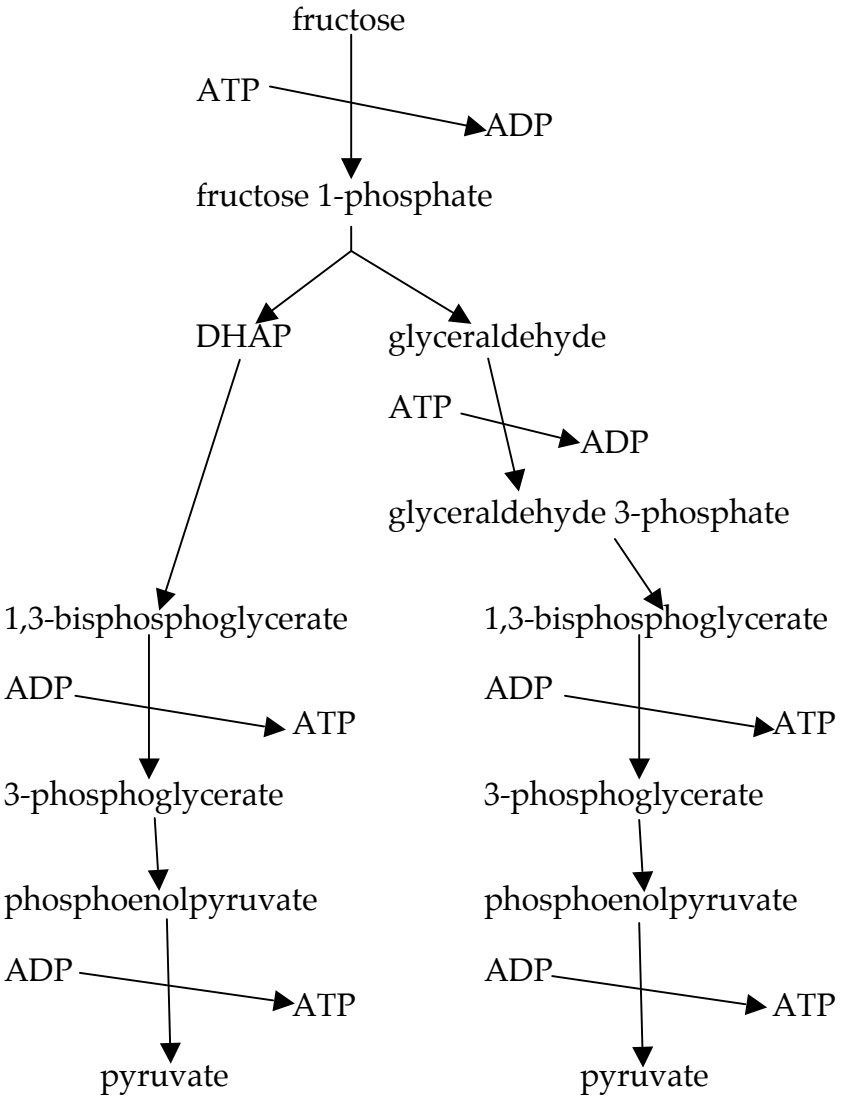
b) Growth requires energy and a cell gets roughly 36 ATP/glucose with O_2 around, as opposed to 2 ATP/glucose without O_2. Therefore, cells require less glucose for the same growth rate (ATP consumption rate) in the presence of O_2.

c) NAD^+ is a cofactor, while glucose is a substrate. Thus, glucose is consumed in large amounts and not recycled. NAD^+ is used to carry the electrons removed from glucose and its derivatives (becoming NADH), but it is recycled to NAD^+ by transferring electrons to other substrate molecules: under anaerobic conditions, to pyruvate; under aerobic conditions, to O_2 via the electron transport chain. Since NAD^+ is recycled, only a small amount is necessary to process a large amount of glucose.

(3.3.3)
a) ATP is the most likely source of phosphate and energy for this reaction. By analogy to reaction 1 it would most likely be:

glyceraldehyde + ATP ⇒ glyceraldehyde 3-phosphate + ADP

b)



c)

	Reaction	ATP used or produced per fructose
Fructose utilization	fructose to fructose-1-P	1 used
	glyceraldehyde to glyceraldehyde-3-P	1 used
	two 1,3-bisphosphoglycerates to two 3-phosphoglycerates	2 produced
	two phosphoenolpyruvates to two pyruvates	2 produced

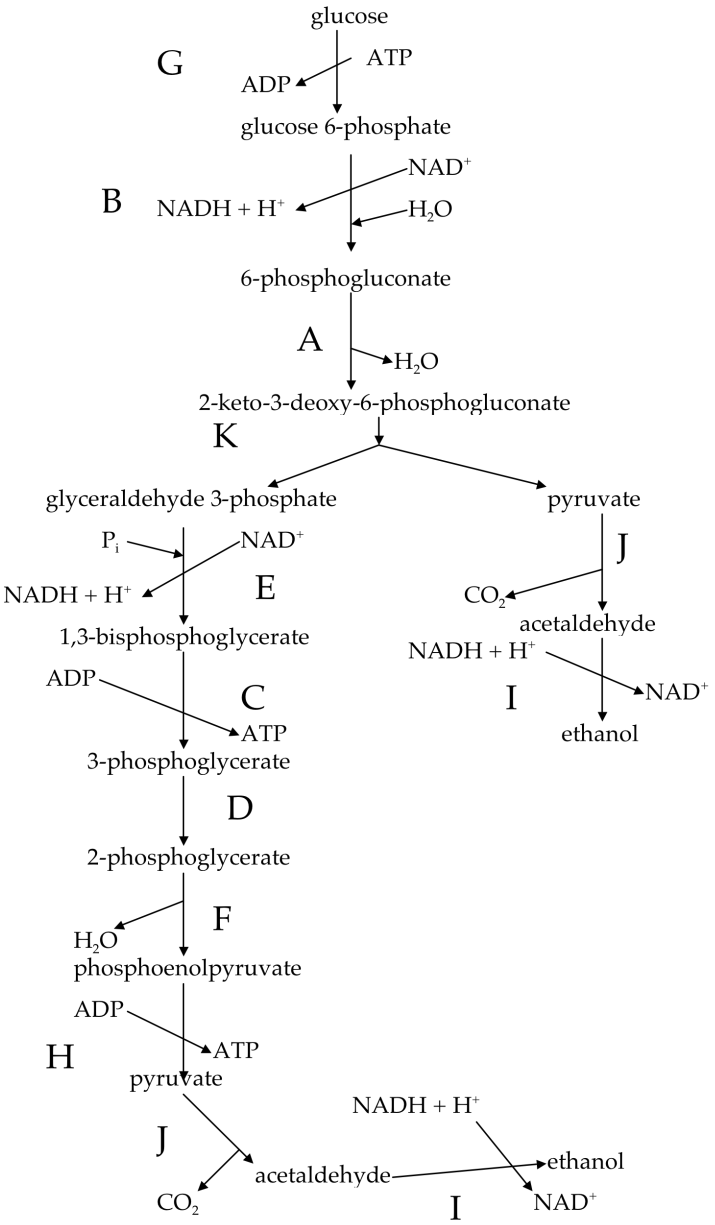
Net: +2

	Reaction	ATP used or produced per fructose
Glucose utilization	glucose to glucose-6-P	1 used
	fructose-6-P to fructose 1,6-bisphosphate	1 used
	two 1,3 -bisphosphoglycerates to two 3-phosphoglycerates	2 produced
	two phosphoenolpyruvates to two pyruvates	2 produced

Net: +2

(3.3.4)
a)

(3.3.4)
a)


glucose
G
ATP
ADP
glucose 6-phosphate
B
NAD+
NADH + H+
H2O
6-phosphogluconate
A
H2O
2-keto-3-deoxy-6-phosphogluconate
K
glyceraldehyde 3-phosphate
pyruvate
Pi
NAD+
E
NADH + H+
J
CO2
acetaldehyde
1,3-bisphosphoglycerate
NADH + H+
ADP
C
I
NAD+
ATP
ethanol
3-phosphoglycerate
D
2-phosphoglycerate
F
H2O
phosphoenolpyruvate
ADP
H
ATP
pyruvate
NADH + H+
J
acetaldehyde
ethanol
CO2
I
NAD+

b) The overall reaction is:

$$\text{glucose} + \text{ADP} + P_i \longrightarrow 2CO_2 + 2\ \text{ethanol} + \text{ATP} + H_2O$$

Therefore, the bacterium gets only 1 ATP per glucose as compared with 2 ATP/glucose from the Embden-Meyerhof-Parnas pathway.

c) Consider the fate of the two glucose 6-phosphate and glyceraldehyde 3-phosphate produced from three xyloses:

Each glucose 6-phosphate will enter at the second step of the Entner-Doudoroff pathway, giving the following reaction:

$$\text{glucose 6-phosphate} + 2\ \text{ADP} + P_i \longrightarrow 2\ CO_2 + 2\ \text{ethanol} + H_2O + 2\ \text{ATP}$$

The glyceraldehyde 3-phosphate will enter at the fifth step of the Entner-Doudoroff pathway, giving the following reaction:

$$\text{glyceraldehyde 3-phosphate} + 2\ \text{ADP} + P_i \longrightarrow CO_2 + \text{ethanol} + H_2O + 2\ \text{ATP}$$

d) Adding the three reactions:

	3 xylose + 3ATP	⇒	2 glucose 6-phosphate + glyceraldehyde 3-phosphate (G3P) + 3 ADP
+	2 glucose 6-phosphate + 4 ADP + 2 P_i	⇒	4 CO_2 + 4 ethanol + 2 H_2O + 4 ATP
+	glyceraldehyde 3-phosphate + 2 ADP + P_i	⇒	CO_2 + ethanol + H_2O + 2 ATP
	3 xylose + 3 ADP + 3 P_i	⇒	5 CO_2 + 5 ethanol + 3 H_2O + 3 ATP

e) From the above, 3 ATP for 3 xylose = 1 ATP per xylose.

(3.3.5)

a) The biochemical process responsible for the plant's absorption of O_2 and production of CO_2 in the dark is respiration. The plant cells are using O_2 to oxidize stored carbohydrates to CO_2, to produce energy.

b) Yes, this process continues when the plant is exposed to light. The plant always needs energy from respiration to perform cellular reactions. In the light, the rate of photosynthesis is greater than the rate of respiration, so the result is net O_2 production and net CO_2 absorption. In the dark, there is no photosynthesis, so the basal respiration level predominates (O_2 absorption and CO_2 production).

(3.3.6)

a and b) Since NADPH will no longer be produced, the dark reactions (Calvin-Benson cycle) will stop. As a result, these reactions will no longer consume ATP, causing ATP to build up and ADP to disappear. Without ADP, the H^+ATPase will not be able to let

H^+ flow down the concentration gradient and the H^+ gradient will build up. When the H^+ gradient gets large enough, e^- transport will stop because there won't be enough energy to pump H^+ against the gradient. If this happens, O_2 will no longer be produced. Since it will take time for all this to back up, O_2 will be produced for a while, then stop.

c)

i) No. If e^- can no longer be transferred to pQ, e^- will back up in pheophytin I (sometimes called simply "I" in various textbooks) and e^- transport will come to a halt. Without a place for the e^- from H_2O to go, H_2O will no longer be oxidized to O_2.

ii) No. With no e^- flowing down the transport chain, no H^+ will be translocated across the thylakoid membrane, no H^+ gradient will form, and therefore no ATP can be made.

iii) No. This process requires reducing power in the form of NADPH. Since there are no e^- flowing through the transport chain, there won't be any to reduce $NADP^+$, so there will be no NADPH around to reduce the CO_2.

(3.3.7)

a)

Enzyme	Pathway
lactate dehydrogenase	This is the last step in lactic acid fermentation.
alcohol dehydrogenase	This is the last step in alcohol fermentation.
aldolase	This is a key step in glycolysis.
proton ATPase	This is a key enzyme in oxidative phosphorylation.
cytochrome *c*	This is part of electron transport.
citrate synthase	This is the "first" step in the citric acid cycle.

b) Based on the above, you can rewrite the table as follows:

Organism	Lactic acid fermention	Alcohol fermentation	Glycolysis	Oxidative phosph.	Electron transport	Citric acid cycle
Haemophilus influenzae	No	Yes	Yes	Yes	No	No
Mycoplasma genitalium	Yes	No	Yes	Yes	No	No
Mycoplasma pneumoniae	Yes	No	Yes	Yes	Yes	No
Escherichia coli	No	Yes	Yes	Yes	Yes	Yes

Thus,

– in the presence of oxygen:

Haemophilus influenzae: Although this organism has the proton ATPase, it lacks the other components of cellular respiration. It must therefore carry out fermentation. In this case, it would produce alcohol + CO_2 and get about 2 ATP per glucose.

Mycoplasma genitalium: This lacks the capability for electron transport or the citric acid cycle; so, even though it has the proton ATPase, it cannot carry out cellular respiration. It can still ferment glucose to lactic acid, so it will produce lactic acid and roughly 2 ATP per glucose.

Mycoplasma pneumoniae: This also cannot perform cellular respiration, so it must ferment glucose. It has the enzymes to ferment glucose to lactic acid and will get roughly 2 ATP per glucose.

Escherichia coli: This has all the parts needed for cellular respiration so it will make CO_2 + H_2O and get roughly 36 ATP per glucose.

– in the absence of oxygen, the first three bacteria will perform the same fermentations. *Escherichia coli* will ferment glucose to ethanol and CO_2 and get roughly 2 ATP per glucose.