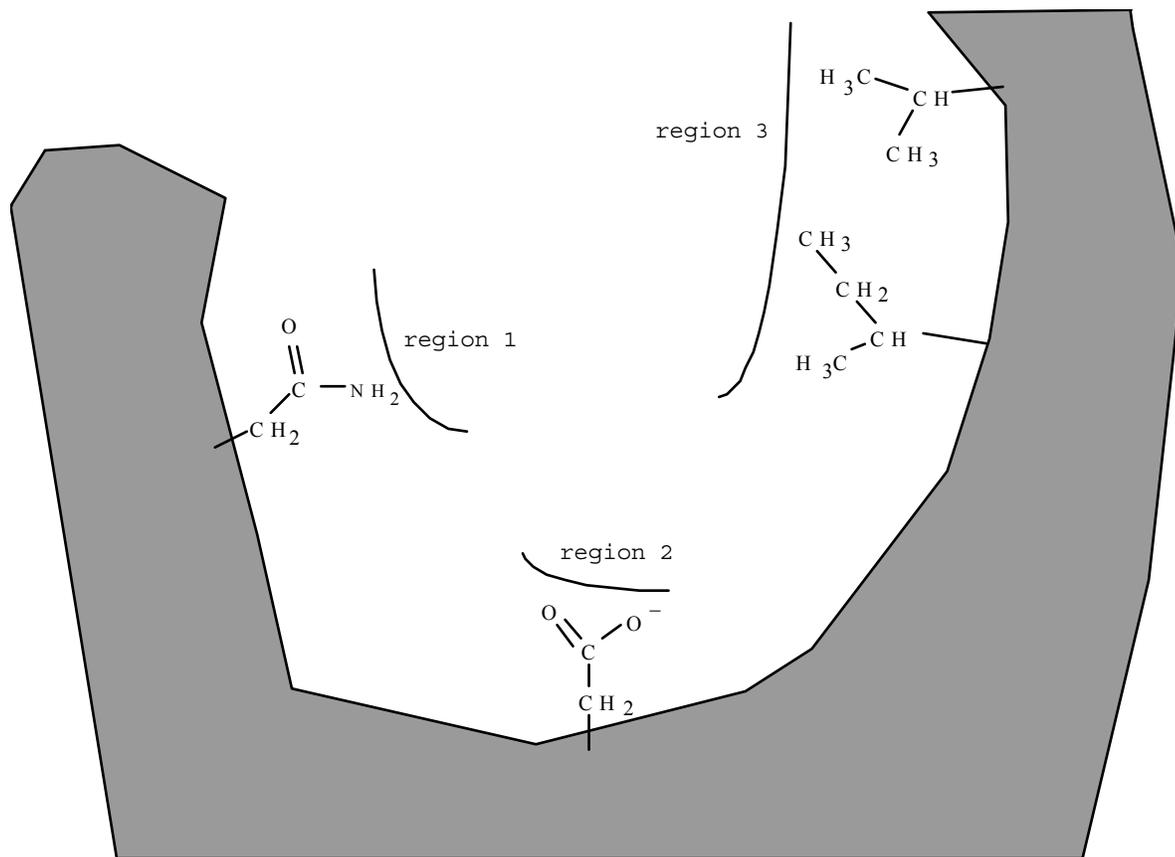


Question 3 (25 points)

A drug company has isolated the protein shown in schematic below.



a) What amino acid is present in region 2?

b) The substrate for this protein has not been identified. Given the diagram above...

i) What is the strongest interaction possible between the amino acid in region 1 and the substrate?

ii) What is the strongest interaction possible between the amino acid in region 2 and the substrate?

iii) What is the strongest interaction possible between the amino acids in region 3 and the substrate?

Question 3, continued

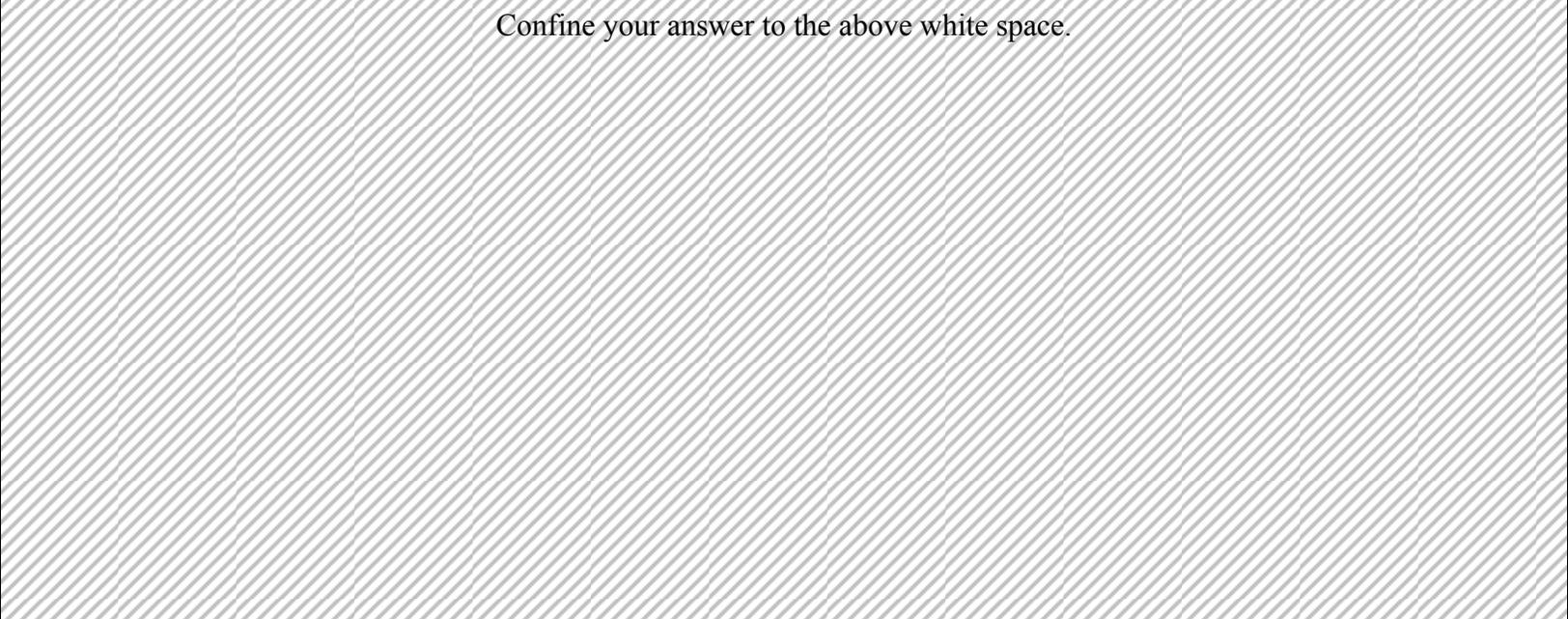
c) The drug company has asked you to design a protein that binds tightly in this pocket.

i) Would Alanine or Serine interact more strongly with region 1? Why?

ii) Would Lysine or Glutamic Acid interact more strongly with region 2? Why?

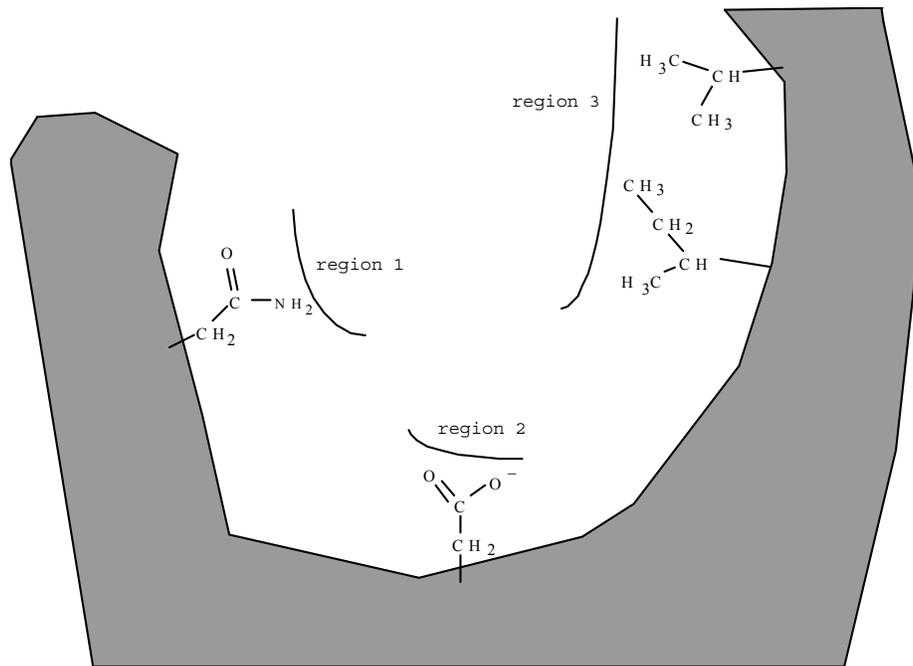
d) You design many proteins that bind tightly in this pocket. One of them has isoleucine associated with region 3. You substitute phenylalanine for isoleucine and find this prevents binding of this protein. Phenylalanine and isoleucine form the same kinds of interactions with the binding pocket, so why can't the phenylalanine version of the protein bind?

Confine your answer to the above white space.



Question 3 (25 points)

A drug company has isolated the protein shown in schematic below.



a) What amino acid is present in region 2? *Aspartic acid*

b) The substrate for this protein has not been identified. Given the diagram above...

i) What is the strongest interaction possible between the amino acid in region 1 and the substrate?

Hydrogen bonds.

ii) What is the strongest interaction possible between the amino acid in region 2 and the substrate?

Ionic bonds

iii) What is the strongest interaction possible between the amino acids in region 3 and the substrate?

van der Waals forces

c) The drug company has asked you to design a protein that binds tightly in this pocket.

i) Would Alanine or Serine interact more strongly with region 1? Why?

Serine, it is polar and can form hydrogen bonds with region 1. Alanine would only interact with van der Waals forces

ii) Would Lysine or Glutamic Acid interact more strongly with region 2? Why?

Lysine, it is (+) charged and can form ionic bonds with region 2. Glutamic acid is also (-) charged and would repel.

d) You design many proteins that bind tightly in this pocket. One of them has isoleucine associated with region 3. You substitute phenylalanine for isoleucine and find this prevents binding of this protein. Phenylalanine and isoleucine form the same kinds of interactions with the binding pocket, so why can't the phenylalanine version of the protein bind?
Phenylalanine has a large side chain that prevents the substrate from fitting into the pocket. Steric hinderence.