

UNIT VII

GENETICS AND EVOLUTION

Chapter 5

Principles of Inheritance
and Variation

Chapter 6

Molecular Basis of Inheritance

Chapter 7

Evolution

The work of Mendel and others who followed him gave us an idea of inheritance patterns. However the nature of those 'factors' which determine the phenotype was not very clear. As these 'factors' represent the genetic basis of inheritance, understanding the structure of genetic material and the structural basis of genotype and phenotype conversion became the focus of attention in biology for the next century. The entire body of molecular biology was a consequent development with major contributions from Watson, Crick, Nirenberg, Khorana, Kornbergs (father and son), Benzer, Monod, Brenner, etc. A parallel problem being tackled was the mechanism of evolution. Awareness in the areas of molecular genetics, structural biology and bio informatics have enriched our understanding of the molecular basis of evolution. In this unit the structure and function of DNA and the story and theory of evolution have been examined and explained.



James Dewey Watson was born in Chicago on 6 April 1928. In 1947, he received B.Sc. degree in Zoology. During these years his interest in bird-watching had matured into a serious desire to learn genetics. This became possible when he received a Fellowship for graduate study in Zoology at Indiana University, Bloomington, where he received his Ph.D. degree in 1950 on a study of the effect of hard X-rays on bacteriophage multiplication.

He met Crick and discovered their common interest in solving the DNA structure. Their first serious effort, was unsatisfactory. Their second effort based upon more experimental evidence and better appreciation of the nucleic acid literature, resulted, early in March 1953, in the proposal of the complementary double-helical configuration.

Francis Harry Compton Crick was born on 8 June 1916, at Northampton, England. He studied physics at University College, London and obtained a B.Sc. in 1937. He completed Ph.D. in 1954 on a thesis entitled "X-ray Diffraction: Polypeptides and Proteins".

A critical influence in Crick's career was his friendship with J. D. Watson, then a young man of 23, leading in 1953 to the proposal of the double-helical structure for DNA and the replication scheme. Crick was made an F.R.S. in 1959.

The honours to Watson with Crick include: the John Collins Warren Prize of the Massachusetts General Hospital, in 1959; the Lasker Award, in 1960; the Research Corporation Prize, in 1962 and above all, the Nobel Prize in 1962.



JAMES WATSON
FRANCIS CRICK

CHAPTER 5



PRINCIPLES OF INHERITANCE AND VARIATION

- 5.1 *Mendel's Laws of Inheritance*
- 5.2 *Inheritance of One Gene*
- 5.3 *Inheritance of Two Genes*
- 5.4 *Sex Determination*
- 5.5 *Mutation*
- 5.6 *Genetic Disorders*

Have you ever wondered why an elephant always gives birth only to a baby elephant and not some other animal? Or why a mango seed forms only a mango plant and not any other plant?

Given that they do, are the offspring identical to their parents? Or do they show differences in some of their characteristics? Have you ever wondered why siblings sometimes look so similar to each other? Or sometimes even so different?

These and several related questions are dealt with, scientifically, in a branch of biology known as Genetics. This subject deals with the inheritance, as well as the variation of characters from parents to offspring. Inheritance is the process by which characters are passed on from parent to progeny; it is the basis of heredity. Variation is the degree by which progeny differ from their parents.

Humans knew from as early as 8000-1000 B.C. that one of the causes of variation was hidden in sexual reproduction. They exploited the variations that were naturally present in the wild populations of plants and animals to selectively breed and select for organisms that possessed desirable characters. For example, through artificial selection and domestication from ancestral

Character	Dominant trait	Recessive trait
Seed shape	Round	Wrinkled
Seed colour	Yellow	Green
Flower colour	Violet	White
Pod shape	Full	Constricted
Pod colour	Green	Yellow
Flower position	Axial	Terminal
Stem height	Tall	Dwarf

Figure 5.1 Seven pairs of contrasting traits in pea plant studied by Mendel

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continuous self-pollination, shows the stable trait inheritance and expression for several generations. Mendel selected 14 true-breeding pea plant varieties, as pairs which were similar except for one character with contrasting traits. Some of the contrasting traits selected were smooth or wrinkled seeds, yellow or green seeds, inflated (full) or constricted green or yellow pods and tall or dwarf plants (Figure 5.1, Table 5.1).

wild cows, we have well-known Indian breeds, e.g., Sahiwal cows in Punjab. We must, however, recognise that though our ancestors knew about the inheritance of characters and variation, they had very little idea about the scientific basis of these phenomena.

5.1 MENDEL'S LAWS OF INHERITANCE

It was during the mid-nineteenth century that headway was made in the understanding of inheritance. Gregor Mendel, conducted hybridisation experiments on garden peas for seven years (1856–1863) and proposed the laws of inheritance in living organisms. During Mendel's investigations into inheritance patterns it was for the first time that statistical analysis and mathematical logic were applied to problems in biology. His experiments had a large sampling size, which gave greater credibility to the data that he collected. Also, the confirmation of his inferences from experiments on successive generations of his test plants, proved that his results pointed to general rules of inheritance rather than being unsubstantiated ideas. Mendel investigated characters in the garden pea plant that were manifested as two opposing traits, e.g., tall or dwarf plants, yellow or green seeds. This allowed him to set up a basic framework of rules governing inheritance, which was expanded on by later scientists to account for all the diverse natural observations and the complexity inherent in them.

Mendel conducted such artificial pollination/cross pollination experiments using several true-breeding pea lines. A true-breeding line is one that, having undergone



Table 5.1: Contrasting Traits Studied by Mendel in Pea

S.No.	Characters	Contrasting Traits
1.	Stem height	Tall/dwarf
2.	Flower colour	Violet/white
3.	Flower position	Axial/terminal
4.	Pod shape	Inflated/constricted
5.	Pod colour	Green/yellow
6.	Seed shape	Round/wrinkled
7.	Seed colour	Yellow/green

5.2 INHERITANCE OF ONE GENE

Let us take the example of one such hybridisation experiment carried out by Mendel where he crossed tall and dwarf pea plants to study the inheritance of one gene (Figure 5.2). He collected the seeds produced as a result of this cross and grew them to generate plants of the first hybrid generation. This generation is also called the **Filial₁ progeny** or the **F₁**. Mendel observed that all the F₁ progeny plants were tall, like one of its parents; none were dwarf (Figure 5.3). He made similar observations for the other pairs of traits – he found that the F₁ always resembled either one of the parents, and that the trait of the other parent was not seen in them.

Mendel then self-pollinated the tall F₁ plants and to his surprise found that in the Filial₂ generation some of the offspring were ‘dwarf’; the character that was not seen in the F₁ generation was now expressed. The proportion of plants that were dwarf were 1/4th of the F₂ plants while 3/4th of the F₂ plants were tall. The tall and dwarf traits were identical to their parental type and did not show any blending, that is all the offspring were either tall or dwarf, none were of in-between height (Figure 5.3).

Similar results were obtained with the other traits that he studied: only one of the parental traits was expressed in the F₁ generation while at the F₂ stage both the traits were expressed in the proportion 3:1. The contrasting traits did not show any blending at either F₁ or F₂ stage.

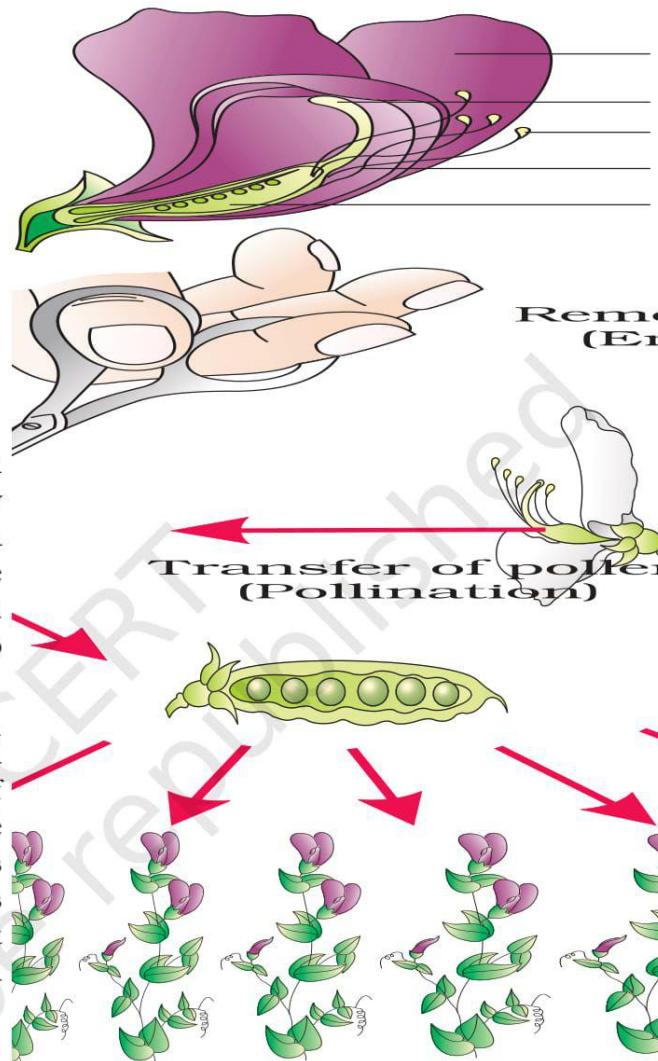


Figure 5.2 Steps in making a cross in pea

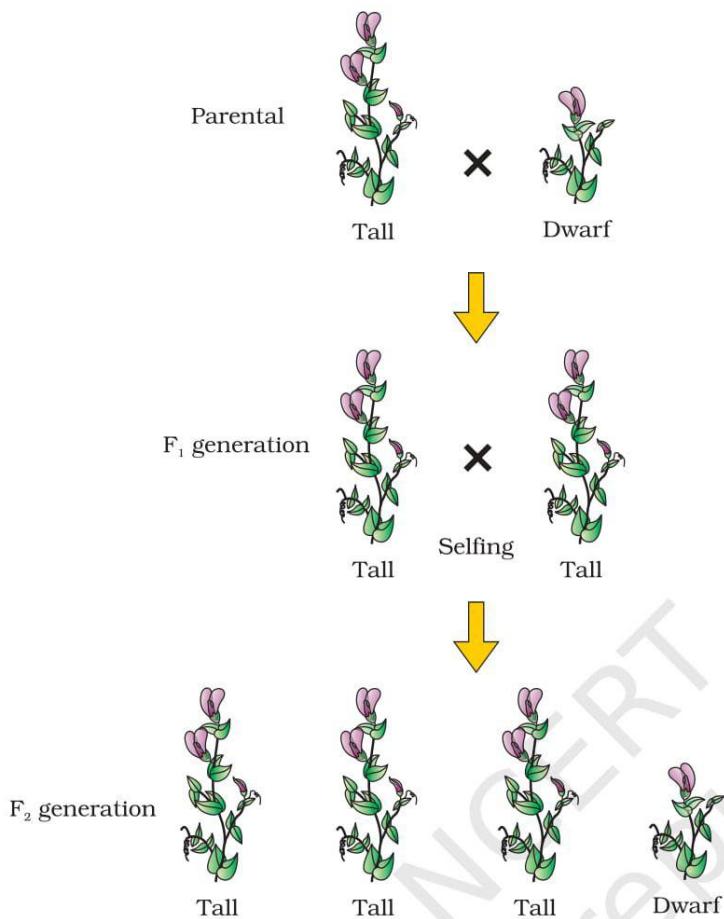


Figure 5.3 Diagrammatic representation of monohybrid cross

Based on these observations, Mendel proposed that something was being stably passed down, unchanged, from parent to offspring through the gametes, over successive generations. He called these things as 'factors'. Now we call them as **genes**. Genes, therefore, are the units of inheritance. They contain the information that is required to express a particular trait in an organism. Genes which code for a pair of contrasting traits are known as **alleles**, i.e., they are slightly different forms of the same gene.

If we use alphabetical symbols for each gene, then the capital letter is used for the trait expressed at the F₁ stage and the small alphabet for the other trait. For example, in case of the character of height, **T** is used for the Tall trait and **t** for the 'dwarf', and **T** and **t** are alleles of each other. Hence, in plants the pair of alleles for height would be **TT**, **Tt** or **tt**. Mendel also proposed that in a true breeding, tall or dwarf pea variety the allelic pair of genes for height are

identical or **homozygous**, **TT** and **tt**, respectively. **TT** and **tt** are called the **genotype** of the plant while the descriptive terms **tall** and **dwarf** are the **phenotype**. What then would be the phenotype of a plant that had a genotype **Tt**?

As Mendel found the phenotype of the F₁ heterozygote **Tt** to be exactly like the **TT** parent in appearance, he proposed that in a pair of dissimilar factors, one dominates the other (as in the F₁) and hence is called the **dominant** factor while the other factor is **recessive**. In this case **T** (for tallness) is dominant over **t** (for dwarfness), that is recessive. He observed identical behaviour for all the other characters/trait-pairs that he studied.

It is convenient (and logical) to use the capital and lower case of an alphabetical symbol to remember this concept of dominance and recessiveness. (Do not use **T** for tall and **d** for dwarf because you will find it difficult to remember whether **T** and **d** are alleles of the same gene/character or not). Alleles can be similar as in the case of homozygotes **TT** and **tt** or can be dissimilar as in the case of the heterozygote **Tt**. Since



the **Tt** plant is heterozygous for genes controlling one character (height), it is a **monohybrid** and the cross between **TT** and **tt** is a **monohybrid cross**.

From the observation that the recessive parental trait is expressed without any blending in the F_2 generation, we can infer that, when the tall and dwarf plant produce gametes, by the process of meiosis, the alleles of the parental pair separate or **segregate** from each other and only one allele is transmitted to a gamete. This segregation of alleles is a random process and so there is a 50 per cent chance of a gamete containing either allele, as has been verified by the results of the crossings. In this way the gametes of the tall **TT** plants have the allele **T** and the gametes of the dwarf **tt** plants have the allele **t**. During fertilisation the two alleles, **T** from one parent say, through the pollen, and **t** from the other parent, then through the egg, are united to produce zygotes that have one **T** allele and one **t** allele. In other words the hybrids have **Tt**. Since these hybrids contain alleles which express contrasting traits, the plants are **heterozygous**. The production of gametes by the parents, the formation of the zygotes, the F_1 and F_2 plants can be understood from a diagram called **Punnett Square** as shown in Figure 5.4. It was developed by a British geneticist, Reginald C. Punnett. It is a graphical representation to calculate the probability of all possible genotypes of offspring in a genetic cross. The possible gametes are written on two sides, usually the top row and left columns. All possible combinations are represented in boxes below in the squares, which generates a square output form.

The Punnett Square shows the parental tall **TT** (male) and dwarf **tt** (female) plants, the gametes produced by them and, the F_1 **Tt** progeny. The F_1 plants of genotype **Tt** are self-pollinated. The symbols ♀ and ♂ are used to denote the female (eggs) and male (pollen) of the F_1 generation, respectively. The F_1 plant of the genotype **Tt** when self-pollinated, produces gametes of the genotype **T** and **t** in equal proportion. When fertilisation takes place, the pollen grains of genotype **T** have a 50 per cent chance to pollinate eggs of the genotype **T**, as well as of genotype **t**. Also pollen grains of genotype **t** have a 50 per cent chance of pollinating eggs of genotype **T**, as well as of

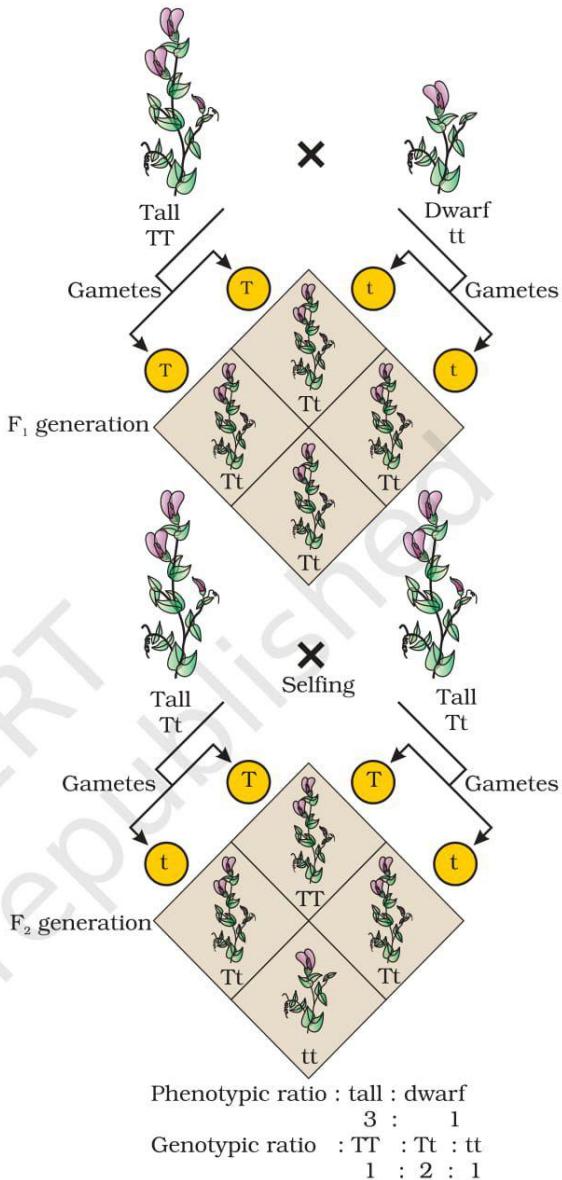


Figure 5.4 A Punnett square used to understand a typical monohybrid cross conducted by Mendel between true-breeding tall plants and true-breeding dwarf plants

genotype **t**. As a result of random fertilisation, the resultant zygotes can be of the genotypes **TT**, **Tt** or **tt**.

From the Punnett square it is easily seen that $1/4^{\text{th}}$ of the random fertilisations lead to **TT**, $1/2$ lead to **Tt** and $1/4^{\text{th}}$ to **tt**. Though the F_1 have a genotype of **Tt**, but the phenotypic character seen is 'tall'. At F_2 , $3/4^{\text{th}}$ of the plants are tall, where some of them are **TT** while others are **Tt**. Externally it is not possible to distinguish between the plants with the genotypes **TT** and **Tt**. Hence, within the genotypic pair **Tt** only one character 'T' tall is expressed. Hence the character **T** or 'tall' is said to dominate over the other allele **t** or 'dwarf' character. It is thus due to this dominance of one character over the other that all the F_1 are tall (though the genotype is **Tt**) and in the F_2 $3/4^{\text{th}}$ of the plants are tall (though genetically $1/2$ are **Tt** and only $1/4^{\text{th}}$ are **TT**). This leads to a phenotypic ratio of $3/4^{\text{th}}$ tall : ($1/4$ **TT** + $1/2$ **Tt**) and $1/4^{\text{th}}$ **tt**, i.e., a 3:1 ratio, but a genotypic ratio of 1:2:1.

The $1/4 : 1/2 : 1/4$ ratio of **TT**:**Tt**:**tt** is mathematically condensable to the form of the binomial expression $(ax+by)^2$, that has the gametes bearing genes **T** or **t** in equal frequency of $\frac{1}{2}$. The expression is expanded as given below :

$$(1/2\mathbf{T} + 1/2\mathbf{t})^2 = (1/2\mathbf{T} + 1/2\mathbf{t}) \times (1/2\mathbf{T} + 1/2\mathbf{t}) = 1/4\mathbf{TT} + 1/2\mathbf{Tt} + 1/4\mathbf{tt}$$

Mendel self-pollinated the F_2 plants and found that dwarf F_2 plants continued to generate dwarf plants in F_3 and F_4 generations. He concluded that the genotype of the dwarfs was homozygous – **tt**. What do you think he would have got had he self-pollinated a tall F_2 plant?

From the preceding paragraphs it is clear that though the genotypic ratios can be calculated using mathematical probability, by simply looking at the phenotype of a dominant trait, it is not possible to know the genotypic composition. That is, for example, whether a tall plant from F_1 or F_2 has **TT** or **Tt** composition, cannot be predicted. Therefore, to determine the genotype of a tall plant at F_2 , Mendel crossed the tall plant from F_2 with a dwarf plant. This he called a **test cross**. In a typical test cross an organism (pea plants here) showing a dominant phenotype (and whose genotype is to be determined) is crossed with the recessive parent instead of self-crossing. The progenies of such a cross can easily be analysed to predict the genotype of the test organism. Figure 5.5 shows the results of typical test cross where violet colour flower (W) is dominant over white colour flower (w).

Using Punnett square, try to find out the nature of offspring of a test cross.

What ratio did you get?

Using the genotypes of this cross, can you give a general definition for a test cross?

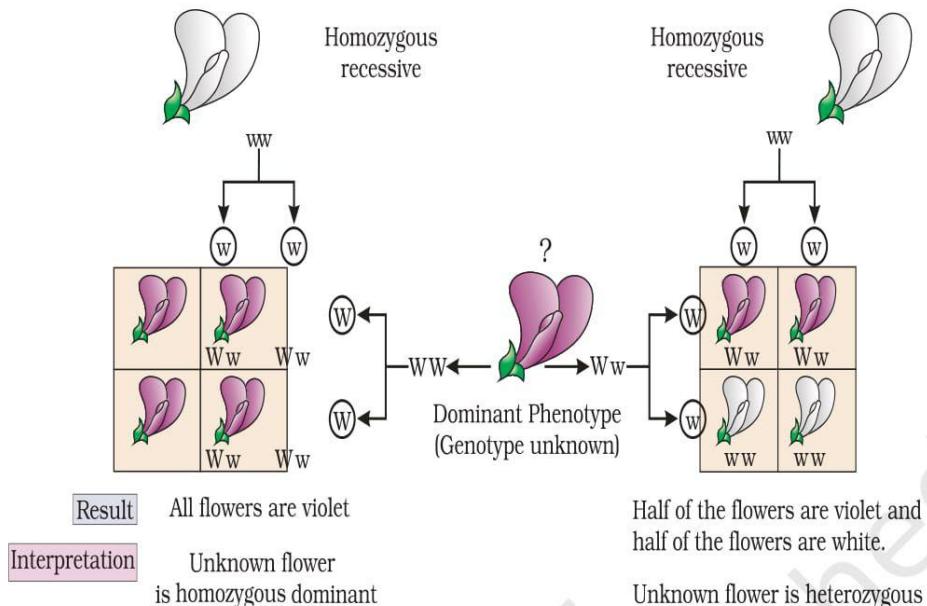


Figure 5.5 Diagrammatic representation of a test cross

Based on his observations on monohybrid crosses Mendel proposed two general rules to consolidate his understanding of inheritance in monohybrid crosses. Today these rules are called the **Principles or Laws of Inheritance**: the First Law or **Law of Dominance** and the Second Law or **Law of Segregation**.

5.2.1 Law of Dominance

- (i) Characters are controlled by discrete units called **factors**.
- (ii) Factors occur in pairs.
- (iii) In a dissimilar pair of factors one member of the pair dominates (dominant) the other (recessive).

The law of dominance is used to explain the expression of only one of the parental characters in a monohybrid cross in the F₁ and the expression of both in the F₂. It also explains the proportion of 3:1 obtained at the F₂.

5.2.2 Law of Segregation

This law is based on the fact that the alleles do not show any blending and that both the characters are recovered as such in the F₂ generation though one of these is not seen at the F₁ stage. Though the parents contain two alleles during gamete formation, the factors or alleles of a pair segregate from each other such that a gamete receives only one of the two factors. Of course, a homozygous parent produces all gametes that are similar while a heterozygous one produces two kinds of gametes each having one allele with equal proportion.

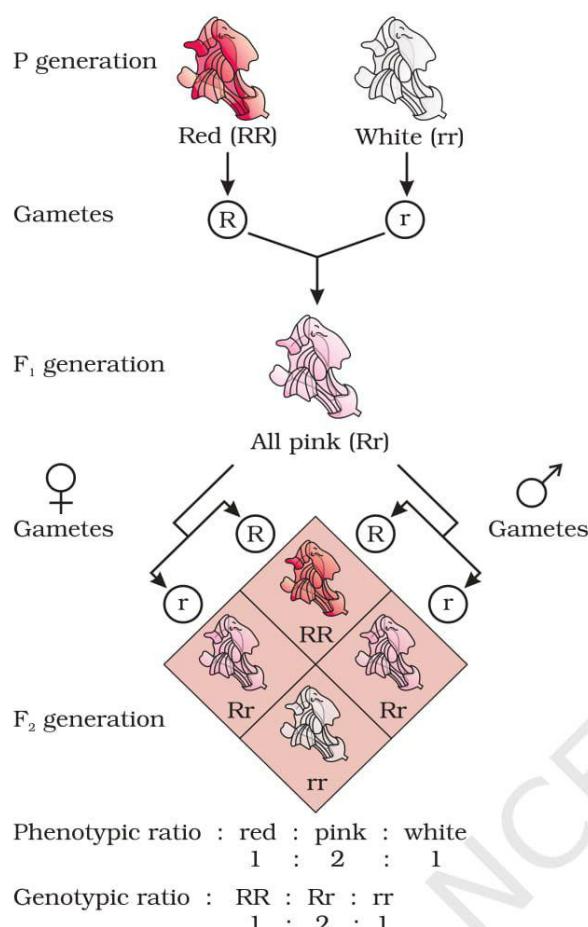


Figure 5.6 Results of monohybrid cross in the plant Snapdragon, where one allele is incompletely dominant over the other allele

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substrate S. Theoretically, the modified allele could be responsible for production of –

- (i) the normal/less efficient enzyme, or
- (ii) a non-functional enzyme, or
- (iii) no enzyme at all

5.2.2.1 Incomplete Dominance

When experiments on peas were repeated using other traits in other plants, it was found that sometimes the F₁ had a phenotype that did not resemble either of the two parents and was in between the two. The inheritance of flower colour in the dog flower (snapdragon or *Antirrhinum sp.*) is a good example to understand incomplete dominance. In a cross between true-breeding red-flowered (**RR**) and true-breeding white-flowered plants (**rr**), the F₁ (**Rr**) was pink (Figure 5.6). When the F₁ was self-pollinated the F₂ resulted in the following ratio 1 (**RR**) Red : 2 (**Rr**) Pink : 1 (**rr**) White. Here the genotype ratios were exactly as we would expect in any mendelian monohybrid cross, but the phenotype ratios had changed from the 3:1 dominant : recessive ratio. What happened was that **R** was not completely dominant over **r** and this made it possible to distinguish **Rr** as pink from **RR** (red) and **rr** (white).

Explanation of the concept of dominance:

What exactly is dominance? Why are some alleles dominant and some recessive? To tackle these questions, we must understand what a gene does. Every gene, as you know by now, contains the information to express a particular trait. In a diploid organism, there are two copies of each gene, i.e., as a pair of alleles. Now, these two alleles need not always be identical, as in a heterozygote. One of them may be different due to some changes that it has undergone (about which you will read further on, and in the next chapter) which modifies the information that particular allele contains.

Let's take an example of a gene that contains the information for producing an enzyme. Now there are two copies of this gene, the two allelic forms. Let us assume (as is more common) that the normal allele produces the normal enzyme that is needed for the transformation of a



In the first case, the modified allele is equivalent to the unmodified allele, i.e., it will produce the same phenotype/trait, i.e., result in the transformation of substrate S. Such equivalent allele pairs are very common. But, if the allele produces a non-functional enzyme or no enzyme, the phenotype may be effected. The phenotype/trait will only be dependent on the functioning of the unmodified allele. The unmodified (functioning) allele, which represents the original phenotype is the dominant allele and the modified allele is generally the recessive allele. Hence, in the example above the recessive trait is seen due to non-functional enzyme or because no enzyme is produced.

5.2.2.2 Co-dominance

Till now we were discussing crosses where the F_1 resembled either of the two parents (dominance) or was in-between (incomplete dominance). But, in the case of co-dominance the F_1 generation resembles both parents. A good example is different types of red blood cells that determine ABO blood grouping in human beings. ABO blood groups are controlled by the gene **I**. The plasma membrane of the red blood cells has sugar polymers that protrude from its surface and the kind of sugar is controlled by the gene. The gene (**I**) has three alleles **I^A**, **I^B** and **i**. The alleles **I^A** and **I^B** produce a slightly different form of the sugar while allele **i** does not produce any sugar. Because humans are diploid organisms, each person possesses any two of the three **I** gene alleles. **I^A** and **I^B** are completely dominant over **i**, in other words when **I^A** and **i** are present only **I^A** expresses (because **i** does not produce any sugar), and when **I^B** and **i** are present **I^B** expresses. But when **I^A** and **I^B** are present together they both express their own types of sugars: this is because of co-dominance. Hence red blood cells have both A and B types of sugars. Since there are three different alleles, there are six different combinations of these three alleles that are possible, and therefore, a total of six different genotypes of the human ABO blood types (Table 5.2). *How many phenotypes are possible?*

Table 5.2: Table Showing the Genetic Basis of Blood Groups in Human Population

Allele from Parent 1	Allele from Parent 2	Genotype of offspring	Blood types of offspring
I^A	I^A	$I^A I^A$	A
I^A	I^B	$I^A I^B$	AB
I^A	i	$I^A i$	A
I^B	I^A	$I^A I^B$	AB
I^B	I^B	$I^B I^B$	B
I^B	i	$I^B i$	B
i	i	$i i$	O

Do you realise that the example of ABO blood grouping also provides a good example of **multiple alleles**? Here you can see that there are more than two, i.e., three alleles, governing the same character. Since in an individual only two alleles can be present, multiple alleles can be found only when population studies are made.

Occasionally, a single gene product may produce more than one effect. For example, starch synthesis in pea seeds is controlled by one gene. It has two alleles (**B** and **b**). Starch is synthesised effectively by **BB** homozygotes and therefore, large starch grains are produced. In contrast, **bb** homozygotes have lesser efficiency in starch synthesis and produce smaller starch grains. After maturation of the seeds, **BB** seeds are round and the **bb** seeds are wrinkled. Heterozygotes produce round seeds, and so **B** seems to be the dominant allele. But, the starch grains produced are of intermediate size in **Bb** seeds. So if starch grain size is considered as the phenotype, then from this angle, the alleles show incomplete dominance.

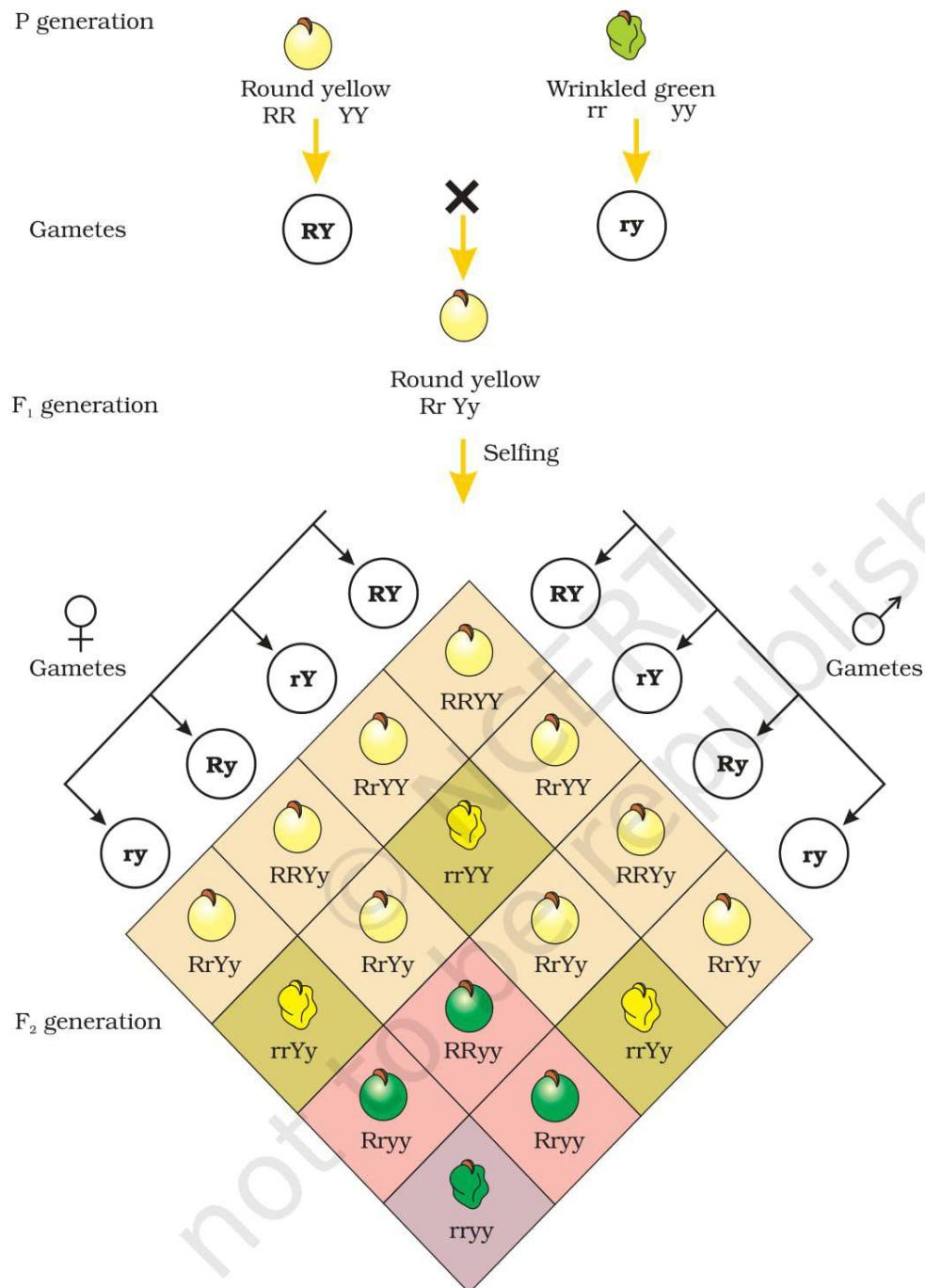
Therefore, dominance is not an autonomous feature of a gene or the product that it has information for. It depends as much on the gene product and the production of a particular phenotype from this product as it does on the particular phenotype that we choose to examine, in case more than one phenotype is influenced by the same gene.

5.3 INHERITANCE OF TWO GENES

Mendel also worked with and crossed pea plants that differed in two characters, as is seen in the cross between a pea plant that has seeds with yellow colour and round shape and one that had seeds of green colour and wrinkled shape (Figure 5.7). Mendel found that the seeds resulting from the crossing of the parents, had yellow coloured and round shaped seeds. *Here can you tell which of the characters in the pairs yellow/green colour and round/wrinkled shape was dominant?*

Thus, yellow colour was dominant over green and round shape dominant over wrinkled. These results were identical to those that he got when he made separate monohybrid crosses between yellow and green seeded plants and between round and wrinkled seeded plants.

Let us use the genotypic symbols **Y** for dominant yellow seed colour and **y** for recessive green seed colour, **R** for round shaped seeds and **r** for wrinkled seed shape. The genotype of the parents can then be written as **RRYY** and **rryy**. The cross between the two plants can be written down as in Figure 5.7 showing the genotypes of the parent plants. The gametes **RY** and **ry** unite on fertilisation to produce the F_1 hybrid **RrYy**. When Mendel self hybridised the F_1 plants he found that $3/4^{\text{th}}$ of F_2 plants had yellow seeds and $1/4^{\text{th}}$ had green. The yellow and green colour segregated in a 3:1 ratio. Round and wrinkled seed shape also segregated in a 3:1 ratio; just like in a monohybrid cross.



Phenotypic ratio : round yellow : round green : wrinkled yellow : wrinkled green
9 3 3 1

Figure 5.7 Results of a dihybrid cross where the two parents differed in two pairs of contrasting traits: seed colour and seed shape

5.3.1 Law of Independent Assortment

In the dihybrid cross (Figure 5.7), the phenotypes round, yellow; wrinkled, yellow; round, green and wrinkled, green appeared in the ratio 9:3:3:1. Such a ratio was observed for several pairs of characters that Mendel studied.

The ratio of 9:3:3:1 can be derived as a combination series of 3 yellow: 1 green, with 3 round : 1 wrinkled. This derivation can be written as follows:

$$(3 \text{ Round} : 1 \text{ Wrinkled}) (3 \text{ Yellow} : 1 \text{ Green}) = 9 \text{ Round, Yellow} : 3 \text{ Wrinkled, Yellow} : 3 \text{ Round, Green} : 1 \text{ Wrinkled, Green}$$

Based upon such observations on **dihybrid crosses** (crosses between plants differing in two traits) Mendel proposed a second set of generalisations that we call Mendel's Law of Independent Assortment. The law states that 'when two pairs of traits are combined in a hybrid, segregation of one pair of characters is independent of the other pair of characters'.

The Punnett square can be effectively used to understand the independent segregation of the two pairs of genes during meiosis and the production of eggs and pollen in the F_1 **RrYy** plant. Consider the segregation of one pair of genes **R** and **r**. Fifty per cent of the gametes have the gene **R** and the other 50 per cent have **r**. Now besides each gamete having either **R** or **r**, it should also have the allele **Y** or **y**. The important thing to remember here is that segregation of 50 per cent **R** and 50 per cent **r** is *independent* from the segregation of 50 per cent **Y** and 50 per cent **y**. Therefore, 50 per cent of the **r** bearing gametes has **Y** and the other 50 per cent has **y**. Similarly, 50 per cent of the **R** bearing gametes has **Y** and the other 50 per cent has **y**. Thus there are four genotypes of gametes (four types of pollen and four types of eggs). The four types are **RY**, **Ry**, **rY** and **ry** each with a frequency of 25 per cent or $1/4^{\text{th}}$ of the total gametes produced. When you write down the four types of eggs and pollen on the two sides of a Punnett square it is very easy to derive the composition of the zygotes that give rise to the F_2 plants (Figure 5.7). *Although there are 16 squares how many different types of genotypes and phenotypes are formed?* Note them down in the format given.

Can you, using the Punnett square data work out the genotypic ratio at the F_2 stage and fill in the format given? Is the genotypic ratio also 9:3:3:1?

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S.No.	Genotypes found in F_2	Their expected Phenotypes

5.3.2 Chromosomal Theory of Inheritance

Mendel published his work on inheritance of characters in 1865 but for several reasons, it remained unrecognised till 1900. Firstly,



communication was not easy (as it is now) in those days and his work could not be widely publicised. Secondly, his concept of **genes** (or **factors**, in Mendel's words) as stable and discrete units that controlled the expression of traits and, of the pair of alleles which did not 'blend' with each other, was not accepted by his contemporaries as an explanation for the apparently continuous variation seen in nature. Thirdly, Mendel's approach of using mathematics to explain biological phenomena was totally new and unacceptable to many of the biologists of his time. Finally, though Mendel's work suggested that factors (genes) were discrete units, he could not provide any physical proof for the existence of factors or say what they were made of.

In 1900, three Scientists (de Vries, Correns and von Tschermak) independently rediscovered Mendel's results on the inheritance of characters. Also, by this time due to advancements in microscopy that were taking place, scientists were able to carefully observe cell division. This led to the discovery of structures in the nucleus that appeared to double and divide just before each cell division. These were called **chromosomes** (*colored bodies*, as they were visualised by staining). By 1902, the chromosome movement during meiosis had been worked out. Walter Sutton and Theodore Boveri noted that the behaviour of chromosomes was parallel to the behaviour of genes and used chromosome movement (Figure 5.8) to explain Mendel's laws (Table 5.3). Recall that you have studied the behaviour of chromosomes during mitosis (equational division) and during meiosis (reduction division). The important things to remember are that chromosomes as well as genes occur in pairs. The two alleles of a gene pair are located on homologous sites on homologous chromosomes.

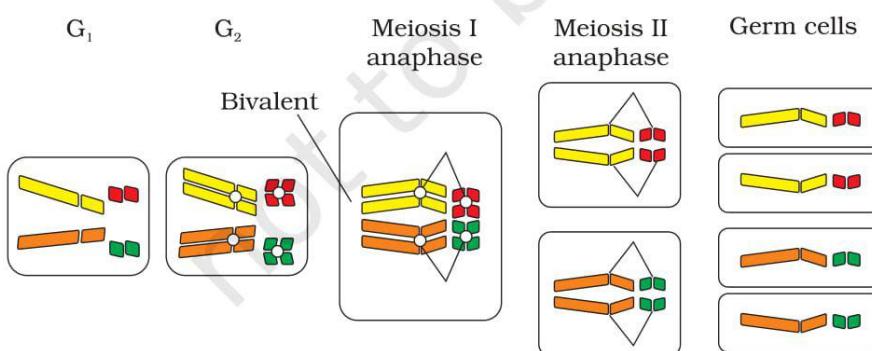


Figure 5.8 Meiosis and germ cell formation in a cell with four chromosomes. Can you see how chromosomes segregate when germ cells are formed?

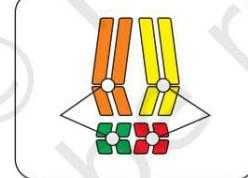
Table 5.3: A Comparison between the Behaviour of Chromosomes and Genes

A	B
Occur in pairs	Occur in pairs
Segregate at the time of gamete formation such that only one of each pair is transmitted to a gamete	Segregate at gamete formation and only one of each pair is transmitted to a gamete
Independent pairs segregate independently of each other	One pair segregates independently of another pair
Can you tell which of these columns A or B represent the chromosome and which represents the gene? How did you decide?	

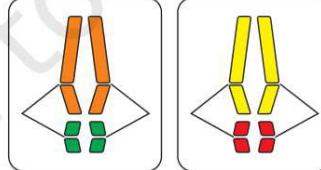
During Anaphase of meiosis I, the two chromosome pairs can align at the metaphase plate independently of each other (Figure 5.9). To understand this, compare the chromosomes of four different colour in the left and right columns. In the left column (Possibility I) orange and green is segregating together. But in the right hand column (Possibility II) the orange chromosome is segregating with the red chromosomes.

Possibility I
One long orange and short green chromosome and long yellow and short red chromosome at the same pole

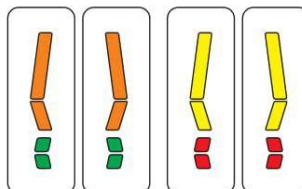
Meiosis I - anaphase



Meiosis II - anaphase

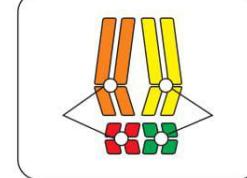


Germ cells

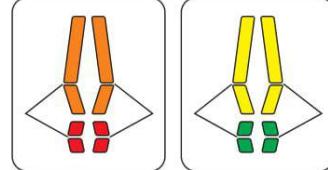


Possibility II
One long orange and short red chromosome and long yellow and short green chromosome at the same pole

Meiosis I - anaphase



Meiosis II - anaphase



Germ cells

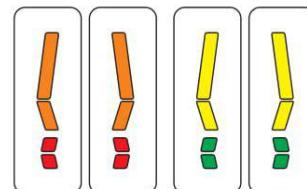


Figure 5.9 Independent assortment of chromosomes

Sutton and Boveri argued that the pairing and separation of a pair of chromosomes would lead to the segregation of a pair of factors they carried. Sutton united the knowledge of chromosomal segregation with Mendelian principles and called it the **chromosomal theory of inheritance**.

Following this synthesis of ideas, experimental verification of the chromosomal theory of inheritance by Thomas Hunt Morgan and his colleagues, led to discovering the basis for the variation that sexual reproduction produced. Morgan worked with the tiny fruit flies, *Drosophila melanogaster* (Figure 5.10), which were found very suitable for such studies. They could be grown on simple synthetic medium in the laboratory. They complete their life cycle in about two weeks, and a single mating could produce a large number of progeny flies. Also, there was a clear differentiation of the sexes – the male and female flies are easily distinguishable. Also, it has many types of hereditary variations that can be seen with low power microscopes.

5.3.3 Linkage and Recombination

Morgan carried out several dihybrid crosses in *Drosophila* to study genes that were sex-linked. The crosses were similar to the dihybrid crosses carried out by Mendel in peas. For example Morgan hybridised yellow-bodied, white-eyed females to brown-bodied, red-eyed males and intercrossed their F_1 progeny. He observed that the two genes did not segregate independently of each other and the F_2 ratio deviated very significantly from the 9:3:3:1 ratio (expected when the two genes are independent).

Morgan and his group knew that the genes were located on the X chromosome (Section 5.4) and saw quickly that when the two genes in a dihybrid cross were situated on the same chromosome, the proportion of parental gene combinations were much higher than the non-parental type. Morgan attributed this due to the physical association or linkage of the two genes and coined the term **linkage** to describe this physical association of genes on a chromosome and the term **recombination** to describe the generation of non-parental gene combinations (Figure 5.11). Morgan and his group also found that even when genes were grouped on the same chromosome, some genes were very tightly linked (showed very low recombination) (Figure 5.11, Cross A) while others were loosely linked (showed higher recombination) (Figure 5.11, Cross B). For example he found that the genes white and yellow were very tightly linked and showed only 1.3 per cent recombination while white and miniature wing showed 37.2 per cent recombination. His student Alfred Sturtevant used the frequency of recombination between gene pairs on the same chromosome as a measure of the distance between genes and ‘mapped’ their position on the chromosome. Today genetic maps

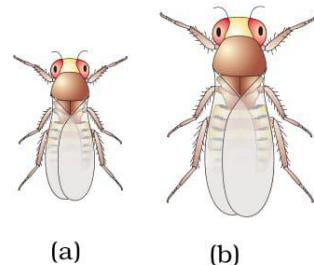


Figure 5.10 *Drosophila melanogaster* (a) Male
(b) Female

are extensively used as a starting point in the sequencing of whole genomes as was done in the case of the Human Genome Sequencing Project, described later.

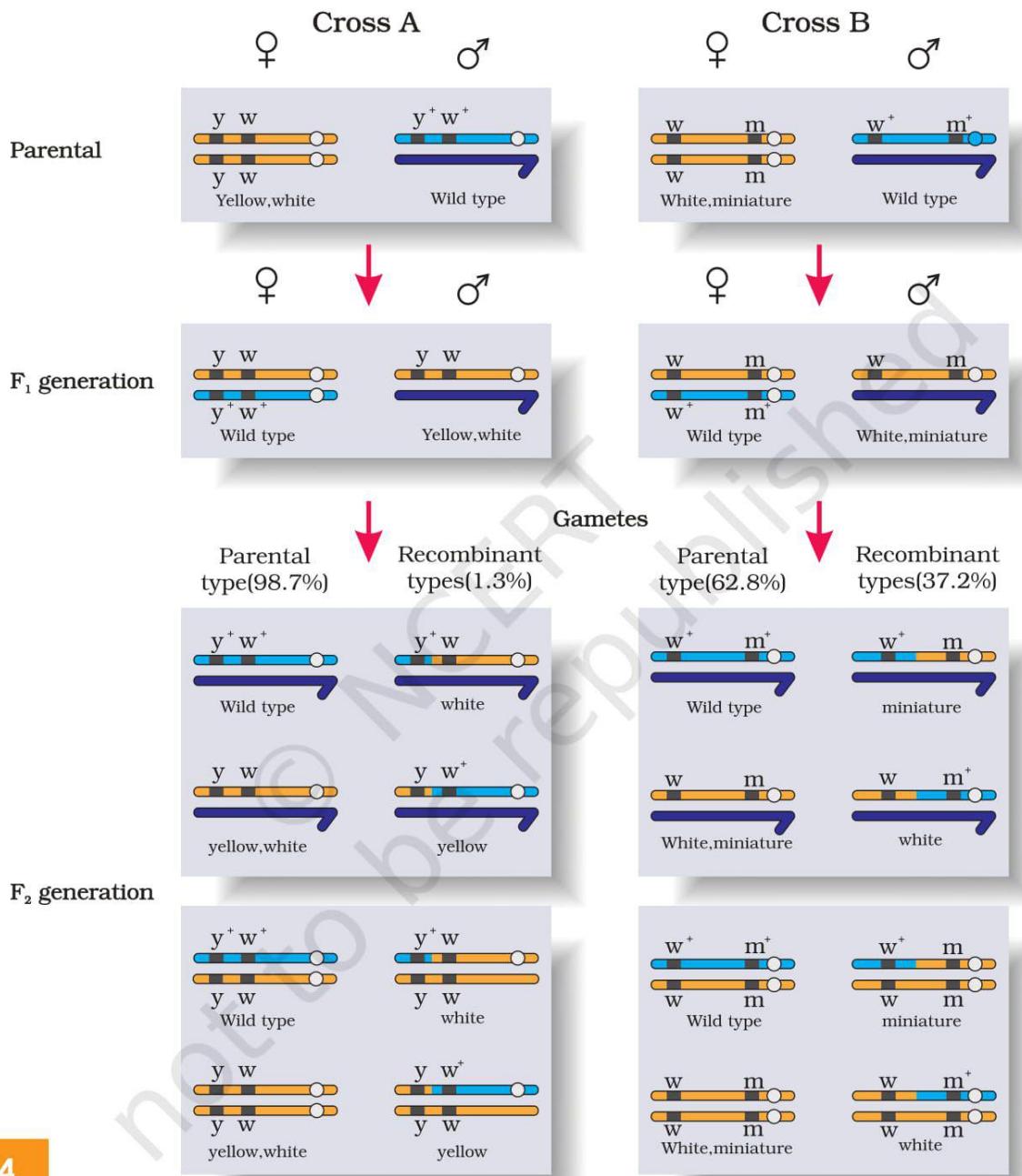


Figure 5.11 Linkage: Results of two dihybrid crosses conducted by Morgan. Cross A shows crossing between gene y and w; Cross B shows crossing between genes w and m. Here dominant wild type alleles are represented with (+) sign in superscript

Note: The strength of linkage between y and w is higher than w and m.



5.4 SEX DETERMINATION

The mechanism of sex determination has always been a puzzle before the geneticists. The initial clue about the genetic/chromosomal mechanism of sex determination can be traced back to some of the experiments carried out in insects. In fact, the cytological observations made in a number of insects led to the development of the concept of genetic/chromosomal basis of sex-determination. Henking (1891) could trace a specific nuclear structure all through spermatogenesis in a few insects, and it was also observed by him that 50 per cent of the sperm received this structure after spermatogenesis, whereas the other 50 per cent sperm did not receive it. Henking gave a name to this structure as the **X body** but he could not explain its significance. Further investigations by other scientists led to the conclusion that the 'X body' of Henking was in fact a chromosome and that is why it was given the name X-chromosome. It was also observed that in a large number of insects the mechanism of sex determination is of the XO type, i.e., all eggs bear an additional X-chromosome besides the other chromosomes (autosomes). On the other hand, some of the sperms bear the X-chromosome whereas some do not. Eggs fertilised by sperm having an X-chromosome become females and, those fertilised by sperms that do not have an X-chromosome become males. *Do you think the number of chromosomes in the male and female are equal?* Due to the involvement of the X-chromosome in the determination of sex, it was designated to be the **sex chromosome**, and the rest of the chromosomes were named as **autosomes**. Grasshopper is an example of XO type of sex determination in which the males have only one X-chromosome besides the autosomes, whereas females have a pair of X-chromosomes.

These observations led to the investigation of a number of species to understand the mechanism of sex determination. In a number of other insects and mammals including man, XY type of sex determination is seen where both male and female have same number of chromosomes.

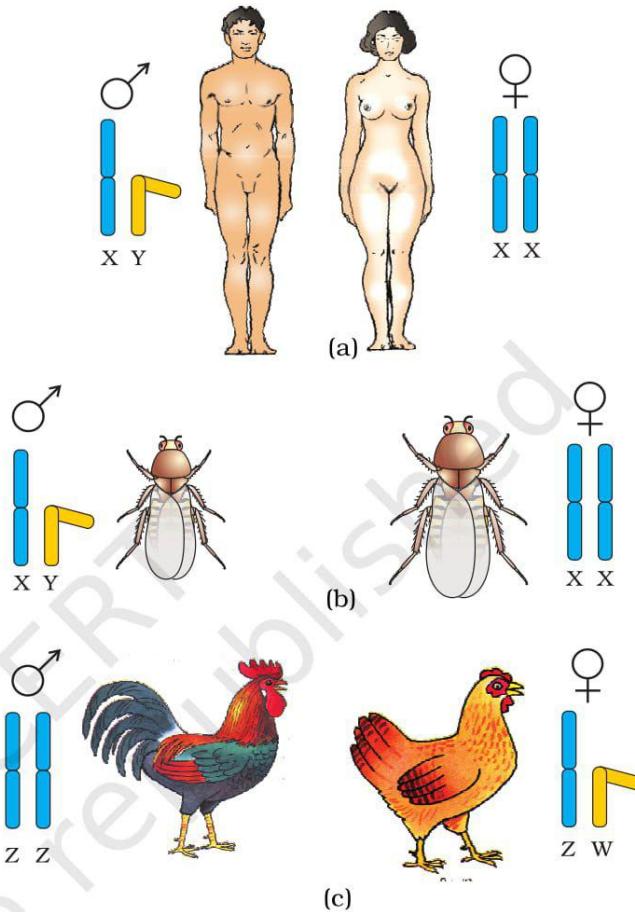


Figure 5.12 Determination of sex by chromosomal differences: (a,b) Both in humans and in *Drosophila*, the female has a pair of XX chromosomes (homogametic) and the male XY (heterogametic) composition; (c) In many birds, female has a pair of dissimilar chromosomes ZW and male two similar ZZ chromosomes

Among the males an X-chromosome is present but its counter part is distinctly smaller and called the Y-chromosome. Females, however, have a pair of X-chromosomes. Both males and females bear same number of autosomes. Hence, the males have autosomes plus XY, while female have autosomes plus XX. In human beings and in *Drosophila* the males have one X and one Y chromosome, whereas females have a pair of X-chromosomes besides autosomes (Figure 5.12 a, b).

In the above description you have studied about two types of sex determining mechanisms, i.e., XO type and XY type. But in both cases males produce two different types of gametes, (a) either with or without X-chromosome or (b) some gametes with X-chromosome and some with Y-chromosome. Such types of sex determination mechanism is designated to be the example of **male heterogamety**. In some other organisms, e.g., birds, a different mechanism of sex determination is observed (Figure 5.12 c). In this case the total number of chromosome is same in both males and females. But two different types of gametes in terms of the sex chromosomes, are produced by females, i.e., **female heterogamety**. In order to have a distinction with the mechanism of sex determination described earlier, the two different sex chromosomes of a female bird has been designated to be the Z and W chromosomes. In these organisms the females have one Z and one W chromosome, whereas males have a pair of Z-chromosomes besides the autosomes.

5.4.1 Sex Determination in Humans

It has already been mentioned that the sex determining mechanism in case of humans is XY type. Out of 23 pairs of chromosomes present, 22 pairs are exactly same in both males and females; these are the autosomes. A pair of X-chromosomes are present in the female, whereas the presence of an X and Y chromosome are determinant of the male characteristic. During spermatogenesis among males, two types of gametes are produced. 50 per cent of the total sperm produced carry the X-chromosome and the rest 50 per cent has Y-chromosome besides the autosomes. Females, however, produce only one type of ovum with an X-chromosome. There is an equal probability of fertilisation of the ovum with the sperm carrying either X or Y chromosome. In case the ovum fertilises with a sperm carrying X-chromosome the zygote develops into a female (XX) and the fertilisation of ovum with Y-chromosome carrying sperm results into a male offspring. Thus, it is evident that it is the genetic makeup of the sperm that determines the sex of the child. It is also evident that in each pregnancy there is always 50 per cent probability of either a male or a female child. It is unfortunate that in our society women are blamed for giving birth to female children and have been ostracised and ill-treated because of this false notion.

How is the sex-determination mechanism different in the birds?
Is the sperm or the egg responsible for the sex of the chicks?