**Chapter 1 Study Questions**

*Genetic Analysis: Genes, Genomes, and Networks in Eukaryotes*

1. Briefly describe how the principles of inheritance, as elucidated by Mendel, Morgan, and others, are used as a means to analyze a biological question.
	1. What are the minimal components needed to perform a genetic analysis?
	2. What are the desirable but possibly not essential components necessary to do a genetic analysis?
	3. What are the strengths of using a genetic-based approach to the analysis of a biological question?
	4. What are the limitations of using a genetic-based approach to the analysis of a biological question?
2. Try to compose a definition of a gene that includes all of its known properties. Is it useful to distinguish different types of genes? If so, what would be the basis for making the distinction between gene types?
3. Is the “one gene, one polypeptide” axiom helpful in understanding the properties of a gene or are the exceptions so frequent that this principle is misleading?
4. Why will the numbers of alternatively spliced transcripts and the numbers of non-coding RNAs always be minimal estimates? What would be necessary to have a definitive and complete census of all transcripts? Is it realistic and important to have such a census of all transcripts?
5. When it was realized that transposable elements were found in many eukaryotic species and not only corn, it was also recognized that different categories of transposable elements might move by different mechanisms and might have different sequence or structural features. However, DNA sequencing was fairly difficult at that time, so other methods were used to analyze their movement and structure. The following question is based on the series of experiments that showed that there is more than one type of transposable element, which move by different mechanisms. The exact data have been heavily modified for this question. Two elements were found in yeast, called element A and element B. The sizes of the native unmodified elements are represented in the diagram of the agarose gel below (lanes 1 and 3). The investigator inserted an intron of 500 bp into a copy of each element, which he called Aint and Bint; the sizes of each element with the intron inserted are also shown in the gel (lanes 2 and 4). He introduced Aint into one yeast cell and Bint into a different cell, and grew up the cultures separately, allowing Aint and Bint to move. (In retrospect, these elements moved only because there were functional A and B elements in the cells; the insertion of the intron probably made Aint and Bint into non-autonomous elements.) He then selected for mutants in which the element had inserted into the *ura3* gene and disrupted its function. He then isolated the disrupted *ura3* gene from each culture and analyzed its size. The results are also shown on the gel (lanes 5, 6 and 7).



1. What can be learned from this experiment about the mechanisms by which A elements and B elements transpose?
2. The A and the B elements have now been sequenced so their DNA sequences and sequence-related structures are known. What are some of the sequence or structural features that distinguish the two types of elements from each other?
3. Imagine that you are the head of a genome project to analyze the genome of a previously uncharacterized species of a tardigrade. Since this is an imaginary project, you can also imagine that you have as much money as you need, with all of the necessary equipment and qualified and contented colleagues to carry out the analysis. You and members of your lab have recently completed sequencing more than 250,000 ESTs or partial transcripts from this species, using many different developmental stages and ages as your source material. You have also been actively sequencing the genome itself so that these ESTs can be located and analyzed, although some of the genome sequence is not yet done.
	1. What is a tardigrade and what biological or evolutionary questions might be approached from an analysis of its genome? What arguments would you use to persuade your investors and the granting agencies that the tardigrade genome project is worth pursuing?
	2. What is some of the information you will obtain from genome sequencing that you will not obtain from sequencing ESTs?
	3. What is some of the information you will obtain by sequencing ESTs that you will not get from sequencing the genome itself?
	4. Describe how you will use the ESTs in combination with the genome sequence to identify protein-coding genes and begin to annotate the genome.
4. Being a somewhat old-fashioned molecular biologist who likes to do to your own experiments when no one in the lab is watching, you decide to do a different type of genome analysis with the tardigrade genome. You isolate DNA from a tardigrade species and shear it into random fragments, with an average size of 1 kb. The fragmented DNA is heated to denature it to single-strands and then allowed to reanneal by lowering the temperature. The percentage of the DNA that remains single-stranded is assayed at various times and plotted on a graph as shown below. Three components of the genome are observed. “Cot” on the X axis is a composite of the concentration at time 0 and the time, so this type of experiment was called a Cot curve.
	1. What is component A, and why does it become double-stranded so quickly?
	2. If the tardigrades are like most other metazoans, which component of the genome will account for most of the transcripts found in Question 6, and why?
	3. Which component is likely to include most of the transposable elements, and why?
	4. microRNA genes were not known at the time Cot curves were commonly done. If they had been known about, which component is likely to include the microRNA genes?