Biochemistry CUME October 2020

Topic: Protein Structure Analysis
(Please submit this open-book exam within 4 hours.)

1. Protein Primary Structure (25 points)

a) (5 points) Proteins are polypeptide chains of amino acids linked by peptide bonds. What are the common chemical features among 20 naturally occurring amino acids? What chemical features make them distinct?

b) (5 points) Given the peptide sequence "`MFDGYNQKPEEDWDSTR`", sort the amino acids according to the following groups.

Non-polar: _____

Polar: _____

Charged: _____

(5 points) At pH 8.0, would this peptide carry a POSITIVE or NEGATIVE net charge? Explain why?

c) (10 points) What chemical features of a protein molecule account for the absorption peaks around the wavelengths of 220 nm and 280 nm, respectively?

2. Protein Secondary Structure (25 points)

a) **(5 points)** Use chemical drawing to illustrate the major differences between the parallel β-sheet and antiparallel β-sheet.

b) (**10 points**) Describe the main geometric features of α-helices. Why are α-helices right-handed?

c) **(10 points)** Circular dichroism (CD) spectroscopy is often used to probe protein secondary structures. Describe the CD spectral characteristics for three common secondary structures: α-helix, β-sheet and random coil. Explain the structural origin of such optical properties.

3. Protein Tertiary Structure (25 points)

a) (15 points) TEM-1 belongs to a family of β-lactamases responsible for antibiotics resistance in bacteria. Three conserved residues (Ser68, Glu164 and Lys232) at the active site of TEM-1 are involved in the β-lactam hydrolysis. What phenotype would you expect for each of the three single mutants in TEM-1? Explain why.

S68A

E164R

K232R

b) (10 points) Name three major methods for protein structure determination at atomic resolution. Use a table to highlight their key differences in sample preparation, physical principles, information content as well as major strengths and limitations.

4. Protein Quaternary Structure (25 points)

Large protein assemblies often employ multiple polypeptide chains to achieve the biological functions in a regulated manner. Describe (with illustration) the biological assembly of the prokaryotic chaperonin GroEL, and explain how such protein architecture facilitates the GroEL functions.