Biology 5357

Chemistry & Physics of Biomolecules

Examination #2

Nucleic Acids Module

November 3, 2023

Name: _____

Question 1 (15 points; A-C = 5 pts each)

In human dsDNA, 70-80% of 5´dCpG sites are modified to contain 5-Me-C.

(A) Draw the structure of a 5-Me-C nucleobase.

(B) Is the methyl group found in the Major or the Minor groove of a DNA B-form duplex?

(C) What effect would you expect this modification to have on DNA structure and stability? Explain.

Question 2 (15 points)

RNA backbone cleavage via transesterification reactions occurs most often at rUpA sites, but any dinucleotide can suffer such cleavage. Given the relative ease of this chemistry, how do RNA molecules retain their integrity in a cell?

Question 3 (15 points)

Probing an RNA secondary structure with nucleases, specifically RNase T1 (cleaves after single-stranded rG↓) and cobra venom V1 (cleaves dsRNA), identifies single and double-stranded regions. How would you interpret a result showing cleavage by both enzymes at the same position in an RNA?

Question 4 (15 points)

The imino protons of DNA and RNA are used in NMR experiments to identify what structural features?

Question 5 (10 points; A & C = 2 pts each, B & D = 3 pts each)

(A) Which of the following is a prerequisite for an ideal chain?

1. no interactions
2. fixed bond length
3. freely rotating bond angle
4. short persistence length
5. definition of a Kuhn segment

(B) What is the expression for the free energy of an ideal chain?

(C) What is referred to as an entropic spring? Based upon your free energy in part (B), what is the spring constant?

(D) Under which solvent conditions does a disordered protein behave as a purely entropic spring?

Question 6 (10 points; A = 4 pts, B-D = 2 pts each)

(A) What are the two definitions of the radius of gyration? Explain in words and mathematical representation.

Definition 1:

Definition 2:

(B) What is the relation between the mean square end-to-end distance and the mean square radius of gyration?

(C) What is the distribution associated with the radius of gyration? Is it the same as the distribution of the end-to-end distance?

(D) What are the scaling exponents expected for the radius of gyration in a poor solvent, a theta solvent, and a good solvent?

Question 7 (10 points; A-E = 2pts each)
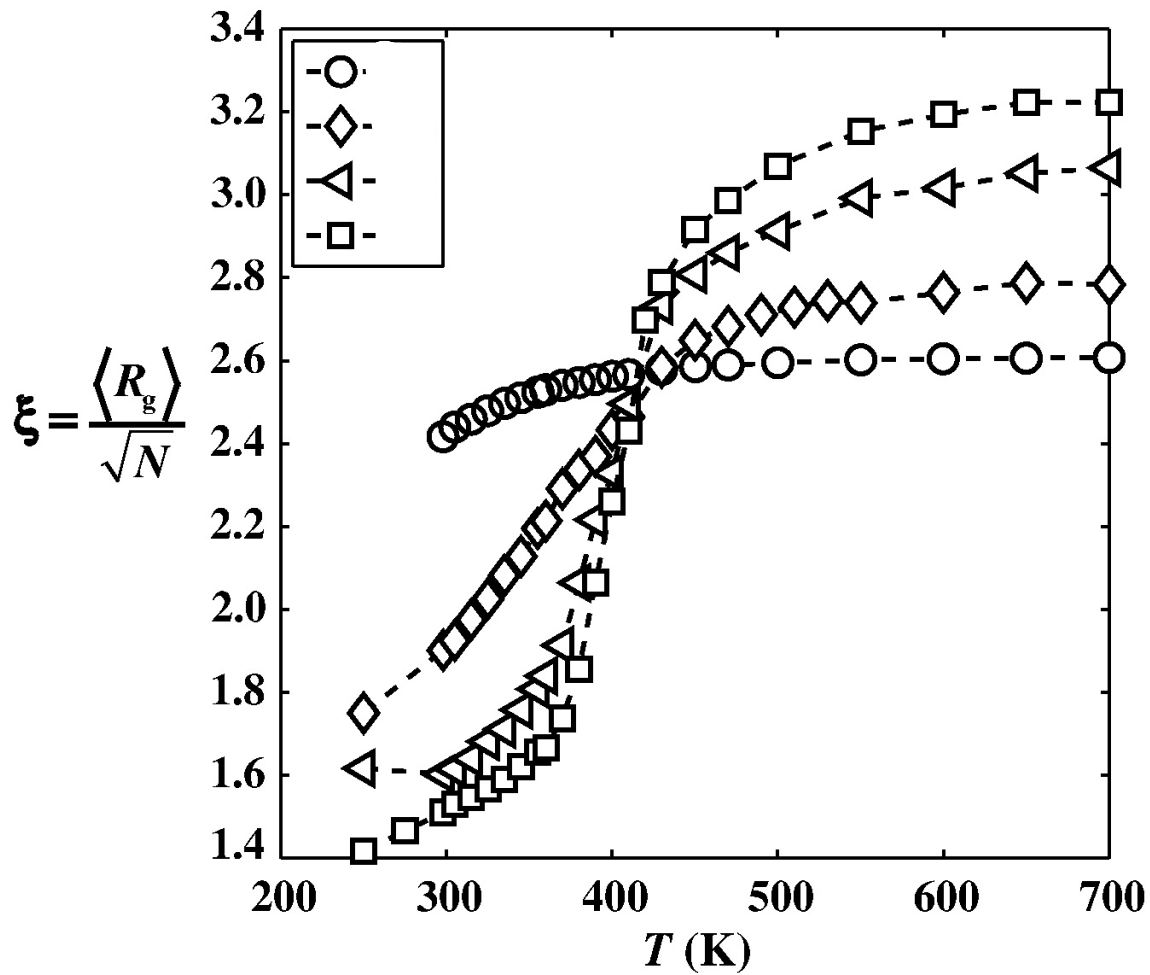
The data above are obtained with a Monte Carlo simulation of polyQ chains, which are relevant to Huntington's disease (data from Vitalis, *et al.*, 2008).

(A) By inspecting the dataset, can you rank the curves from the shortest to the largest?

(B) Based on the simulation results, which range of temperatures represents approximately good solvent and poor solvent conditions? Identify them on the graph and report the value here.

(C) What is the theta temperature for a polymer?

(D) Why the authors may have chosen that specific type of quantity for the y-axis?

(E) What have been observed experimentally about the dimensions of disordered proteins as a function of temperature?

Question 8 (10 points; A = 4 pts, B-C = 3 pts each)

(A) What are some advantages and disadvantages of cryo-EM *vs* X-ray crystallography in the determination of biomolecular structures?

(B) In reconstruction and refinement of cryo-EM images, what is the relationship between the contrast transfer function (CTF) and point spread function (PSF)?

(C) Briefly, explain the differences between cryo-electron microscopy (EM) and cryo-electron tomography (ET)?