

**1. Hemoglobin allostery and oxygen transport (35 pts):**

(a; 10 pts) Briefly describe three steps, in terms of changes in protein and heme structure, in the allosteric induction of the R state of hemoglobin upon binding a molecule of O<sub>2</sub>. What one word describes the shape of the resulting binding curve?

(b; 25 pts: 5 pts each) For each of the following ligands, indicate whether it binds better to the R state or the T state of hemoglobin, and briefly describe the significance of the preference to physiological oxygen transport.

O<sub>2</sub> (Circle one: R T ) Significance:

H<sup>+</sup> (Circle one: R T ) Significance:

CO<sub>2</sub> (Circle one: R T ) Significance:

NO (Circle one: R T ) Significance:

BPG (Circle one: R T ) Significance:

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## 2. Protein folding and prions (25 pts):

(a; 9 pts) What is the molten globule in protein folding? How does the activity of chaperones in unfolding molten globules enhance the overall rate of folding to the native state?

(b; 8 pts) Name a protein folding disease. Give two possible general causes for disease arising from protein folding defects.

(c; 8 pts) Give two rationales for the prevalence of independently folding 100-200 residue domains in proteins. How might you identify domain boundaries, either experimentally or by sequence analysis (pick one)?

### 3. Protein sequence analysis and evolution (25 pts):

(a; 6 pts) The sequence below shows three segments of a protein region that binds retinol, a large hydrophobic ligand. Do you think the binding region is an  $\alpha$ -helix or a  $\beta$ -sheet? Explain your reasoning. (Exaggerated from the actual sequence given by Branden and Tooze.)

... Ile – Ala – Val – Glu – Phe – Ser – Val – Asp ...  
... Met – Ser – Ala – Thr – Val – Lys – Gly – Arg ...  
... Ala – Asp – Met – Val – Trp – Cys – Phe – Thr ...

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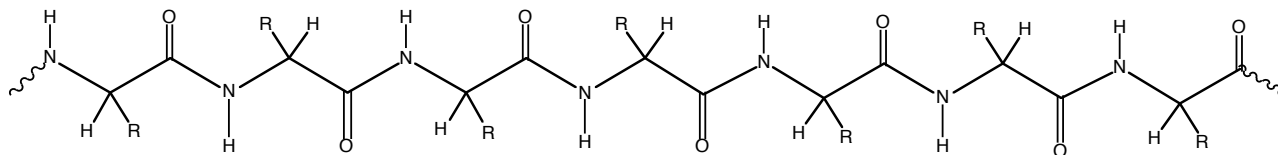
(b; 5 pts) Which is more conserved in evolution, primary sequence or tertiary structure? Why?

(c; 9 pts) How are protein sequences used in constructing phylogenetic trees? Why does the phylogeny of a protein sometimes not match up with the phylogeny of the organisms it inhabits?

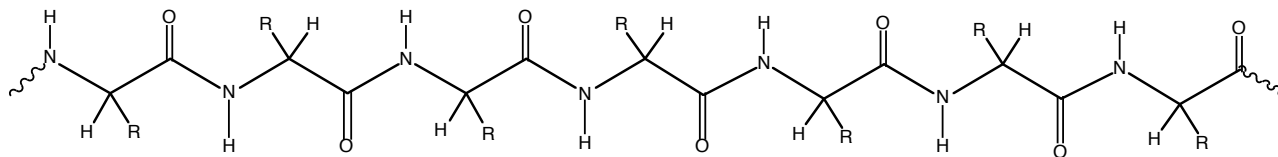
(d; 5 pts) How can the analysis of protein families improve homology searches? Name a program that extends BLAST in this way.

#### 4. Secondary structure (15 pts):

(a; 6 pts) On the extended peptide representation below, diagram the hydrogen bonding pattern of the  $\alpha$ -helix. In other words, draw in which three carbonyls are H-bonded to which three amides.



If you mess up, try again here:



(b; 5 pts) What is the number of residues per turn for the  $\alpha$ -helix? The  $i \rightarrow i \pm$  (some number) H-bonding pattern you diagrammed in (a) connects amino acids that are one above another along the direction of the helix axis. How can this be consistent with a non-integral number of residues per turn?

(c; 4 pts) Why does leucine have a greater propensity to be found in the  $\alpha$ -helix than isoleucine, whereas Ile has the greater  $\beta$ -sheet propensity of the two?

Score: 1. Hemoglobin allostery and oxygen transport (35 pts): \_\_\_\_\_

2. Protein folding and prions (25 pts): \_\_\_\_\_

3. Protein sequence analysis and evolution (25 pts): \_\_\_\_\_

4. Secondary structure (15 pts): \_\_\_\_\_

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**Total: out of 100** \_\_\_\_\_