

1. (23 pts) Amino acid structure and the peptide bond

(a; 5 pts) What is the **H-bonding pattern in an α -helix**? You don't need to draw the structure, just specify which atoms are H-bonded to each other. **Why is it important that all of the moieties involved are backbone atoms**, not side-chain atoms?

(b; 13 pts) Draw **Ile-Pro with a *cis* peptide bond**, in the ionization state observed at pH 7. Include C α stereochemistry and indicate the C β stereocenter on the dipeptide. **Why are X-Pro peptide bonds the only ones that are observed to be either *cis* or *trans***, as opposed to exclusively *trans* for other dipeptides? (X = any amino acid)

(c; 5 pts) For each of the five amino acids on the left, **circle the one on the right that is most likely to substitute for it** in a homologous protein.

Ile Leu Val Asp Cys

Lys Glu Met Arg Ala

Ser Tyr Thr Asn Ile

Tyr Gly Trp Gln Lys

Glu Phe Ser Asp His

Score for the page _____

2. (20 pts) Peptide structure and Henderson-Hasselbach

(a; 10 pts) Draw the **tripeptide EFH** in an extended form (i.e. the way we usually draw peptide sequences), in its predominant ionization state at pH 5. Include the stereochemistry at each $C\alpha$. If the tripeptide in this conformation were part of a **secondary structure element**, which one would it be?

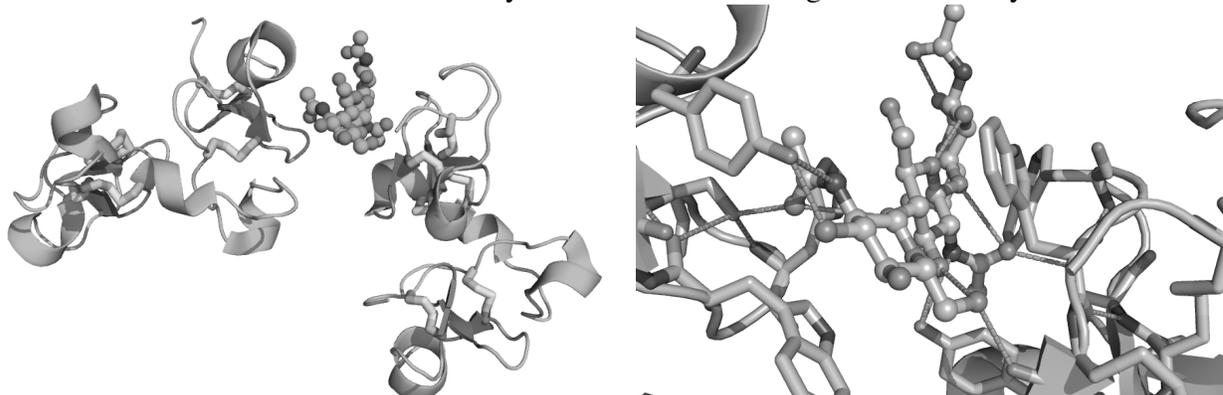
(b; 3 pts) It turns out the pK_a of the EFH Histidine in this protein is 7.5, rather than whatever it was as an isolated amino acid. (This should not change your answer for the structure.) **Explain why the pK_a changed** in this way.

(c; 7 pts) **At what pH would the average charge on the histidine side chain above be +0.25 (i.e. what pH gives 75% dissociation of HisH⁺)?**

3. (15 pts) Biomolecules and Molecular Recognition:

(a; 8 pts) Give **two reasons that fat is a denser source of dietary calories** than carbohydrates. When yeast grows fermentatively, it leaves behind an excellent fuel, ethanol. **Why don't the yeast burn the ethanol** to continue growing? **Why do they grow more efficiently under aerobic conditions?**

The pictures below show two molecules of a plant lectin protein binding to NAG₃ in the middle; NAG = N-acetylglucosamine, a modified sugar. The dashed lines in the close-up on the right indicate putative hydrogen bonds – since we don't see H in X-ray structures, one has to guess where they are.



(b; 7 pts) We claimed that sugars have tremendous information density. **How is the information in sugars encoded and read? Why isn't this encoding suitable for carrying genetic information?**

4. (22 pts) Tertiary structure and protein folding

(a; 3 pts) We have made the analogy that tertiary and quaternary structure in proteins is held together by Velcro, not nails. **What does this mean in terms of molecular structure and interactions?**

(b; 6 pts) How does the Velcro vs. nails analogy help explain a) **cooperative protein folding** and b) **evolution**?

(c; 13 pts) Protein folding and misfolding: A misfolded protein folding intermediate can follow several pathways. **What is ironic about calling the GroEL/GroES chaperone a “foldase”?** The steric zipper is one common failure mode leading from misfolding to protein aggregation. **Name and sketch another mode.** Both modes explain how aggregates can form that contain only one kind of protein, even though the failure modes are generic. **List two different ways in which a protein aggregate might be responsible for disease. What else can happen to a misfolded intermediate (besides chaperone-mediated refolding or irreversible aggregation)?**

4. (20 pts) Hemoglobin

Carbon monoxide is a poison at least in part because it binds to hemoglobin. Carboxyhemoglobin looks like the O₂-bound state but CO binds with ~200-fold higher affinity than O₂. CO poisoning leads to headache, dizziness, hallucinations, and confusion. Fatal levels CO are much lower than the amount needed to saturate all the O₂ binding sites.

(a; 8 pts) CO binds the R state much better than the T state. Sketch and explain the linked equilibria that **demonstrate that CO binding will have the effect of stabilizing the R state.**

(b; 8 pts) On one graph, sketch the **oxygen binding curves** (\bar{Y} = fractional saturation of Hb with O₂ vs. pO₂) for (1) **Hb in normal blood** and for (2) **Hb in blood that contains enough CO** to saturate one site per tetramer. There is room on the next page to recopy the graph if you need to.

(c; 3 pts) **How does CO interfere with O₂ delivery?**

(d; 1 pts) Why do people who live in old houses with faulty furnaces sometimes think that the houses are **haunted** (according to Wikipedia)?

Page	Score
1	/5
2	/18
3	/13
4	/15
5	/10
6	/19
7	/16
8	/4
Total	/100

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