**Chem 791B** **Biomolecular Structure** **Exam #2**

**Exam Due: Tuesday, December 12 in class - no exceptions**

This examination is open book, but is to be worked on ***independently***. Once you have begun working on the exam, you may not discuss any aspect of the exam with *anyone* other than C. Martin. This includes any discussions with anyone after you are done with the exam, but before December 12.

*You are on your honor.*

*Note: The following questions are looking for short, concise, but complete answers. Overly long responses typically indicate a lack of thorough understanding, and will be scored accordingly. Be concise. Lay out all of your thoughts before you write your final answer. Choose only those relevant.*

**1.** a) (10 points) In a recent study of protein folding, the authors note that "it can be argued that the introduction of hydrophobic residues onto the surface of a protein will not destabilize" the protein's folding. Explain this statement.

b) (10 points) Assuming that the above statement is true, why is that nature has placed largely polar groups on the surfaces of proteins?

c) (5 points) For a membrane protein, would the introduction of polar groups at the protein-lipid interface destabilize the protein's folding?

2. a) (10 points) Circle the statement below which most closely resembles the definition of the transition state for folding, as presented in class:

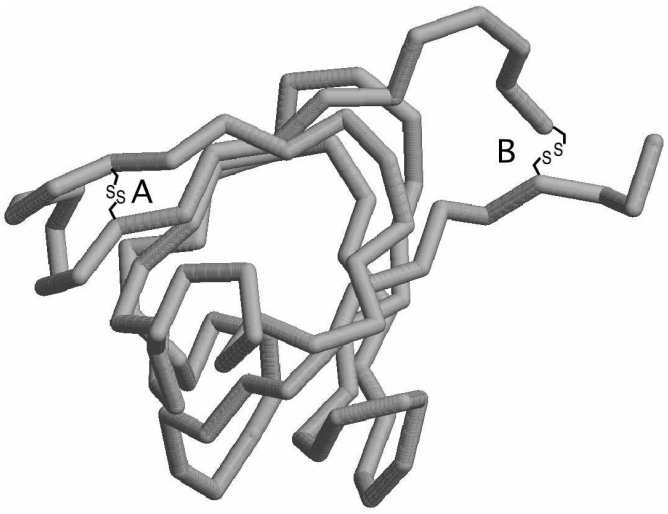
"The transition state resembles an expanded form of the folded state with extensive native-like structure."

"The transition state resembles an unproductive randomly collapsed ensemble containing non-native structure that has to be undone before productive folding can occur."

b) (10 points) What would you call the species described by the sentence that you ***did not*** circle?

3. a) (25 points) Examine the two structures linked to from our home page. Each of these macromolecular assemblies binds the same ligand (defined as "Lignd" for CHIME purposes). Describe the ***similarities*** in the way that these two macromolecules interact with their respective target ligands.

4. Consider the following hypothetical protein which in its native state contains no Cys residues. You create two engineered mutants. Mutant A incorporates two Cys as shown in the figure, which are optimally positioned to allow disulfide formation. Similarly, mutant B incorporates two Cys residues as shown, which are also optimally positioned to allow disulfide formation.




a) (15 points) All other things being equal and under oxidizing conditions, which of the two mutants (A or B) do you expect to be more stable *thermodynamically*? Explain your answer.

b) (15 points) All other things being equal and assuming a pre-formed disulfide bond, which of the two mutants (A or B) do you expect might fold *more rapidly*? Explain your answer.