

Exercise 8: Replication, transcription, translation

The DNA molecule is a polymer comprised of repeating units called **nucleotides**. For convenience, DNA is said to be "read" (i.e. transcribed) from the **3'** (pronounced "three prime") end to the **5'** (five prime) end (the terminology is related to organic chemistry). A **gene** is the portion of the DNA molecule that codes for an actual **protein**. The word "**base**" is sometimes used in place of the word "nucleotide". Thus, the DNA double helix is said to comprise **base-pairs**. You will need the genetic code handout.

Suppose you have the following strand of DNA (oriented with 5' on the left and 3' on the right):

TTTTTTTACCCCCCTGGGGGAATTTTACTTAAAAAAAATTTTATTTT

1. Write the **complementary** strand of DNA, which attaches to the segment above.
2. Write the strand of **RNA** generated from the original strand of DNA.
3. Find the **start codon** (three RNA nucleotide sequence) and mark it. Hint: break up the RNA strand into groups of three bases and translate the groups.
4. Mark on the RNA sequence you have generated, the portion which is the gene. Hint: you will need to find the **stop** or **end** codon.
5. What is the **amino acid sequence** (protein) for which this RNA codes? See Table 22.4, page 729 in the text for the genetic code.
6. a. What **percentage** of the RNA (and therefore the DNA) actually codes for a protein? (Hint: for this one, don't count the start and stop signals)

b. Including the regulatory parts (like start and stop signals), what percentage of the RNA is truly functional?

A **mutation** is any change in the base (nucleotide) sequence of DNA, brought about by radiation or chemical interactions.

7. Suppose a cosmic ray strikes the original strand of DNA and alters **one** base (nucleotide). This type of mutation is called a **substitution**. Suppose the change occurs in the second letter (position) of the first codon (i.e., the CCC becomes a CGC). What will the resulting amino acid sequence be?

8. What is the **probability** that a substitutional mutation will occur in an actual functional codon? Express the probability as a fraction or a decimal. Hint: compare this answer to the answer to question 6b.

9. Suppose the cosmic ray does strike somewhere in the **gene** (the part of the RNA that will be translated into amino acids) and alters **one** nucleotide. What is the probability that the change will affect the resulting amino acid sequence? (Hint: the answer is **not** 100% — look at the redundancies in the genetic code)

10. What is the **probability** that a cosmic ray will cause an actual change in this protein? (Hint: this is not as hard as it sounds; simply multiply the fractions or decimals from the previous two questions). Notice that this is how nature protects itself against lots of mutations occurring with every generation!

11. Recall that glycine is a small molecule and that the other amino acids are all larger (see genetic code handout). Glycine is used in proteins that need to be long and flexible, like keratin in hair and fingernails. Other amino acids tend to be used in proteins that are bulky, like the protein hemoglobin in blood. What will the **shape change** in the protein be, due to the mutation?

Perhaps more frightening are the **reading frame shift** mutations brought on by either the **insertion** or **deletion** of a base or bases.

12. Suppose, in the original sequence, a **mutagen** (a chemical which induces mutations) removes the sixth T base from the left (just that base). In other words, the original strand of DNA begins with six T residues, not seven. Will the start sequence still be recognized?

13. In fact, write the new complementary RNA sequence (it should not be a lot different from what you wrote in question 2), and mark the new start codon.

14. What is the **amino acid sequence** for which this RNA codes?

15. Is this sequence significantly different from the sequence in question 5? More importantly, is the shape of the protein going to be significantly different?

By removing or adding one base to the DNA sequence, then, results in a reading frame shift, so whole genes can become inactive, and hitherto inactive genes can become activated. In fact, there are plenty of inactive genes in the human **genome** which await only a frame shift to become active again.

In sexual reproduction, a double strand of DNA from the mother and a double strand of DNA from the father unite to form the chromosomes that will generate a unique individual. However, the mitochondria of the first cell of the new individual all come from the mother. Furthermore, the mitochondria, having been an independent organism at one time (see adaptation the third), retains its own DNA and replicates using this DNA.

16. In principle, then, if there were no mutations, should your **mitochondrial DNA** (mDNA) differ at all from your great-great-great grandmother's (on your mother's mother's mother's side)?

17. Mutations, then, are about the only way to change mitochondrial DNA (yeah, there are other mechanisms, but they aren't that significant). This can give us a way to calculate the rate of **genetic evolution**, the change in genes over time. You are lucky enough to find a human hair follicle cell 50,000 years old with its mDNA intact (you get its age by carbon-14 dating). When you compare its mDNA sequence to your own mDNA, you find that the two mDNAs differ by 10 bases. What is the mutation rate (or the rate of genetic evolution)? Express this as the number of bases per year.

18. You find another human hair follicle cell, which cannot be dated by carbon-14 because it is too old and there is no detectable amount of carbon-14 left. However, its mDNA is intact and, upon analysis, differs from your mDNA by 100 bases. How many years old do you estimate the sample to be?

19. In fact, this sort of **linear extrapolation** of the mutation rate may not be valid for figuring out the dates of human evolution. Stephen Jay Gould, a Harvard paleontologist, suggests that evolution of organisms proceeds by **punctuated equilibrium**. What is punctuated equilibrium and how might this mechanism mess up our age estimates?

Of course, if the mutation rate is averaged over a sufficient number of years, even punctuated equilibrium will seem to be gradual...