

You have 80 minutes for this exam.

Exams written in pencil or erasable ink will not be re-graded under any circumstances.

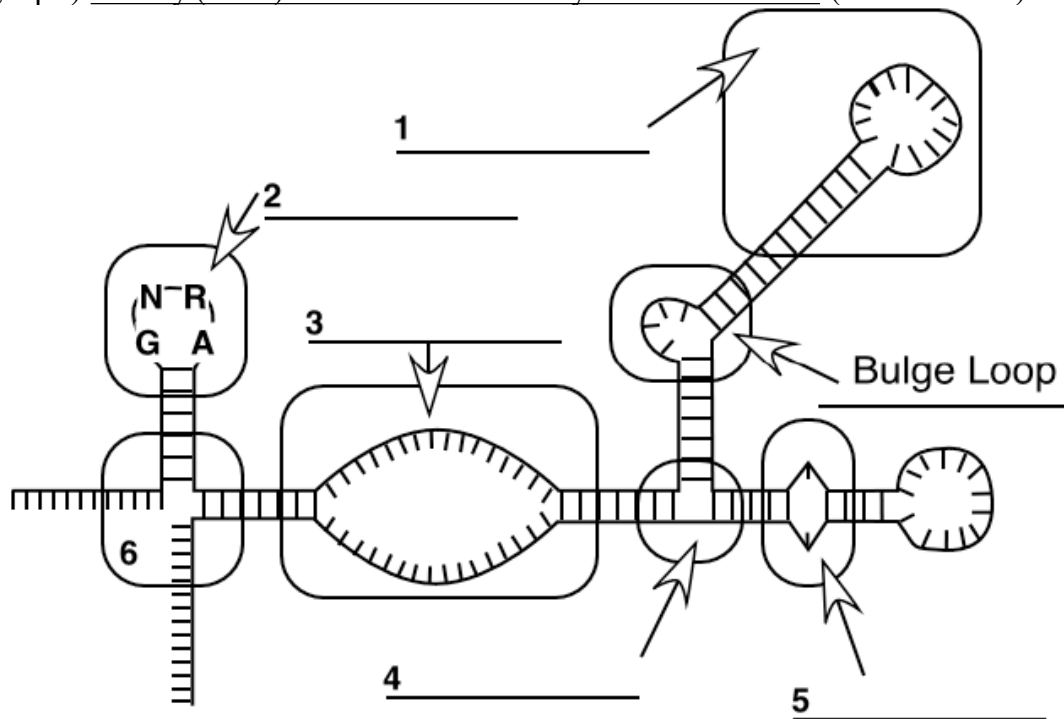
Explanations should be concise and clear.

You may need a calculator for this exam. No other study aids or materials are permitted.

Generous partial credit will be given, *i.e.*, if you don't know, guess.

1. Secondary Structure and Thermodynamics (25 pts):

(a; 5 pts) Identify (name) the indicated secondary structure elements (numbered 1-5) in the RNA below.



(b; 3 pts) What is the likely three-dimensional conformation of the junction labeled 6 above (sketch).
What is this arrangement called (cf. tRNA in class)?

(c; 9 pts) List the ten unique nearest-neighbor dinucleotides for DNA. In addition to the database of ΔH° and ΔS° values for forming each dinucleotide, what other thermodynamic parameters (in general) do the prediction programs use in order to make the most accurate possible predictions of RNA secondary structure? What additional information derived from looking out into genome land is most useful for predicting RNA secondary structure?

(d; 8 pts) Briefly discuss the tradeoff between stability and specificity in designing oligonucleotide primers or hybridization probes.

2. DNA Flexibility and Topology (23 pts):

(a; 12 pts) A ~1000bp circular DNA with a $\Delta Lk = -4$ relative to relaxed can assume many different shapes. Sketch (1) the shape one would expect for free DNA just in buffer, (2) the shape observed if enough ethidium is bound to induce $\Delta Tw = -6$, (3) the shape expected if all superhelical strain appears as toroidal writhe, and (4) the shape expected if the DNA has a 42 bp heteroduplex (i.e. unpaired) region. [#3 is vaguely like the structure wrapped around the nucleosome, with several wrinkles we haven't studied yet.] Indicate node signs where appropriate.

1	2
3	4

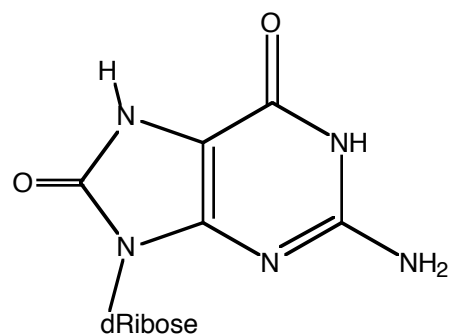
(b; 5 pts) Why do intercalating dyes bind with higher affinity to negatively supercoiled DNA than to relaxed DNA?

(c; 6 pts) Briefly describe what “persistence length” means. What effect would magically doubling the persistence length have on the Shore and Baldwin curve of J factor vs. length in bp?

3. Base Pairing and DNA geometry (18 pts):

(a; 6 pts) Draw the structure of dTTP, including the numbering of the sugar and the base and identifying the phosphates.

(b; 12 pts) The miscoding oxidative lesion 8-oxoG (right) is much more likely than G itself to adopt the *syn* conformation. Why?
Draw *syn* 8-oxoG with its sugar and propose (sketch) a likely base pairing partner for it in the context of an otherwise Watson-Crick helix.



4. RNA Tertiary structure (16 pts):

(a; 4 pts) Briefly describe the A-minor motif.

(b; 4 pts) What often constitutes the core of a large structured RNA?

(c; 8 pts) It has been found that a given ssRNA often adopts a more stable and ordered 3-D structure than the corresponding ssDNA. What chemical difference between RNA and DNA is likely to be the cause of this, and why? Speculate on the interactions that might be responsible for stabilizing RNA but not DNA tertiary structure.

5. Miscellaneous (18 pts):

(a; 8 pts) Why are roll, tilt, and twist the three base pair geometric parameters which are critical for describing long-range DNA shape (e.g. as opposed to slide, buckle, propeller twist etc.). Sketch a picture defining one of the angles (roll, tilt, or twist).

(b; 2 pts) Name a molecular visualization program:

(c; 8 pts) Some nucleic acid analogues made with sugars other than ribose can form stable base-paired structures which are not helical. Speculate on why (in terms of evolution) our own genetic material is in fact helical.

Score:	Question 1: _____ out of 25: 2° Structure and Thermo
	Question 2: _____ out of 23: DNA Flexibility and Topology
	Question 3: _____ out of 18: Base Pairing and Geometry
	Question 4: _____ out of 16: RNA Tertiary Structure
	<u>Question 5: _____ out of 18: Miscellaneous</u>
Total:	_____ out of 100