6.3 Stochastic models of genetics

MATHEMATICAL TECHNIQUES

♠ Compute the following probabilities for a selfing plant using figure 6.15.

• EXERCISE **6.3.1**
The fraction of grand-offspring (second generation) with genotype **AA**.

• EXERCISE **6.3.2**
The fraction of third generation offspring with genotype **AA**.

• EXERCISE **6.3.3**
The fraction of fourth generation offspring with genotype **AA**.

• EXERCISE **6.3.4**
The fraction of offspring with genotype **AA** in generation t.

♠ In normal plants, the probability that an offspring of a heterozygous parent is heterozygous is 0.5. However, suppose that the survival of heterozygous offspring differs from that of homozygous offspring, and the probability that a surviving offspring is heterozygous is not equal to 0.5. For the following values of the probability, write a discrete-time dynamical system for the fraction of heterozygous offspring over time, find the solution, and compute the fraction that will be heterozygous after 10 generations. How does this compare with the fraction for a normal plant?

• EXERCISE **6.3.5**
The probability that an offspring is heterozygous is 0.6.

• EXERCISE **6.3.6**
The probability that an offspring is heterozygous is 0.4.

• EXERCISE **6.3.7**
The probability that an offspring is heterozygous is 0.2.

• EXERCISE **6.3.8**
The probability that an offspring is heterozygous is 0.9.

♠ Suppose that the fraction of homozygous and heterozygous offspring that survive self-fertilization by a heterozygote is measured. Find the fraction of surviving offspring that are heterozygous in the following cases.

• EXERCISE **6.3.9**
All of the homozygous offspring survive and half of the heterozygous offspring survive.

• EXERCISE **6.3.10**
Half of the homozygous offspring survive and one third of the heterozygous offspring survive.

♠ Consider the following case of blending inheritance. A population of plants starts out with an equal number of individuals of heights 40 and 60 cm. The parents mate randomly, and the height of an offspring is exactly equal to the average height of its parents.

• EXERCISE **6.3.11**
What are all the possible matings? What would be the heights of the offspring? What is the probability that a 40 cm tall plant mates with a 40 cm tall plant?

• EXERCISE **6.3.12**
What is the probability that a 60 cm tall plant mates with a 60 cm tall plant, and the probability that a 40 cm tall plant mates with a 60 cm tall plant?

• EXERCISE **6.3.13**
Suppose that these offspring now mate with each other. Find all possible matings and the resulting offspring heights.

• EXERCISE **6.3.14**
Find the probability of each of the possible matings of the offspring. Out of 100 plants, about how many would have height 50?

• EXERCISE **6.3.15**
With blending inheritance, the height of the offspring of the offspring is equal to the average height of the four grandparents. Find the probability that all four grandparents have height 40 and thus the probability that a plant in the second generation has height 40.

• EXERCISE **6.3.16**
Find the probability that three grandparents have height 40 and that one grandparent has height 60. Make sure to count up all possible identities of the 60 cm grandparent (maternal grandmother etc).

APPLICATIONS

♠ A heterozygous plant with genotype **Aa** self-pollinates. Find the probability that an offspring is tall for the following genetic systems.

• EXERCISE **6.3.17**
Only plants that have two **A** alleles are tall (the allele **A** is recessive).

• EXERCISE **6.3.18**
Plants that have either one or two **A** alleles are tall (the allele **A** is dominant).

• EXERCISE **6.3.19**
Heterozygous plants are tall and homozygous plants are short.

• EXERCISE **6.3.20**
Half of heterozygous plants and one fourth of homozygous plants are tall (it depends on their position in the greenhouse).

♠ A heterozygous plant with genotype **Aa** self-pollinates, and then its offspring also self-pollinate. Find the probability that the offspring of the offspring are tall for the following genetics systems.

• EXERCISE **6.3.21**
Only plants that have two **A** alleles are tall.

• EXERCISE **6.3.22**
Plants that has either one or two **A** alleles are tall.

• EXERCISE **6.3.23**
Heterozygous plants are tall and that homozygous plants are short.

• EXERCISE **6.3.24**
Half of heterozygous plants and one fourth of homozygous plants are tall (it depends on their position in the greenhouse).

♠ Suppose we allow a plant and its offspring to self-pollinate for many generations, and that the original parent is heterozygous at locus 1 with alleles **a** and **A** and is also heterozygous at locus 2 with alleles **b** and **B**.

• EXERCISE **6.3.25**
What fraction of the first generation offspring will have the the genotype **AABb**?

• EXERCISE **6.3.26**
What fraction of the first generation offspring will have the completely heterozygous genotype **AaBb**?

• EXERCISE **6.3.27**
How many different genotypes at the two loci will remain after many generations? What fraction will be heterozygous at least one locus after a long time?

• EXERCISE **6.3.28**
What fraction of offspring will have the genotype **AABB** after a long time?

♠ Often geneticists want to change one allele in an outcrossing organism while keeping the rest of the genome the same. For example, they might wish to take a specially designed stock of flies and alter the eye color from red to white. Suppose that the white eye allele is dominant, meaning that flies with one or two white eye alleles will have white eyes. One procedure used is to take a white-eyed fly and cross it with the red-eyed stock. The white-eyed offspring are then considered to be the first generation, and are crossed with the red-eyed stock. Their white-eyed offspring are considered to be the second generation, and are again crossed with the red-eyed stock, and so forth. The special red-eyed stock is homozygous for the desirable allele **A** at some other locus, but the white-eyed fly is homozygous for the inferior **a** allele at that locus.

• EXERCISE **6.3.29**
What is the genotype at the eye color locus in the first generation?

• EXERCISE **6.3.30**
What is the genotype at the eye color locus in the second and subsequent generations?

• EXERCISE **6.3.31**

What fraction of flies will have the **a** allele (at the second locus) after 1 generation?

• EXERCISE **6.3.32**

What fraction of flies will have the **a** allele (at the second locus) after 2 generations?

• EXERCISE **6.3.33**

What fraction of flies will have the **a** allele (at the second locus) after t generations?

• EXERCISE **6.3.34**

How many back-crosses would be necessary to purge 99.9999% of the inferior genes from the white-eyed fly?

♠ One force that can alter the ratio of heterozygotes produced by a selfing heterozygote is **meiotic drive**. This means that one allele, say **A**, pushes its way into more than half of the gametes (ovules or pollen).

• EXERCISE **6.3.35**

Suppose meiotic drive affects the pollen only and that 80% of the pollen grains from a heterozygote carry the **A** allele. Ovules are normal and 50% of them carry the **A** allele. What fraction of offspring from a selfing heterozygote will be heterozygous?

• EXERCISE **6.3.36**

Suppose meiotic drive affects both pollen and ovules and that 80% of the pollen grains and ovules from a heterozygote carry the **A** allele. What fraction of offspring from a selfing heterozygote will be heterozygous?

• EXERCISE **6.3.37**

Suppose meiotic drive affects both pollen and ovules but that 80% of the pollen grains carry the **A** allele while 80% of ovules carry the **a** allele. What fraction of offspring from a selfing heterozygote will be heterozygous?

• EXERCISE **6.3.38**

How many generations would it take before the probability of a descendent of a plant described in exercise 6.3.37 would have less than a 0.01 chance of being a heterozygote? Compare this with the number of generations required in the absence of meiotic drive.

♠ Suppose height is governed by two genes, and follows the rule that each **B** allele increases height by 1 cm (as in equation 6.11). A short plant with two copies of the short allele at each locus (genotype $\mathbf{b_1b_1b_2b_2}$) is crossed with a tall plant with two copies of the tall allele at each locus (genotype $\mathbf{B_1B_1B_2B_2}$).

• EXERCISE **6.3.39**

Find all possible heights of the offspring of these plants, and compute the the probability of each.

• EXERCISE **6.3.40**

Suppose two of these offspring are crossed. Find all possible heights of the offspring, and compute the the probability of each.

♠ Consider the same case as in exercises 6.3.39 and 6.3.40 but that the **B** genes are dominant. That is, a plant gets a 2 cm boost in height from the first locus if it has at least one allele of type $\mathbf{B_1}$, and a 2 cm boost in height from the second locus if it has at least one allele of type $\mathbf{B_2}$.

• EXERCISE **6.3.41**

Find the height of the offspring of these plants.

• EXERCISE **6.3.42**

Find the heights and their probabilities of the next generation of plants.

♠ Heterozygosity in inbreeding organisms can be restored by mutation. Suppose that mutations always create brand new alleles. Suppose that each parental allele has a probability 0.01 of mutating.

• EXERCISE **6.3.43**

Suppose first that the parent has genotype **AA**. What is the probability that the allele that came from the pollen is type **A**? What is the probability that the allele that came from the ovule is type **A**?

• EXERCISE **6.3.44**

The probability that both alleles in the offspring are type **A** is the **product** of the probability that allele from the pollen is **A** and the probability that the allele from the ovule is **A** (we will derive this in section 6.6). What is the probability that the offspring of a homozygous parent is homozygous? What is the probability that the offspring of a homozygous parent is heterozygous?

- EXERCISE **6.3.45**

  Suppose a plant is heterozygous with genotype **Aa**. What is the probability that the allele that came from the pollen is type **A**? What is the probability that the allele that came from the ovule is type **A**?

- EXERCISE **6.3.46**

  Find the probability that the offspring is **AA**. Find the probability that the offspring is **aa**. What is the probability that the offspring of a heterozygous parent is homozygous? What is the probability that the offspring of a heterozygous parent is heterozygous? How does this compare with the result in the absence of mutation?

Chapter 7

Answers

6.3.1. All the **AA** offspring (0.25) + one fourth of the heterozygous offspring $(0.25 \cdot 0.5)$ gives $0.25+0.125 = 0.375$. Alternatively, we know that $h_2 = 0.5^2 = 0.25$ are heterozygous. The remaining 0.75 are split evenly between **AA** and **aa**, so the fraction is 0.75/2=0.375.
6.3.3. All the **AA** great grand-offspring (0.4375) + one fourth of the heterozygous offspring $(0.125 \cdot 0.25)$ gives 0.46875. Alternatively, we know that $h_4 = 0.5^4 = 0.0625$ are heterozygous. The remaining 0.9375 are split evenly between **AA** and **aa**, so the fraction is 0.9375/2=0.46875.
6.3.5. The updating function is $h_{t+1} = 0.6h_t$, with solution $h + t = 0.6^t$. After 10 generations, a fraction $h_{10} = 0.006$ will be heterozygous. This is only six times as many as for a normal plant.
6.3.7. The updating function is $h_{t+1} = 0.2h_t$, with solution $h + t = 0.2^t$. After 10 generations, a fraction $h_{10} = 1.02 \times 10^{-7}$ will be heterozygous. This is vanishingly small.
6.3.9. There should be an equal fraction, 0.5, of each type produced. However, after mortality, 0.25 of the original offspring are living heterozygotes and 0.5 of the original offspring are living homozygotes. Out of the total of 0.75 that survive, a fraction 0.25/0.75=0.33 are heterozygotes and 0.5/0.75=0.67 are homozygotes.
6.3.11. There are 3 possible matings, 40 cm with 40 cm, 40 cm with 60 cm, and 60 cm with 60 cm. The first produces offspring with height 40 cm, the second offspring with height 50 cm, and the last offspring with height 60 cm. The probability that both parents have height 40 cm is $0.5 \cdot 0.5 = 0.25$.
6.3.13. There are now 6 possible matings: (40,40), (40,50), (40,60), (50,50), (50,60), and (60,60). They produce offspring of heights 40, 45, 50, 50, 55 and 60 respectively.
6.3.15. The probability that any one grandparent has height 40 cm is 0.5, so the probability that all four have height 40 cm is $0.5 \cdot 0.5 \cdot 0.5 \cdot 0.5 = 0.0625$.
6.3.17. 1/4 of the offspring have genotype **AA** and are tall.
6.3.19. Half will be heterozygous, and hence half will be tall.
6.3.21. 3/8 of the grandoffspring have genotype **AA** and are tall.
6.3.23. After 2 generations, only 1/4 are heterozygous and tall.
6.3.25. The chance that an offspring has genotype **AA** at the first locus is 1/4, and the chance that is has genotype **Bb** at the second locus is 1/2, so the chance of this exact genotype is 1/16.
6.3.27. There will be four: **aabb**, **aaBB**, **AAbb**, **AABB**. None will be heterozygous because all plants are eventually homozygous.
6.3.29. The flies are white-eyed, and hence have at least one of the white-eyed alleles. Because each has a parent from the red-eyed stock, it must also have one red-eyed allele. Therefore, these flies will also be heterozygous at the eye color locus.
6.3.31. In the first generation, all the flies will have genotype **Aa** at the second locus.
6.3.33. Half of the **a** alleles will be lost each generation. Let p_t be the probability that a fly has an **a** allele in generation t. Then

$$p_{t+1} = 0.5p_t$$

with initial condition $p_1 = 1$. The solution is

$$p_t = 0.5^{t-1}.$$

6.3.35. A heterozygote could have gotten **a** from the ovule and **A** from the pollen or **A** from the ovule and **a** from the pollen. The probability of **a** from ovule is 0.5 and the probability of **A** from pollen is 0.8, giving a probability of 0.4 of a heterozygous offspring in this way. The probability of **A** from ovule is 0.5 and the probability of **a** from the pollen is 0.2, giving a probability of 0.1 of a heterozygous offspring in this way. The total is 0.4+0.1 = 0.5 as in a normal plant.
6.3.37. A heterozygote could have gotten **a** from the ovule and **A** from the pollen or **A** from the ovule and **a** from the pollen. The probability of **a** from ovule is 0.8 and the probability of **A** from pollen is 0.8, giving a probability of 0.64 of a heterozygous offspring in this way. The probability of **A** from ovule is 0.2 and the probability of **a** from the pollen is 0.2, giving a probability of 0.04 of a heterozygous offspring in this way. The total is 0.64+0.04 = 0.68.
6.3.39. All offspring have height 42 cm The probability is 1.
6.3.41. All are tall, height 44 cm.
6.3.43. 0.99 (probability it does not mutate).
6.3.45. Multiply 0.5 (probability it started out as **A**) times the probability it didn't mutate (0.99) to get 0.495.