**READ INSTRUCTIONS FIRST!!!!!!!!!!!!!!!!**

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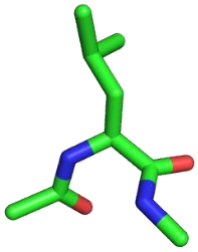
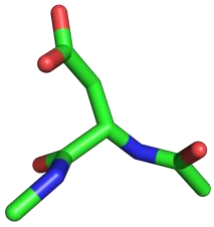
**1. Proteins (25 points)**

a) Predict the kind of secondary structure for each of the following three sequences (one each for alpha-helix, beta-strand, random coil). Which sequence would you expect to bind a metal ion? Why?

i. KLTVRLNISVE
ii. ACYNCGQPGHPSRECPT
iii. TLSKITNDLNELADTL

b) Identify the following amino acid side chains and label the dihedral angles for the amino acid (Φ, Ψ & Xs don't worry about the direction convention). In what secondary structure element would each amino acid be based on the given angles?

i. Φ=-90 Ψ=-30  ii. Φ=-90 Ψ=90 

c) Briefly describe the hydrophobic effect in terms of protein structure in water. Why do denaturants like urea or guanidinium chloride work? Consider free energy costs in your answer.

d) Chaperonins (Hsp60 class) and Hsp70s are both chaperones that facilitate protein folding despite different mechanisms. Give two ways they are similar and two ways in which they are different.

e) In bacteria, protein aggregates typically contain dominant ordered structural features. What are these and why are they favored?

**2. Nucleic acids (25 points)**

a) Nucleic acid polymers adopt two main helical conformations called the A and B form. What main forms can RNA and DNA take and what constraint keeps RNA in only one form?

b) Proteins that bind specifically to DNA generally recognize which groove (minor or major)? What features of this groove make it more suitable for sequence discrimination? Identify two amino acid side chains that can be used to read the base pairs in either groove and explain how they distinguish base pairs?

c) Predicting secondary structure is an important part of designing experiments that involve nucleic acids. Large folded RNA secondary structure is difficult to predict based purely on base pairing. Describe two additional things you could use to predict correct

secondary structure in a large conserved RNA considering energetics, sequence information and tertiary structures.

d) Amino-acylating a tRNA with an incorrect amino acid has been an important tool for protein engineering. In the context of translation, why is this compatible with protein synthesis? Explain two reasons why this might be troublesome for an organism.

**3. Lipids and Membrane proteins (25 points)**

a) In considering lipids, what features make them suited to forming lipid bilayers? Explain the effect you would expect by introducing fewer saturated bonds in the acyl chains in a bilayer?

b) Describe (draw) the various parts of the lipid bilayer. Where would you expect an amphipathic helix to reside? Would you expect an amphipathic helix to be accessible to soluble proteins? Why? (feel free to use a diagram)

c) In general terms, why do 'lipid rafts' form? What role does cholesterol play?

d) Unlike cytoplasmic proteins, membrane proteins often contain conserved glycines in helices. Why is this unusual in terms of secondary structure? What would be the advantage to maintaining these residues for a membrane protein?

e) In terms of reconstituting membrane proteins *in vitro*, describe three membrane-replacing systems you can use and possible uses for each?

**4. Carbohydrates (25 points)**

a) Why do glycan polymers offer more diversity in terms of sequence than proteins? What would be required in a cell to achieve this additional level of diversity distinct mechanistically from template driven processes?

b) Give three different mechanisms that would lead to congenital diseases of glycosylation (diseases that result in incorrect glycosylation of a protein)?

c) Explain two aspects of glycobiology are potential tools for treatment of cancer?

d) Briefly explain why it is difficult for avian flu to make the jump to humans?

e) Lectins often consist of multiple carbohydrate binding domains or are clustered on membrane surfaces. Why are multiple binding sites necessary? Give two advantages this provides?