

1

THE GENETICS REVOLUTION

PROBLEMS

In each chapter, a set of problems tests the reader's comprehension of the concepts in the chapter and their relation to concepts in previous chapters. Each problem set begins with some problems based on the figures in the chapter, which embody important concepts. These are followed by problems of a more general nature.

WORKING WITH THE FIGURES

1. If the white-flowered parental variety in Figure 1-3 were crossed to the first-generation hybrid plant in that figure, what types of progeny would you expect to see and in what proportions?

Answer: You would get a 1:1 ratio of purple to white. This is because the first-generation hybrid plant has one copy of the purple allele and one copy of the white allele, and as a result, 50 percent of the gametes would carry the purple allele and 50 percent of the gametes would carry the white allele. The white-flowered parental variety has two copies of the white allele, and all the gametes produced from the white plant will carry the white allele. Hence, a cross between the two would produce a 1:1 ratio of purple to white.

Hybrid plant P/p \times white plant p/p

Gametes $50\% P$ $50\% p$ \times $100\% p$

$50\% P/p$: $50\% p/p$

Purple : white

2. In Mendel's 1866 publication as shown in Figure 1-4, he reports 705 purple (violet) flowered offspring and 224 white-flowered offspring. The ratio he obtained is 3.15:1 for purple:white. How do you think he explained the fact that the ratio is not exactly 3:1?

Answer: This depends on the sample size. When the sample size was large, the proportions were close to 3:1 (e.g., for round and wrinkled seeds the ratio was 2.95:1 and the total population size

was 7324), whereas for a small sample size such as the purple and white petal flowered plants (929 plants), the ratio was not as close to 3:1.

3. In Figure 1-6, the students have 1 of 15 different heights plus there are two height classes (4 ft 11 in and 5 ft 0 in) for which there are no observed students. That is a total of 17 height classes. If a single Mendelian gene can only account for two classes of a trait (such as purple or white flowers), how many Mendelian genes would be minimally required to explain the observation of 17 height classes?

Answer: If a single gene can only account for two classes of a trait, minimum of 9 genes are required to explain the 17 height classes.

4. Figure 1-7 shows a simplified pathway for arginine synthesis in *Neurospora*. Suppose you have a special strain of *Neurospora* that makes citrulline but not arginine. Which gene(s) are likely mutant or missing in your special strain? You have a second strain of *Neurospora* that makes neither citrulline nor arginine but does make ornithine. Which gene(s) are mutant or missing in this strain?

Answer: If the mutant strain makes citrulline, that means genes A and B must be functional. Therefore, the only gene that is missing or mutant in the first *Neurospora* strain must be gene C.

In the second strain, gene A must be functional since it is able to make ornithine. Gene B must be missing or mutant since it is unable to make citrulline. However, gene C may or may not be missing/mutant. Enzyme C converts citrulline into arginine (they are in the same sequential pathway), and enzyme C is dependent on the availability of citrulline for its function.

5. Consider Figure 1-8a.
- What do the small blue spheres represent?
 - What do the brown slabs represent?
 - Do you agree with the analogy that DNA is structured like a ladder?

Answer:

- The blue ribbon represents sugar phosphate backbone (deoxyribose and a phosphate group), while the blue spheres signify atoms.
 - Brown slabs show complementary bases (A, T, G, and C).
 - Yes, it is a helical structure.
6. In Figure 1-8b, can you tell if the number of hydrogen bonds between adenine and thymine is the same as that between cytosine and guanine? Do you think that a DNA molecule with a high content of A + T would be more stable than one with a high content of G + C?

Answer: There are two hydrogen bonds between adenine and thymine; three between guanine and cytosine. No, the molecule with a high content of G-C would be more stable.

7. Which of three major groups (domains) of life in Figure 1-11 is not represented by a model organism?

Answer: Archaea

8. Figure 1-13b shows the human chromosomes in a single cell. The green dots show the location of a gene called *BAPXI*. Is the cell in this figure a sex cell (gamete)? Explain your answer.

Answer: It is not a sex cell. Cloned *BAPXI* gene has hybridized to two chromosomes in the cell, indicating there are two copies of the *BAPXI* gene. If it were a gamete, it would have only one copy of each chromosome and of the *BAPXI* gene.

9. Figure 1-15 shows the family tree or pedigree for Louise Bengé (Individual VI-1) who suffers from the disease ACDC because she has two mutant copies of the *CD73* gene. She has four siblings (VI-2, VI-3, VI-4, and VI-5) who have this disease for the same reason. Do all the 10 children of Louise and her siblings have the same number of mutant copies of the *CD73* gene, or might this number be different for some of the 10 children?

Answer: All 10 children have one mutant copy of the *CD73* gene. Children get one *CD73* copy from their mom and one from their dad. Since Louise and her four siblings each carry two defective genes, all their children will get one mutant *CD73* copy.

BASIC QUESTIONS

10. Below is the sequence of a single strand of a short DNA molecule. On a piece of paper, rewrite this sequence and then write the sequence of the complementary strand below it.

GTTCGCGGCCGCGAAC

Comparing the top and bottom strands, what do you notice about the relationship between them?

Answer:

GTTCGCGGCCGCGAAC
CAAGCGCCGCGCTTG

They are complementary to each other and run in the opposite direction (antiparallel). The sequences are also palindromic; they read the same in either direction.

11. Mendel studied a *tall* variety of pea plants with stems that are 20 cm long and a *dwarf* variety with stems that are only 12 cm long.
- Under blending theory, how long would you expect the stems of first and second hybrids to be?
 - Under Mendelian rules, what would you expect to observe in the second-generation hybrids if all the first-generation hybrids were tall?

Answer:

- a. First-generation hybrids would have stems 16 cm long because that is the average between 20 cm and 12 cm. The second generation would be a product of two 16-cm stemmed plants mating, so they would also have stems 16 cm long.
- b. If the first-generation hybrids are all tall, then tall must be dominant, and you would expect a 3:1 ratio of tall:dwarf in the second generation.

12. If a DNA double helix that is 100 base pairs in length has 32 adenines, how many cytosines, guanines, and thymines must it have?

Answer: Thymines = 32, Cytosines = 68, Guanines = 68

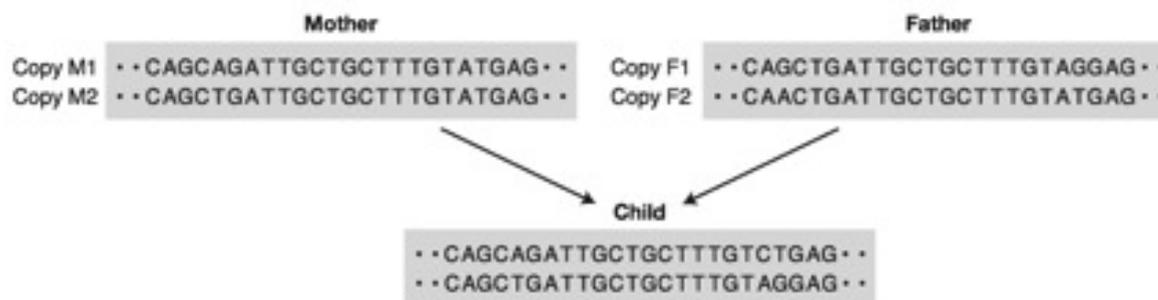
Number of thymines is 32 because thymine and adenine are paired, so the number of adenines equals the number of thymines. The remaining 136 base pairs must be cytosines and guanines. The number of cytosines equals the number of guanines because those bases are paired. Therefore, there are $136 \div 2 = 68$ base pairs of each.

13. The complementary strands of DNA in the double helix are held together by hydrogen bonds: $G \equiv C$ or $A = T$. These bonds can be broken (denatured) in aqueous solutions by heating to yield two single strands of DNA (see Figure 1-13a). How would you expect the relative amounts of GC versus AT base pairs in a DNA double helix to affect the amount of heat required to denature it? How would you expect the length of a DNA double helix in base pairs to affect the amount of heat required to denature it?

Answer: Double-stranded DNA with a high GC content would be more stable because GC pairs have three hydrogen bonds and hence would require more heat to denature compared with a double-stranded DNA with high AT content.

As the length of the double helix increases, the heat required to denature would also increase. This is because there would be more hydrogen bonds to break.

14. The figure that follows shows the DNA sequence of a portion of one of the chromosomes from a trio (mother, father, and child). Can you spot any new point mutations in the child that are not in either parent? In which parent did the mutation arise?



Answer: There is a new point mutation from an A to a C. The child inherited copy F1 from the father without any de novo mutations, as shown on the bottom. The other copy (as shown on the top) must therefore be from the mother. The mother has an SNP (A/T) at the fifth nucleotide shown, so we know the child inherited copy M1 (A). The A-to-C mutation in copy M1 is not observed in either of the parents, so it must be a new mutation.

CHALLENGING PROBLEMS

15. a. There are three nucleotides in each codon, and each of these nucleotides can have one of four different bases. How many possible unique codons are there?
 b. If DNA had only two types of bases instead of four, how long would codons need to be to specify all 20 amino acids?

Answer:

- a. There are 64 unique codons ($4 \times 4 \times 4 = 64$).
 b. In order to specify 20 amino acids using only two bases, a codon must be five bases long ($2 \times 2 \times 2 \times 2 \times 2 = 32$). This would give 32 unique codons that could specify 20 amino acids.
16. Fathers contribute more new point mutations to their children than mothers. You may know from general biology that people have sex chromosomes—two X chromosomes in females and an X plus a Y chromosome in males. Both sexes have the autosomes (As).
 a. On which type of chromosome (A, X, or Y) would you expect the genes to have the greatest number of new mutations per base pair over many generations in a population? Why?
 b. On which type of chromosome would you expect the least number of new mutations per base pair? Why?
 c. Can you calculate the expected number of new mutations per base pair for a gene on the X and Y chromosome for every 1 new mutation in a gene on an autosome if the mutation rate in males is twice that in females?

Answer:

- a. Y chromosome. All, or 100 percent of, Y chromosomes are passed through the male lineage via sperm. The production of sperm (spermatogenesis) continues throughout a man's life, undergoing many rounds of cell division. Each round of cell division include DNA replication, which provides opportunity for new mutations, so the male lineage has a higher mutation rate than the female lineage, as explained in the text.
 b. X chromosome. Two out of every three X chromosomes (66.7 percent) are transmitted through the female lineage, which has a lower mutation rate than the male lineage. By comparison, 50 percent of autosomes are inherited through females with the lower mutation rate and 50 percent through males with the higher mutation rate.
 c. Set the male mutation rate (μ_M) as 2.0 per unit time and the female mutation rate (μ_F) as 1.0 per unit time. Since autosomes are transmitted equally through males and females, then the autosomal rate is the average of the male and female rates:

$$(\mu_A) = (2 + 1)/2 = 1.5$$

Since genes on the Y are transmitted only through males, the Y rate equals the male rate:

$$\mu_Y = \mu_M = 2$$

Since 1/3 of X chromosomes are inherited through males and 2/3 through females:

$$\mu_X = (1/3 \mu_M) + (2/3 \mu_F) = (1/3 \times 2) + (2/3 \times 1) = 1.33$$

The expected number of new mutation on the Y for every 1 on an autosome is $2/1.5 = 1.33$. The expected number of new mutation on the X for every 1 on an autosome is $1.33/1.5 = 0.889$.

- 17.** For young men of age 20, there have been 150 rounds of DNA replication during sperm production as compared with only 23 rounds for a woman of age 20. That is a 6.5-fold greater number of cell divisions and proportionately greater opportunity for new point mutations. Yet, on average, 20-year-old men contribute only about twice as many new point mutations to their offspring as do women. How can you explain this discrepancy?

Answer: While experimental evidence to explain this observation are not available, one hypothesis is that sperm cells are physiologically weak and their normal function is easily disrupted by mutations. Thus, sperm that carry deleterious new mutations are less likely to survive and form a zygote with an egg cell. Therefore, many sperm with new mutations are eliminated prezygotically.

- 18.** In computer science, a bit stores one of two states, 0 or 1. A byte is a group of 8 bits, which has $2^8 = 256$ possible states. Modern computer files are often mega-bytes (10^6 bytes), or even giga-bytes (10^9 bytes), in size. The human genome is approximately 3 billion base pairs in size. How many nucleotides are needed to encode a single byte? How large of a computer file would it take to store the same amount of information as a single human genome?

Answer: Four nucleotides, with four possible states (A, T, C, G) can encode $4 \times 4 \times 4 \times 4 = 4^4 = 256 = 1$ byte. If one byte can encode four nucleotides, then 3×10^9 nucleotides can be encoded in $(3 \times 10^9) / 4 = 7.5 \times 10^8$ bytes = 750×10^6 , or 750 megabytes.

- 19.** The human genome is approximately 3 billion base pairs in size.
- Using standard 8.5-in \times 11-in paper with one-inch margins, a 12-point font size and single-spaced lines, how many sheets of paper printed on one side would be required to print out the human genome?
 - A ream of 500 sheets of paper is about 5 cm thick. How tall would the stack of paper with the entire human genome be?
 - Would you want a backpack, shopping cart, or a semi trailer truck to haul around this stack?

Answer:

- Assuming a single one-sided page can fit 23 lines, with 56 letters in each line, $23 \times 56 = 1288$ letters per sheet. The human genome is 3×10^9 base pairs, so the number of sheets required to print out the entire human genome = $3 \times 10^9 / 1288 = 2,329,192$ sheets of paper.

- b.** If a ream of 500 sheets = 5 cm thick, the thickness of 2,329,192 sheets = $5 \text{ cm}/500 \text{ sheets} \times 2,329,192 \text{ sheets} = 23,291 \text{ cm} = 233 \text{ meters}$.
- c.** Semitrailer truck