

# Supplemental Material

*CBE—Life Sciences Education*

Halmo *et al.*

## Supplemental Material

### Table of Contents

	<b>Page</b>
<b>Additional Tables</b>	
• Table 1. Demographic information of research participants	3
• Table 2. Unadjusted basic knowledge pre- and posttest performance	3
<b>Instructional Materials</b>	
• Slides and Instructor Notes	
I. Worked Examples Plus Practice	5
II. Productive Failure	19
III. Unscaffolded Guidance	33
IV. Scaffolded Guidance	37
• Student Handouts	
I. Worked Examples Plus Practice	40
II. Productive Failure	47
III. Unscaffolded Guidance	52
IV. Scaffolded Guidance	60
<b>Assessments</b>	
• Basic Knowledge Post-Test	75
• Near Transfer Problems	79
• Far Transfer Problems	82
<b>Analytical Codebooks</b>	
• Near Transfer Problems	86
• Far Transfer Problems	93
<b>Scoring Rubrics</b>	
• Near Transfer Problems	97
• Far Transfer Problems	100

## **Additional Tables**

**Supplemental Material Table I. Demographic information of research participants**

	Gender	Race/Ethnicity	Average GPA
Total (N=189)	81.5% Female (n=154) 18.5% Male (n=35)	23.3% Asian (n=44) 19.6% Black or African-American (n=37) 4.8% Hispanic or Latinx (n=9) 1.6% Not reported (n=3) 2.1% Two or more races (n=4) 48.7% White (n=92)	3.46
Worked examples plus practice (n=41)	75.6% Female (n=31) 24.4% Male (n=10)	9.8% Asian (n=4) 17.1% Black or African-American (n=7) 7.3% Hispanic or Latinx (n=3) 0% Not reported (n=0) 2.4% Two or more races (n=1) 63.4% White (n=26)	3.40
Productive failure (n=78)	88.5% Female (n=69) 11.5% Male (n=9)	25.6% Asian (n=20) 25.6% Black or African-American (n=20) 5.1% Hispanic or Latinx (n=4) 2.6% Not reported (n=2) 1.3% Two or more races (n=1) 39.7% White (n=31)	3.50
Unscaffolded guidance (n=42)	66.7% Female (n=28) 33.3% Male (n=14)	19% Asian (n=8) 11.9% Black or African-American (n=5) 4.8% Hispanic or Latinx (n=2) 0% Not reported (n=0) 4.8% Two or more races (n=2) 59.5% White (n=25)	3.41
Scaffolded guidance (n=28)	92.9% Female (n=26) 7.1% Male (n=2)	42.9% Asian (n=12) 17.9% Black or African-American (n=5) 0% Hispanic or Latinx (n=0) 3.6% Not reported (n=1) 0% Two or more races (n=0) 35.7% White (n=10)	3.53

**Supplemental Material Table 2. Unadjusted basic knowledge pre- and posttest performance**

	Pretest Mean (s.d.)	Posttest Mean (s.d.)
Worked examples plus practice (n=41)	-0.98 (0.77)	-0.44 (0.57)
Productive failure (n=78)	-0.81 (0.67)	-0.60 (0.66)
Unscaffolded guidance (n=42)	-0.95 (0.73)	-0.44 (0.69)
Scaffolded guidance (n=28)	-0.68 (0.63)	-0.70 (0.48)

**Instructional Materials: Slides and Instructor Notes**

Worked Examples Plus  
Practice Slides

## Learning Objectives

- Given a model of biological molecules, identify, categorize, and compare the important features.
- Recall that chemical composition affects the structure and interactions of macromolecules.
- Compare different types of non-covalent interactions occurring in biological molecules.
- Explain why and how it is that *all* non-covalent interactions are attractions of opposite charges.
- Predict the impact of changes in the building blocks of biological molecules on the structure of the macromolecules.
- Formulate a scientific explanation for your prediction.
- Solve new problems that extend your thinking about the role of non-covalent interactions across biology.

This lesson should support your learning of the following objectives.

Let's get started.

**PROBLEM 1.** Protein B, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and white). The environment has a pH of 7.4. The blue line represents the Protein B backbone; some but not all of the amino acid side chains (R groups) are shown.

4. This is an ionic interaction between two polar, charged R groups.

6. There are no hydrogen bonds here

5. Van der Waals forces are attracting these nonpolar R groups.

7. A hydrogen bond is attracting the polar R groups of asparagine and serine.

1. This is the R group. It contributes to noncovalent interactions.

2. Isoleucine's R group is nonpolar because C and H don't differ in electronegativity.

3. The amino acid backbone is not shown, because typically it does not contribute to non-covalent interactions relevant to this problem.

8. Isoleucine's R group is nonpolar like alanine's but also bigger.

The amino acids shown are: (A) aspartate, (B) arginine, (C) leucine, (D) alanine, (E) asparagine, and (F) serine. Sometimes, a mutation occurs that substitutes alanine (yellow circle) with isoleucine (above right).

**Predict what will happen to the noncovalent interactions shown when alanine is substituted with isoleucine. Explain your reasoning.**

Here is a problem.

I will walk you through how to solve this problem.

First, let me read it to you [Read the problem]

Now that we've read the problem, let's walk through it.

Because proteins are made up of amino acids, we know that it is the individual amino acids that will determine the structure of this protein. (not on the screen). Notice the amino acid side chains - which I'll also call R groups. Six of them are shown for Protein B (A, B, C, D, E, and F). There is also one shown here (Isoleucine).

1. This is the R group of the amino acid isoleucine. It contributes to noncovalent interactions.
2. The R group of isoleucine is nonpolar because Carbon and Hydrogen don't differ in electronegativity.
3. The amino acid backbone, which is the same among all amino acids, is not shown here, because typically it does not contribute to the non-covalent interactions relevant to this problem.
4. Notice that an ionic interaction is attracting the charged polar R group of aspartate and



the charged polar R group of arginine.

5. Notice that van der Waals forces are attracting nonpolar leucine and alanine.

[BUILD] Van der Waals forces occur due to the fact that electrons are always in motion.

When electrons are momentarily distributed unevenly in the alanine R group, the R group has a temporary positive charge that is close to the R group of leucine.

[BUILD] The positive charge attracts electrons in the R group of leucine, temporarily creating an induced dipole in the leucine R group. These temporary partial charges attract each other.

[POINT] Compare the representation of the charges in the ionic interaction above with the van der Waals forces shown here. Even though both of these interactions are due to the attraction of opposite charges, the charges are usually drawn in for the R groups above, because these charges are permanent at pH 7.4. In contrast, the charges involved in van der Waals forces are not usually shown for these R groups because they are temporary.

6. There are NO hydrogen bonds attracting leucine and alanine.

[POINT] We will come back to this interaction in a moment, but first we need to consider what's happening over here.

7. A hydrogen bond is occurring between the R groups of asparagine and serine. Due to the covalently bound electronegative oxygen, the hydrogen in the hydroxyl group of serine has a permanent partial positive charge that is attracted to the permanent partial negative charge on the oxygen of asparagine.

[POINT] Compare the representation of the charges in the ionic interaction above with the hydrogen bond shown here. Even though both of these interactions are due to the attraction of opposite charges, the charges are usually drawn in for the R groups in the ionic interaction, because these charges are full at pH 7.4. In contrast, the charges involved in the hydrogen bond are partial, so often they are not drawn. If they are drawn, the lowercase delta is used to indicate that the charge is partial.

[POINT] Now let's go back to the leucine/alanine interaction. We need to predict the impact of substituting isoleucine for alanine.

8. Isoleucine is nonpolar like alanine but also bigger. Because isoleucine has a non polar R group like alanine, it can only participate in attractive non-covalent interactions with leucine through van der Waals forces. Because isoleucine's R group is bigger, this could impact the distance between the two R groups. But it is possible that the molecule is flexible enough to accommodate this change in size of the R group.

[POINT] Therefore, we can predict that substituting isoleucine for alanine should not have an impact on the noncovalent interactions of Protein B.

[POINT] However, there's a chance it could, even though this is a subtle change. So to confirm this prediction, it would be necessary to test this with an experiment in which we measured the impact of the substitution on the noncovalent interaction shown.

Next slide ...

**PROBLEM 1.** Protein B, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and white). The environment has a pH of 7.4. The blue line represents the Protein B backbone; some but not all of the amino acid side chains (R groups) are shown.

The amino acids shown are: (A) aspartate, (B) arginine, (C) alanine, (D) valine, (E) asparagine, and (F) serine. Sometimes, a mutation occurs that substitutes alanine with isoleucine (above right).

**9. Explain given non-covalent interaction**

**10. Categorize amino acids**

**11. Explain new non-covalent interaction**

**12. State your prediction**

**13. Reflect on predictions**

Leucine and alanine are attracted to each other due to van der Waals forces. Both of them have nonpolar R groups, so no other type of non-covalent attraction is possible. However, due to temporary partial charges on the R groups an attraction can occur. Because isoleucine is nonpolar, like alanine, it also could participate in van der Waals interactions with leucine. The only potential problem is if its bigger size causes a problem with these interactions. But my best prediction is no impact on the noncovalent interaction from isoleucine. To know for sure if I'm right, I would need experimental evidence.

**Predict what will happen to the noncovalent interactions shown when alanine is substituted with isoleucine. Explain your reasoning.**

Here is a good scientific explanation for our prediction. [read solution] This solution has 5 parts.

9. First, you should explain the given non-covalent interaction
10. Second, you should include a categorization of all the relevant amino acids
11. Third, you should explain the new non-covalent interaction.
12. Fourth, state your prediction.
13. Finally, reflect on your predictions.

## It's Your Turn

- Work problem 2 on page 2 of your handout.
- Be sure to write a scientific explanation for your prediction on page 5.
- If you have questions about the instructions, we are happy to help you. We cannot answer questions about the content of the problem. Just do your very best based on the instruction you've received.

## Compare Your Answers

- Take 5 minutes to compare your Problem 2 answer with the two people sitting closest to you.
- If you make notes on your original answer, please only do so with a blue pen.

**PROBLEM 3.** Protein W, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and white). The environment has a pH of 7.4. The blue line represents the Protein W backbone; some but not all of the amino acid side chains (R groups) are shown.

7. A hydrogen bond is attracting the polar R groups of glutamine and threonine.

3. The amino acid backbone is not shown, because typically it does not contribute to non-covalent interactions relevant to this problem.

1. This is the R group. It contributes to noncovalent interactions

2. Leucine's R group is nonpolar because C and H don't differ in electronegativity.

5. Van der Waals forces are attracting the three nonpolar alanines.

4. This is an ionic interaction between two polar, charged R groups.

6. There are no hydrogen bonds here

8. The atoms of leucine do not differ in electronegativity, so leucine cannot be a hydrogen bond donor or acceptor.

The amino acids shown are: (A) glutamine, (B) threonine, (C) alanine, (D) glutamate, and (E) lysine. Sometimes, a mutation occurs that substitutes glutamine (yellow circle) with leucine (right).

**Predict what will happen to the noncovalent interactions shown when glutamine is substituted with leucine. Explain your reasoning.**

Here is the third problem.

I will walk you through how to solve this problem.

First, let me read it to you [Read the problem]

Now that we've read the problem, let's walk through it.

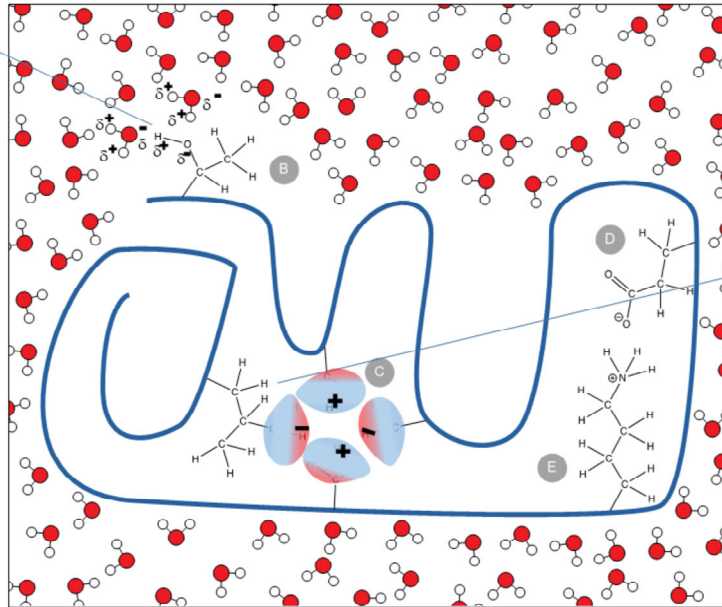
Again we have a protein made up of amino acids, whose structure is determined by its amino acids.

1. Here we have the R group of Leucine. Remember that even though amino acids have a backbone and an R group, it is the R groups that contribute to the non-covalent interactions that stabilize the 3-D structure of Protein W.
2. The R group of leucine is nonpolar because Carbon and Hydrogen don't differ in electronegativity.
3. Even though amino acids consist of an R group and a backbone, only the R group is shown, because typically the backbone does not contribute to the non-covalent interactions relevant to this problem.
4. Notice that an ionic interaction is attracting the charged polar R group of glutamate and

- the charged polar R group of lysine.
5. Notice the van der Waals forces are occurring again, this time among three nonpolar alanine R groups. [BUILD] Even though these alanines are non-polar, they can undergo attractions among their side chains because the temporary negative charge that occurs in this alanine due to the constant movement of electrons induces a temporary positive charge in the alanines that are close to it. [POINT] And remember that we don't usually show these charges on the figure, because they are temporary. In contrast, we do typically show the charges when they are permanent – as in this ionic interaction.
  6. No hydrogen bonds occur among these R groups.
  7. Notice, however, that a hydrogen bond is attracting the R groups of glutamine and threonine. Due to the covalently bound electronegative nitrogen, the hydrogen in the amine group of glutamine has a permanent partial positive charge that is attracted to the permanent partial negative charge on the oxygen of threonine [POINT] Compare the representation of the charges in the ionic interaction on the right with the hydrogen bond shown here. Even though both of these interactions are due to the attraction of opposite charges, the charges are usually drawn in for the R groups in the ionic interaction, because these charges are full at pH 7.4. In contrast, the charges involved in the hydrogen bond are partial, so often they are not drawn. If they are drawn, the lowercase delta is used to indicate that the charge is partial.
  8. [POINT] Let's go back to our substitution. The question is what is the impact of a leucine for glutamine substitution. We need to predict the impact of the leucine substitution on the noncovalent interaction shown. Leucine is nonpolar. However, glutamine is polar. The leucine atoms do not differ from each other in electronegativity, so leucine cannot be a hydrogen bond donor or acceptor. So if leucine were substituted, the hydrogen bond would not form.
  9. What would happen instead?

**PROBLEM 3.** Protein W, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and white). The environment has a pH of 7.4. The blue line represents the Protein W backbone; some but not all of the amino acid side chains (R groups) are shown.

The protein may rearrange so that threonine can hydrogen bond with something else – like water as shown here.



The protein may also rearrange so that the new leucine is in close proximity to other nonpolar R groups. Then van der Waals forces will occur.

Pick up from previous slide.

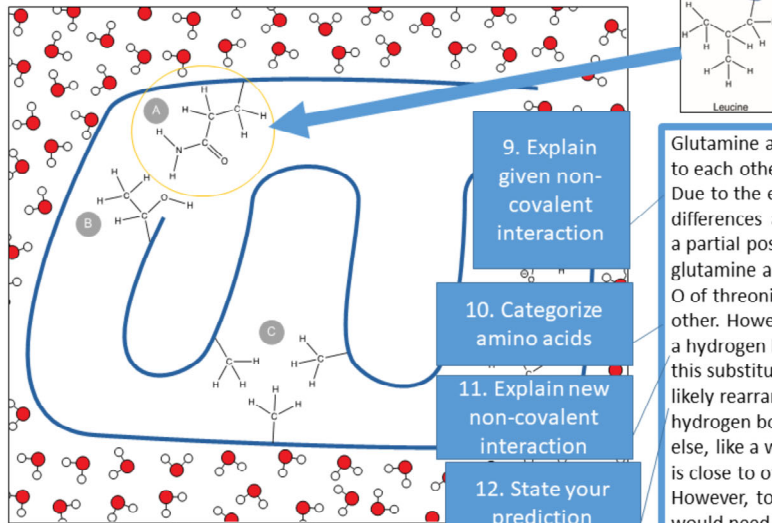
[BUILD] A good possibility is that the protein structure may rearrange to enable threonine to hydrogen bond with something else. As shown here, it could hydrogen bond with water.

[BUILD] If that rearrangement were to take place, the protein likely would arrange itself also so that the new leucine is associated with other nonpolar residues, because relatively speaking it is not as energetically favorable for a polar R group to form a dipole-induced dipole interaction as it is for it to form a dipole-dipole interaction, such as a hydrogen bond.

[POINT] This is one example of the type of changes that could take place in terms of non-covalent interactions due to a leucine substitution. But there are other possibilities.

[STATE] To know for sure what would happen, we would have to test the substitution with experiments in the laboratory.

**PROBLEM 3.** Protein W, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and white). The environment has a pH of 7.4. The blue line represents the Protein W backbone; some but not all of the amino acid side chains (R groups) are shown.



The amino acids shown are: (A) glutamine, (B) threonine, (C) alanine, (D) gl  
Sometimes, a mutation occurs that substitutes glutamine (yellow circle) with leucine (right).

9. Explain given non-covalent interaction

10. Categorize amino acids

11. Explain new non-covalent interaction

12. State your prediction

Glutamine and threonine are attracted to each other due to a hydrogen bond. Due to the electronegativity differences among N, H, and O, there is a partial positive charge on the H of glutamine and partial negative on the O of threonine. These attract each other. However, leucine is nonpolar, so a hydrogen bond is not possible. With this substitution, the protein would likely rearrange so that threonine is hydrogen bonding with something else, like a water molecule, and leucine is close to other nonpolar R groups. However, to know for sure if I'm right, I would need experimental evidence.

13. Reflect on predictions

Predict what will happen to the noncovalent interactions shown when glutamine is substituted with leucine. Ex

Here is a good scientific explanation for the prediction. It has 5 parts.

9. First, you should explain the given non-covalent interaction
10. Second, you should include a categorization of all the relevant amino acids
11. Third, you should explain the new non-covalent interaction.
12. Fourth, state your prediction.
13. Finally, reflect on your predictions.



## It's Your Turn

- Work problem 4 on of page 4 your handout.
- Be sure to write a scientific explanation for your prediction on page 5.
- If you have questions about the instructions, we are happy to help you. We cannot answer questions about the content of the problem. Just do your very best based on the instruction you've received.

## Compare Your Answers

- Take 5 minutes to compare your Problem 4 answer with the two people sitting closest to you.
- If you make notes on your original answer, please only do so with a blue pen.

## Problem-Solving Assessment

Sign out on the paper form by the door before you leave!

- The lesson is now complete.
- Please check your UGA email for the survey link. Enter your UGA MyID and password to access the assessment.
- Thank you for doing your very best on the assessment, so we can have good information about the best approach for teaching students this material.
- Once you have completed the problem set and signed out on the paper form by the door, you are free to go.

# Productive Failure Slides

## Learning Objectives

- Given a model of biological molecules, identify, categorize, and compare the important features.
- Recall that chemical composition affects the structure and interactions of macromolecules.
- Compare different types of non-covalent interactions occurring in biological molecules.
- Explain why and how it is that *all* non-covalent interactions are attractions of opposite charges.
- Predict the impact of changes in the building blocks of biological molecules on the structure of the macromolecules.
- Formulate a scientific explanation for your prediction.
- Solve new problems that extend your thinking about the role of non-covalent interactions across biology.

This lesson should support your learning of the following objectives.

Let's get started.

## It's time to explore...

- Work on the problem on your handout with the people sitting next to you. You should look at pages 2 and 3 to solve the problem. Record your answer on page 4.
- Be sure to write a scientific explanation for your predictions.

Remember:

- Try to generate solutions
- But the goal is NOT to get correct answers
- The goal is to imagine possible solutions and what the two scenarios have in common
- Think about what knowledge you have that is helpful for solving this problem and what you'd like to know more about

We will begin this evening by exploring the problem at your table.

You should work on the problem with the people sitting next to you.

Look at pp. 1-2 to solve the problem. Record your answer on p. 3.

Be sure to write a scientific explanation for your prediction.

Remember these things:

- 1) Try your best to generate solutions to the problem
- 2) But remember that the goal of this activity is NOT to get the correct answers.
- 3) The goal is to imagine possible solutions and what the two problems have in common
- 4) As you work on the problem, think about what knowledge you have that is helpful for solving this problem and what you'd like to know more about.

You will have ~15 minutes for exploring the problem.

After this exploration phase, we will share some possible solutions and help you construct knowledge necessary to solve these types of problems.

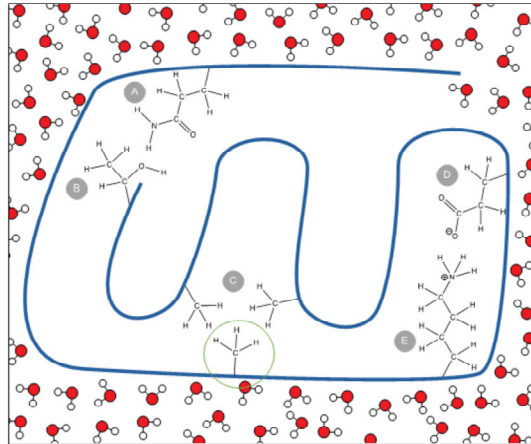
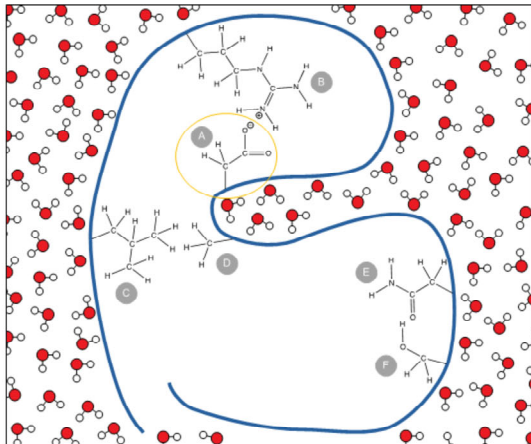
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**DO NOT SAY:**

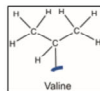
Instructors and PLAs will be walking around during this phase. We will not comment on correctness of ideas or direct students to the canonical solution. We will:

1. ask the students to explain what they are doing
2. push students to expand their thinking to all 4 scenarios

## Discussion of Problem Exploration



To solve this problem you need to consider (1) the chemical composition of the R groups, (2) the interactions happening between R groups, and (3) how these two ideas are related.



Let's come back together and discuss some possible solutions to this problem.

Reasoning:

You could have ranked based on differences between Protein B and Protein W. However, this is not a good approach to the problem. Because when you look at all of the non-covalent interactions in B and then in W, you'll see that the same non-covalent interactions are at play in both proteins.

You could have ranked based on similarity of R group chemical composition. This is a good place to start. You'll notice that valine and alanine have a very similar chemical composition, all composed of carbons and hydrogens. You might have noticed that aspartate has an oxygen with a negative charge. Serine also has a negative charge on its oxygen, but it's partial and not shown here.

You could have compared the differences among having C, H, N, or O atoms. That's good. The way to think about that for this problem is to consider their differences in electronegativity and what this means in terms of full, partial, permanent, or temporary charges.



You may have thought of some of these interactions as repulsions and others as attractions, but actually they are all attractions.

You may have tried to name all of the types of non-covalent interactions. Being able to name these is not that important compared to being able to recognize that all of the interactions involve an attraction of opposite charges.

You may have wondered if the solid lines between atoms are covalent bonds or noncovalent interactions (like hydrogen bonds). You should know that across biology and chemistry, anytime we draw a straight line between atoms we are indicating a covalent bond.

**To solve this problem you need to consider (1) the chemical composition of the R groups, (2) the interactions happening between R groups, and (3) how these two ideas are related.**

**PROBLEM 2.** Protein B, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and white). The environment has a pH of 7.4. The blue line represents the Protein B backbone; some but not all of the amino acid side chains (R groups) are shown.

4. This is an ionic interaction between two polar, charged R groups.

6. There are no hydrogen bonds here

5. Van der Waals forces are attracting these nonpolar R groups.

1. This is the R group. It contributes to noncovalent interactions.

2. Isoleucine's R group is nonpolar because C and H don't differ in electronegativity.

3. The amino acid backbone is not shown, because typically it does not contribute to non-covalent interactions relevant to this problem.

7. A hydrogen bond is attracting the polar R groups of asparagine and serine.

8. Isoleucine's R group is nonpolar like alanine's but also bigger.

The amino acids shown are: (A) aspartate, (B) arginine, (C) leucine, (D) alanine, (E) asparagine, and (F) serine. Sometimes, a mutation occurs that substitutes alanine (yellow circle) with isoleucine (above right).

**Predict what will happen to the noncovalent interactions shown when alanine is substituted with isoleucine. Explain your reasoning.**

You've done some great work exploring problems. I'm now going to walk you through how to solve problems of this type.

Here is another similar problem.

I will walk you through how to solve this problem.

First, let me read it to you [Read the problem]

Now that we've read the problem, let's walk through it.

Because proteins are made up of amino acids, we know that it is the individual amino acids that will determine the structure of this protein. (not on the screen). Notice the amino acid side chains - which I'll also call R groups. Six of them are shown for Protein B (A, B, C, D, E, and F). There is also one shown here (Isoleucine).

1. This is the R group of the amino acid isoleucine. It contributes to noncovalent interactions.
2. The R group of isoleucine is nonpolar because Carbon and Hydrogen don't differ in electronegativity.
3. The amino acid backbone, which is the same among all amino acids, is not shown here,

because typically it does not contribute to the non-covalent interactions relevant to this problem.

4. Notice that an ionic interaction is attracting the charged polar R group of aspartate and the charged polar R group of arginine.

5. Notice that van der Waals forces are attracting nonpolar leucine and alanine.

[BUILD] Van der Waals forces occur due to the fact that electrons are always in motion.

When electrons are momentarily distributed unevenly in the alanine R group, the R group has a temporary positive charge that is close to the R group of leucine.

[BUILD] The positive charge attracts electrons in the R group of leucine, temporarily creating an induced dipole in the leucine R group. These temporary partial charges attract each other.

[POINT] Compare the representation of the charges in the ionic interaction above with the van der Waals forces shown here. Even though both of these interactions are due to the attraction of opposite charges, the charges are usually drawn in for the R groups above, because these charges are permanent at pH 7.4. In contrast, the charges involved in van der Waals forces are not usually shown for these R groups because they are temporary.

6. There are NO hydrogen bonds attracting leucine and alanine.

[POINT] We will come back to this interaction in a moment, but first we need to consider what's happening over here.

7. A hydrogen bond is occurring between the R groups of asparagine and serine. Due to the covalently bound electronegative oxygen, the hydrogen in the hydroxyl group of serine has a permanent partial positive charge that is attracted to the permanent partial negative charge on the oxygen of asparagine.

[POINT] Compare the representation of the charges in the ionic interaction above with the hydrogen bond shown here. Even though both of these interactions are due to the attraction of opposite charges, the charges are usually drawn in for the R groups in the ionic interaction, because these charges are full at pH 7.4. In contrast, the charges involved in the hydrogen bond are partial, so often they are not drawn. If they are drawn, the lowercase delta is used to indicate that the charge is partial.

[POINT] Now let's go back to the leucine/alanine interaction. We need to predict the impact of substituting isoleucine for alanine.

8. Isoleucine is nonpolar like alanine but also bigger. Because isoleucine has a non polar R group like alanine, it can only participate in attractive non-covalent interactions with leucine through van der Waals forces. Because isoleucine's R group is bigger, this could impact the distance between the two R groups. But it is possible that the molecule is flexible enough to accommodate this change in size of the R group.

[POINT] Therefore, we can predict that substituting isoleucine for alanine should not have an impact on the noncovalent interactions of Protein B.

[POINT] However, there's a chance it could, even though this is a subtle change. So to confirm this prediction, it would be necessary to test this with an experiment in which we measured the impact of the substitution on the noncovalent interaction shown.

Next slide ...

**PROBLEM 2.** Protein B, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and white). The environment has a pH of 7.4. The blue line represents the Protein B backbone; some but not all of the amino acid side chains (R groups) are shown.

The amino acids shown are: (A) aspartate, (B) arginine, (C) alanine, (D) serine, (E) asparagine, and (F) isoleucine. Sometimes, a mutation occurs that substitutes alanine with isoleucine (above right).

**9. Explain given non-covalent interaction**

**10. Categorize amino acids**

**11. Explain new non-covalent interaction**

**12. State your prediction**

**13. Reflect on predictions**

Leucine and alanine are attracted to each other due to van der Waals forces. Both of them have nonpolar R groups, so no other type of non-covalent attraction is possible. However, due to temporary partial charges on the R groups an attraction can occur. Because isoleucine is nonpolar, like alanine, it also could participate in van der Waals interactions with leucine. The only potential problem is if its bigger size causes a problem with these interactions. But my best prediction is no impact on the noncovalent interaction from isoleucine. To know for sure if I'm right, I would need experimental evidence.

**Predict what will happen to the noncovalent interactions shown when alanine is substituted with isoleucine. Explain your reasoning.**

Here is a good scientific explanation for our prediction. [read explanation] It has 5 parts.

9. First, you should explain the given non-covalent interaction
10. Second, you should include a categorization of all the relevant amino acids
11. Third, you should explain the new non-covalent interaction.
12. Fourth, state your prediction.
13. Finally, reflect on your predictions.

**PROBLEM 3.** Protein W, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and white). The environment has a pH of 7.4. The blue line represents the Protein W backbone; some but not all of the amino acid side chains (R groups) are shown.

7. A hydrogen bond is attracting the polar R groups of glutamine and threonine.

3. The amino acid backbone is not shown, because typically it does not contribute to non-covalent interactions relevant to this problem.

1. This is the R group. It contributes to noncovalent interactions

2. Leucine's R group is nonpolar because C and H don't differ in electronegativity.

5. Van der Waals forces are attracting the three nonpolar alanines.

4. This is an ionic interaction between two polar, charged R groups.

6. There are no hydrogen bonds here

8. The atoms of leucine do not differ in electronegativity, so leucine cannot be a hydrogen bond donor or acceptor.

The amino acids shown are: (A) glutamine, (B) threonine, (C) alanine, (D) glutamate, and (E) lysine. Sometimes, a mutation occurs that substitutes glutamine (yellow circle) with leucine (right).

**Predict what will happen to the noncovalent interactions shown when glutamine is substituted with leucine. Explain your reasoning.**

Here is the third problem.

I will walk you through how to solve this problem.

First, let me read it to you [Read the problem]

Now that we've read the problem, let's walk through it.

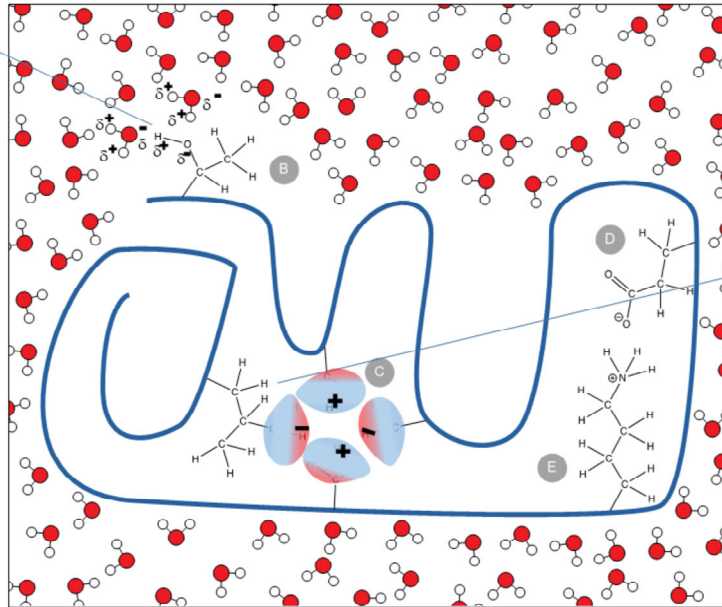
Again we have a protein made up of amino acids, whose structure is determined by its amino acids.

1. Here we have the R group of Leucine. Remember that even though amino acids have a backbone and an R group, it is the R groups that contribute to the non-covalent interactions that stabilize the 3-D structure of Protein W.
2. The R group of leucine is nonpolar because Carbon and Hydrogen don't differ in electronegativity.
3. Even though amino acids consist of an R group and a backbone, only the R group is shown, because typically the backbone does not contribute to the non-covalent interactions relevant to this problem.
4. Notice that an ionic interaction is attracting the charged polar R group of glutamate and

- the charged polar R group of lysine.
5. Notice the van der Waals forces are occurring again, this time among three nonpolar alanine R groups. [BUILD] Even though these alanines are non-polar, they can undergo attractions among their side chains because the temporary negative charge that occurs in this alanine due to the constant movement of electrons induces a temporary positive charge in the alanines that are close to it. [POINT] And remember that we don't usually show these charges on the figure, because they are temporary. In contrast, we do typically show the charges when they are permanent – as in this ionic interaction.
  6. No hydrogen bonds occur among these R groups.
  7. Notice, however, that a hydrogen bond is attracting the R groups of glutamine and threonine. Due to the covalently bound electronegative nitrogen, the hydrogen in the amine group of glutamine has a permanent partial positive charge that is attracted to the permanent partial negative charge on the oxygen of threonine [POINT] Compare the representation of the charges in the ionic interaction on the right with the hydrogen bond shown here. Even though both of these interactions are due to the attraction of opposite charges, the charges are usually drawn in for the R groups in the ionic interaction, because these charges are full at pH 7.4. In contrast, the charges involved in the hydrogen bond are partial, so often they are not drawn. If they are drawn, the lowercase delta is used to indicate that the charge is partial.
  8. [POINT] Let's go back to our substitution. The question is what is the impact of a leucine for glutamine substitution. We need to predict the impact of the leucine substitution on the noncovalent interaction shown. Leucine is nonpolar. However, glutamine is polar. The leucine atoms do not differ from each other in electronegativity, so leucine cannot be a hydrogen bond donor or acceptor. So if leucine were substituted, the hydrogen bond would not form.
  9. What would happen instead?

**PROBLEM 3.** Protein W, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and white). The environment has a pH of 7.4. The blue line represents the Protein W backbone; some but not all of the amino acid side chains (R groups) are shown.

The protein may rearrange so that threonine can hydrogen bond with something else – like water as shown here.



The protein may also rearrange so that the new leucine is in close proximity to other nonpolar R groups. Then van der Waals forces will occur.

Pick up from previous slide.

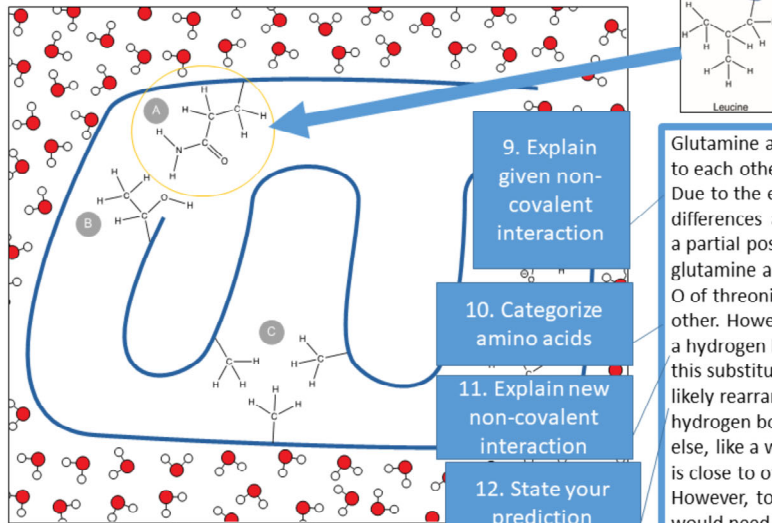
[BUILD] A good possibility is that the protein structure may rearrange to enable threonine to hydrogen bond with something else. As shown here, it could hydrogen bond with water.

[BUILD] If that rearrangement were to take place, the protein likely would arrange itself also so that the new leucine is associated with other nonpolar residues, because relatively speaking it is not as energetically favorable for a polar R group to form a dipole-induced dipole interaction as it is for it to form a dipole-dipole interaction, such as a hydrogen bond.

[POINT] This is one example of the type of changes that could take place in terms of non-covalent interactions due to a leucine substitution. But there are other possibilities.

[STATE] To know for sure what would happen, we would have to test the substitution with experiments in the laboratory.

**PROBLEM 3.** Protein W, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and white). The environment has a pH of 7.4. The blue line represents the Protein W backbone; some but not all of the amino acid side chains (R groups) are shown.



The amino acids shown are: (A) glutamine, (B) threonine, (C) alanine, (D) gl  
Sometimes, a mutation occurs that substitutes glutamine (yellow circle) with leucine (right).

9. Explain given non-covalent interaction

10. Categorize amino acids

11. Explain new non-covalent interaction

12. State your prediction

Glutamine and threonine are attracted to each other due to a hydrogen bond. Due to the electronegativity differences among N, H, and O, there is a partial positive charge on the H of glutamine and partial negative on the O of threonine. These attract each other. However, leucine is nonpolar, so a hydrogen bond is not possible. With this substitution, the protein would likely rearrange so that threonine is hydrogen bonding with something else, like a water molecule, and leucine is close to other nonpolar R groups. However, to know for sure if I'm right, I would need experimental evidence.

13. Reflect on predictions

Predict what will happen to the noncovalent interactions shown when glutamine is substituted with leucine. Ex

Here is a good scientific explanation for the prediction. [read explanation] It has 5 parts.

9. First, you should explain the given non-covalent interaction
10. Second, you should include a categorization of all the relevant amino acids
11. Third, you should explain the new non-covalent interaction.
12. Fourth, state your prediction.
13. Finally, reflect on your predictions.



Sign out on the paper form by  
the door before you leave!

## Problem-Solving Assessment

- The lesson is now complete.
- Please check your UGA email for the survey link. Enter your UGA MyID and password to access the assessment.
- Thank you for doing your very best on the assessment, so we can have good information about the best approach for teaching students this material.
- Once you have completed the problem set and signed out on the paper form by the door, you are free to go.

# Unscaffolded Guidance Slides

## Learning Objectives

- Given a model of biological molecules, identify, categorize, and compare the important features.
- Recall that chemical composition affects the structure and interactions of macromolecules.
- Compare different types of non-covalent interactions occurring in biological molecules.
- Explain why and how it is that *all* non-covalent interactions are attractions of opposite charges.
- Predict the impact of changes in the building blocks of biological molecules on the structure of the macromolecules.
- Formulate a scientific explanation for your prediction.
- Solve new problems that extend your thinking about the role of non-covalent interactions across biology.

This lesson should support your learning of the following objectives.

Let's get started.

## Problem Solving

- Work problems 1-4 on your handout with the two people sitting closest to you.
- Be sure to write a scientific explanation for your predictions on page 5-6.

### Remember:

- If you need help or feel stuck, raise your hand and we will come assist you.

35-45 minutes

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### DO NOT SAY:

Instructors and PLAs will be walking around during this phase. Our goal is to help students get to the right answer. We will comment on correctness of ideas or direct students to the canonical solution. We will follow this process in our interactions with students:

1. Ask the students to explain where they are or what they've done so far.
2. Once we understand where they are stuck, we will ask about what they know about related content, i.e. of they are stuck at understanding what interaction is present, say "tell me what you know about noncovalent interactions" to activate their prior knowledge
3. If it is clear a student does not have the necessary prior knowledge, then we can do some explaining.
4. If it's clear several students do not have the necessary prior knowledge, we can come together whole group for some direct instruction.

Sign out on the paper form by  
the door before you leave!

## Problem-Solving Assessment

- The lesson is now complete.
- Please check your UGA email for the survey link. Enter your UGA MyID and password to access the assessment.
- Thank you for doing your very best on the assessment, so we can have good information about the best approach for teaching students this material.
- Once you have completed the problem set and signed out on the paper form by the door, you are free to go.

# Scaffolded Guidance Slides

## Learning Objectives

- Given a model of biological molecules, identify, categorize, and compare the important features.
- Recall that chemical composition affects the structure and interactions of macromolecules.
- Compare different types of non-covalent interactions occurring in biological molecules.
- Explain why and how it is that *all* non-covalent interactions are attractions of opposite charges.
- Predict the impact of changes in the building blocks of biological molecules on the structure of the macromolecules.
- Formulate a scientific explanation for your prediction.
- Solve new problems that extend your thinking about the role of non-covalent interactions across biology.

This lesson should support your learning of the following objectives.

Let's get started.

## Problem Worksheet

- Work through the problem worksheet at your seat with the two people sitting closest to you.

Remember:

- If you need help or feel stuck, raise your hand and we will come assist you.

35-45 minutes

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DO NOT SAY:

Instructors and PLAs will be walking around during this phase. Our goal is to help students get to the right answer. We will comment on correctness of ideas or direct students to the canonical solution. We will follow this process in our interactions with students:

1. Ask the students to explain where they are or what they've done so far.
2. Once we understand where they are stuck, we will ask about what they know about related content, i.e. if they are stuck at understanding what interaction is present, say "tell me what you know about noncovalent interactions" to activate their prior knowledge
3. If it is clear a student does not have the necessary prior knowledge, then we can do some explaining.



**Instructional Materials: Student Handout for Worked Examples Plus Practice**

Name: \_\_\_\_\_

## Problem Worksheet

### Learning Objectives:

- Given a model of biological molecules, identify, categorize, and compare the important features.
- Recall that chemical composition affects the structure and interactions of macromolecules.
- Compare different types of noncovalent interactions occurring in biological molecules.
- Explain why and how it is that all noncovalent interactions are attractions of opposite charges.
- Predict the impact of changes in the building blocks of biological molecules on the structure of the macromolecules and formulate a scientific explanation for your prediction.
- Solve new problems that extend your thinking about the role of noncovalent interactions across biology.

## Problem 1: Worked Example

**PROBLEM 1.** Protein B, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and white). The environment has a pH of 7.4. The blue line represents the Protein B backbone; some but not all of the amino acid side chains (R groups) are shown.

4. This is an ionic interaction between two polar, charged R groups.

6. There are no hydrogen bonds here

5. Van der Waals forces are attracting these nonpolar R groups.

1. This is the R group. It contributes to noncovalent interactions.

2. Isoleucine's R group is nonpolar because C and H don't differ in electronegativity.

3. The amino acid backbone is not shown, because typically it does not contribute to non-covalent interactions relevant to this problem.

7. A hydrogen bond is attracting the polar R groups of asparagine and serine.

8. Isoleucine's R group is nonpolar like alanine's but also bigger.

The amino acids shown are: (A) aspartate, (B) arginine, (C) leucine, (D) alanine, (E) asparagine, and (F) serine. Sometimes, a mutation occurs that substitutes alanine (yellow circle) with isoleucine (above right).

**Predict what will happen to the noncovalent interactions shown when alanine is substituted with isoleucine. Explain your reasoning.**

**PROBLEM 1.** Protein B, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and white). The environment has a pH of 7.4. The blue line represents the Protein B backbone; some but not all of the amino acid side chains (R groups) are shown.

9. Explain given non-covalent interaction

10. Categorize amino acids

11. Explain new non-covalent interaction

12. State your prediction

13. Reflect on predictions

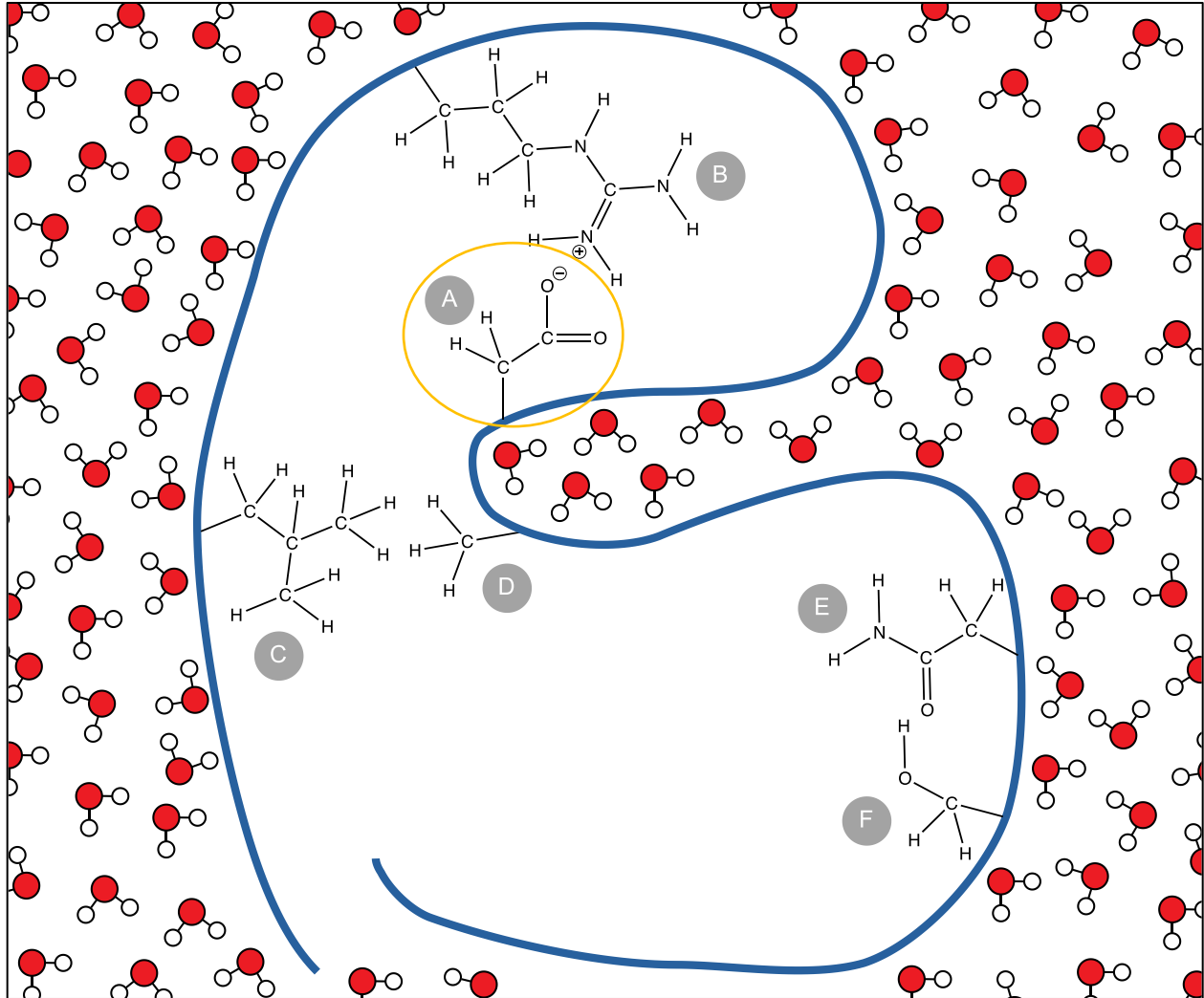
The amino acids shown are: (A) aspartate, (B) arginine, (C) leucine, (D) alanine, (E) asparagine, and (F) serine. Sometimes, a mutation occurs that substitutes alanine (yellow circle) with isoleucine (above right).

**Predict what will happen to the noncovalent interactions shown when alanine is substituted with isoleucine. Explain your reasoning.**

Leucine and alanine are attracted to each other due to van der Waals forces. Both of them have nonpolar R groups, so no other type of non-covalent attraction is possible. However, due to temporary partial charges on the R groups an attraction can occur. Because isoleucine is nonpolar, like alanine, it also could participate in van der Waals interactions with leucine. The only potential problem is if its bigger size causes a problem with these interactions. But my best prediction is no impact on the noncovalent interaction from isoleucine. To know for sure if I'm right, I would need experimental evidence.

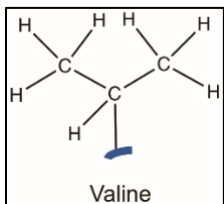
## Problem 2:

Protein B, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and white). The environment has a pH of 7.4. The blue line represents the Protein B backbone; some but not all of the amino acid side chains (R groups) are shown.



The amino acids shown are: (A) aspartate, (B) arginine, (C) leucine, (D) alanine, (E) asparagine, and (F) serine.

Sometimes, a mutation occurs that substitutes aspartate (yellow circle) with valine (below).



**Predict what will happen to the noncovalent interactions shown when aspartate is substituted with valine. Explain your reasoning.**

### Problem 3: Worked Example

**PROBLEM 3.** Protein W, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and white). The environment has a pH of 7.4. The blue line represents the Protein W backbone; some but not all of the amino acid side chains (R groups) are shown.

7. A hydrogen bond is attracting the polar R groups of glutamine and threonine.

5. Van der Waals forces are attracting the three nonpolar alanines.

6. There are no hydrogen bonds here.

4. This is an ionic interaction between two polar, charged R groups.

3. The amino acid backbone is not shown, because typically it does not contribute to non-covalent interactions relevant to this problem.

1. This is the R group. It contributes to noncovalent interactions

2. Leucine's R group is nonpolar because C and H don't differ in electronegativity.

8. The atoms of leucine do not differ in electronegativity, so leucine cannot be a hydrogen bond donor or acceptor.

The amino acids shown are: (A) glutamine, (B) threonine, (C) alanine, (D) glutamate, and (E) lysine. Sometimes, a mutation occurs that substitutes glutamine (yellow circle) with leucine (right).

**Predict what will happen to the noncovalent interactions shown when glutamine is substituted with leucine. Explain your reasoning.**

**PROBLEM 3.** Protein W, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and white). The environment has a pH of 7.4. The blue line represents the Protein W backbone; some but not all of the amino acid side chains (R groups) are shown.

9. Explain given non-covalent interaction

10. Categorize amino acids

11. Explain new non-covalent interaction

12. State your prediction

13. Reflect on predictions

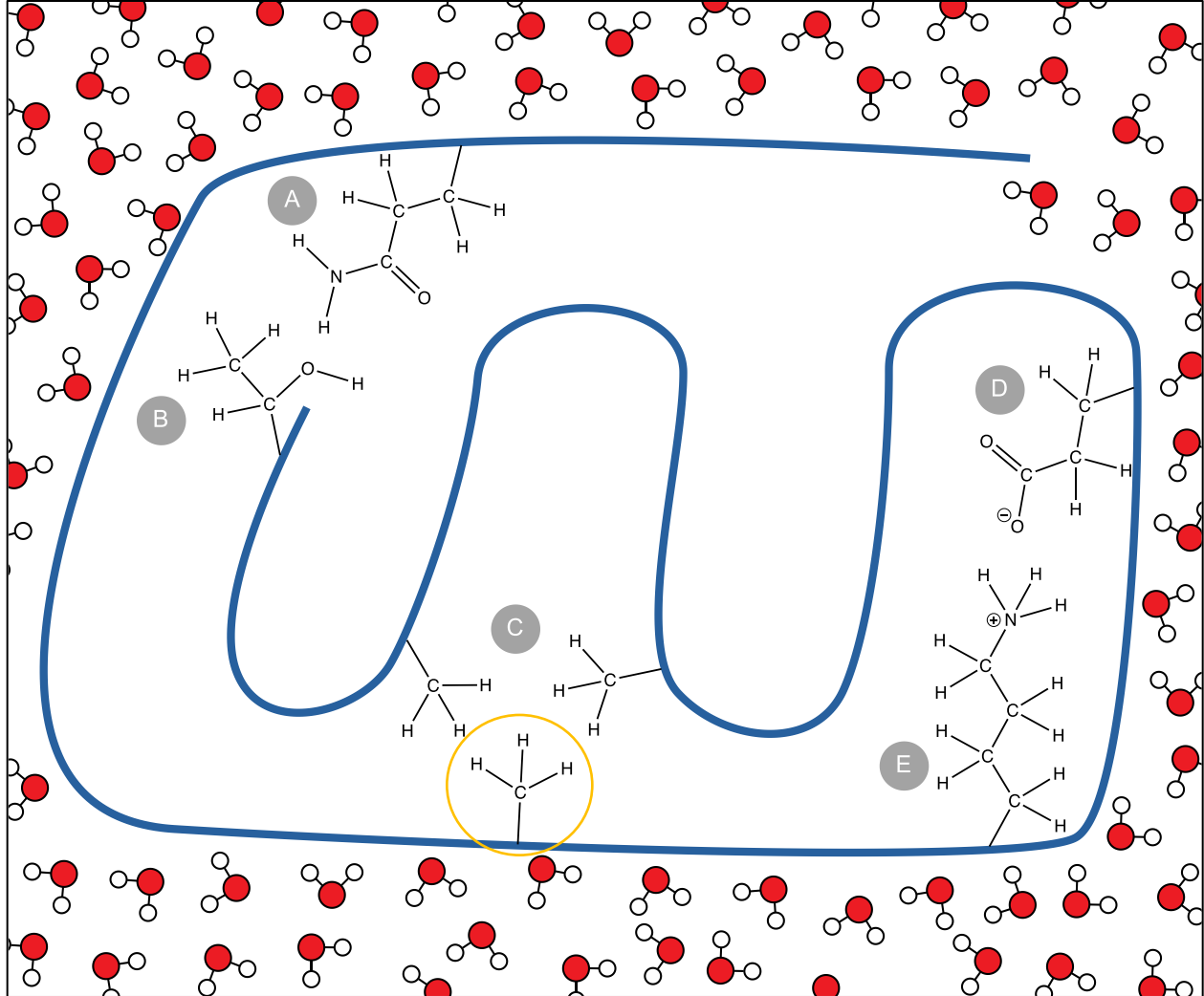
Glutamine and threonine are attracted to each other due to a hydrogen bond. Due to the electronegativity differences among N, H, and O, there is a partial positive charge on the H of glutamine and partial negative on the O of threonine. These attract each other. However, leucine is nonpolar, so a hydrogen bond is not possible. With this substitution, the protein would likely rearrange so that threonine is hydrogen bonding with something else, like a water molecule, and leucine is close to other nonpolar R groups. However, to know for sure if I'm right, I would need experimental evidence.

The amino acids shown are: (A) glutamine, (B) threonine, (C) alanine, (D) glutamate, and (E) lysine. Sometimes, a mutation occurs that substitutes glutamine (yellow circle) with leucine (right).

**Predict what will happen to the noncovalent interactions shown when glutamine is substituted with leucine. Explain your reasoning.**

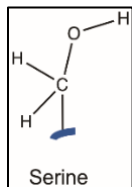
#### Problem 4:

Protein W, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and white). The environment has a pH of 7.4. The blue line represents the Protein W backbone; some but not all of the amino acid side chains (R groups) are shown.



The amino acids shown are: (A) glutamine, (B) threonine, (C) alanine, (D) glutamate, and (E) lysine.

Sometimes, a mutation occurs that substitutes alanine (yellow circle) with serine (below).



**Predict what will happen to the noncovalent interactions shown when alanine is substituted with serine. Explain your reasoning.**

Write your predictions and explanations here.

**Problem 2**

**Problem 4**

**Instructional Materials: Student Handout for Productive Failure**



Name: \_\_\_\_\_

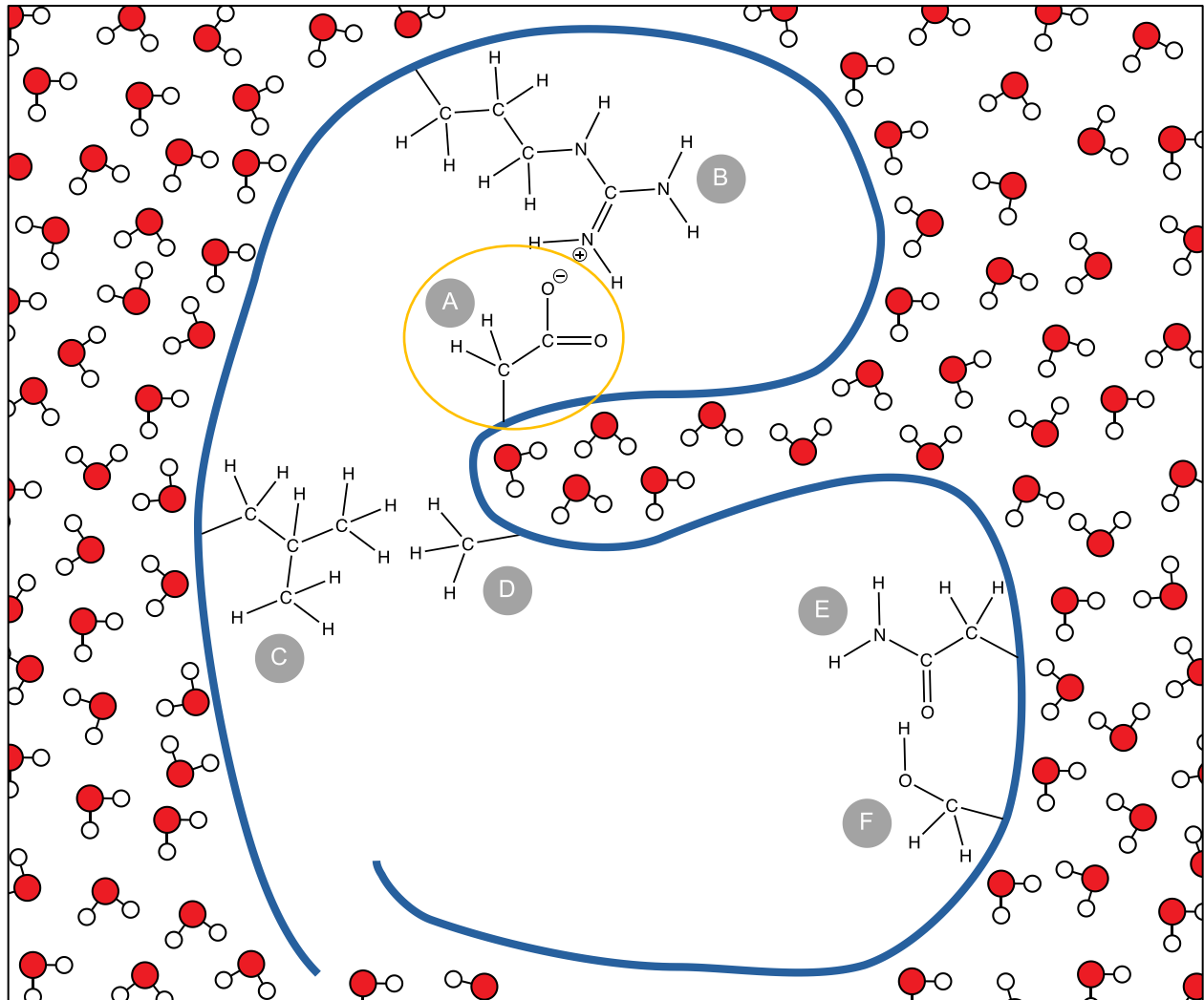
## Problem Worksheet

### Learning Objectives:

- Given a model of biological molecules, identify, categorize, and compare the important features.
- Recall that chemical composition affects the structure and interactions of macromolecules.
- Compare different types of noncovalent interactions occurring in biological molecules.
- Explain why and how it is that all noncovalent interactions are attractions of opposite charges.
- Predict the impact of changes in the building blocks of biological molecules on the structure of the macromolecules and formulate a scientific explanation for your prediction.
- Solve new problems that extend your thinking about the role of noncovalent interactions across biology.

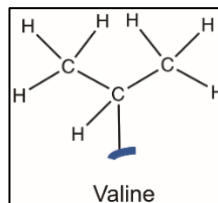
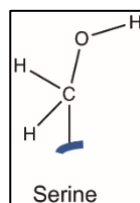
Protein B and Protein W, both cytoplasmic proteins, are folded into their tertiary structure, surrounded by water molecules (red and white). The environment has a pH of 7.4. The blue line represents the protein backbone; some but not all of the amino acid side chains (R groups) are shown for each protein. Sometimes, mutations occur that substitute aspartate (yellow circle) in Protein B and alanine (green circle) in Protein W with serine or valine (below).

**Protein B:**

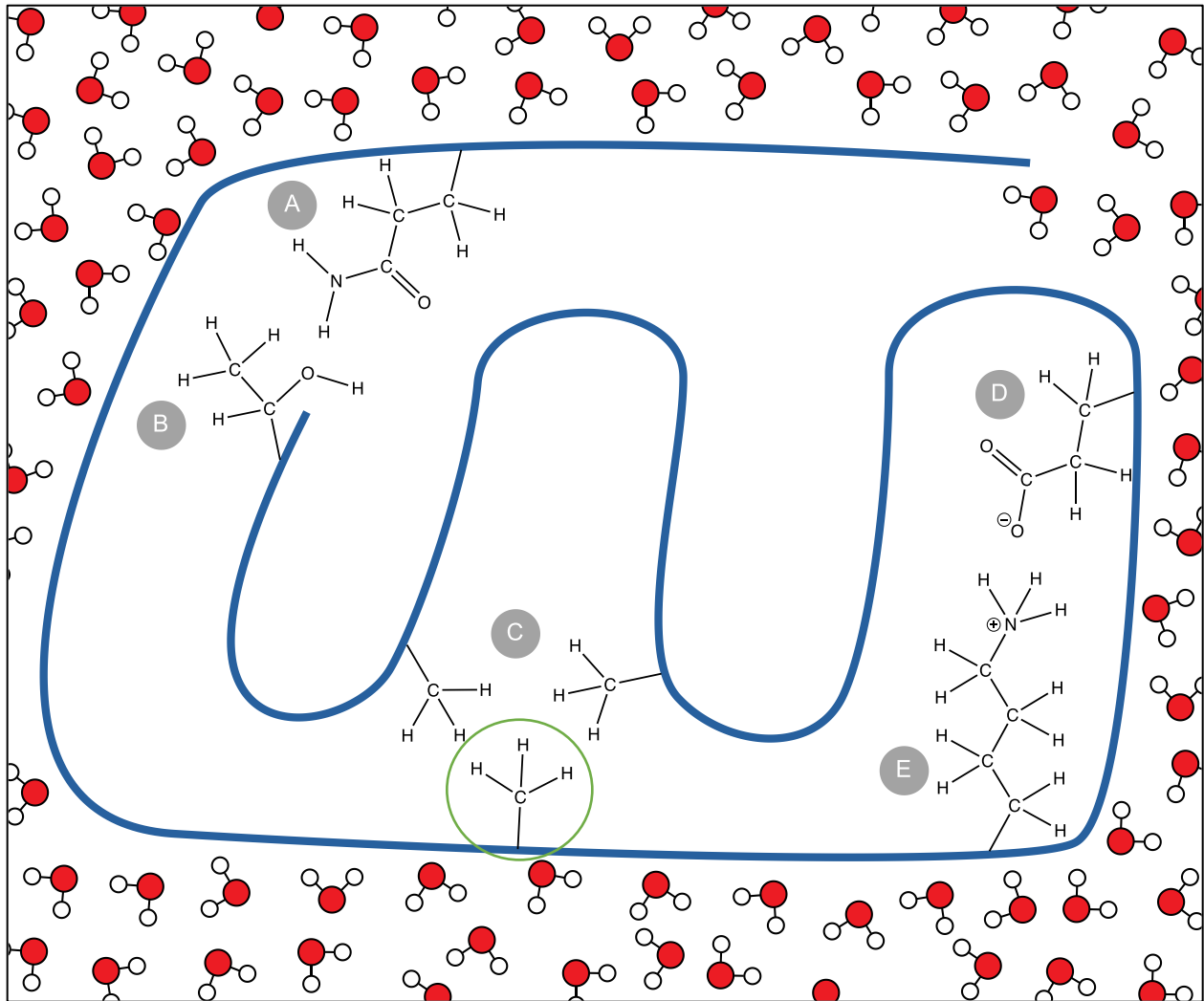


The amino acids shown are: (A) aspartate, (B) arginine, (C) leucine, (D) alanine, (E) asparagine, and (F) serine.

**Substituted Amino Acids:**

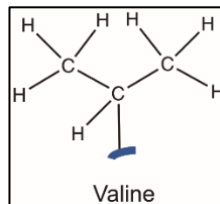
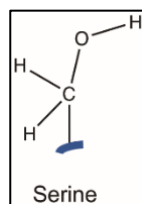


**Protein W:**



The amino acids shown are: (A) glutamine, (B) threonine, (C) alanine, (D) glutamate, and (E) lysine.

**Substituted Amino Acids:**



**Predict the effect of each amino acid substitution on the existing noncovalent interactions. Compare and contrast the effects of the four amino acid substitutions. Explain your reasoning.**

**Predictions and Explanations:**

<b>Protein B with Serine Substitution</b>	<b>Protein B with Valine Substitution</b>	<b>Protein W with Serine Substitution</b>	<b>Protein W with Valine Substitution</b>

**Instructional Materials: Student Handout for Unscaffolded Guidance**

Name: \_\_\_\_\_

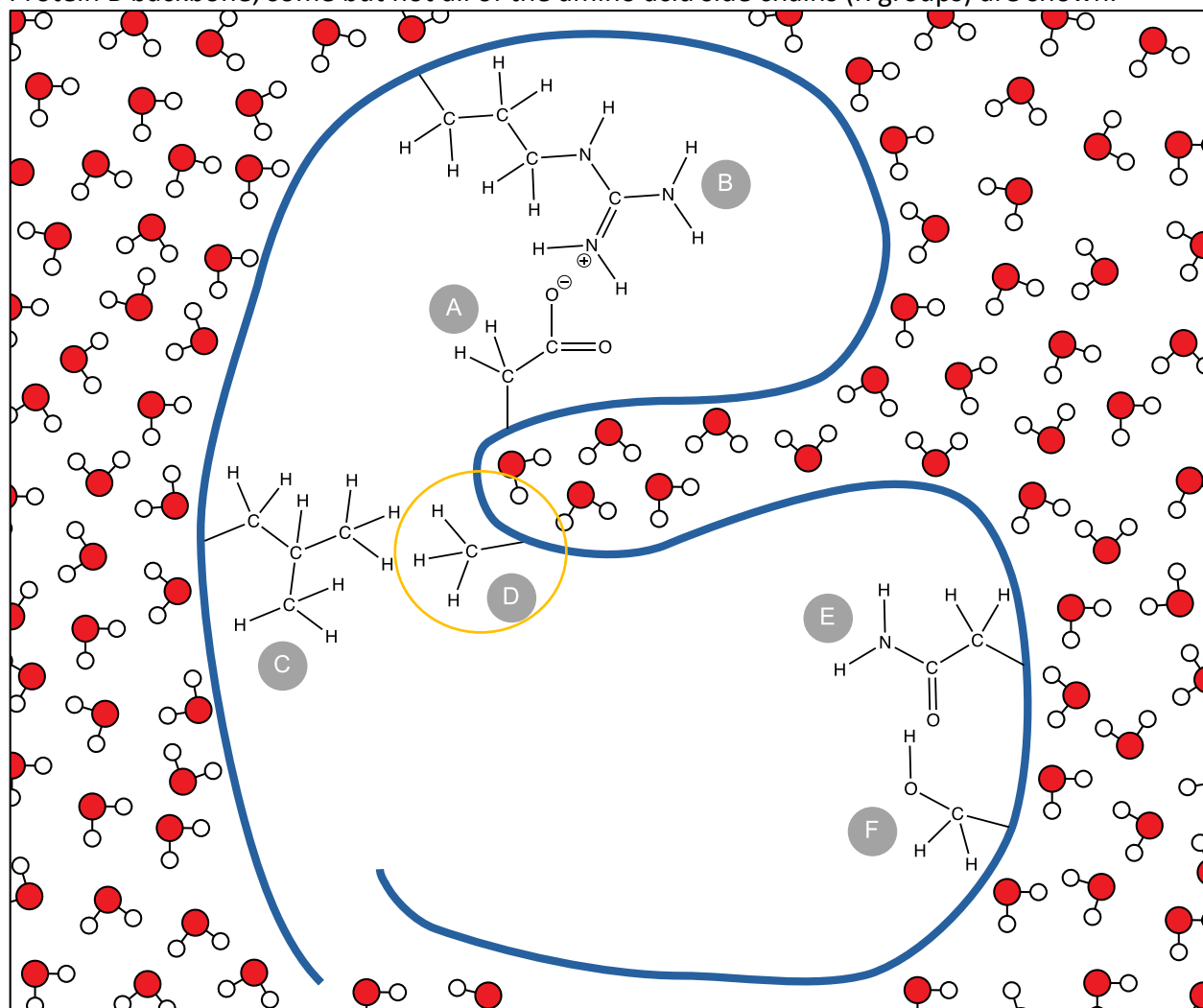
## Problem Worksheet

### Learning Objectives:

- Given a model of biological molecules, identify, categorize, and compare the important features.
- Recall that chemical composition affects the structure and interactions of macromolecules.
- Compare different types of noncovalent interactions occurring in biological molecules.
- Explain why and how it is that all noncovalent interactions are attractions of opposite charges.
- Predict the impact of changes in the building blocks of biological molecules on the structure of the macromolecules and formulate a scientific explanation for your prediction.
- Solve new problems that extend your thinking about the role of noncovalent interactions across biology.

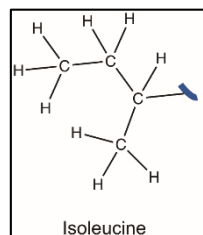
### Problem 1:

Protein B, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and white). The environment has a pH of 7.4. The blue line represents the Protein B backbone; some but not all of the amino acid side chains (R groups) are shown.



The amino acids shown are: (A) aspartate, (B) arginine, (C) leucine, (D) alanine, (E) asparagine, and (F) serine.

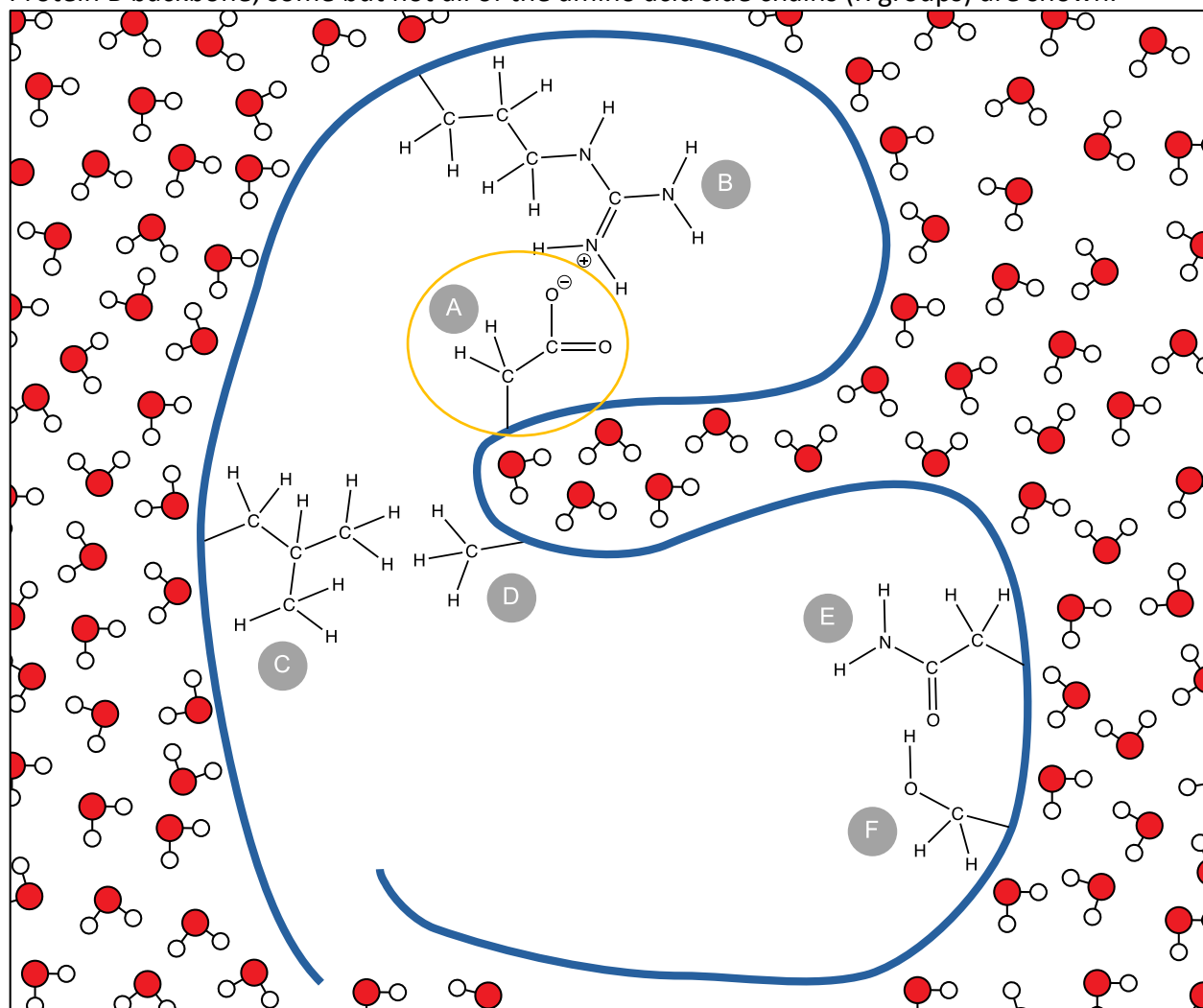
Sometimes, a mutation occurs that substitutes alanine (yellow circle) with isoleucine (below).



**Predict what will happen to the noncovalent interactions shown when alanine is substituted with isoleucine. Explain your reasoning.**

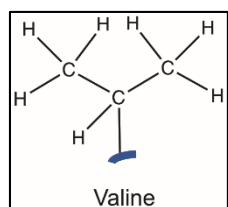
## Problem 2:

Protein B, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and white). The environment has a pH of 7.4. The blue line represents the Protein B backbone; some but not all of the amino acid side chains (R groups) are shown.



The amino acids shown are: (A) aspartate, (B) arginine, (C) leucine, (D) alanine, (E) asparagine, and (F) serine.

Sometimes, a mutation occurs that substitutes aspartate (yellow circle) with valine (below).

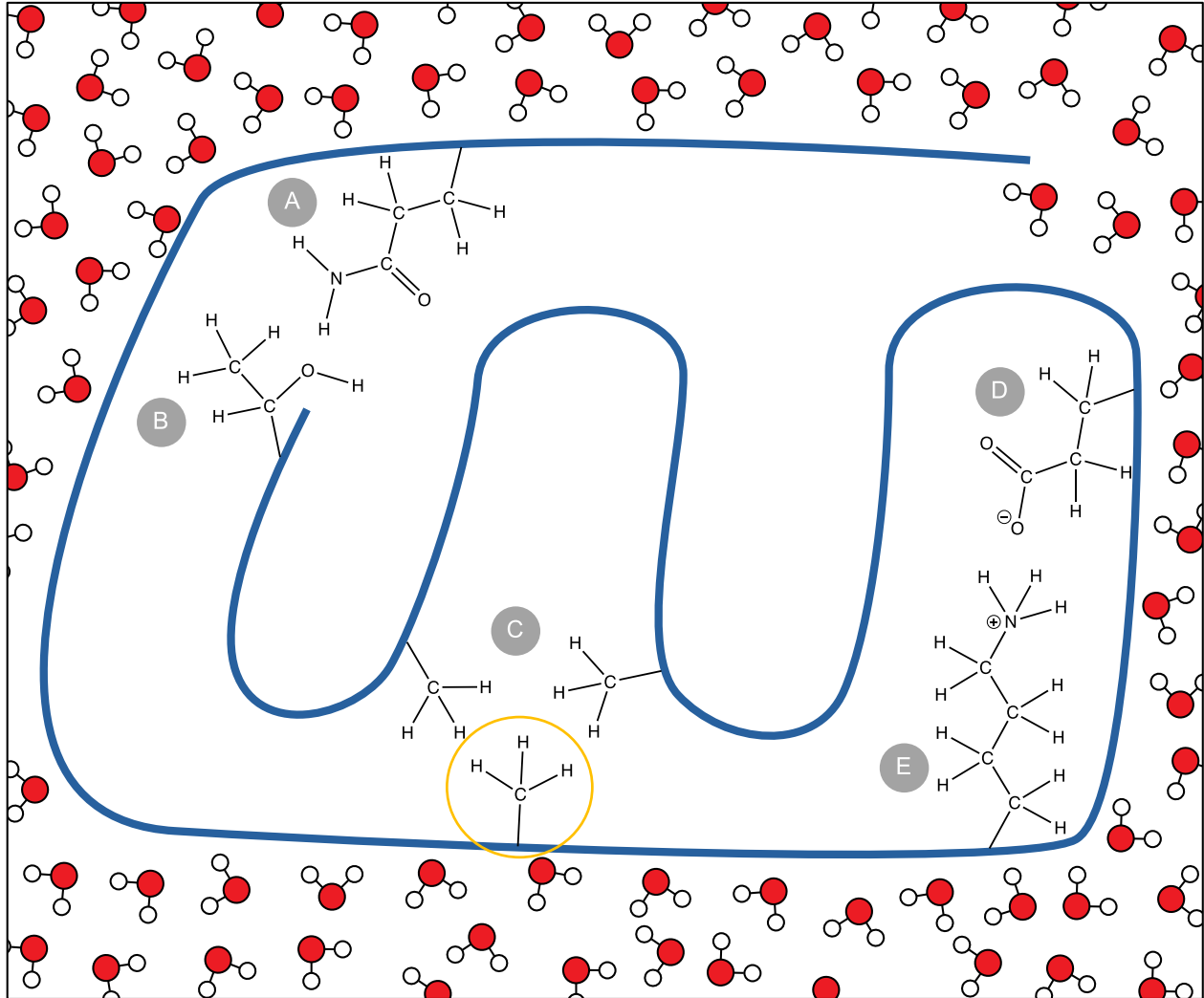


**Predict what will happen to the noncovalent interactions shown when aspartate is substituted with valine. Explain your reasoning.**



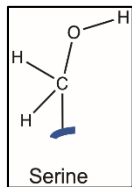
### Problem 3:

Protein W, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and white). The environment has a pH of 7.4. The blue line represents the Protein W backbone; some but not all of the amino acid side chains (R groups) are shown.



The amino acids shown are: (A) glutamine, (B) threonine, (C) alanine, (D) glutamate, and (E) lysine.

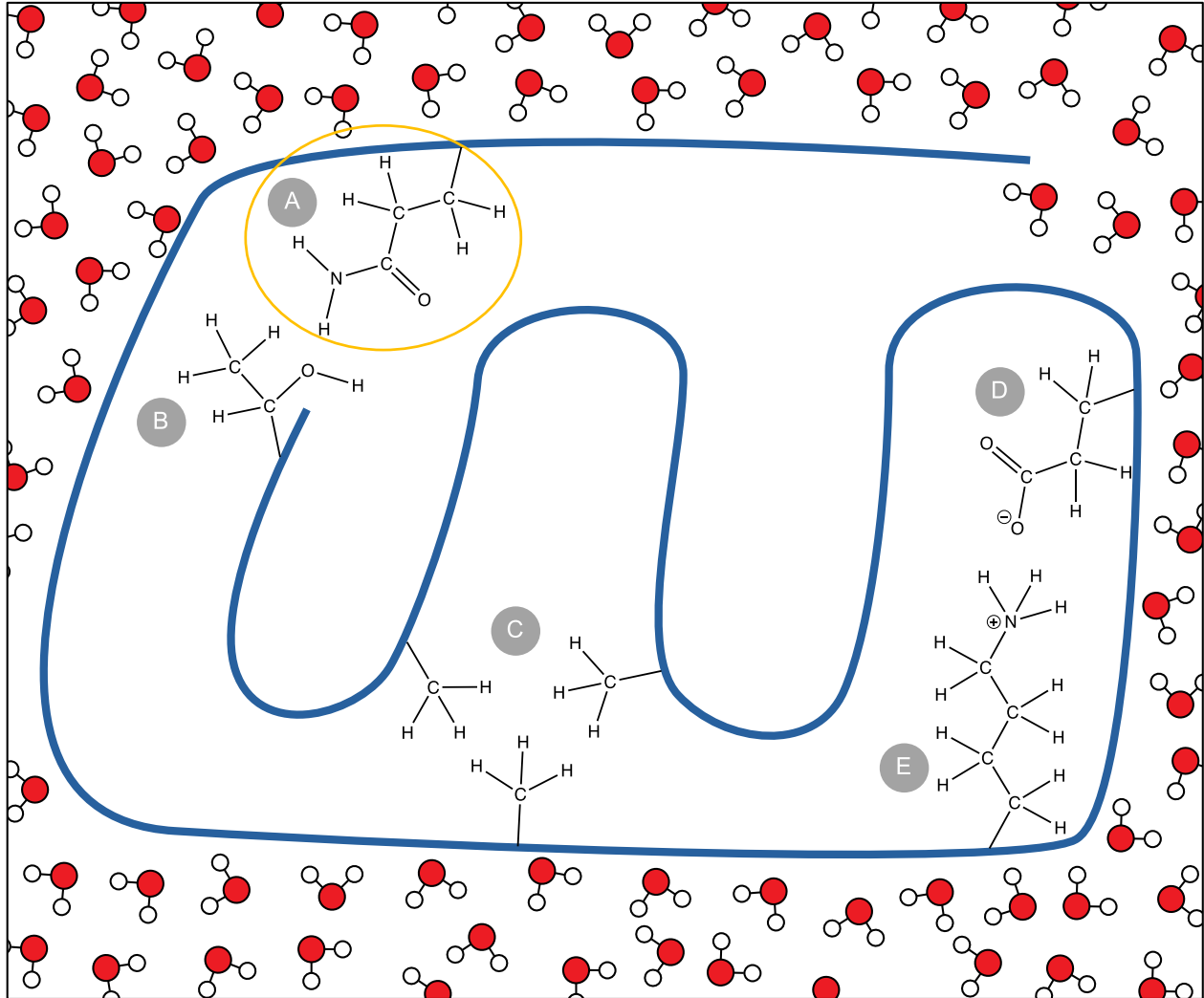
Sometimes, a mutation occurs that substitutes alanine (yellow circle) with serine (below).



**Predict what will happen to the noncovalent interactions shown when alanine is substituted with serine. Explain your reasoning.**

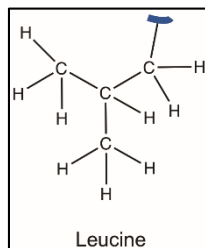
#### Problem 4:

Protein W, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and white). The environment has a pH of 7.4. The blue line represents the Protein W backbone; some but not all of the amino acid side chains (R groups) are shown.



The amino acids shown are: (A) glutamine, (B) threonine, (C) alanine, (D) glutamate, and (E) lysine.

Sometimes, a mutation occurs that substitutes glutamine (yellow circle) with leucine (below).



**Predict what will happen to the noncovalent interactions shown when glutamine is substituted with leucine. Explain your reasoning.**

Write your predictions and explanations here.

**Problem 1**

**Problem 2**

Write your predictions and explanations here.

**Problem 3**

**Problem 4**

**Instructional Materials: Student Handout for Scaffolded Guidance**

## Problem Worksheet

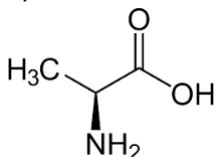
### Learning Objectives:

- Given a model of biological molecules, identify, categorize, and compare the important features.
- Recall that chemical composition affects the structure and interactions of macromolecules.
- Compare how different types of noncovalent interactions occur in biological molecules.
- Explain why and how it is that all noncovalent interactions are attractions of opposite charges.
- Predict the impact of changes in the building blocks of biological molecules on the structure of the macromolecules and formulate a scientific explanation for your prediction.
- Solve new problems that extend your thinking about the role of noncovalent interactions across biology.

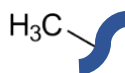
### Model 1: General Structure of an Amino Acid

The building blocks of proteins are amino acids. There are at least 20 different amino acids found in proteins, each differing in their side chain or R group. Investigate the images below of one amino acid, alanine.

A) Alanine



B) Alanine



1. For each image, circle the amino acid R group and draw a box around the peptide backbone.

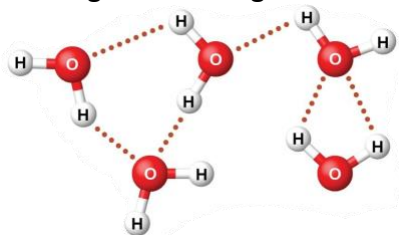
### Part A: Categorizing Amino Acids Based on their R Groups

When looking at amino acid R groups, it can be helpful to categorize the R group as charged, polar, or nonpolar based on its chemical composition. Let's take another look at alanine.

2. What atoms make up the R group of alanine?
3. Compare the electronegativity of the atoms that make up alanine's R group.
4. Is alanine's R group charged? Does alanine's R group have a significant dipole? Explain your reasoning.
5. Using your answers to questions 1-3 questions, how would you classify alanine's R group (charged, polar, or nonpolar)? Explain your reasoning.

### Model 2: Covalent Bonds vs. Noncovalent Interactions

Investigate the image below of water molecules:



6. In the image above, circle and label a covalent bond and a noncovalent interaction.
7. Using your knowledge from general chemistry, define a noncovalent interaction in your own words:

There are three main types of noncovalent interactions: ion pairing, hydrogen bonding, and van der Waals. These three types of noncovalent interactions vary based on the charges involved.

8. Complete the following chart to help you distinguish between the three types of noncovalent interactions:

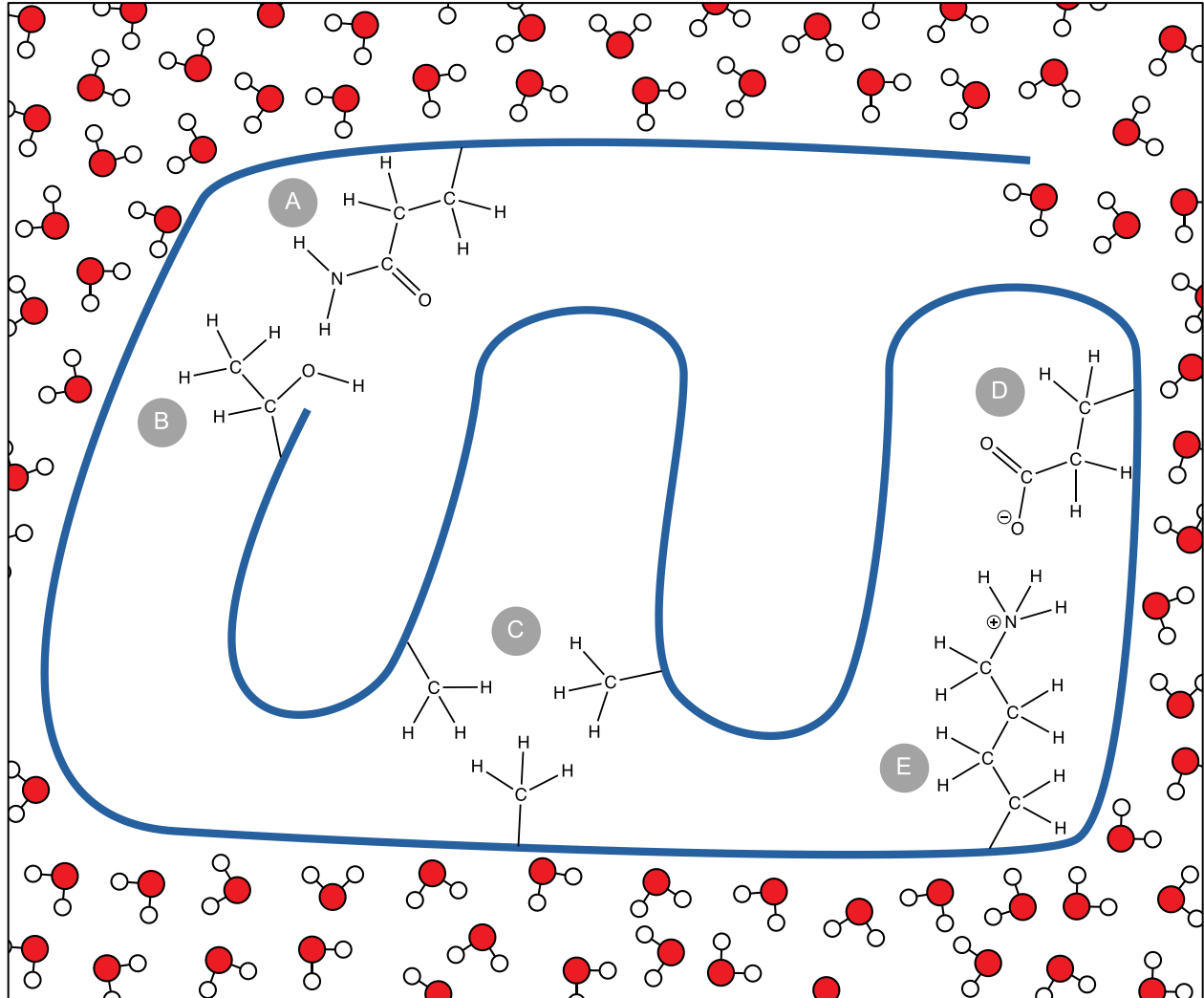
	<b>Ion Pairing</b>	<b>Hydrogen Bond</b>	<b>van der Waals</b>
Full or partial charges involved?			
Permanent or temporary charges involved?			



### Model 3. Noncovalent Interactions in the Context of a Folded Protein

Proteins fold in a way that maximizes the noncovalent interactions between amino acid R groups. Read the model legend in italics and investigate the model below:

*Protein W, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and white). The environment has a pH of 7.4. The blue line represents the Protein W backbone; some but not all of the amino acid side chains (R groups) are shown.*

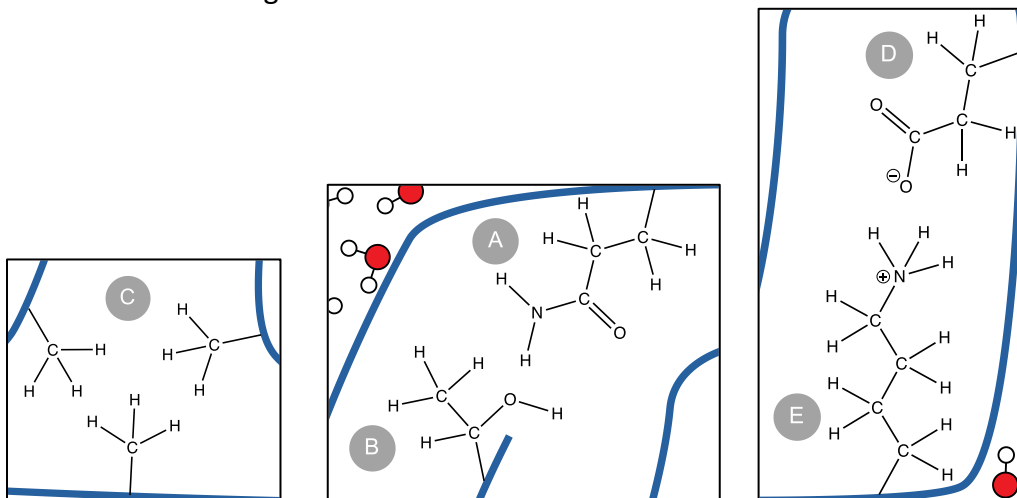


*The amino acids shown are: (A) glutamine, (B) threonine, (C) alanine, (D) glutamate, and (E) lysine.*

9. Circle a noncovalent interaction between amino acid R groups in the model above.

#### Model 4: Noncovalent Interactions Between Amino Acid R groups

Below are zoomed-in images of three noncovalent interactions shown in Protein W (Model 3).



**Part A:** Consider the interaction between the three R groups of amino acid C shown above.

10. Categorize the R group of C (refer to Model 1: Part A for help):

11. What type of noncovalent interaction is occurring among the three amino acids C?  
Explain how this interaction occurs.

**Part B:** Consider the interaction between the R group of amino acid A and the R group of amino acid B shown above.

12. Categorize the R group of A and the R group of B:

13. What type of noncovalent interaction is occurring between amino acid A and B? Explain how this interaction occurs.

**Part C:** Consider the interaction between the R groups of amino acid D and amino acid E shown above.

14. Categorize the R group of D and the R group of E:

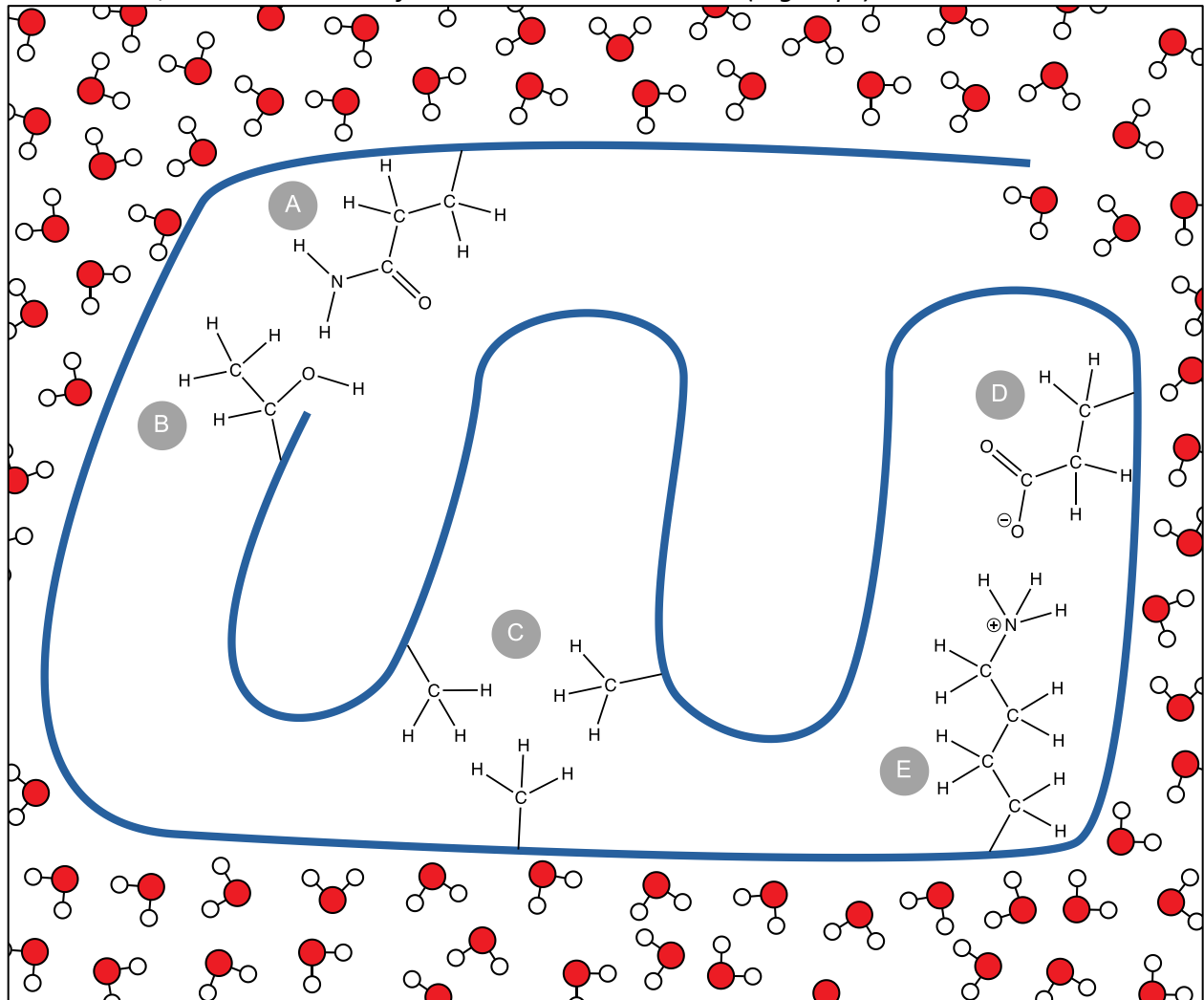
15. What type of noncovalent interaction is occurring between amino acid D and E? Explain how this interaction occurs.

**STOP: Before moving on, double-check your answers with a PLA.**

### Model 5. An Amino Acid Substitution

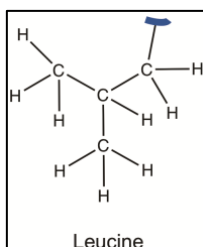
Let's return to Model 3 on page 3.

*Protein W, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and white). The environment has a pH of 7.4. The blue line represents the Protein W backbone; some but not all of the amino acid side chains (R groups) are shown.*



*The amino acids shown are: (A) glutamine, (B) threonine, (C) alanine, (D) glutamate, and (E) lysine.*

Sometimes, a mutation occurs that substitutes glutamine (A) in Protein W with leucine (below).



### Critical Thinking Questions: Considering an Amino Acid Substitution

16. Predict what will happen to the noncovalent interactions shown in Protein W when glutamine is substituted with leucine (Model 5). Explain your reasoning and construct a scientific explanation by filling in the blanks below:

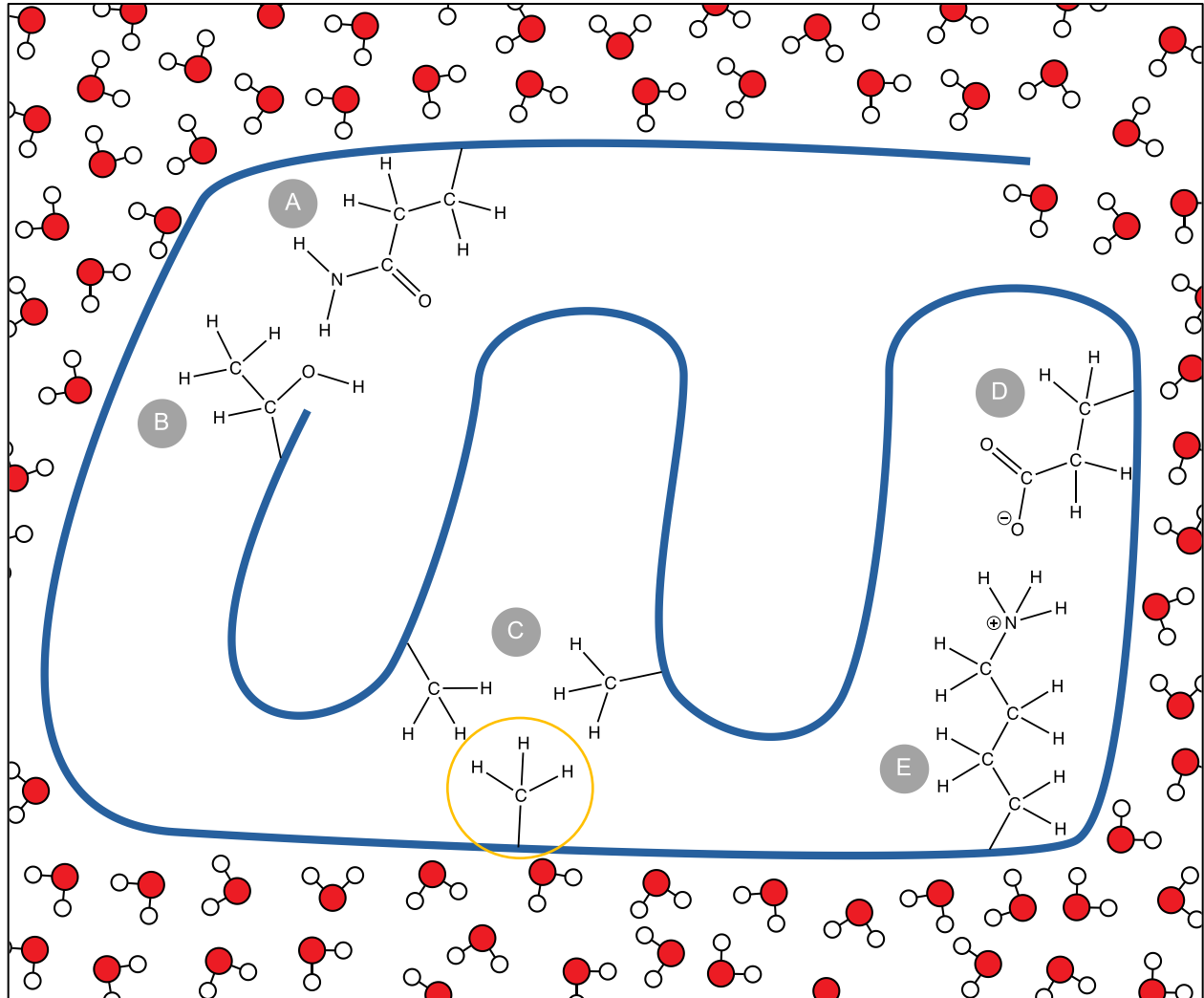
Glutamine is a \_\_\_\_\_ (polar or nonpolar) amino acid. Threonine is a \_\_\_\_\_ (polar or nonpolar) amino acid. In protein W, glutamine (A) and threonine (B) are attracted to each other through a \_\_\_\_\_ (type of noncovalent interaction). This interaction arises because there is a \_\_\_\_\_ (partial or full) positive charge on the H of glutamine and a partial \_\_\_\_\_ (positive or negative) charge on the O of threonine due to the electronegativity \_\_\_\_\_ (similarities or differences) among N, H, and O atoms. These \_\_\_\_\_ (permanent or temporary) charges on glutamine and threonine attract each other. Leucine is a \_\_\_\_\_ (polar or nonpolar) amino acid. If leucine replaced glutamine in the protein sequence, a hydrogen bond would \_\_\_\_\_ (still or no longer) form. With this substitution, the protein would likely rearrange so that threonine forms a \_\_\_\_\_ (type of noncovalent interaction) with something else, like a water molecule. This re-folding would also bring leucine closer to other \_\_\_\_\_ (polar or nonpolar) R groups, like \_\_\_\_\_ (name of amino acid in protein W). This is because leucine can interact noncovalently with these other amino acids through \_\_\_\_\_ (type of noncovalent interaction). Therefore, I predict that the leucine substitution will \_\_\_\_\_ (have or not have) an impact on the noncovalent interaction shown. In order to feel more confident about my prediction an experiment would need to be conducted to test my prediction.

**NOTE: Reflect on the features of the explanation above. Use the structure of this explanation as a model for writing explanations for this type of problem.**

## Model 6: Another Amino Acid Substitution

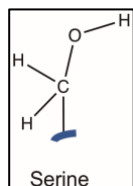
Refer back to Protein W.

*Protein W, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and white). The environment has a pH of 7.4. The blue line represents the Protein W backbone; some but not all of the amino acid side chains (R groups) are shown.*



The amino acids shown are: (A) glutamine, (B) threonine, (C) alanine, (D) glutamate, and (E) lysine.

Sometimes, a mutation occurs that substitutes alanine (yellow circle) with serine (below).



**Critical Thinking Questions: Considering an Amino Acid Substitution**

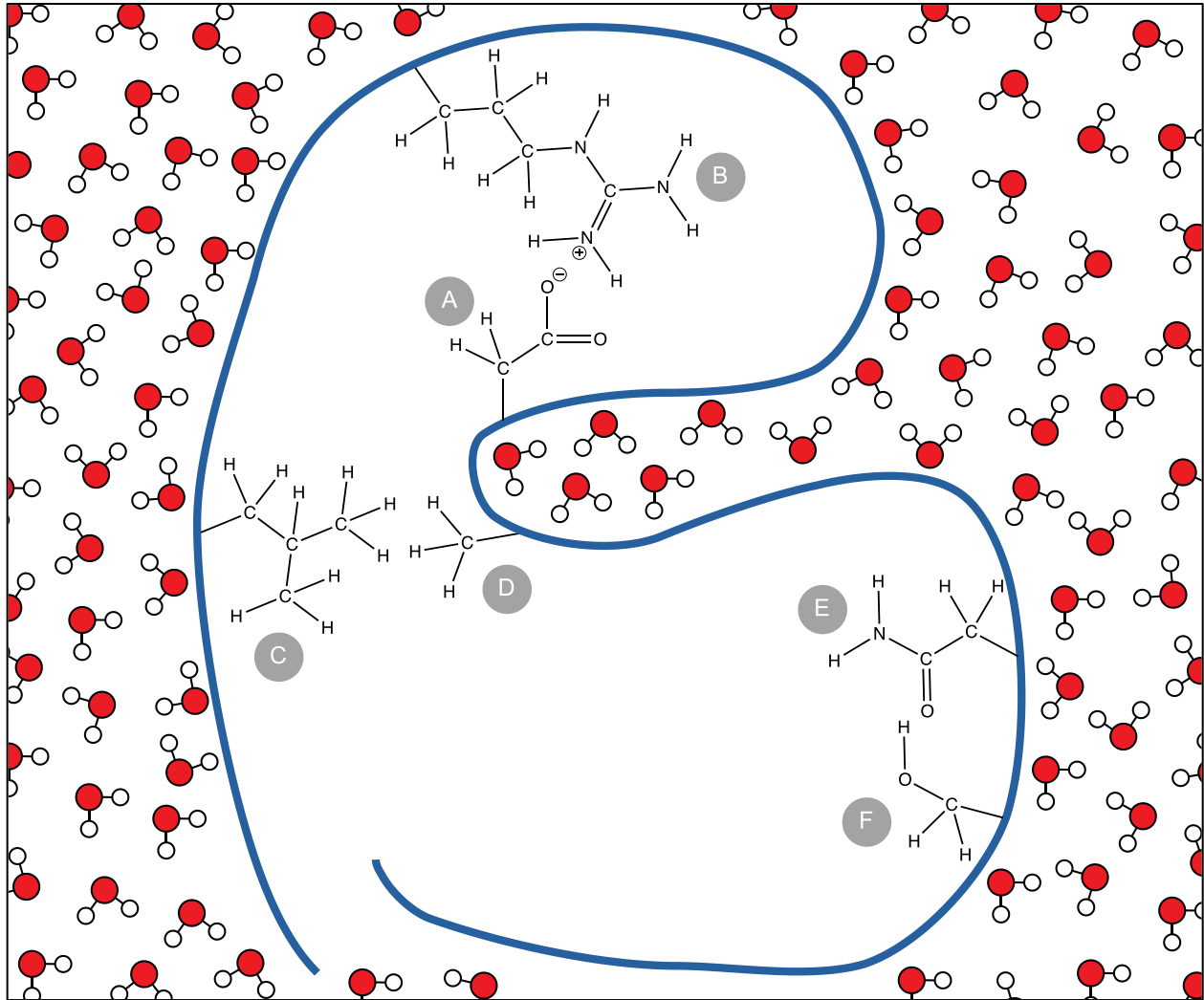
17. Predict what will happen to the noncovalent interactions shown when alanine is substituted with serine. Using complete sentences, explain your reasoning and construct a scientific explanation by completing the table below:

Categorize alanine (C):	
Categorize serine:	
Describe the given noncovalent interaction between the three alanines (C) in Protein W:	
When the substituted Protein W folds, would serine interact with the other alanines?	
State your prediction about the impact of the substitution on the given noncovalent interaction:	
Do you predict any new noncovalent interactions after the substitution? If so, describe them.	
Reflect on your prediction by thinking about what information you would need to feel more confident about your prediction:	

### Model 7. More Noncovalent Interactions in the Context of a Different Folded Protein

Let's consider a new protein, Protein B. Read the model legend in italics:

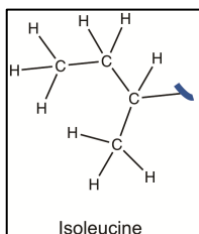
*Protein B, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and white). The environment has a pH of 7.4. The blue line represents the Protein B backbone; some but not all of the amino acid side chains (R groups) are shown.*



The amino acids shown are: (A) aspartate, (B) arginine, (C) leucine, (D) alanine, (E) asparagine, and (F) serine.

18. On the model of Protein B above, circle and name the three noncovalent interactions that are occurring.

Sometimes, a mutation occurs that substitutes alanine (D) in Protein B with isoleucine (below).



**Critical Thinking Questions:**

Predict what will happen to the noncovalent interactions shown in Protein B when alanine is substituted with isoleucine (Model 7). Explain your reasoning and construct a scientific explanation by using the format below:

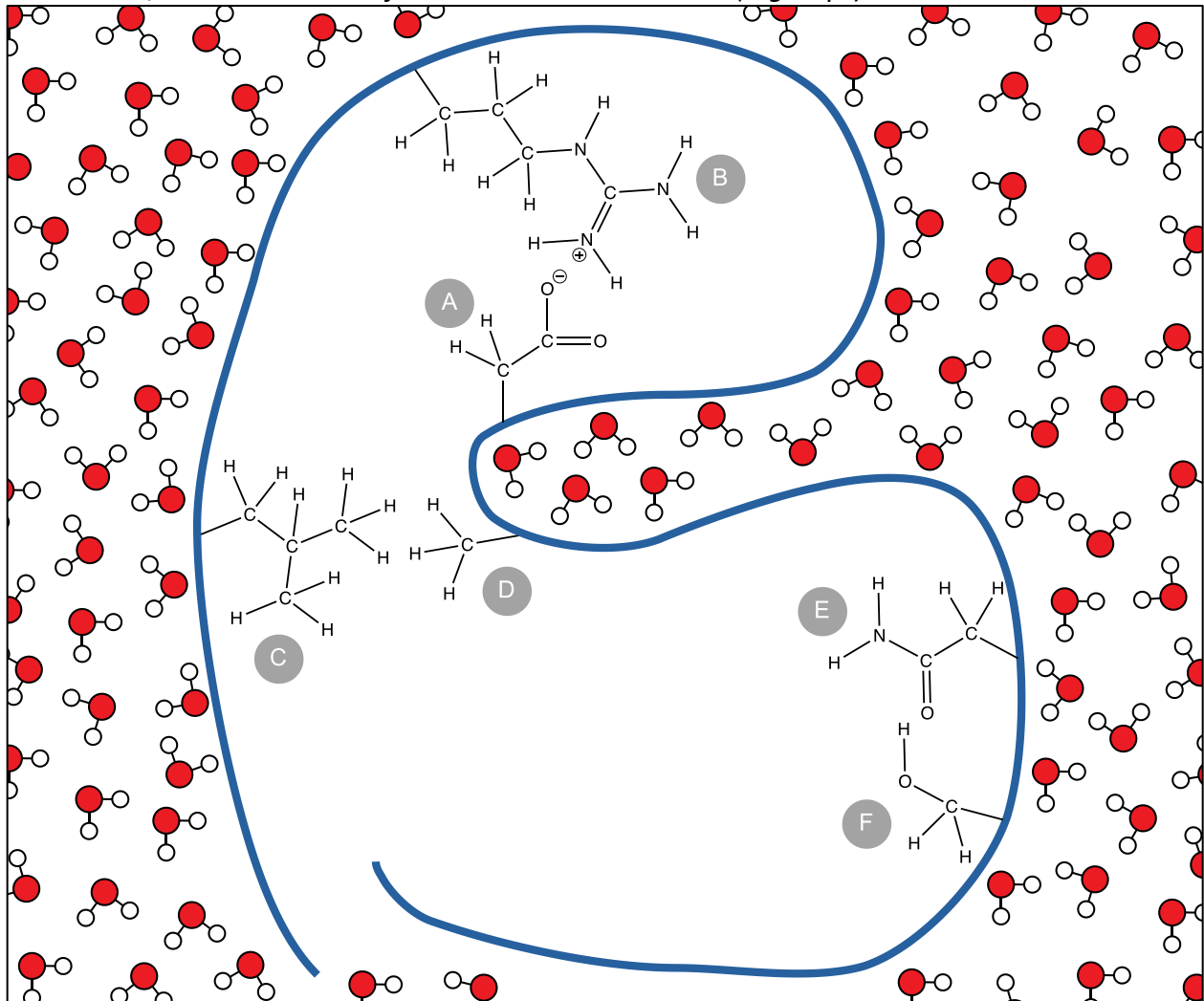
19. Categorize and compare alanine and isoleucine:
  
  
  
  
  
  
  
  
  
  
20. Describe the original noncovalent interaction that alanine (D) participates in and how it arises:
  
  
  
  
  
  
  
  
  
  
21. Will Protein B fold into the same 3D shape when alanine is substituted with isoleucine? Explain.
  
  
  
  
  
  
  
  
  
  
22. Will the original noncovalent interaction still form after substitution?
  
  
  
  
  
  
  
  
  
  
23. Explain any new non-covalent interactions that may occur after the substitution:
  
  
  
  
  
  
  
  
  
  
24. Reflect on your prediction by thinking about what type of evidence you would need to feel confident about your prediction:



## Exercises:

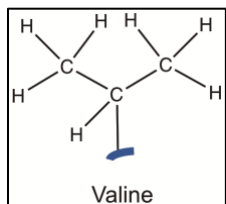
1. Try to solve the following problem on your own.

*Protein B, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and white). The environment has a pH of 7.4. The blue line represents the Protein B backbone; some but not all of the amino acid side chains (R groups) are shown.*



*The amino acids shown are: (A) aspartate, (B) arginine, (C) leucine, (D) alanine, (E) asparagine, and (F) serine.*

Sometimes, a mutation occurs that substitutes aspartate (A) with valine (below).



**Predict what will happen to the noncovalent interactions shown when aspartate is substituted with valine. Explain your reasoning.**

2. The concepts you've learned about noncovalent interactions in proteins also apply to noncovalent interactions in other biological molecules. Consider the noncovalent interaction occurring between DNA and the lambda repressor protein below:

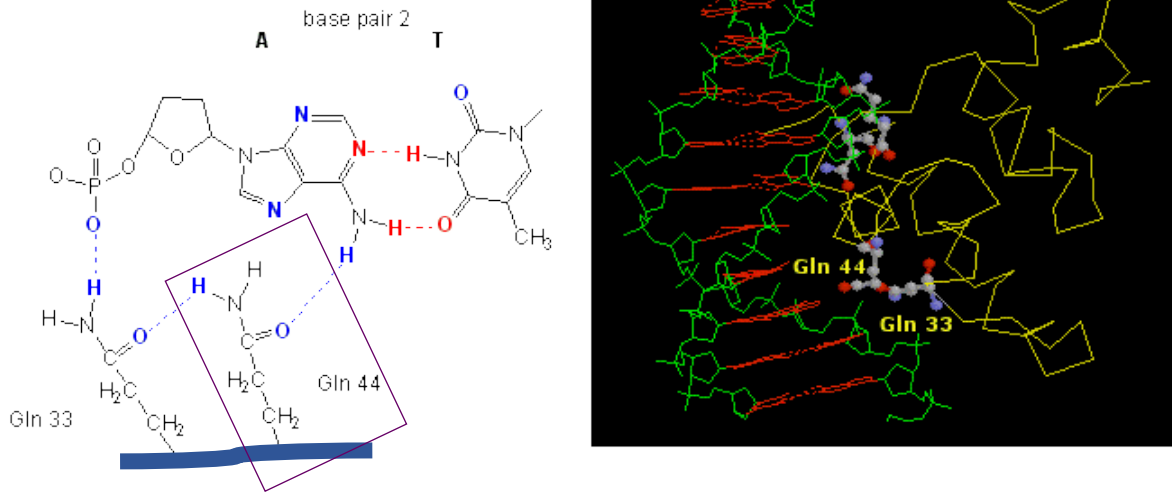


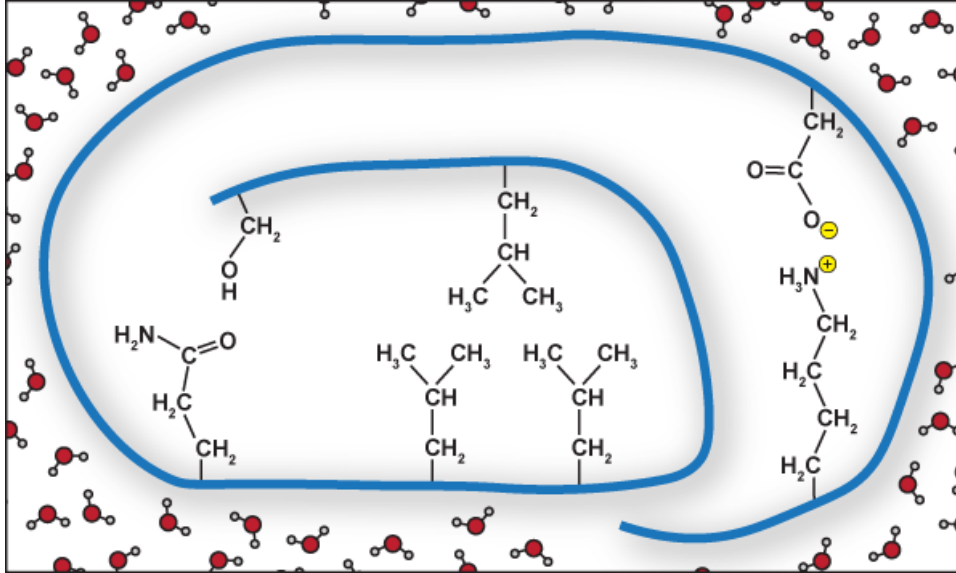
Image: <https://employees.csbsju.edu/hjakubowski/classes/ch331/bind/olbindtranscription.html>

Do you predict that DNA could still interact with the protein if glutamine (boxed in purple) was mutated to leucine? Explain.

## **Assessments**

### Basic Knowledge Post-Test

Protein X, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and gray). This environment has a pH of 7.4. The blue line represents the protein X backbone. Some, but not all, of the amino acid side chains are shown in chemical notation.



For questions that list multiple true/false statements:

- Decide for each statement whether it is more likely to be true, or more likely to be false.
- Multiple statements can be true.
- Multiple statements can be false.

**What occupies the white area inside the protein, where no amino acid side chains are shown?**

a void of empty space (i.e., nothing at all)  
chemical groups

True	False
<input type="radio"/>	<input type="radio"/>
<input type="radio"/>	<input type="radio"/>

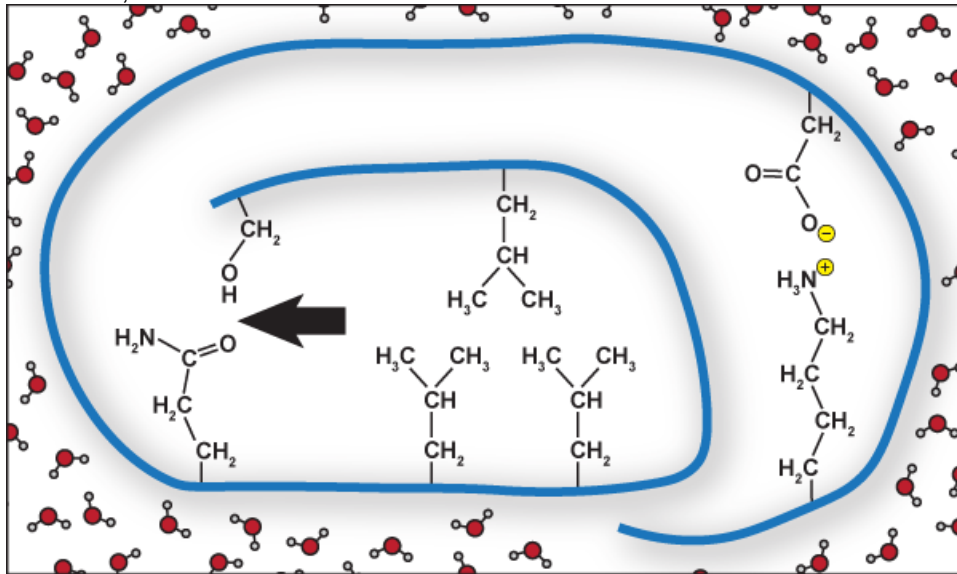
**The blue line represents ...**

peptide bonds  
amino acid side chains

True	False
<input type="radio"/>	<input type="radio"/>
<input type="radio"/>	<input type="radio"/>

Continue

Protein X, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and gray). This environment has a pH of 7.4. The blue line represents the protein X backbone. Some, but not all, of the amino acid side chains are shown in chemical notation.



The items below all relate to the **most prominent** non-covalent interaction occurring in the space pointed to by the arrow.

What is the name of this non-covalent interaction? Select one option.

- hydrogen bond
- ion pairing
- van der Waals interaction

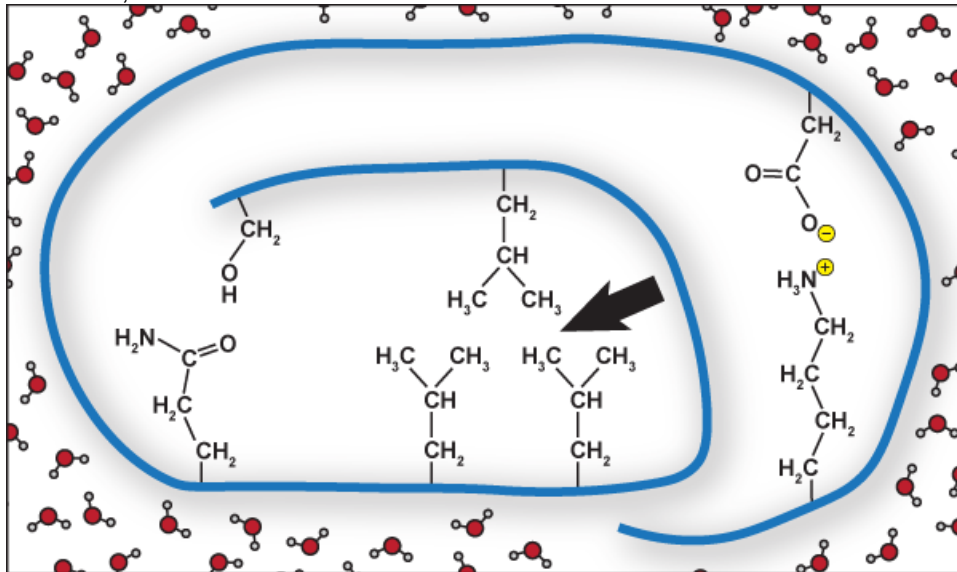
The charges involved in this non-covalent interaction are ...

partial  
temporary  
induced  
due to differences in electronegativity

True	False
<input type="radio"/>	<input type="radio"/>
<input type="radio"/>	<input type="radio"/>
<input type="radio"/>	<input type="radio"/>
<input type="radio"/>	<input type="radio"/>

Continue

Protein X, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and gray). This environment has a pH of 7.4. The blue line represents the protein X backbone. Some, but not all, of the amino acid side chains are shown in chemical notation.



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What is the name of this non-covalent interaction? Select one option.

- hydrogen bond
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- van der Waals interaction

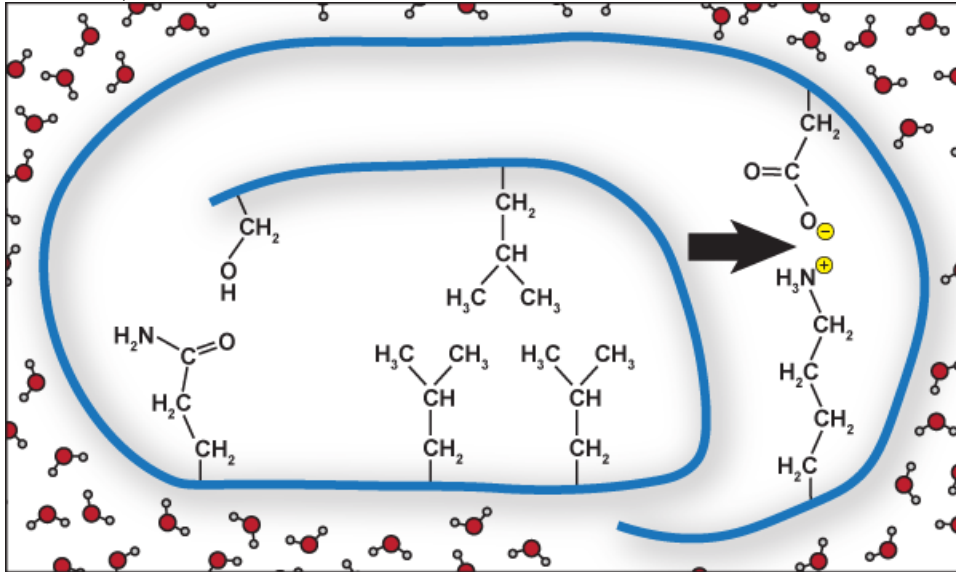
The charges involved in this non-covalent interaction are ...

partial  
temporary  
induced  
due to differences in electronegativity

True	False
<input type="radio"/>	<input type="radio"/>
<input type="radio"/>	<input type="radio"/>
<input type="radio"/>	<input type="radio"/>
<input type="radio"/>	<input type="radio"/>

Continue

Protein X, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and gray). This environment has a pH of 7.4. The blue line represents the protein X backbone. Some, but not all, of the amino acid side chains are shown in chemical notation.



The items below all relate to the **most prominent** non-covalent interaction occurring in the space pointed to by the arrow.

What is the name of this non-covalent interaction? Select one option.

- hydrogen bond
- ion pairing
- van der Waals interaction

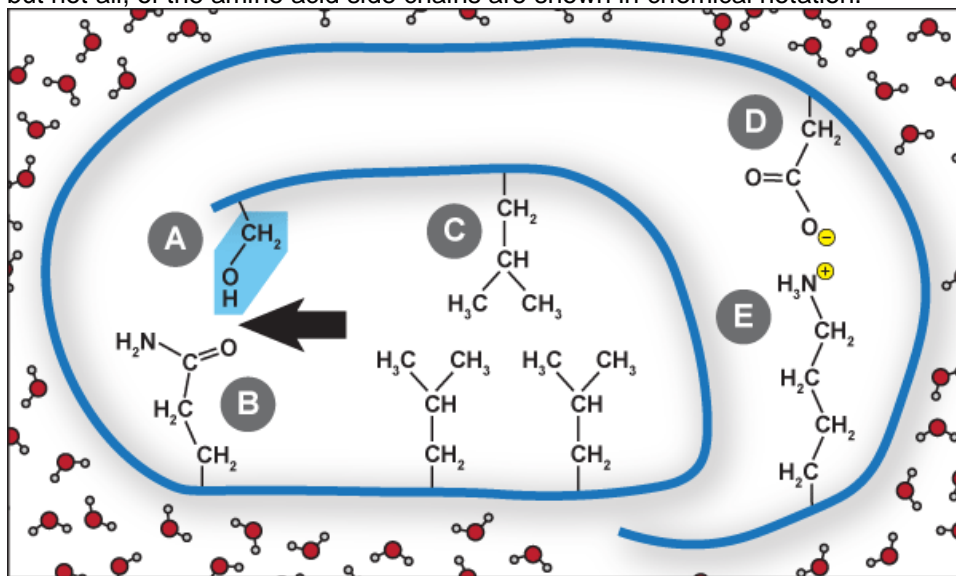
The charges involved in this non-covalent interaction are ...

partial  
 temporary  
 induced  
 due to differences in electronegativity

True	False
<input type="radio"/>	<input type="radio"/>
<input type="radio"/>	<input type="radio"/>
<input type="radio"/>	<input type="radio"/>
<input type="radio"/>	<input type="radio"/>

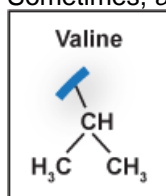
### Near Transfer Problems

Protein X, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and gray). This environment has a pH of 7.4. The blue line represents the protein X backbone. Some, but not all, of the amino acid side chains are shown in chemical notation.



The amino acids shown are: (A) serine, (B) glutamine, (C) leucine, (D) aspartate, and (E) lysine.

Sometimes, a mutation occurs that substitutes serine (blue highlight) with valine (below).



Do you predict that such a mutation would affect the non-covalent interaction pointed to by the arrow?

- Yes, the interaction would be affected.  
 No, the interaction would not be affected.

Provide a scientific explanation to support your prediction.

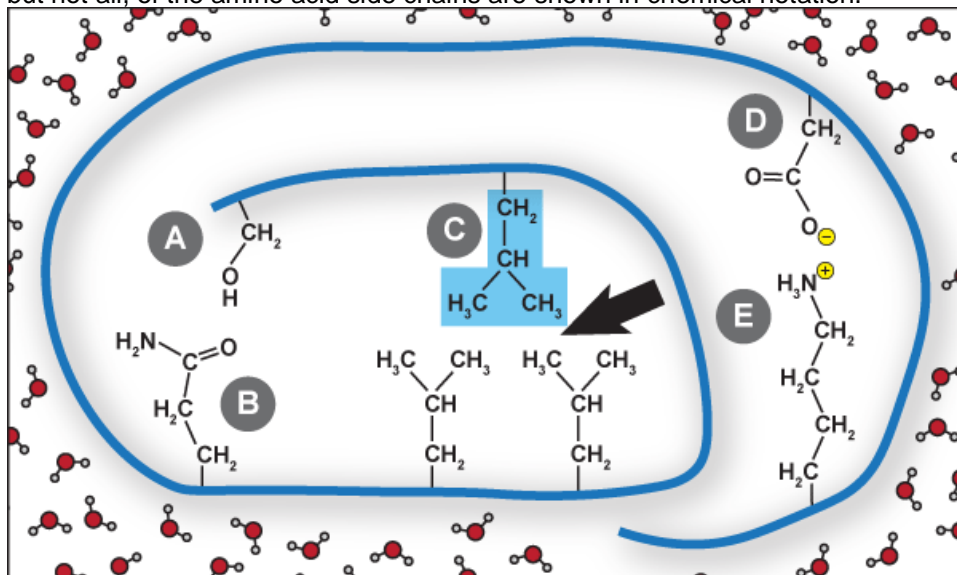
(The following prompt is shown only if “Yes” is selected above)

Predict any new non-covalent interactions that might occur with such a mutation, and provide scientific explanations of them.

Continue

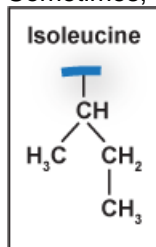


Protein X, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and gray). This environment has a pH of 7.4. The blue line represents the protein X backbone. Some, but not all, of the amino acid side chains are shown in chemical notation.



The amino acids shown are: (A) serine, (B) glutamine, (C) leucine, (D) aspartate, and (E) lysine.

Sometimes, a mutation occurs that substitutes leucine (blue highlight) with isoleucine (below).



**Do you predict that such a mutation would affect the non-covalent interaction pointed to by the arrow?**

- Yes, the interaction would be affected.
- No, the interaction would not be affected.

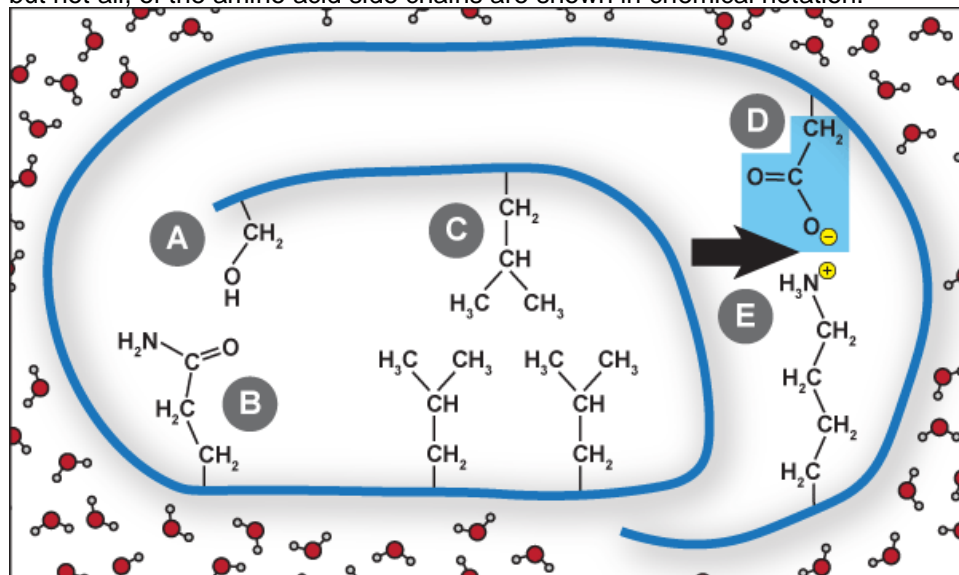
**Provide a scientific explanation to support your prediction.**

(The following prompt is shown only if “Yes” is selected above)

**Predict any new non-covalent interactions that might occur with such a mutation, and provide scientific explanations of them.**

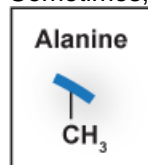
Continue

Protein X, a cytoplasmic protein, is folded into its tertiary structure, surrounded by water molecules (red and gray). This environment has a pH of 7.4. The blue line represents the protein X backbone. Some, but not all, of the amino acid side chains are shown in chemical notation.



The amino acids shown are: (A) serine, (B) glutamine, (C) leucine, (D) aspartate, and (E) lysine.

Sometimes, a mutation occurs that substitutes aspartate (blue highlight) with alanine (below).



**Do you predict that such a mutation would affect the non-covalent interaction pointed to by the arrow?**

- Yes, the interaction would be affected.
- No, the interaction would not be affected.

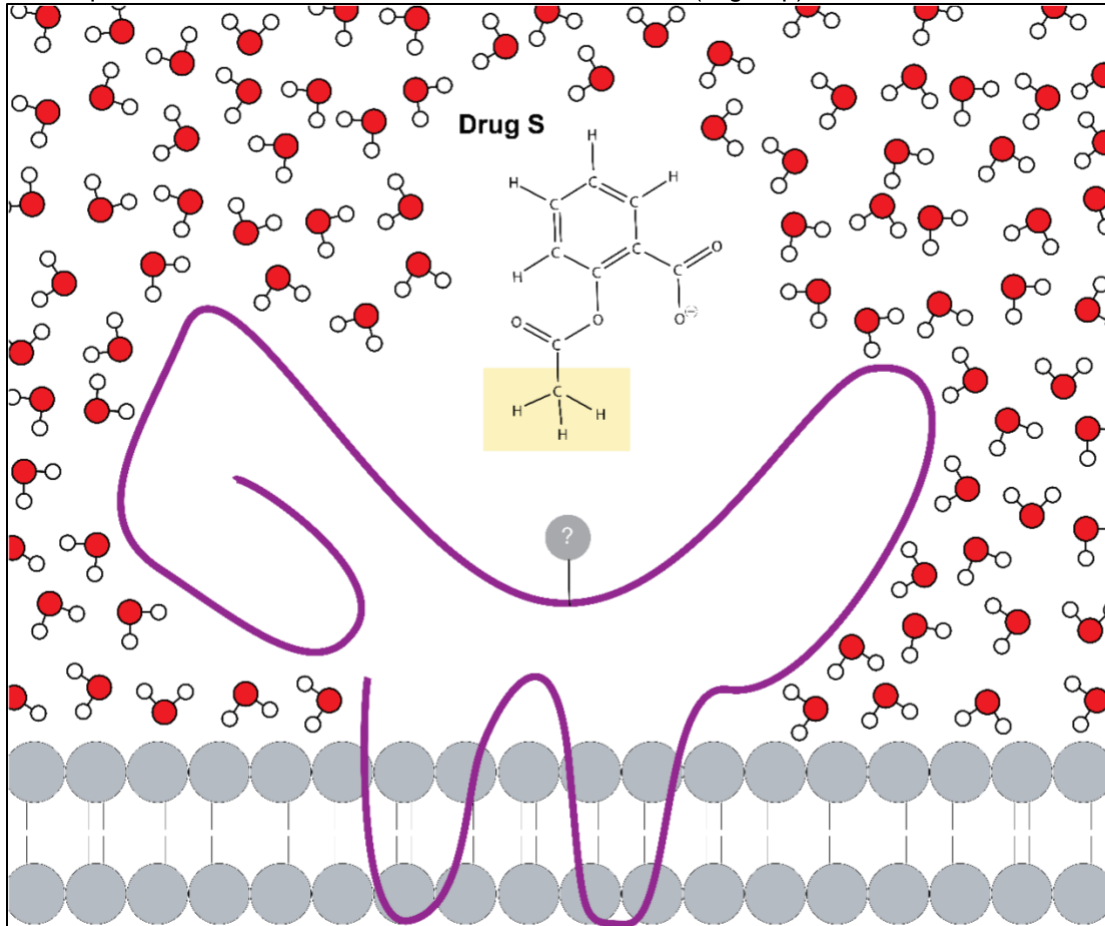
**Provide a scientific explanation to support your prediction.**

(The following prompt is shown only if "Yes" is selected above)

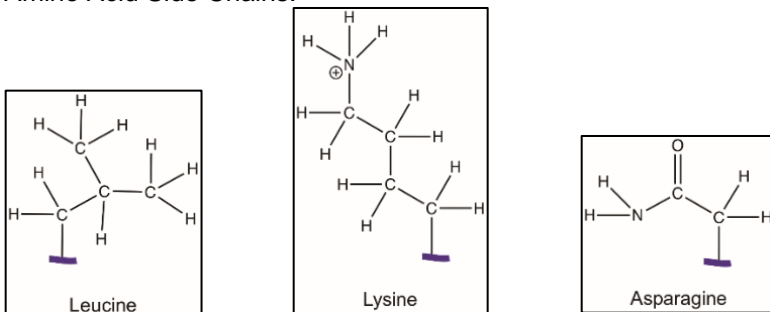
**Predict any new non-covalent interactions that might occur with such a mutation, and provide scientific explanations of them.**

## Far Transfer Problems

Below is a model of Drug S and a protein with which it may interact. The protein is located on the cell surface situated within the cell membrane and surrounded by water molecules (red and white). The environment has a pH of 7.4. The purple line represents the protein backbone, and the section labeled with a question mark is a site for an amino acid side chain (R group).

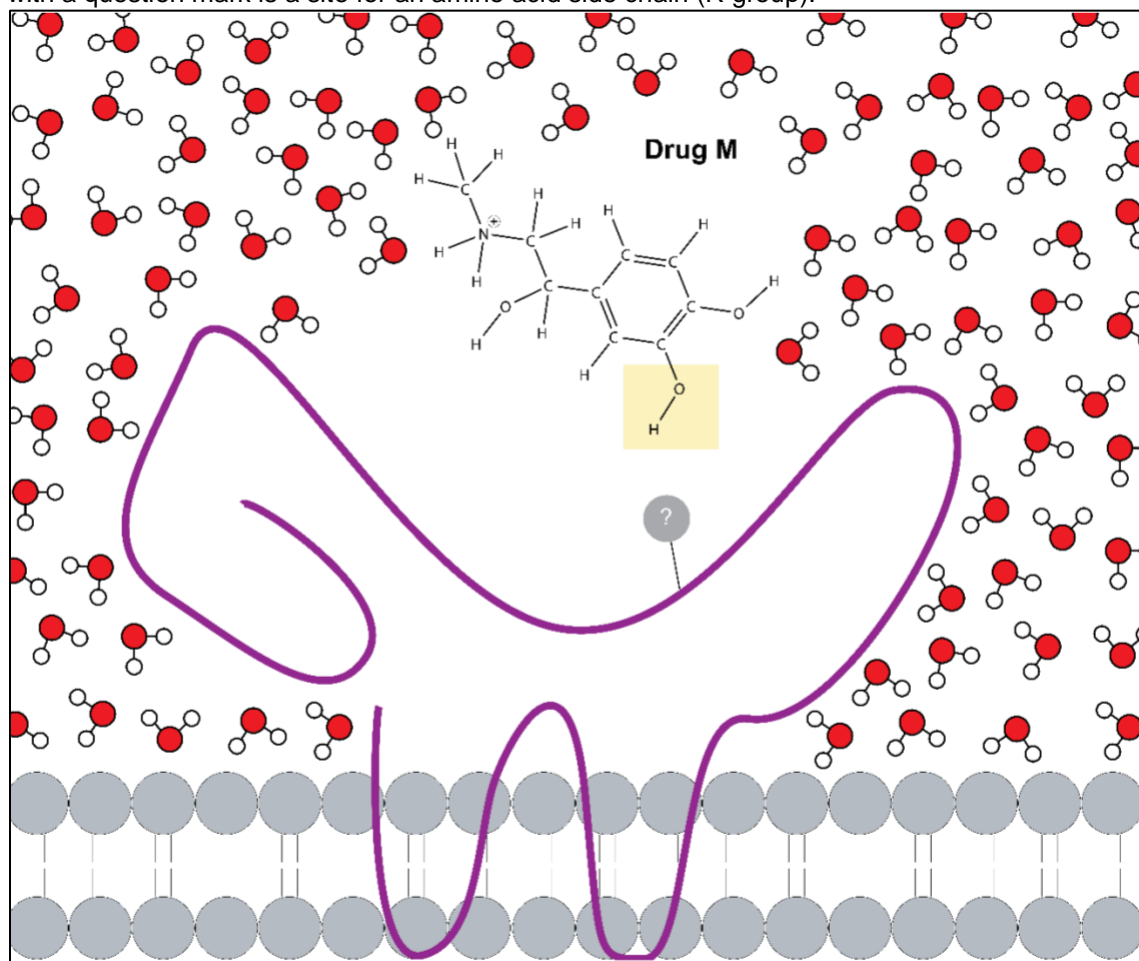


Amino Acid Side Chains:

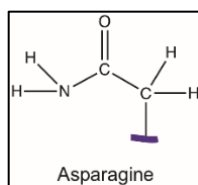
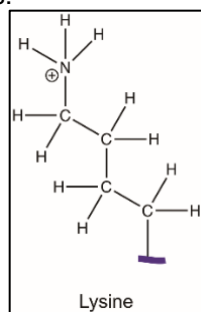
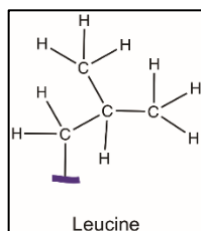


**Which amino acid would interact non-covalently with the yellow highlighted section of Drug S? Provide a scientific explanation describing how Drug S interacts non-covalently with the amino acid you selected. Be sure to describe how this interaction forms.**

Below is a model of Drug M and a protein with which it may interact. The protein is located on the cell surface situated within the cell membrane and surrounded by water molecules (red and white). The environment has a pH of 7.4. The purple line represents the protein backbone, and the section labeled with a question mark is a site for an amino acid side chain (R group).

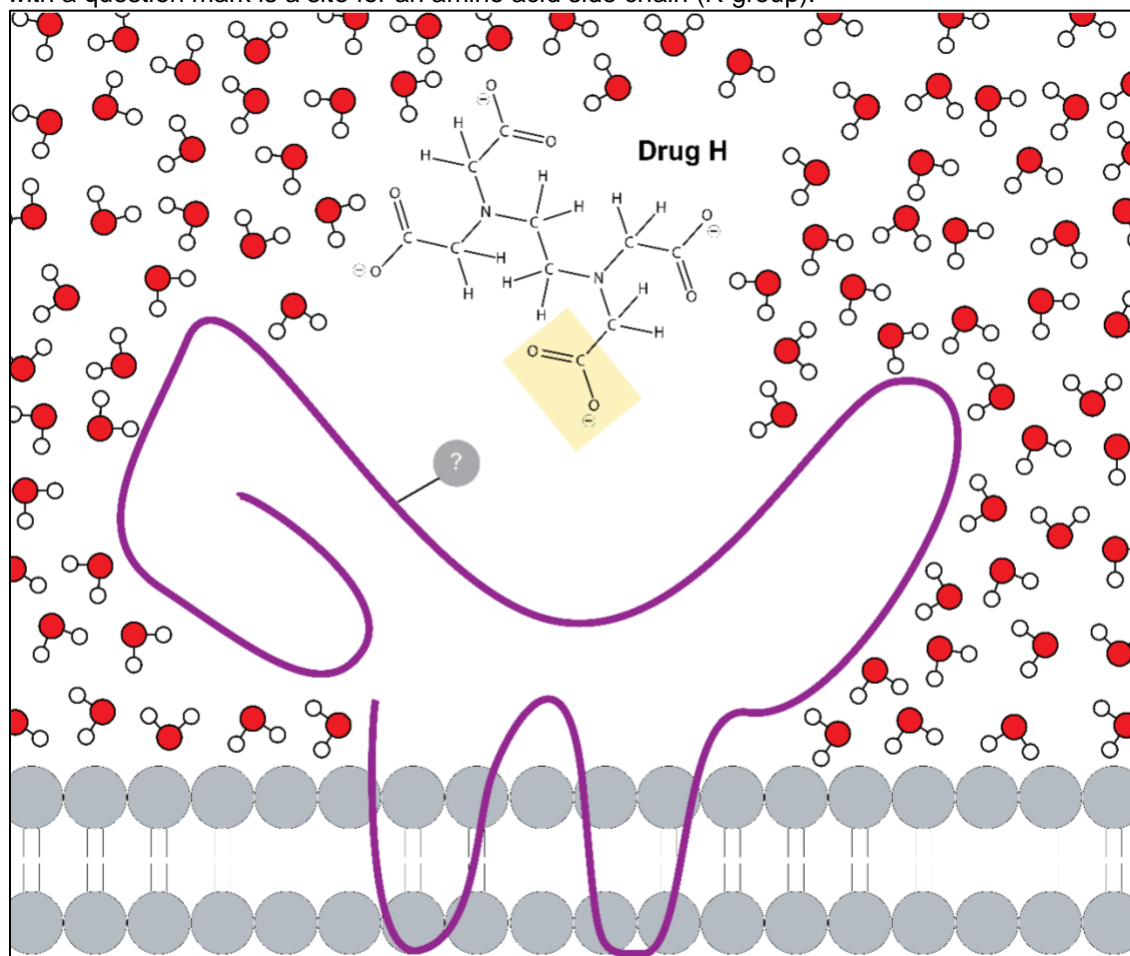


Amino Acid Side Chains:

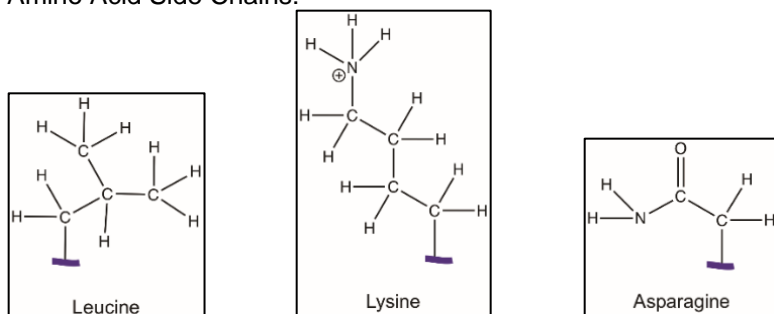


Which amino acid would interact non-covalently with the yellow highlighted section of Drug M? Provide a scientific explanation describing how Drug M interacts non-covalently with the amino acid you selected. Be sure to describe how this interaction forms.

Below is a model of Drug H and a protein with which it may interact. The protein is located on the cell surface situated within the cell membrane and surrounded by water molecules (red and white). The environment has a pH of 7.4. The purple line represents the protein backbone, and the section labeled with a question mark is a site for an amino acid side chain (R group).



Amino Acid Side Chains:



Which amino acid would interact non-covalently with the yellow highlighted section of Drug H? Provide a scientific explanation describing how Drug H interacts non-covalently with the amino acid you selected. Be sure to describe how this interaction forms.

## Analytical Codebooks

## Near Transfer Analytical Codebooks

### Protein X – Valine Substitution Codebook

Code #	Code Description
1	<p><b>General comparison of amino acids</b></p> <ul style="list-style-type: none"> <li>• Chemical properties are compared; there is some difference/similarity IN GENERAL               <ul style="list-style-type: none"> <li>• Appearance, atoms, size, electronegativity or structure                   <ul style="list-style-type: none"> <li>○ <i>“The hydrogen bonding that typically would occur between these two side chains would no longer be able to occur if serine was substituted for valine because valine does not have a hydrogen atom that can readily participate in this interaction.”</i></li> <li>○ <i>“The hydrogen attached to the oxygen in serine will be gone. The other hydrogens in valine are all attached to carbons.”</i></li> <li>○ <i>“This would happen because these 2 exhibit very similar chemical properties”</i></li> </ul> </li> </ul> </li> <li>• Double-coding with codes 2-7 is okay IF specific differences are ALSO mentioned</li> </ul>
2	<p><b>Serine categorized correctly</b></p> <p>Level 1 – polar</p> <p>Level 2 – polar <i>and</i> partially charged/dipole <i>or</i> permanently charged</p> <p>Level 3 – polar <i>and</i> partially charged/dipole <i>and</i> permanently charged</p>
3	<p><b>Glutamine categorized correctly</b></p> <p>Level 1 – polar</p> <p>Level 2 – polar <i>and</i> partially charged/dipole <i>or</i> permanently charged</p> <p>Level 3 – polar <i>and</i> partially charged/dipole <i>and</i> permanently charged</p>
4	<p><b>Valine categorized correctly</b></p> <p>Level 1 – nonpolar/hydrophobic</p> <p>Level 2 – nonpolar <i>and</i> induced partial charge/dipole <i>or</i> temporarily charged</p> <p>Level 3 – nonpolar <i>and</i> induced partial charge/dipole <i>and</i> temporarily charged</p>
5	<p><b>Serine categorized incorrectly</b></p> <ul style="list-style-type: none"> <li>• Non-polar or hydrophobic</li> <li>• Positively charged (overall)</li> <li>• Charged (overall)</li> <li>• More/less polar</li> <li>• Do NOT use this for “uncharged”</li> </ul>
6	<p><b>Glutamine categorized incorrectly</b></p> <ul style="list-style-type: none"> <li>• Non-polar or hydrophobic</li> <li>• Positively charged (overall)</li> <li>• Charged (overall)</li> <li>• More/less polar</li> <li>• Do NOT use this for “uncharged”</li> </ul>
7	<p><b>Valine categorized incorrectly</b></p> <ul style="list-style-type: none"> <li>• Polar           <ul style="list-style-type: none"> <li>○ <i>“the CH3 bonds are polar”</i></li> </ul> </li> <li>• More/less polar</li> </ul>

8	<p><b>Electronegativity of specific atoms discussed</b></p> <p>For Serine:</p> <ul style="list-style-type: none"> <li>• Hydrogen is less electronegative</li> <li>• Oxygen is more electronegative</li> </ul> <p>For Glutamine:</p> <ul style="list-style-type: none"> <li>• Carbon is less electronegative</li> <li>• Oxygen is more electronegative</li> </ul> <p>For Valine:</p> <ul style="list-style-type: none"> <li>• Neither carbon nor hydrogen are electronegative; no difference in electronegativities <ul style="list-style-type: none"> <li>• Do NOT count references to chemical groups, i.e. “stable CH3/methyl” would not receive this code</li> </ul> </li> </ul> <p>“Serine allows for hydrogen bonding because there is a hydrogen on the molecule which is attached to an electronegative atom.”</p> <p>“The new interaction would be hydrogen bonding with glutamine because the difference in electronegativity causes partial charges to occur which causes the hydrogen off the oxygen of the mutated R-group to be attracted to the oxygen of serine.”</p> <p>NOTE – can receive this code without amino acid category codes (2-7).</p>
9	<p><b>Given interaction would no longer occur after substitution</b></p> <p>Do NOT double-code simply because other codes about new interactions apply</p> <ul style="list-style-type: none"> <li>• Literal statements <ul style="list-style-type: none"> <li>○ “Hydrogen bonding would no longer occur.”</li> <li>○ “The reaction (read, ‘interaction’) would no longer be able to take place.”</li> <li>○ “The bond is disrupted”</li> </ul> </li> <li>• Use code 15 for statements regarding the ABSENCE of any new interaction</li> <li>• “instead of” and “change to” statements do not qualify for this code</li> </ul>
10	<p><b>Valine shape/size will affect the interaction</b></p>
11	<p><b>Valine and glutamine could interact – correct</b></p> <p>NOT for hydrogen bonds (see code 14)</p> <ul style="list-style-type: none"> <li>• Van der Waals interactions</li> <li>• London dispersion forces</li> <li>• Dipole-induced dipole interaction</li> <li>• Methyl and carbonyl O (or N) could interact <ul style="list-style-type: none"> <li>• Through the methyl/non-polar groups of valine</li> </ul> </li> </ul> <p>NOTE: assume if they say “new interaction”, then they mean between valine and glutamine</p>
12	<p><b>Valine could interact with another residue</b></p> <ul style="list-style-type: none"> <li>• Leucine, hydrophobic core, or a non-polar residue not shown</li> </ul> <p>NOTE: must be specific about what valine will interact with in order to receive this code</p>
13	<p><b>Glutamine could interact with another residue or water</b></p>
14	<p><b>Valine and glutamine could interact through a hydrogen bond</b></p> <p>Do NOT also apply code 11</p> <ul style="list-style-type: none"> <li>• Hydrogen bond could still be intact <ul style="list-style-type: none"> <li>○ “ There are still hydrogens that can be bonded”</li> </ul> </li> </ul> <p>Through the methyl/non-polar groups of valine</p>
15	<p><b>New interaction predicted incorrectly</b></p> <ul style="list-style-type: none"> <li>• Incorrect predictions other than hydrogen bonding <ul style="list-style-type: none"> <li>○ “An ionic bond may form because of the increased differences in electronegativity”</li> </ul> </li> <li>• No interaction would occur after substitution (lack or absence of an interaction) <ul style="list-style-type: none"> <li>○ “There is no new non-covalent interaction”</li> <li>○ “No interaction would occur because one is polar and one is non-polar”</li> <li>○ “The amino acid cannot interact with anything.”</li> </ul> </li> </ul>
16	<p><b>Structure/folding/function affected or NOT affected by valine shape and/or size</b></p>
17	<p><b>Structure/folding/function affected or NOT affected by mutation and/or new interactions</b></p>



18	<b>Contradicting without a resolution</b> Do NOT use if contradiction is resolved
19	<b>Need for empirical evidence</b> <ul style="list-style-type: none"> <li>• “more info” does not count, but “more scientific info” does count.</li> </ul>
20	<b>Given interaction (hydrogen bond) identified correctly</b>
21	<b>Given interaction identified incorrectly</b> <ul style="list-style-type: none"> <li>• Anything but a hydrogen bond.</li> </ul>
22	<b>Mechanism for existing interaction described correctly</b> <i>“attraction due to opposite charges”</i> NOTE: must use the word attract to receive this code
23	<b>Mechanism for new interaction(s) described correctly</b> <i>“attraction due to opposite charges”</i> NOTE: must use the word attract to receive this code
24	<b>Mechanism for existing interaction described incorrectly</b> <i>“repulsion”</i> <ul style="list-style-type: none"> <li>• Residues would repel each other <ul style="list-style-type: none"> <li>○ <i>“... there would be a great deal of repulsion between the two compounds because both are nonpolar.”</i></li> </ul> </li> </ul>
25	<b>Mechanism for new interaction(s) described incorrectly</b> <i>“repulsion”</i> <ul style="list-style-type: none"> <li>• Residues would repel each other <ul style="list-style-type: none"> <li>○ <i>“... there would be a great deal of repulsion between the two compounds because both are nonpolar.”</i></li> </ul> </li> </ul>

**Protein X – Isoleucine Substitution Codebook**

Code #	Code Description
1	<b>General comparison of amino acids</b> <ul style="list-style-type: none"> <li>Chemical properties are compared; there is some difference/similarity IN GENERAL <ul style="list-style-type: none"> <li>Appearance, atoms, size, electronegativity or structure <ul style="list-style-type: none"> <li><i>"Isoleucine is an isomer of leucine."</i></li> <li><i>"the molecules differ in orientation"</i></li> </ul> </li> <li>Polarity <ul style="list-style-type: none"> <li><i>"Leucine and isoleucine have the same polarity."</i></li> </ul> </li> </ul> </li> <li>Double-coding with codes 2-5 is okay IF specific similarities are ALSO mentioned</li> </ul>
2	<b>Leucine categorized correctly</b> Level 1 – nonpolar/hydrophobic Level 2 – nonpolar <i>and</i> induced partial charge/dipole <i>or</i> temporarily charged Level 3 – nonpolar <i>and</i> induced partial charge/dipole <i>and</i> temporarily charged
3	<b>Isoleucine categorized correctly</b> Level 1 – nonpolar/hydrophobic Level 2 – nonpolar <i>and</i> induced partial charge/dipole <i>or</i> temporarily charged Level 3 – nonpolar <i>and</i> induced partial charge/dipole <i>and</i> temporarily charged
4	<b>Leucine categorized incorrectly</b>
5	<b>Isoleucine categorized incorrectly</b>
6	<b>Electronegativity of specific atoms discussed</b> <ul style="list-style-type: none"> <li>Neither carbon nor hydrogen are electronegative; no difference in electronegativities Do NOT count references to chemical groups, i.e. <i>"stable CH3/methyl"</i> would not receive this code. Must specify atoms.</li> </ul> NOTE – can receive this code without amino acid category codes (2-5).
7	<b>Confuse hydrophobic amino acid with hydrophobic effect</b>
8	<b>Given interaction would no longer occur after substitution</b> <ul style="list-style-type: none"> <li>Do NOT double-code simply because other codes about new interactions apply</li> <li>Literal statements <ul style="list-style-type: none"> <li><i>"Ion pairing would no longer occur."</i></li> <li><i>"The reaction (read, 'interaction') would no longer be able to take place."</i></li> <li><i>"The bond is disrupted"</i></li> </ul> </li> <li>Use code 11 for statements regarding the ABSENCE of any new interaction</li> <li>"instead of" and "change to" statements do not qualify for this code</li> </ul>
9	<b>A new or different van der Waals interaction is formed</b> <ul style="list-style-type: none"> <li>Okay to say "the interaction" instead of van der Waals</li> <li>Between isoleucine and a lower leucine (see Note)</li> </ul> NOTE – Interaction: <ul style="list-style-type: none"> <li>Anything going on with the three residues</li> <li>Do not differentiate between isoleucine with left leucine vs. isoleucine with right leucine</li> <li><i>"The interaction will remain the same"</i> counts for this code if they also got code 16</li> </ul>
10	<b>Isoleucine shape/size will affect or NOT affect the interaction</b> <ul style="list-style-type: none"> <li>a general acknowledgement that size may have an effect qualifies for this code</li> <li>Explanation of what causes a new van der Waals interaction (code 9)</li> <li>Between isoleucine and a lower leucine (see Note 1) <ul style="list-style-type: none"> <li><i>"This mutation would affect the distance of the bottom left leucine from the isoleucine methyl group. This mutation might get rid of or severely weaken the bond between these two."</i></li> <li><i>"... the interaction with the molecule to the left will be affected due to the distance between the two (interacting) compounds."</i></li> </ul> </li> </ul>

11	<p><b>New interaction predicted incorrectly</b></p> <ul style="list-style-type: none"> <li>• Incorrect predictions other than LDF or VDW <ul style="list-style-type: none"> <li>○ <i>"An ionic bond may form because of the increased differences in electronegativity"</i></li> </ul> </li> <li>• Residues would repel each other <ul style="list-style-type: none"> <li>○ <i>"... there would be a great deal of repulsion between the two compounds because both are nonpolar."</i></li> </ul> </li> <li>• No interaction would occur after substitution <ul style="list-style-type: none"> <li>○ <i>"There is no non-covalent interaction"</i></li> </ul> </li> <li>• Don't code unintelligible answers that can't be interpreted as definitely incorrect</li> </ul>
12	<b>Structure/folding/function affected or NOT affected by isoleucine shape and/or size</b>
13	<p><b>Structure/folding/function affected or NOT affected by mutation and/or new interactions</b></p> <p>Capture both affected and not affected answers</p>
14	<b>Contradicting without a resolution</b>
15	<p><b>Need for empirical evidence</b></p> <ul style="list-style-type: none"> <li>• "more info" does not count, but "more scientific info" does count.</li> </ul>
16	<p><b>Given interaction (van der Waals) identified correctly</b></p> <ul style="list-style-type: none"> <li>• Induced dipole – induced dipole, London dispersion force, van der Waals</li> </ul>
17	<p><b>Given interaction identified incorrectly</b></p> <p>Anything but van der Waals, London dispersion force, or induced dipole - induced dipole</p>
18	<p><b>Mechanism for existing interaction described correctly</b></p> <p><i>"attraction due to opposite charges"</i></p> <p>NOTE: must use the word attract to receive this code</p>
19	<p><b>Mechanism for new interaction(s) described correctly</b></p> <p><i>"attraction due to opposite charges"</i></p> <p>NOTE: must use the word attract to receive this code</p>
20	<p><b>Mechanism for existing interaction described incorrectly</b></p> <p><i>"repulsion"</i></p> <ul style="list-style-type: none"> <li>• Residues would repel each other</li> </ul> <p><i>"... there would be a great deal of repulsion between the two compounds because both are nonpolar."</i></p>
21	<p><b>Mechanism for new interaction(s) described incorrectly</b></p> <p><i>"repulsion"</i></p> <ul style="list-style-type: none"> <li>• Residues would repel each other</li> </ul> <p><i>"... there would be a great deal of repulsion between the two compounds because both are nonpolar."</i></p>

**Protein X – Alanine Substitution Codebook**

<b>Code #</b>	<b>Code Description</b>
1	<p><b>General comparison of amino acids</b></p> <ul style="list-style-type: none"> <li>• Chemical properties are compared; there is some difference/similarity IN GENERAL <ul style="list-style-type: none"> <li>• Appearance, atoms, size, electronegativity, or structure</li> <li>• Double-coding with codes 2-7 is okay IF specific differences are ALSO mentioned</li> </ul> </li> </ul>
2	<p><b>Aspartate categorized correctly</b></p> <p>Level 1 – polar or charged  Level 2 – polar or charged <i>and</i> fully charged <i>or</i> permanently charged  Level 3 – polar or charged <i>and</i> fully charged <i>and</i> permanently charged</p>
3	<p><b>Lysine categorized correctly</b></p> <p>Level 1 – polar or charged  Level 2 – polar or charged <i>and</i> fully charged <i>or</i> permanently charged  Level 3 – polar or charged <i>and</i> fully charged <i>and</i> permanently charged</p>
4	<p><b>Alanine categorized correctly</b></p> <p>Level 1 – nonpolar/hydrophobic  Level 2 – nonpolar <i>and</i> induced partial charge/dipole <i>or</i> temporarily charged  Level 3 – nonpolar <i>and</i> induced partial charge/dipole <i>and</i> temporarily charged</p>
5	<p><b>Aspartate categorized incorrectly</b></p> <ul style="list-style-type: none"> <li>• Non-polar or hydrophobic</li> <li>• Uncharged</li> </ul>
6	<p><b>Lysine categorized incorrectly</b></p> <ul style="list-style-type: none"> <li>• Non-polar or hydrophobic</li> <li>• Uncharged</li> </ul>
7	<p><b>Alanine categorized incorrectly</b></p> <ul style="list-style-type: none"> <li>• Partially charged</li> <li>• Hydrogen is partially positively charged</li> </ul>
8	<p><b>Electronegativity of specific atoms discussed</b></p> <p>For Aspartate:</p> <ul style="list-style-type: none"> <li>• Carbon is less electronegative</li> <li>• Oxygen is more electronegative</li> </ul> <p>For Lysine:</p> <ul style="list-style-type: none"> <li>• Hydrogen is less electronegative</li> <li>• Nitrogen is more electronegative</li> </ul> <p>For Alanine:</p> <ul style="list-style-type: none"> <li>• Neither carbon nor hydrogen are electronegative; no difference in electronegativities <ul style="list-style-type: none"> <li>• Do NOT count references to chemical groups, i.e. “<i>stable CH3/methyl</i>” would not receive this code</li> </ul> </li> </ul> <p>NOTE – can receive this code without amino acid category codes (2-4).</p>
9	<p><b>Given interaction would no longer occur after substitution</b></p> <ul style="list-style-type: none"> <li>• Do NOT double-code simply because other codes about new interactions apply</li> <li>• Literal statements <ul style="list-style-type: none"> <li>○ “<i>Ion pairing would no longer occur.</i>”</li> <li>○ “<i>The reaction (read, ‘interaction’) would no longer be able to take place.</i>”</li> <li>○ “<i>The reaction (read, ‘interaction’) would not form between the alanine and the lysine.</i>”</li> <li>○ “<i>The bond is disrupted</i>”</li> </ul> </li> <li>• Use code 15 for statements regarding the ABSENCE of any new interaction</li> <li>• “instead of” and “change to” statements do not qualify for this code</li> </ul>
10	<p><b>Alanine shape and/or size will affect or NOT affect the interaction</b></p>

11	<p><b>Alanine and lysine could interact - correct</b></p> <ul style="list-style-type: none"> <li>• NOT for ion pairing (see code 16)</li> <li>• Interaction MUST be named</li> <li>• Assume named interaction is between alanine and lysine unless otherwise specified</li> <li>• Ion-induced dipole interaction</li> <li>• Van der Waals interaction</li> </ul>
12	<p><b>Alanine could interact with another residue</b></p> <ul style="list-style-type: none"> <li>• Leucine, hydrophobic core, or a non-polar residue not shown</li> <li>• Van der Waals interaction</li> <li>• London dispersion forces</li> </ul>
13	<p><b>Lysine could interact with another residue or water</b></p> <ul style="list-style-type: none"> <li>• Note: It's okay for students to call this hydrogen bonding, ion-dipole interaction</li> </ul>
14	<p><b>Ion pairing could still be intact or not affected</b></p> <ul style="list-style-type: none"> <li>• Explanation of why intact or not affected, beyond answer for part a.</li> <li>• Do NOT also apply code 11</li> <li>• Between alanine and lysine</li> <li>• Through the methyl/non-polar groups of alanine</li> </ul>
15	<p><b>New interaction predicted incorrectly</b></p> <ul style="list-style-type: none"> <li>• Incorrect predictions other than ion pairing (e.g., hydrogen bonding between alanine and lysine, repelling each other)</li> <li>• No interaction would occur after substitution <ul style="list-style-type: none"> <li>○ <i>"There is no new non-covalent interaction"</i></li> <li>○ <i>"... no bond will form because van der waals interactions are only bonded between neutral atoms. Since there is a positively charged nitrogen, there will not be any interaction taking place."</i></li> </ul> </li> </ul>
16	<b>Structure/folding/function affected or NOT affected by alanine shape and/or size</b>
17	<b>Structure/folding/function affected or NOT affected by mutation and/or new interactions</b>
18	<p><b>Contradicting without a resolution</b></p> <ul style="list-style-type: none"> <li>○ <i>"I do not see any new non-covalent interactions that might occur. There maybe van Der waals forces interacting because of the nonpolar group of alanine."</i></li> </ul>
19	<p><b>Need for empirical evidence</b></p> <ul style="list-style-type: none"> <li>• "more info" does not count, but "more scientific info" does count.</li> </ul>
20	<p><b>Given interaction (ion pairing) identified correctly</b></p> <ul style="list-style-type: none"> <li>• other acceptable terms: ionic interaction, ionic bonding, ionic bond, ion pair, ion-ion pair/interaction, ionic attraction</li> </ul>
21	<p><b>Given interaction identified incorrectly</b></p> <ul style="list-style-type: none"> <li>• Anything but ion pairing</li> </ul>
22	<p><b>Mechanism for existing interaction described correctly</b></p> <p><i>"attraction due to opposite charges"</i></p> <p>NOTE: must use the word attract to receive this code</p>
23	<p><b>Mechanism for new interaction(s) described correctly</b></p> <p><i>"attraction due to opposite charges"</i></p> <p>NOTE: must use the word attract to receive this code</p>
24	<p><b>Mechanism for existing interaction described incorrectly</b></p> <p><i>"repulsion"</i></p> <ul style="list-style-type: none"> <li>• Residues would repel each other</li> </ul> <p><i>"... there would be a great deal of repulsion between the two compounds because both are nonpolar."</i></p>
25	<p><b>Mechanism for new interaction(s) described incorrectly</b></p> <p><i>"repulsion"</i></p> <ul style="list-style-type: none"> <li>• Residues would repel each other</li> </ul> <p><i>"... there would be a great deal of repulsion between the two compounds because both are nonpolar."</i></p>

## Far Transfer Analytical Codebooks

### Drug S Codebook

Code #	Code Description
1	<b>General comparison of amino acids/drug (chemical composition, polarity)</b>
2	<b>Electronegativity of specific atoms discussed</b> <ul style="list-style-type: none"> <li>• O, N are more electronegative than C, H</li> <li>• C and H have no real difference in electronegativity</li> </ul>
3	<b>Comparison of strength of intermolecular forces</b> <ul style="list-style-type: none"> <li>• van der Waals, induced dipole-induced dipole &lt; dipole-induced dipole &lt; dipole-dipole, hydrogen bond &lt; ion-induced dipole &lt; ion-dipole &lt; ion-ion pairing</li> <li>• Interactions being compared need to be clearly stated</li> </ul>
4	<b>Need for empirical evidence</b>
5	<b>Contradicting self</b> <ul style="list-style-type: none"> <li>• Without resolution</li> </ul>
6	<b>Categorizing chosen amino acid correctly</b> For Leucine: nonpolar with induced partial temporary charges, For Asparagine: polar with partial permanent charges For Lysine: polar with full permanent charge <ul style="list-style-type: none"> <li>• Level 1 – category</li> <li>• Level 2 – category AND magnitude OR permanency described</li> <li>• Level 3 – category AND magnitude AND permanency described</li> </ul>
7	<b>Categorizing chosen amino acid incorrectly</b>
8	<b>Characterizing highlighted portion of drug correctly</b> Nonpolar methyl with induced partial temporary charges <ul style="list-style-type: none"> <li>• Level 1 – category</li> <li>• Level 2 – category AND magnitude OR permanency described</li> <li>• Level 3 – category AND magnitude AND permanency described</li> </ul>
9	<b>Characterizing highlighted portion of drug incorrectly</b>
10	<b>Predicting interaction correctly</b> van der Waals between Leucine and Drug Dipole-induced dipole between Asparagine and Drug (or vdw, but must name groups involved) Ion-induced dipole between Lysine and Drug (or vdw, but must name groups involved) <ul style="list-style-type: none"> <li>• MUST name interaction</li> </ul>
11	<b>Predicting interaction incorrectly</b>
12	<b>Describing how interaction will form correctly (mechanistic reasoning)</b> <i>“Attraction due to opposite charges”</i> van der Waals: attraction of oppositely signed induced temporary dipoles/charges on two nonpolar molecules <u>Dipole-induced dipole</u> : attraction between charge on a dipole and the opposite signed induced charge on a nonpolar molecule <u>Ion-induced dipole</u> : attraction between fully charged species and the opposite signed induced charge on a nonpolar molecule
13	<b>Describing how interaction will form incorrectly</b> <ul style="list-style-type: none"> <li>• <i>“repulsion”</i></li> </ul>

## Drug M Codebook

Code #	Code Description
1	<b>General comparison of amino acids/drug (chemical composition, polarity)</b>
2	<b>Electronegativity of specific atoms discussed</b> <ul style="list-style-type: none"> <li>O, N are more electronegative than C, H</li> <li>C and H have no real difference in electronegativity</li> </ul>
3	<b>Comparison of strength of intermolecular forces</b> <ul style="list-style-type: none"> <li>van der Waals, induced dipole-induced dipole &lt; dipole-induced dipole &lt; dipole-dipole, hydrogen bond &lt; ion-induced dipole &lt; ion-dipole &lt; ion-ion pairing</li> <li>Interactions being compared need to be clearly stated</li> </ul>
4	<b>Need for empirical evidence</b>
5	<b>Contradicting self</b> <ul style="list-style-type: none"> <li>Without resolution</li> </ul>
6	<b>Categorizing chosen amino acid correctly</b> For Leucine: nonpolar with induced partial temporary charges, For Asparagine: polar with partial permanent charges For Lysine: polar with full permanent charge <ul style="list-style-type: none"> <li>Level 1 – category</li> <li>Level 2 – category AND magnitude OR permanency described</li> <li>Level 3 – category AND magnitude AND permanency described</li> </ul>
7	<b>Categorizing chosen amino acid incorrectly</b>
8	<b>Characterizing highlighted portion of drug correctly</b> Polar hydroxyl with partial permanent charges (O is partially negative, H is partially positive) <ul style="list-style-type: none"> <li>Level 1 – category</li> <li>Level 2 – category AND magnitude OR permanency described</li> <li>Level 3 – category AND magnitude AND permanency described</li> </ul>
9	<b>Characterizing highlighted portion of drug incorrectly</b>
10	<b>Predicting interaction correctly</b> Dipole-induced dipole between drug and Leucine Dipole-dipole/hydrogen bond between drug and Asparagine Ion-dipole between Lysine and drug <ul style="list-style-type: none"> <li>MUST name interaction</li> </ul>
11	<b>Predicting interaction incorrectly</b>
12	<b>Describing how interaction will form correctly (mechanistic reasoning)</b> <i>“attraction due to opposite charges”</i> Dipole-induced dipole: attraction between partially charged species and the oppositely signed induced temporary dipole/charge on a nonpolar molecule Dipole-dipole/hydrogen bond: attraction between two oppositely partially charged species Ion-dipole: attraction between fully charged ionic species and the oppositely signed partial charge on a polar molecule
13	<b>Describing how interaction will form incorrectly</b> <i>“repulsion”</i>

## Drug H Codebook

Code #	Code Description
1	<b>General comparison of amino acids/drug (chemical composition, polarity)</b>
2	<b>Electronegativity of specific atoms discussed</b> <ul style="list-style-type: none"> <li>O, N are more electronegative than C, H</li> <li>C and H have no real difference in electronegativity</li> </ul>
3	<b>Comparison of strength of intermolecular forces</b> <ul style="list-style-type: none"> <li>van der Waals, induced dipole-induced dipole &lt; dipole-induced dipole &lt; dipole-dipole, hydrogen bond &lt; ion-induced dipole &lt; ion-dipole &lt; ion-ion pairing</li> <li>Interactions being compared need to be clearly stated</li> </ul>
4	<b>Need for empirical evidence</b>
5	<b>Contradicting self</b> <ul style="list-style-type: none"> <li>Without resolution</li> </ul>
6	<b>Categorizing chosen amino acid correctly</b> For Leucine: nonpolar with induced partial temporary charges, For Asparagine: polar with partial permanent charges For Lysine: polar with full permanent charge <ul style="list-style-type: none"> <li>Level 1 – category</li> <li>Level 2 – category AND magnitude OR permanency described</li> <li>Level 3 – category AND magnitude AND permanency described</li> </ul>
7	<b>Categorizing chosen amino acid incorrectly</b>
8	<b>Characterizing highlighted portion of drug correctly</b> Polar carboxylate with full permanent negative charge on O <ul style="list-style-type: none"> <li>Level 1 – category</li> <li>Level 2 – category AND magnitude OR permanency described</li> <li>Level 3 – category AND magnitude AND permanency described</li> </ul>
9	<b>Characterizing highlighted portion of drug incorrectly</b>
10	<b>Predicting interaction correctly</b> Ion-induced dipole between drug and Leucine Ion-dipole between drug and Asparagine Ion-ion between drug and Lysine <ul style="list-style-type: none"> <li>MUST name interaction</li> </ul>
11	<b>Predicting interaction incorrectly</b>
12	<b>Describing how interaction will form correctly (mechanistic reasoning)</b> <i>“attraction due to opposite charges”</i> Ion-induced dipole: attraction between fully charged ionic species and the oppositely signed induced temporary dipole/charge on a nonpolar molecule Ion-dipole: attraction between fully charged ionic species and the oppositely signed partial charge on a polar molecule Ion-pairing: attraction between two oppositely fully charged species
13	<b>Describing how interaction will form incorrectly</b> <i>“repulsion”</i>



## Scoring Rubrics

## Near Transfer Scoring Rubrics

### Protein X – Valine Substitution Rubric

Evidence (up to 3 pts)						Prediction (up to 3 pts)		Linkage (up to 1 pt)	
Categorize given amino acids	pts	Categorize new amino acid	pts	Identify given interaction	pts	Predict new interaction	pts	Linking evidence and prediction	pts
Ser and Gln both categorized correctly	1	Val categorized correctly	1	Hydrogen bond identified correctly	1	High quality prediction	3	At least one piece of evidence and a prediction made	1
Only Ser categorized	1	Different	0.5	Mixed ideas	0.5	Low quality prediction	2	Evidence or prediction missing	0
Only Gln categorized	1	Mixed ideas	0.5	Missing	0	Mixed ideas	1		
Mixed ideas	0.5	Missing	0	Interaction identified incorrectly	0	Missing	0		
Missing	0	Val categorized incorrectly	0			Unacceptable hydrogen bond prediction	0		
Ser or Gln categorized incorrectly	0					Other unacceptable prediction	0		

**Protein X – Isoleucine Substitution Rubric**

Evidence (up to 3 pts)						Prediction (up to 3 pts)		Linkage (up to 1 pt)	
Categorize given amino acids	pts	Categorize new amino acid	pts	Identify given interaction	pts	Predict new interaction	pts	Linking evidence and prediction	pts
Leu categorized correctly	1	Ile categorized correctly	1	van der Waals identified correctly	1	High quality prediction	3	At least one piece of evidence and a prediction made	1
Mixed ideas	0.5	Different	0.5	Mixed ideas	0.5	Low quality prediction	2	Evidence or prediction missing	0
Missing	0	Mixed ideas	0.5	Missing	0	Mixed ideas	1		
Leu categorized incorrectly	0	Missing	0	Interaction identified incorrectly	0	Missing	0		
		Ile categorized incorrectly	0			Unacceptable prediction	0		

### Protein X – Alanine Substitution Rubric

Evidence (up to 3 pts)						Prediction (up to 3 pts)		Linkage (up to 1 pt)	
Categorize given amino acids	pts	Categorize new amino acid	pts	Identify given interaction	pts	Predict new interaction	pts	Linking evidence and prediction	pts
Asp and Lys both categorized correctly	1	Ala categorized correctly	1	Ion pairing identified correctly	1	High quality predictions	3	At least one piece of evidence and a prediction made	1
Only Asp categorized	1	Different	0.5	Mixed ideas	0.5	Low quality predictions	2	Evidence or prediction missing	0
Only Lys categorized	1	Mixed ideas	0.5	Missing	0	Mixed ideas	1		
Mixed ideas	0.5	Missing	0	Interaction identified incorrectly	0	Missing	0		
Missing	0	Ala categorized incorrectly	0			Unacceptable ion pairing prediction	0		
Asp or Lys categorized incorrectly	0					Other unacceptable prediction	0		

## Far Transfer Scoring Rubrics

### Drug S Rubric

Evidence (up to 3 pts)					Prediction (up to 3 pts)				Linkage (up to 1 pt)		
Categorize Drug S	pts	Categorize chosen amino acid	pts	Mechanistic Reasoning	pts	Predict new interaction	pts	Chosen amino acid	pts	Linking evidence and prediction	pts
Correctly (8)	1	Correctly (6)	1	Described how interaction will form correctly (12)	1	Predict interaction correctly (10)	2	Leu	1	At least one piece of evidence and a prediction made	1
Mixed (8 and 9)	0.5	General Comparison (1)	0.5	Mixed (12 and 13)	0.5	Mixed (10 and 11)	1	Lys	0	Evidence or prediction missing	0
Missing	0	Mixed (1 or 6 and 7)	0.5	Missing	0	Missing	0	Asn	0		
Incorrectly (9)	0	Missing	0	Incorrectly (13)	0	Incorrectly (11)	0				
		Incorrectly (7)	0								

Numbers in parentheses correspond to code numbers in codebook.

### Drug M Rubric

Evidence (up to 3 pts)					Prediction (up to 3 pts)				Linkage (up to 1 pt)		
Categorize Drug S	pts	Categorize chosen amino acid	pts	Mechanistic Reasoning	pts	Predict new interaction	pts	Chosen amino acid	pts	Linking evidence and prediction	pts
Correctly (8)	1	Correctly (6)	1	Described how interaction will form correctly (12)	1	Predict interaction correctly (10)	2	Asn	1	At least one piece of evidence and a prediction made	1
Mixed (8 and 9)	0.5	General Comparison (1)	0.5	Mixed (12 and 13)	0.5	Mixed (10 and 11)	1	Lys	0	Evidence or prediction missing	0
Missing	0	Mixed (1 or 6 and 7)	0.5	Missing	0	Missing	0	Leu	0		
Incorrectly (9)	0	Missing	0	Incorrectly (13)	0	Incorrectly (11)	0				
		Incorrectly (7)	0								

Numbers in parentheses correspond to code numbers in codebook.

## Drug H Rubric

Evidence (up to 3 pts)					Prediction (up to 3 pts)				Linkage (up to 1 pt)		
Categorize Drug S	pts	Categorize chosen amino acid	pts	Mechanistic Reasoning	pts	Predict new interaction	pts	Chosen amino acid	pts	Linking evidence and prediction	pts
Correctly (8)	1	Correctly (6)	1	Described how interaction will form correctly (12)	1	Predict interaction correctly (10)	2	Lys	1	At least one piece of evidence and a prediction made	1
Mixed (8 and 9)	0.5	General Comparison (1)	0.5	Mixed (12 and 13)	0.5	Mixed (10 and 11)	1	Leu	0	Evidence or prediction missing	0
Missing	0	Mixed (1 or 6 and 7)	0.5	Missing	0	Missing	0	Asn	0		
Incorrectly (9)	0	Missing	0	Incorrectly (13)	0	Incorrectly (11)	0				
		Incorrectly (7)	0								

Numbers in parentheses correspond to code numbers in codebook.