Linear Algebra in the Context of Autosomal Inheritance

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1 Introduction

An Austrian monk named Gregor Mendel laid the groundwork for the chromosome theory of inheritance in 1865 when he worked out the rules of inheritance through a series of experiments on garden peas. Another key insight emerged during the final decades of the nineteenth century, when biologists described meiosis. Walter Sutton and Theodor Boveri linked these two discoveries in 1902 to form the chromosome theory of inheritance. This theory states that genes are located on chromosomes, and that the transmission of chromosomes to daughter cells at meiosis accounts for the patterns of inheritance that Mendel observed [1]. The chromosome theory of inheritance launched the study of genetics, the branch of biology that focuses on the inheritance of traits.

In this project we examine autosomal inheritance, a type of inheritance studied widely in genetics. More specifically, we use spectral theory to model different scenarios in which a farmer fertilizes plants with partners of various genotypes. The process begins with a matrix of probabilities for the genotype of offspring given the genotype of its parents. We can apply this matrix as a transformation to get the genotype proportions for the next generation, and after diagonalization extrapolate our results to an arbitrary number of generations.

2 Definitions

It would be helpful for the reader to be familiar with the following concepts from genetics and linear algebra.

Autosomal inheritance. The pattern of inheritance of any genes not on a sex chromosome. It is the "standard" kind of inheritance that was studied by Mendel. It is not dependent on the sex of the parent or offspring, as the offspring inherits one allele of the gene from each parent.

Gene. A hereditary factor that influences a particular trait, that is, physical characteristic visible in an individual. Allele. A particular form of a gene, represented in autosomal inheritance by a single letter - in our example, by A or a.

Dominant allele. The allele which expresses itself and controls the particular trait in the individual even when present with the other allele. Conventionally it is represented by the uppercase, for example, A.

Recessive allele. The allele which expresses itself and controls the particular trait in the individual only when the other allele is absent. Conventionally it is represented by the lowercase, for example, a.

Genotype. A listing of the alleles of particular genes in an individual, consisting of two alleles. Possible genotypes for alleles A and a are AA, Aa and aa.

Eigenvalue. For a linear transformation $T: V \to V$, a scalar λ such that $T\mathbf{v} = \lambda \mathbf{v}$ for some nonzero $\mathbf{v} \in V$.

Eigenvector. Given a linear transformation $T: V \to V$, a vector \mathbf{v} for which $T\mathbf{v} = \lambda \mathbf{v}$. $\lambda \in \mathbb{R}$ is its corresponding eigenvalue.

Diagonalization. A process that takes a matrix A and finds matrices S and D such that D is diagonal and

$$A = SDS^{-1}. (1)$$

The importance of diagonalizing operators comes from the fact that powers and functions of diagonal matrices are easy to compute. If we diagonalize a matrix, we can more readily compute functions of it.

In the following sections we will study two different breeding programs for plants. To do so, we will first have to establish the distribution probabilities for the genotypes of the studied population of plants.

3 Genotype probabilities

Consider a farmer in an experimental farm that has a large population of plants consisting of some distribution of three possible plant genotypes: AA, Aa, aa. Our aim is to derive a distribution for the genotype probabilities of different breeding programs. Thus, we examine each possible breeding combination. It must be noted that, in order to simplify the calculations, we will assume that each parent has a 50% chance of passing each of their alleles.

To calculate the probability of each genotype on the offspring, we find the probability of inheriting each allele from either parent, and calculate the total probabilities appropriately. For example, in the cross $Aa \times Aa$, each parent has a 0.5 chance of passing on the A allele, and a 0.5 chance of passing on the a allele, to a particular offspring. The probability of the offspring being AA is $0.5 \cdot 0.5 = 0.25$ since the only way for this to happen is for an A to be inherited from each parent. The probability of aa is similarly 0.25, since an a must be inherited from each parent. There are two ways the offspring can have Aa — the offspring could receive the A from their first parent and the a from their second, or vice versa. The probability of Aa is therefore $2(0.5 \cdot 0.5) = 0.5$. This can be generalized to fill the table below.

Danasat	Probability	Probability	Probability	Probability	Probability	Probability	Probability
Parent Genotypes	offspring	offspring	offspring	offspring	offspring	offspring	offspring
(P1, P2)	receives A	receives a	receives A	receives a	genotype is	genotype is	genotype is
(1 1, 1 2)	from P1	from P1	from P2	from P2	AA	Aa	aa
AA, AA	1	0	1	0	1	0	0
AA, Aa	1	0	0.5	0.5	0.5	0.5	0
AA, aa	1	0	0	1	0	1	0
Aa, Aa	0.5	0.5	0.5	0.5	0.25	0.5	0.25
Aa, aa	0.5	0.5	0	1	0	0.5	0.5
aa, aa	0	1	0	1	0	0	1

Table 1: Generalized table for genotype probabilities

However, we're only interested in the allele combination of the offspring, regardless of the specific origin of each allele. Therefore, in our calculations we will only be using the information of the last 3 columns of Table 1. Focusing on this information (and taking the transpose of the columns), we arrive at the following table.

		Parent Genotype							
		AA, AA	AA, Aa	AA, aa	Aa, Aa	Aa, aa	aa, aa		
Offenning	AA	1	0.5	0	0.25	0	0		
Offspring Genotype	Aa	0	0.5	1	0.5	0.5	0		
Genotype	aa	0	0	0	0.25	0.5	1		

Table 2: Offspring genotype probabilities

Now that we have the distribution probabilities of each offspring, let us dive into the first breeding program, one in which the farmer always fertilizes with a plant of genotype AA through the generations.

4 Breeding with plants of genotype AA

As just mentioned, in this specific scenario the farmer undertakes a breeding program in which each plant in the population is always fertilized with a plant of genotype AA. We will use linear algebra to model the genotype proportions across generations.

To denote the portions of the initial population with genotypes AA, Aa, and aa we'll use a_0 , b_0 , c_0 respectively.

We represent this as

$$\mathbf{v}_0 = \begin{pmatrix} a_0 \\ b_0 \\ c_0 \end{pmatrix}. \tag{2}$$

We define a transition matrix T, which has the property that it takes in a vector representing the current genotype distribution and outputs a vector representing the genotype distribution for the next generation. As each plant is always fertilized with one of genotype AA, we use the 3-by-3 matrix formed by the first three columns of Table 2.

$$T = \begin{pmatrix} 1 & 0.5 & 0 \\ 0 & 0.5 & 1 \\ 0 & 0 & 0 \end{pmatrix} \tag{3}$$

We first derive an expression for the distribution of the three possible genotypes in the population after one generation in terms of the fractions present in the initial population.

It is sufficient to apply our transition matrix once, so to calculate the proportions of the first generation, we multiply \mathbf{v}_0 with T to compute \mathbf{v}_1 .

$$\mathbf{v}_{1} = T\mathbf{v}_{0} = \begin{pmatrix} 1 & 0.5 & 0 \\ 0 & 0.5 & 1 \\ 0 & 0 & 0 \end{pmatrix} \begin{pmatrix} a_{0} \\ b_{0} \\ c_{0} \end{pmatrix} = \begin{pmatrix} a_{0} + \frac{b_{0}}{2} \\ \frac{b_{0}}{2} + c_{0} \\ 0 \end{pmatrix}$$
(4)

Now, generalizing this step, to find an expression for the distribution of the three possible genotypes in the population after n generations in terms of the fractions present after n-1 generations, we can calculate the nth generation by multiplying T with \mathbf{v}_{n-1} :

$$\mathbf{v}_{n} = T\mathbf{v}_{n-1} = \begin{pmatrix} 1 & 0.5 & 0 \\ 0 & 0.5 & 1 \\ 0 & 0 & 0 \end{pmatrix} \begin{pmatrix} a_{n-1} \\ b_{n-1} \\ c_{n-1} \end{pmatrix} = \begin{pmatrix} a_{n-1} + \frac{b_{n-1}}{2} \\ \frac{b_{n-1}}{2} + c_{n-1} \\ 0 \end{pmatrix} = \begin{pmatrix} a_{n} \\ b_{n} \\ c_{n} \end{pmatrix}$$
(5)

And therefore, we can create a recursion whereby the n^{th} generation is calculated by applying T to \mathbf{v}_0 n times;

that is, we can compute the proportions for any generation by repeatedly multiplying the initial vector \mathbf{v}_0 by T until the desired generation is reached.

$$\mathbf{v}_n = T^n \, \mathbf{v}_0 \tag{6}$$

However, taking powers of a matrix isn't easy, and T must be diagonalized to ease the computations. To begin we factor out a $\frac{1}{2}$ from T to make every element an integer.

$$T = \frac{1}{2} \begin{pmatrix} 2 & 1 & 0 \\ 0 & 1 & 2 \\ 0 & 0 & 0 \end{pmatrix} \tag{7}$$

We ignore the $\frac{1}{2}$ for now, and which we calculate the values of λ that make the determinant of the characteristic matrix equal to 0.

$$\begin{vmatrix} 2 - \lambda & 1 & 0 \\ 0 & 1 - \lambda & 2 \\ 0 & 0 & -\lambda \end{vmatrix} = 0 \tag{8}$$

$$(2 - \lambda)(1 - \lambda)(-\lambda) = 0 \tag{9}$$

(10)

The characteristic equation equals 0 when λ equals 0, 1, or 2, so these are our eigenvalues (notwithstanding the need to scale them down, which will be done later). We now use row reduction to obtain our eigenvectors.

In the $\lambda_1 = 1$ case:

$$\begin{pmatrix}
2-1 & 1 & 0 \\
0 & 1-1 & 2 \\
0 & 0 & 0-1
\end{pmatrix}
\xrightarrow{r_3 \to -r_3}
\begin{pmatrix}
1 & 1 & 0 \\
0 & 0 & 2 \\
0 & 0 & 1
\end{pmatrix}
\xrightarrow{r_2 \to r_2 - 2r_3}
\begin{pmatrix}
1 & 1 & 0 \\
0 & 0 & 0 \\
0 & 0 & 1
\end{pmatrix}$$
(11)

Which yields the eigenvector $\begin{pmatrix} -1 & 1 & 0 \end{pmatrix}^T$.

In the $\lambda_2 = 2$ case:

$$\begin{pmatrix}
2-2 & 1 & 0 \\
0 & 1-2 & 2 \\
0 & 0 & 0-2
\end{pmatrix} = \begin{pmatrix}
0 & 1 & 0 \\
0 & -1 & 2 \\
0 & 0 & -2
\end{pmatrix} \xrightarrow{r_2 \to \frac{1}{2}(r_2 + r_1)} \begin{pmatrix}
0 & 1 & 0 \\
0 & 0 & 1 \\
0 & 0 & 0
\end{pmatrix} \xrightarrow{r_2 \rightleftharpoons r_3} \begin{pmatrix}
0 & 0 & 0 \\
0 & 1 & 0 \\
0 & 0 & 1 \\
0 & 0 & 0
\end{pmatrix} \xrightarrow{r_1 \rightleftharpoons r_2} \begin{pmatrix}
0 & 1 & 0 \\
0 & 1 & 0 \\
0 & 0 & 1
\end{pmatrix}$$
(12)

Thus, a corresponding eigenvector is $\begin{pmatrix} -1 & 0 & 0 \end{pmatrix}^T$.

In the $\lambda_3 = 0$ case:

$$\begin{pmatrix}
2 - 0 & 1 & 0 \\
0 & 1 - 0 & 2 \\
0 & 0 & 0 - 0
\end{pmatrix}
\xrightarrow{r_1 \to \frac{1}{2}(r_1 - r_3)}
\begin{pmatrix}
1 & 0 & -1 \\
0 & 1 & 2 \\
0 & 0 & 0
\end{pmatrix}$$
(13)

Our final eigenvector is therefore $\begin{pmatrix} 1 & -2 & 1 \end{pmatrix}^T$. Before creating our diagonal matrix of eigenvalues we must scale their current values by $\frac{1}{2}$, to account for the $\frac{1}{2}$ we factored out of T at the start. Because of this our eigenvalues are actually $0, \frac{1}{2}, 1$. The result of our diagonalization is thus

$$T = SDS^{-1}$$
, where $S = \begin{pmatrix} -1 & -1 & 1 \\ 1 & 0 & -2 \\ 0 & 0 & 1 \end{pmatrix}$ and $D = \begin{pmatrix} \frac{1}{2} & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 0 \end{pmatrix}$. (14)

Additionally, by the properties of diagonal and invertible matrices, $T^n = SD^nS^{-1}$. Combining this result with (6) and taking the inverse of S we see that

$$\mathbf{v}_{n} = SD^{n}S^{-1}\mathbf{v}_{0} = \begin{pmatrix} -1 & -1 & 1\\ 1 & 0 & -2\\ 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} 2^{-n} & 0 & 0\\ 0 & 1 & 0\\ 0 & 0 & 0 \end{pmatrix} \begin{pmatrix} 0 & 1 & 2\\ -1 & -1 & -1\\ 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} a_{0}\\ b_{0}\\ c_{0} \end{pmatrix}. \tag{15}$$

Performing matrix multiplication with (24), we obtain the following.

$$\mathbf{v}_{n} = \begin{pmatrix} -1 & -1 & 1\\ 1 & 0 & -2\\ 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} 2^{-n} & 0 & 0\\ 0 & 1 & 0\\ 0 & 0 & 0 \end{pmatrix} \begin{pmatrix} 0 & 1 & 2\\ -1 & -1 & -1\\ 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} a_{0}\\ b_{0}\\ c_{0} \end{pmatrix}$$
(16)

$$= \begin{pmatrix} 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} 0 & 0 & 0 \end{pmatrix} \begin{pmatrix} 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} c_0 \end{pmatrix}$$

$$= \begin{pmatrix} -1 & -1 & 1 \\ 1 & 0 & -2 \\ 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} 2^{-n} & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 0 \end{pmatrix} \begin{pmatrix} b_0 + 2c_0 \\ -a_0 - b_0 - c_0 \\ c_0 \end{pmatrix}$$

$$(17)$$

$$= \begin{pmatrix} -1 & -1 & 1 \\ 1 & 0 & -2 \\ 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} 2^{-n}(b_0 + 2c_0) \\ -a_0 - b_0 - c_0 \\ 0 \end{pmatrix}$$

$$\tag{18}$$

$$= \begin{pmatrix} a_0 + b_0 + c_0 - 2^{-n}(b_0 + 2c_0) \\ 2^{-n}(b_0 + 2c_0) \\ 0 \end{pmatrix}$$
(19)

With a bit of simplification we obtain the following distribution for the three genotypes after n generations, $n \ge 0$.

$$AA: a_0 + b_0 + c_0 - \frac{b_0}{2^n} + \frac{c_0}{2^{n-1}}$$

$$Aa: \frac{b_0}{2^n} - \frac{c_0}{2^{n-1}}$$

$$aa: 0$$
(20)

Analyzing (20) as n gets larger and larger, it is clear how the proportions of the plants with genotype Aa tend to 0 whereas the plants with genotype AA reach the $a_0 + b_0 + c_0$, which is 100% of the population. It isn't surprising, as the farmer constantly force-breeds every plant and increases the chances of AA offspring in every generation. Let us now look at a more interesting scenario.

5 Fertilizing population with a plant of its own genotype

In this scheme, another farmer modifies the fertilization procedure by undertaking a breeding program in which each plant in the population is fertilized with a plant of its own. Now the final result isn't as transparent as the previous breeding program. The steps to model such are the same as the previous one. We firstly redefine our transition matrix T.

In this scenario, the farmer is inbreeding the plants, and therefore the transition matrix from one generation to the next will be given by the columns AA, AA, Aa, Aa and aa, aa in Table 2.

$$T = \begin{pmatrix} 1 & \frac{1}{4} & 0 \\ 0 & \frac{1}{2} & 0 \\ 0 & \frac{1}{4} & 1 \end{pmatrix} = \frac{1}{4} \begin{pmatrix} 4 & 1 & 0 \\ 0 & 2 & 0 \\ 0 & 1 & 4 \end{pmatrix}$$
 (21)

We will set aside the common factor of $\frac{1}{4}$ to simplify the calculations, and once the computations have been performed, we will adjust to account for it. We'll be working with 4T instead. To diagonalize the matrix, we first solve the characteristic equation:

$$\det(4T - \lambda I) = \begin{vmatrix} 4 - \lambda & 1 & 0 \\ 0 & 2 - \lambda & 0 \\ 0 & 1 & 4 - \lambda \end{vmatrix} = (4 - \lambda)(2 - \lambda)(4 - \lambda) = (4 - \lambda)^{2}(2 - \lambda) = 0$$
 (22)

The eigenvalues are $\lambda_1 = 4$, $\lambda_2 = 2$. Now, we seek their corresponding eigenvectors. In the $\lambda_1 = 4$ case:

$$\begin{pmatrix}
4-4 & 1 & 0 \\
0 & 2-4 & 0 \\
0 & 1 & 4-4
\end{pmatrix} = \begin{pmatrix}
0 & 1 & 0 \\
0 & -2 & 0 \\
0 & 1 & 0
\end{pmatrix} \xrightarrow{r_1 \to r_1 + \frac{1}{2}r_2} \begin{pmatrix}
0 & 0 & 0 \\
r_2 \to -\frac{1}{2}r_2 \\
\hline
 & & & & \\
0 & 0 & 0
\end{pmatrix}$$
(23)

This yields the eigenvectors $\begin{pmatrix} 1 & 0 & 0 \end{pmatrix}^T$ and $\begin{pmatrix} 0 & 0 & 1 \end{pmatrix}^T$. In the $\lambda_2=2$ case:

$$\begin{pmatrix}
4-2 & 1 & 0 \\
0 & 2-2 & 0 \\
0 & 1 & 4-2
\end{pmatrix} = \begin{pmatrix}
2 & 1 & 0 \\
0 & 0 & 0 \\
0 & 1 & 2
\end{pmatrix} \xrightarrow{r_1 \to \frac{1}{2}(r_1 - r_3)} \begin{pmatrix}
1 & 0 & -1 \\
0 & 1 & 2 \\
0 & 0 & 0
\end{pmatrix} \tag{24}$$

And therefore yields the eigenvector $\begin{pmatrix} 1 & -2 & 1 \end{pmatrix}^T$. Now, we readjust our eigenvectors in the same manner as with the previous question, leaving us $\lambda_1 = 1$ and $\lambda_2 = \frac{1}{2}$. The diagonalization is the following.

$$T = SDS^{-1}$$
, where $S = \begin{pmatrix} 1 & 0 & 1 \\ 0 & 0 & -2 \\ 0 & 1 & 1 \end{pmatrix}$ and $D = \begin{pmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & \frac{1}{2} \end{pmatrix}$ (25)

Since $T^n = SD^nS^{-1}$, taking the inverse of S we see that

$$\mathbf{v}_{n} = SD^{n}S^{-1}\mathbf{v}_{0} = \begin{pmatrix} 1 & 0 & 1 \\ 0 & 0 & -2 \\ 0 & 1 & 1 \end{pmatrix} \begin{pmatrix} 1^{n} & 0 & 0 \\ 0 & 1^{n} & 0 \\ 0 & 0 & 2^{-n} \end{pmatrix} \begin{pmatrix} 1 & \frac{1}{2} & 0 \\ 0 & \frac{1}{2} & 1 \\ 0 & -\frac{1}{2} & 0 \end{pmatrix} \begin{pmatrix} a_{0} \\ b_{0} \\ c_{0} \end{pmatrix}. \tag{26}$$

Performing matrix multiplication,

$$\mathbf{v}_{n} = \begin{pmatrix} 1 & 0 & 1 \\ 0 & 0 & -2 \\ 0 & 1 & 1 \end{pmatrix} \begin{pmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 2^{-n} \end{pmatrix} \begin{pmatrix} 1 & \frac{1}{2} & 0 \\ 0 & \frac{1}{2} & 1 \\ 0 & -\frac{1}{2} & 0 \end{pmatrix} \begin{pmatrix} a_{0} \\ b_{0} \\ c_{0} \end{pmatrix}$$

$$(27)$$

$$= \begin{pmatrix} 1 & 0 & \frac{1}{2^n} \\ 0 & 0 & -2^{1-n} \\ 0 & 1 & \frac{1}{2^n} \end{pmatrix} \begin{pmatrix} a_0 + \frac{1}{2}b_0 \\ \frac{1}{2}b_0 + c_0 \\ -\frac{1}{2}b_0 \end{pmatrix}$$

$$(28)$$

$$= \begin{pmatrix} \frac{2^{n+1}a_0 + b_0(2^n - 1)}{2^{n+1}} \\ \frac{b_0}{2^n} \\ \frac{b_0(2^n - 1) + 2^{n+1}c_0}{2^{n+1}} \end{pmatrix}. \tag{29}$$

We end up with the following genotype distributions after n generations.

$$AA: \frac{2^{n+1}a_0 + b_0 (2^n - 1)}{2^{n+1}}$$

$$Aa: \frac{b_0}{2^n}$$

$$aa: \frac{b_0 (2^n - 1) + 2^{n+1}c_0}{2^{n+1}}$$
(30)

For instance, looking after 5 generations we would have

$$AA: \frac{2^{6}a_{0} + b_{0}(2^{5} - 1)}{2^{6}} = a_{0} + \frac{31}{64}b_{0}$$

$$Aa: \frac{b_{0}}{2^{5}} = \frac{b_{0}}{32}$$

$$aa: \frac{b_{0}(2^{5} - 1) + 2^{6}c_{0}}{2^{6}} = \frac{31}{64}b_{0} + c_{0}$$
(31)

But the most interesting behavior is the long term one, and therefore we look at the distribution behavior as n tends to infinity,

Letting $n \to \infty$, we have

$$\lim_{n \to \infty} \mathbf{v}_n = \lim_{n \to \infty} \begin{pmatrix} \frac{2^{n+1} a_0 + b_0 (2^n - 1)}{2^{n+1}} \\ \frac{b_0}{2^n} \\ \frac{b_0 (2^n - 1) + 2^{n+1} c_0}{2^{n+1}} \end{pmatrix} = \begin{pmatrix} a_0 + \frac{b_0}{2} \\ 0 \\ \frac{b_0}{2} + c_0 \end{pmatrix}$$
(32)

We can use MATLAB [2] to graph the above with $a_0 = b_0 = 0.4, c_0 = 0.2$:

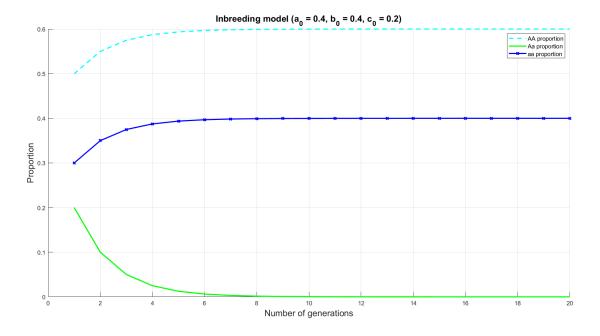


Figure 1: Genotype proportions of inbreeding across generations

It can be seen in both (32) and the figure above how inbreeding eliminates genotypes with mixed alleles. By (32)

we can see how the b_0 proportion is shared by the AA and aa genotypes as n gets larger and larger.

6 Conclusion

The use of spectral theory to calculate genotype frequencies provides interesting insights into the behavior of gene pools over many generations. These results meet our expectations from biological concepts. Our first case illustrates the process of elimination of one of the homozygotes from the population over time - due to repeated breeding with the other allele. This is useful in cases in which the recessive allele a is not suitable for the plant's survival - since its homozygote is removed and it is now present only in conjunction with the dominant allele A, its effects are no longer observed in the population of plants. In our second case, we witness the elimination of heterozygotes - our eventual populations are entirely made up of pure breeds of AA and aa types. This is useful for establishing pure lines with specific characteristics, that could be utilized in further genetic crosses and experiments.

Therefore the models of inheritance that spectral theory provides us are useful for obtaining predictions about the end results of a specifically designed breeding program. Extending this to cases with more than one gene, or more than two alleles for one gene, could help us design more complex models to predict inheritance patterns for an individual plant or animal as a whole.

References

- [1] Freeman, Scott. Biological Science: Pearson New International Edition. *Harlow Pearson Education Limited*, pp. 473-480, 2014.
- [2] MATLAB. Version 9.9.0. (R2010a). Natick, Massachusetts: The Math Works Inc, 2019.