Daniel.SciO Protein Modeling Test:
Enloe Varsity 2018-19
1. a) Define what chirality in a sentence or two:

Chirality is a geometric property of molecules or ions in which there exists two optically active asymmetric forms of the molecule that are the mirror images \[1\] of each other.

b) Different chiral forms are called _enantiomers \[1\]_.

c) i) What are the 2 chiral forms of proteins designated as?
Two types - D \[1\] and L \[1\] configurations.

   ii) Which type is used by enzymes and are synthesized by ribosomes?
   A-acids in proteins almost always have L-configuration \[1\], enzymes responsible for protein synthesis have evolved to utilize only the L-enantiomer.

d) All amino acids are chiral except for which?
   A. Tyrosine
   B. Alanine
   C. Glycine \[1\]
   D. Histidine

e) Explain the difference in the chemical structure of the amino acids you chose for part b that sets it apart from the other chiral amino acids:
   A chiral carbon is any carbon that is bonded to four non-identical types of atoms or groups of atoms. The only amino acid that does not have a chiral carbon is glycine \[1\].

2. a) Fill in the blanks: In proteins, the _Carboxyl \[1\]_ group is acidic, while the _Amino \[1\]_ group is basic. At physiological pH, free amino acids exist mostly as _Zwitterions \[1\]_.

b) Draw the chemical structure of a general amino acid below:
c) What is the isoelectric point of an amino acid and why is it important?
The isoelectric point (pI) is the pH at which a molecule has no net electrical charge, or the point where pKa=pH [1]. pI is very useful for determining the electrical behavior of an amino acid based on the pH of the environment, and thus can also be used to estimate the pH [1] of the amino acid and its location.

d) i) What are pKa values and how are they different from pH?
pKa is a measure of acid strength [1]. It depends on the identity and chemical properties of the acid, while pH is a measure of the concentration of hydrogen ions [1] in an aqueous solution. pKa is related, but more specific, in that it helps you predict what a molecule will do at a specific pH [1].

ii) Why are the pKas of proteins useful for determining the location and behavior of amino acids?
pKa can be used to estimate the pH via the Henderson–Hasselbalch equation. This can allow one to determine the electrical behavior and location of the amino acid. [1]

iii) Match each relationship of pH and pKa to the corresponding characteristic of the amino acid:
   _C [1]_ pH < pKa       A. 0 net charge
   _A [1]_ pH = pKa       B. deprotonated
   _B [1]_ pH > pKa       C. protonated

3. a) Match the properties of each amino acid group to their properties:
   _B [1]_ Group I         A. Acidic
   _D [1]_ Group II        B. Nonpolar
   _A [1]_ Group III       C. Basic
   _C [1]_ Group IV        D. Polar

b) i) Based on the properties of amino acid groups, where would you expect to find each group?
Group I is hydrophobic and thus would be found in the interior [1] of the protein, away from the aqueous environment. Groups II, III, and IV are hydrophilic and would be found on the surface [1] of the protein.
ii) List where you would find each amino acid (use “i” for interior and “e” for exterior). 

Each worth 1
Glycine: i
Valine: i
Glutamic acid: e
Lysine: e
Cysteine: e
Proline: i
Methionine: i
Glutamine: e
Phenylalanine: i
Histidine: e

c) Fill in the blanks: The _imidazole_ ring [1] side chain of Histidine allows it to function as both an _acid [1]_ and a _base [1]_, these types of amino acids are _amphipathic [1]_.

d) The amino acids that contain sulfur atoms are _Cysteine [1]_ and _Methionine [1]_.

d) The two main characteristics of aromatic amino acids are what?
Relatively nonpolar [1], absorb UV light [1].

4. a) i) What are the two main secondary structures? How are they formed?

Alpha helices [1] and beta sheets [1] that fold rapidly b/c they are stabilized by H-bonding [1] between NH and carbonyl.

ii) Give the corresponding secondary structure to the measurements for the following:
_Collagen helix/triple helix [1]_ has 3.3 residues per turn.
.Alpha-helix [1]______________ has 3.6 residues per turn.
_3/10 helix [1]______________ has 3.0 residues per turn.
._π-helix [1]______________ has 4.1 residues per turn.

b) i) How are π-helices derived from alpha-helices?

Derived from _insertion of 1 a-acid into an α-helix. [1]_
ii) Briefly explain why π-helices are so much rarer than alpha-helices:

The insertion of an α-acid is highly destabilizing, thus π-helices are selected against unless for some functional advantage to the protein [1].

c) Where are 3/10 helices usually found in the secondary structure of a protein?

Usually observed as extensions of α-helices [1] found at either their N- or C-termini.

d) Which amino acid is known to destabilize alpha-helices and why?

Proline contains a ring structure that joins its R group to the amino group, which inhibits flexibility of the peptide bond containing the proline amino group. [1]

e) What force dominates secondary structure formation?

A. Hydrophobic Effect
B. Salt Bridges
C. Disulfide Bonds
D. Hydrogen Bonding [1]

f) What is the difference between antiparallel and parallel beta sheets?

Hydrogen bonds with the ideal 180 degree angle vs slanted H-bonds formed by parallel sheet. [1]

5. a) What are the noncovalent forces involved in protein folding?

H-Bonding, Van der Waal forces (London dispersion, dipole-dipole, and hydrogen bonding), Ionic bonding (salt bridges) and Hydrophobic interactions/bonds. [1] Must have ALL

b) Explain the significance of Cysteine in tertiary structure formation:

Thiol (sulfhydryl) of cysteine is highly reactive. The most common reaction of this group is a reversible oxidation that forms a disulfide bridge; two thiols are oxidized to release two electrons and two protons and form a bond between the two sulfur atoms [1]. This bridge is used to stabilize the tertiary structure of proteins [1], and is the strongest interaction involved in tertiary structure formation.

c) i) What types of bonds are involved in salt bridges?

Ionic bonding. [1]
ii) What amino acids are involved in the formation of salt bridges?

Between aspartic acid/glutamic acid (anionic carboxylate group) and lysine (cationic ammonium)/arginine (guanidine) [1]

d) Describe these methods for analyzing tertiary structure:

X-ray Crystallography:  
Used for determining the atomic/molecular structure of a crystal; crystalline structure causes a beam of incident X-rays to diffract into many specific Directions [1].

NMR Spectroscopy:  
Spectroscopic technique to observe local magnetic fields around atomic nuclei. [1]

e) Describe how Gibbs free energy influences protein folding in a sentence or two:

When a protein folds, it tries to minimize its free energy to achieve lowest energy conformation [1]. Conformational entropy is most unfavorable to protein folding: higher entropy = more possible states = destabilization.

f) Explain briefly what the hydrophobic effect is, and how it relates to thermodynamics:  
Phenomenon where hydrophobic chains of a protein collapse into the core (away from hydrophilic environment) [1]. Water molecules aggregate around the hydrophobic regions/side chains, creating hydration spheres of ordered water molecules & a negative change in entropy. Hydrophobic collapse = increased entropy via the breaking of the water cages, freeing the ordered water molecules [1].

6. a) i) Explain transcription in detail:

Transcription: complementary mRNA made from DNA in the nucleus. [1] The mRNA then exits the nucleus into cytoplasm and interacts with ribosomes (assembles a-acids for synth) [1]. The ribosome consists of proteins and ribosome RNA molecules (rRNA), organized in two subunits (60% rRNA, 40% protein).
ii) Explain translation in detail:
The mRNA binds to a ribosome subunits, which synthesizes a protein based on the mRNA. [1] The process of synthesizing a protein from an mRNA template is translation. [1] When mRNA interacts with ribosome subunit, it triggers the approach of tRNA. [1] The tRNA molecule possess an anticodon, which complements a codon (first tRNA binds to start codon). When it finds it, it attaches to the mRNA, as the other end of the tRNA is “loaded” with an a-acid. [1] As the complete ribosome structure is formed, another tRNA molecule approaches. The two a-acids carried by the first two tRNAs are bound together by the ribosome (rRNA). [1]

b) What are transcription factors?
Transcription factors are proteins that bind to specific sequences on DNA controlling (regulating) the transcription from DNA to RNA. [1]

c) Name the function of each site in a ribosome:
The A site is the aminoacyl site [1], the P site is the peptidyl site [1], and the E site is the exit site [1]. P site binds a tRNA [1] that carries a peptide chain, and the A site binds an incoming aminoacyl-tRNA [1]. E site carries an uncharged tRNA that is about to be released from the ribosome [1].

d) mRNA translation begins from its 5’ to 3’ and the polypeptide is synthesized from N [1]-end to C [1]-end

e) i) What process forms polypeptide bonds?
Dehydration synthesis [1]

ii) Draw out a peptide bond below:
f) Why are there only about half as many tRNA molecules as codons?

Wobble: only about half as many tRNA molecules as codons bc of wobble in the third base (5’ end) of the anticodon on the tRNA. [1]

7. a) Which structural motif is this? Two antiparallel b-strands connected by a tight turn of a few amino acids between them.

Beta hairpin [1]

b) Which structural motif is this? Two beta strands with an alpha helix end folded over to bind a zinc ion.

Zinc Finger [1]

8. Briefly explain the four types of proteins:

Globular Proteins, or spheroid proteins are spherical ("globe-like") proteins.
Globular proteins are somewhat water-soluble (forming colloids in water). [1]

Fibrous: Structural/storage proteins. There are many scleroprotein superfamilies, e.g. keratin, collagen, elastin, and fibroin. Their roles include protection/support, forming connective tissue, tendons, bone matrices, and muscle fiber. [1]

Disordered/intrinsically disordered protein (IDP): a protein that lacks a fixed/ordered 3D structure. IDPs are a very large & functionally important class of proteins. [1]

Membrane Proteins: Membrane proteins are proteins that interact with/part of biological membranes. [1]
9. a) What is the Central Dogma, and who was responsible for it?
   Stated by Francis Crick [1]. In cells, info only flows from DNA to RNA to proteins [1]. Cannot flow in reverse direction.

b) What is the Levinthal Paradox?
   sampling all possible conformations of a polypeptide chain to find the lowest-energy state would take millions of years rather than a few seconds, so how do proteins fold so quickly? [1]

d) What is Anfinsen's Dogma? How did Anfinsen come up with this Dogma?
   Explain his experiment:
   for a small globular protein in its standard phys environment, native structure is determined only by the protein's a-acid sequence & the native structure is a unique, stable and kinetically accessible minimum of free energy [1]. After denaturing a protein, it reverted back to normal conformation after the denaturing agent was removed [1].

10. a) What is competitive inhibition?
   Competitive inhibition: when molecules very similar to the substrate molecules bind to the active site and prevent binding of the actual substrate. [1]

b) What is noncompetitive inhibition?
   Noncompetitive inhibition: an inhibitor binds to the enzyme at a location other than the active site. [1]

c) What are molecular chaperones and what do they do in regards to protein folding?
   Molecular chaperones: Large group of unrelated protein families: stabilize unfolded proteins, unfold them for translocation across membranes/degradation, assist in correct folding & assembly. [1]

d) Briefly explain cooperation and allosteric regulation:
   Cooperativity in terms of tertiary protein subunits: Tertiary subunits follow each other changing formation together once one binds a substrate [1]. Allosteric regulation is the regulation of an enzyme by binding an effector molecule at a site other than the enzyme's active site [1].