Genetics

Unit 3

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3.1 Genetic crosses (page 102)	• Work out the outcomes of monohybrid crosses and dihybrid crosses. • Use the Punnett square to determine genetic crosses. • Determine genotypes and phenotypes formed in a genetic cross. • Explain the different types of dominance. • Describe the significance of the fact that not all genes show a straightforward dominant/recessive relationship between different alleles of the gene. • State that some genes have more than two alleles. • Describe the different stages of meiotic division. • Describe the significance of meiosis as both a source of variation through crossing over and independent assortment as well as a method of halving chromosome number in the gametes. • Describe how a knowledge of genetics is important in artificially producing new varieties of crops and stock animals through artificial cross-breeding and inbreeding. • Explain why fruit flies (*Drosophila melanogaster*) have been used in much genetic research. • Explain the genetic basis of gender determination and why it is that some characteristics are sex-linked, sex-influenced or sex-limited.
3.2 Molecular genetics (page 128)	• Describe the structure of a chromosome. • Describe in detail the structure of the DNA molecule. • Name the four nucleotides that build up the DNA molecule. • Construct a model of DNA showing the base pair between complementary nucleotides. • Describe the semi-conservative replication of DNA. • Describe the significance of some of the uses of gene technology in forensic science (such as genetic fingerprinting). • Describe how genetic fingerprints are produced. • Define and give examples of cloning. • Understand that genes can be cloned and explain in outline how this is achieved. • Describe, in outline, the procedures involved in genetic engineering and appreciate that whilst there are many advantages that result from the process, there are also some ethical concerns about some of the procedures.

Contents

3.1 Genetic crosses

By the end of this section you should be able to:

- Work out the outcomes of monohybrid crosses and dihybrid crosses.
- Use the Punnett square to determine genetic crosses.
- Determine genotypes and phenotypes formed in a genetic cross.
- Explain the different types of dominance.
- Describe the significance of the fact that not all genes show a straightforward dominant/recessive relationship between different alleles of the gene.
- State that some genes have more than two alleles.
- Describe the different stages of meiotic division.
- Describe the significance of meiosis as both a source of variation through crossing over and independent assortment as well as a method of halving chromosome number in the gametes.

Activity 3.1

Humans have several genetic traits which are inherited through single genes. These include dangly or attached earlobes, straight or curved thumbs and dimples or no dimples. Carry out a survey of people you know (in class, at home, in your family and friends) and make bar charts to compare the numbers of people who have the different versions of these genetic traits. The more people you ask, the more valid your results will be.

- Describe how a knowledge of genetics is important in artificially producing new varieties of crops and stock animals through artificial cross-breeding and inbreeding.
- Explain why fruit flies (*Drosophila melanogaster*) have been used in much genetic research.
- Explain the genetic basis of gender determination and why it is that some characteristics are sex-linked, sex-influenced or sex-limited.

What is the relationship between chromosomes, genes, alleles and characteristics of an organism?

In grade 11, unit 2, we learned about biological molecules. One of these was the molecule of inheritance – DNA. We shall be learning in more detail how this molecule is able to pass on our features or traits in section 3.2. For now, however, we need to revise a little of the structure of the molecule and where it is situated in cells. Figure 3.1 shows how chromosomes, **genes** and DNA are related.

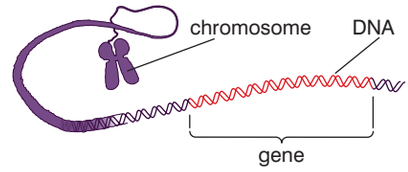


Figure 3.1 *Chromosomes, genes and DNA*

In grade 11, unit 4, we learned that chromosomes are found in the nucleus of a cell and are made from the DNA, which is bound with **histone** proteins to form the chromosomes.

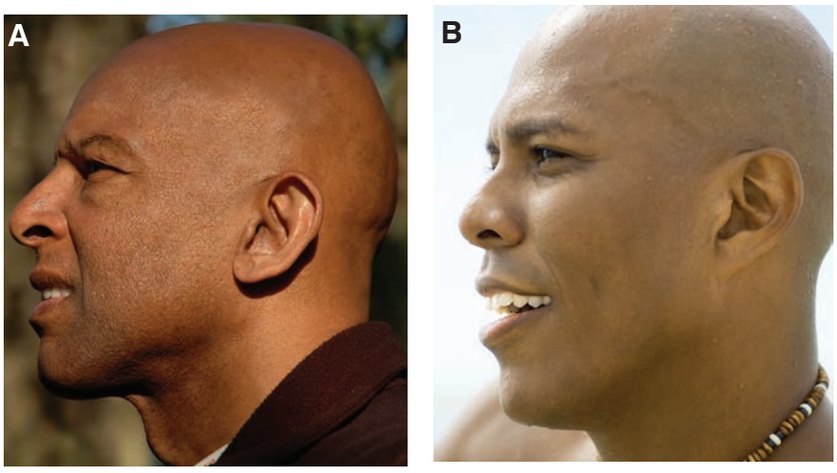


Figure 3.2 *Attached and unattached earlobes.*

A gene is a section of DNA (and therefore a section of a **chromosome**) that determines a particular feature, for example, earlobe attachment in humans. Whether or not your earlobes hang free (figure 3.2A) or are attached (figure 3.2B) is determined by a single gene. However, there are two versions of this gene. One version says 'be attached' and the other says 'don't be attached – be free'.

Different versions of the same gene are called **alleles**.

Because humans reproduce sexually, we receive half of our chromosomes from one parent and half from the other. And the two sets are very similar. In our cells we have 46 chromosomes; 23

KEY WORDS

gene *a section of DNA that determines a specific feature*

histone *the core of a chromosome around which the chromosome's DNA is wrapped*

chromosome *a long strand of DNA on which a large number of genes is stored*

allele *a version of a gene that determines a particular trait*

KEY WORDS

homologous pairs *the chromosomes in a eukaryotic cell usually come in pairs called homologous pairs. Each of the chromosomes in a homologous pair have corresponding genes that together determine the same trait*

locus *(plural* **loci***) the position of a particular gene on a chromosome*

homozygous *an organism is homozygous for a particular gene if it has the same allele for that gene on each of the chromosomes in the homologous pair*

heterozygous *an organism is heterozygous for a particular gene if it has different alleles for that gene on each of the chromosomes in the relevant homologous pair*

genotype *a genotype describes the pair of alleles for a particular gene possessed by a organism*

phenotype *a phenotype describes the trait or traits determined by a particular genotype*

are paternal in origin (came from our fathers) and 23 are maternal in origin (came from our mothers). And when they get together, they form pairs called **homologous pairs**. These homologous pairs have genes controlling the same features in the same position – or **locus** – on the chromosome. However, the alleles may not be the same. Figure 3.3 shows the loci of three genes on a pair of homologous chromosomes.

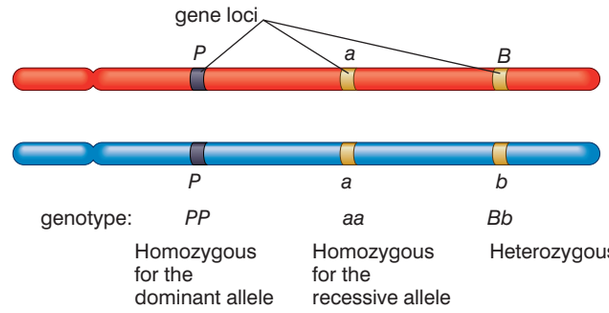


Figure 3.3 *Loci of alleles on homologous chromosomes*

Gene 1 has two alleles P and P. Both chromosomes have the dominant P allele (we say that the individual is **homozygous** for the dominant allele).

Gene 2 has two alleles, a and a. Both chromosomes have the recessive allele a (homozygous for the recessive allele).

Gene 3 has alleles B and b. One chromosome has the dominant allele, B, whilst the other has the recessive allele, b. We say that the individual is **heterozygous** for this particular gene.

The alleles of a particular gene possessed by an individual are its **genotype** (for that feature). The actual result of that genotype (whether or not the earlobes are attached, for example) is the **phenotype** (for that feature). If you know the genotypes of two parents, you can make predictions about the type and proportions of offspring they will have in relation to a particular feature. You can also throw that into reverse: if you know proportions of offspring showing certain versions of a feature, you can often work out the genotypes of the parents. Just how we do this, you will learn in the next part of this section.

How do we predict ratios in a monohybrid cross?

First, let us make clear what we are talking about. A monohybrid cross is a genetic cross or breeding situation that relates to just one trait or feature. The 'father' of genetics, the man who discovered the rules by which genes are inherited, was the Austrian monk Gregor Mendel. Living and experimenting in a monastery in Brno, Mendel experimented with pea plants and was able to deduce the rules of inheritance from his results.

He noticed that pea plants exhibited 'contrasting characteristics'. For example, the plants were either tall or short, had purple flowers

or white flowers. Now not all tall pea plants are exactly the same height, neither are all dwarf ones. But you wouldn't mistake a tall plant for a dwarf one. And obviously, you wouldn't mistake a purple-flowered plant for a white-flowered one. This was the key that enabled Mendel to experiment successfully – there were never any medium-height pea plants or plants with pale purple flowers. Figure 3.4 shows the seven contrasting characteristics that Mendel used in his experiments.

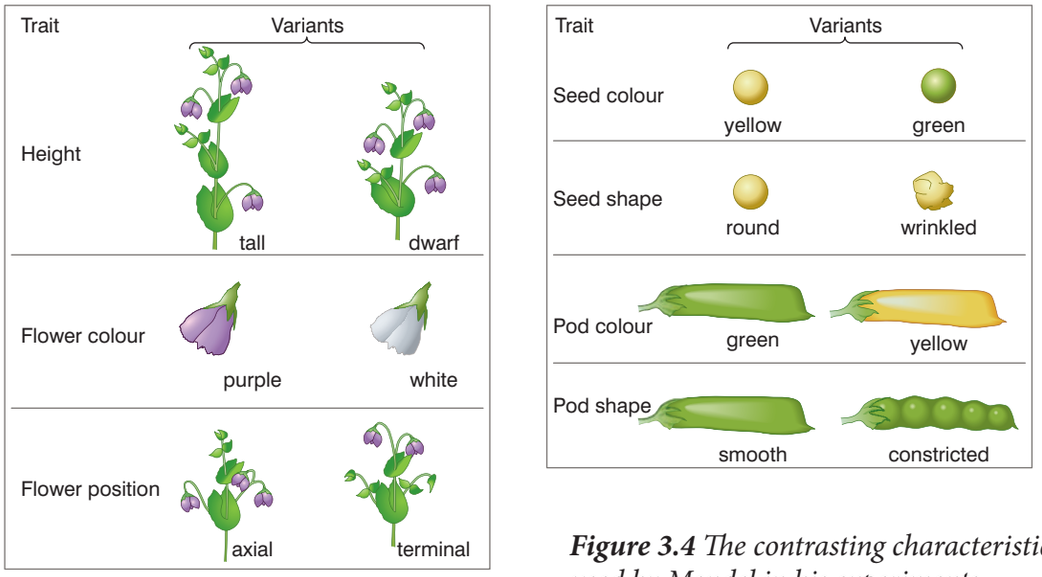


Figure 3.4 *The contrasting characteristics of pea plants used by Mendel in his experiments*

How did he do it?

Mendel was very methodical. His starting point was to wonder what would happen if he cross-bred two pea plants with contrasting features – for example, plants with purple flowers and plants with white flowers. Before he carried out any breeding experiments, he self-pollinated the plants for several generations, and eventually used plants from a 'breeding line' that had contained only purple-flowered plants or white-flowered plants. These he called 'true-breeding' plants. He then cross-bred them in the following way. We will use flower colour as our example, but he used the same procedure for all the contrasting characteristics.

1. He removed stamens from the flowers of the purple-flowered plant (so that these flowers could not pollinate themselves).
2. He used a paintbrush to transfer pollen from the flowers of the white-flowered plant to the carpel of the purple flowers.
3. This pollinated carpel then produced a pea pod containing several pea seeds.
4. He collected and grew all the seeds from all the pods.
5. When the plants were mature, he noted the colour of their flowers.

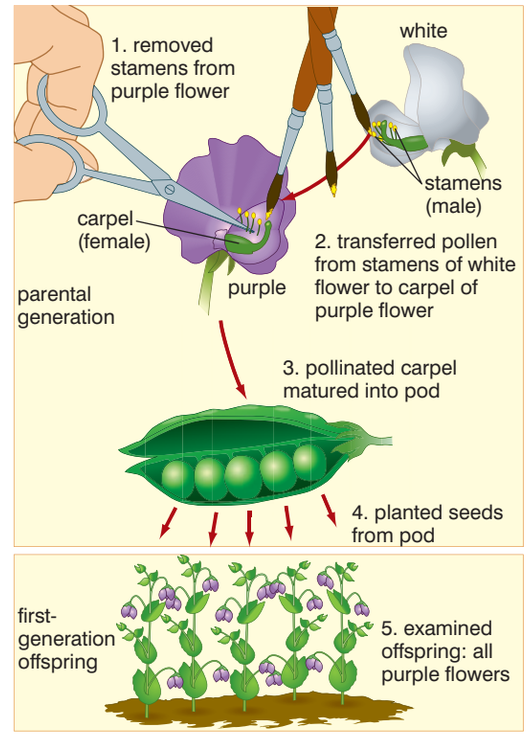


Figure 3.5 *Mendel's technique*

KEY WORDS

F_1/F_2 (first/second filials) *when organisms with different traits are cross-bred, F_1 refers to the offspring from the original organisms, and F_2 refers to the offspring of the F_1 organisms*

trait *a feature of an organism determined by its genes*

dominant allele *a dominant allele is the allele expressed in a heterozygous organism*

recessive allele *a recessive allele is only expressed in a homozygous organism*

Mendel also carried out reciprocal crosses. In this case he also pollinated white-flowered plants with pollen from purple-flowered plants.

In the above cross, all the offspring (which we call the **F_1** or **first filial** generation) have purple flowers. Mendel then allowed these purple-flowered plants to self-pollinate themselves. In the next generation (the **F_2** or **second filial** generation) he found a ratio of very nearly three purple-flowered plants for every one white-flowered plant. This pattern repeated itself in all of his experiments. In each case he:

- crossed pure-breeding plants with contrasting characteristics
- found that only one of the characteristics appeared in the F_1 generation (always the same one – always purple flowers, for example, never white), and
- found a ratio of 3:1 in the F_2 generation (always 3 of the one that had appeared in the F_1 and 1 of the one that hadn't).

It was this pattern that led Mendel to formulate his laws and to coin the terms dominant and recessive. He used the term dominant to describe the allele that determined the **trait** that appeared in the F_1 and the term recessive to describe the allele that determined the trait that did not appear in the F_1. Table 3.1 summarises the results for all Mendel's breeding experiments.

Table 3.1 *Mendel's results*

Character	Dominant trait	×	Recessive trait	F_2 generation dominant : recessive	Ratio
Flower colour	purple	×	white	705:224	3.15:1
Flower position	axial	×	terminal	651:207	3.14:1
Seed colour	yellow	×	green	6022:2001	3.01:1
Seed shape	round	×	wrinkled	5474:1850	2.96:1
Pod shape	inflated	×	constricted	882:299	2.95:1
Pod colour	green	×	yellow	428:152	2.82:1
Stem length	tall	×	dwarf	787:277	2.84:1

The overall ratio for the F_2 generation is 2.99:1. This could hardly be nearer to 3:1 and, indeed, caused some biologists to accuse him of falsifying his results. However, most believe that he was just an exceptionally meticulous experimenter.

Mendel explained these results in the following way:

1. Every trait (like flower colour, or seed shape, or seed colour) is controlled by two 'heritable factors' – these are what we now call genes. The heritable factors (genes) may take different forms (alleles).
2. If the two alleles in an individual are different, one is **dominant** (will be expressed in the organism's appearance or physiology) and one is **recessive** (cannot be expressed unless the individual has two copies of the recessive allele). Dominant traits mask the appearance of recessive traits.
3. The only physical link between the generations is the gametes or sex cells. These must pass the genes from one generation to the next.
4. The heritable factors (alleles) separate when the gametes (sex cells) are formed; each gamete therefore contains only one allele controlling the trait. This is Mendel's 'law of segregation'. He also stated that the gametes (sex cells) fuse randomly at fertilisation.

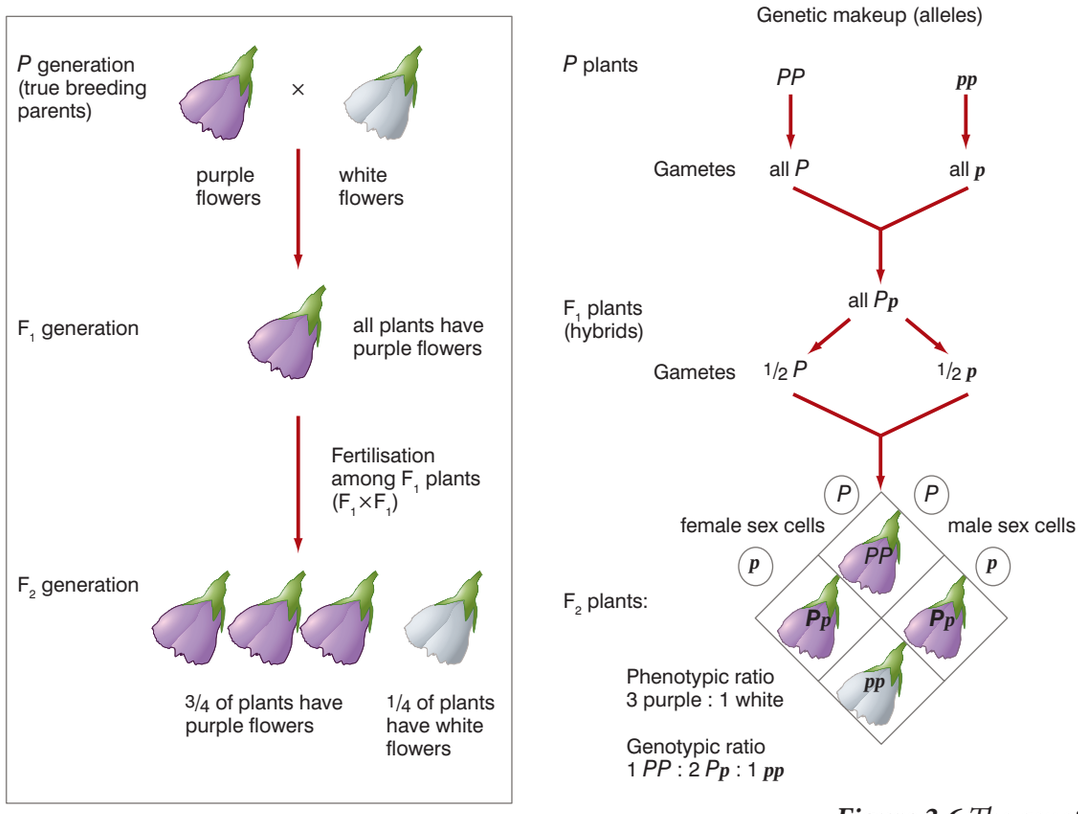


Figure 3.6 *The genetic basis of Mendel's results from crosses between purple-flowered pea plants and white-flowered pea plants*

After further studies and experiments, Mendel also formulated another law called the 'law of independent assortment'. This law states that the inheritance of one trait is independent of the inheritance of another. That is, the alleles of one pair segregate independently of the alleles of another pair controlling a different feature. Whilst this was true for the traits that Mendel studied in pea plants and is true for many traits in many other organisms, we now know that it is not always the case, as we shall see when we look at the phenomenon of linkage.

If we return to our example of the cross between purple-flowered plants and white-flowered plants, we can now explain what is happening in terms of segregation of alleles, random fertilisation and the concepts of dominant and recessive alleles.

In the genetic diagram in Figure 3.6, the symbol **P** represents the dominant allele for purple flowers and **p** represents the recessive allele for white flowers.

Both parents are homozygous.

Alleles segregate and gametes contain only one of the pair.

All F_1 are heterozygous, with purple flowers as **P** is dominant.

Alleles segregate and half of the gametes receive **P** and half **p**.

The gametes fuse at random in fertilisation. All the combinations of gametes are shown in this Punnett square. This represents the possible genotypes of the offspring and the ratio in which they will occur.

Activity 3.2

Make a simple model – for example using beads or clay – to explain how a genetic cross works.

See if you can solve the following

Draw genetic diagrams to show the offspring that would result from the following crosses. Check table 3.1 to see which trait is dominant and which is recessive.

- heterozygous purple-flowered plants and white-flowered plants
- two white-flowered plants
- two heterozygous tall plants
- a heterozygous green-podded plant and a yellow-podded plant

You will need to make up your own symbols to represent the alleles.

So, if we know the genotypes of parents, we can produce genetic diagrams like the one above to work out the possible genotypes of their offspring and the proportions in which they will occur.

How can parents showing one version of a feature have children with the other version?

Let's stick with the gene for earlobes. It has two alleles – free earlobes and attached earlobes. Everyone has two alleles for this feature in all their cells (except the sex cells). A person could have:

- two attached earlobe alleles per cell (homozygous for the recessive allele)
- two free earlobe alleles per cell (homozygous for the dominant allele)
- one attached allele and one free earlobe allele per cell (heterozygous)

We can represent this process diagrammatically. If we use symbols for the different alleles:

E to represent the dominant allele for free earlobes
e to represent the recessive allele for attached earlobes.

Suppose a man homozygous for free earlobes and a woman homozygous for attached earlobes have a child. The possible offspring are shown in Figure 3.7.

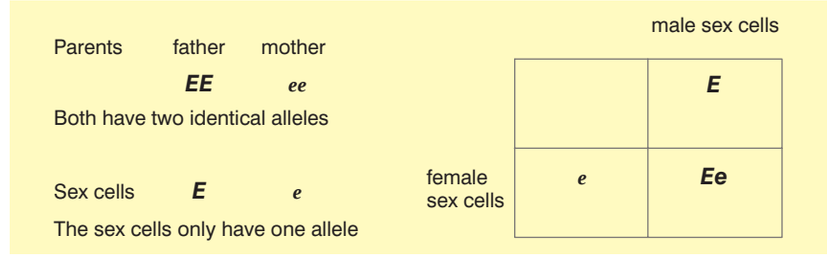


Figure 3.7 *The offspring of parents homozygous for free and attached earlobes, respectively*

		male sex cells	
		E (1/2)	e (1/2)
female sex cells	E (1/2)	EE (1/4)	Ee (1/4)
	e (1/2)	Ee (1/4)	ee (1/4)

Figure 3.8 *The offspring of parents both heterozygous for free earlobes*

Figure 3.8 shows the outcome if both parents had had free earlobes with the genotype **Ee**.

We would expect three out of four children to have free earlobes and one out of four to have attached earlobes – a ratio of 3:1. Put another way there is a 75% or ¾ probability that any particular child will have free earlobes and a 25% or ¼ probability that the child will have attached earlobes.

Remember this ratio …
It occurs in all organisms where two heterozygotes cross-breed.

So now we can answer our question 'how can parents showing one version of a feature have children with the other version?'. If both the parents show the feature determined by the *dominant* allele, but are *heterozygous*, they can produce children that show the feature determined by the recessive allele.

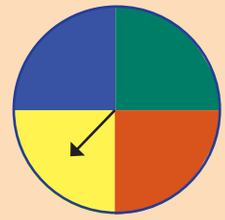
Remember this too …
It is an important idea in solving genetic problems.

KEY WORD

back cross/test cross
an organism showing the dominant trait is bred with one showing the recessive trait. The results allow determination of whether the original organism showing this dominant trait was homozygous or heterozygous

Activity 3.3: Probability

Make a spinner with four colours like the one opposite.



When you spin it, it must land on one of the four colours. There is an equal probability that it will land on each of the colours. Each time, there are the same four possible outcomes, and one of them must happen, so every time there is a probability of 1 in 4, 0.25 or 25%, that it will land on each colour.

Now, you will investigate the number of events on how close the predicted probability matches reality!

Spin the spinner 12 times, record the results and work out the actual percentage occurrence for each. This is found by

$$\frac{\text{number of occurrences of a particular colour}}{\text{total number of spins}} \times 100$$

Record your results in a table like the one below.

Now repeat for 24, 36, 48 and 60 spins.

Number of spins	Percentage occurrence of:			
	Yellow	Blue	Red	Green
12				
24				
36				
48				
60				

How does the percentage occurrence match the predicted 25% as the number of spins changes?

How could you find out if an organism showing the trait determined by a dominant allele is homozygous or heterozygous?

After all, all tall pea plants are tall and all unattached earlobes are unattached. It makes no difference to the appearance whether the organism is homozygous or heterozygous. The only possible way is to carry out a breeding experiment. However, this is not possible with humans, so we must look at any children they may have, or perhaps gain clues from their parents.

But first, let's look at the breeding experiment. The particular experiment to find out if an organism is homozygous or heterozygous for a dominant trait is called the **test cross** or the **back cross**. Let's again use the flower colour in pea plants as our example.

DID YOU KNOW?

Why ratios don't always work out in the real world

What genetic diagrams show are *probabilities* that a certain genotype or phenotype will be produced. For instance, in the cross between two heterozygotes we *predict* that one quarter, 25%, will be homozygous recessive and will show the feature determined by the recessive allele. But a moment's thought will make you realise that it is only a prediction and may not be realised in any particular situation.

You might *predict* that with any toss of a coin there is a 50% chance of the coin landing head side up and if you tossed a coin ten times you would *predict* five heads and five tails. However, if you actually did it, you could easily get seven heads and three tails or four heads and six tails. But if ten people tossed a coin ten times, it would probably come close to 50 heads and 50 tails and even closer to 500 heads and 500 tails if one hundred people tossed a coin ten times.

Predicted ratios from genetic diagrams are only likely to be realised with large numbers of offspring. When the numbers are small, the laws of chance have a disproportionate effect.

Remember …

When fertilisation occurs, any type of male sex cell could fertilise any type of female sex cell; it is a random process. Again, we work out the possible genotypes in the children by drawing a **Punnett square**.

Activity 3.4: Seed counting

In maize (sweetcorn) several features of the seeds on the cob are determined by single genes with dominant and recessive alleles. For example, the allele for purple seeds is dominant to that for yellow seeds.

If two plants that are heterozygous for purple seeds are cross-bred, they will produce corn cobs with purple seeds and yellow seeds.

Count the number of purple seeds and yellow seeds on this maize fruit (cob).

What is the ratio of purple seeds to yellow seeds?

Is this what you would expect from the cross described above?

If we breed the purple-flowered plant with a plant whose genotype is definitely known, we can make predictions about the outcome. This can only be a white-flowered plant, which must have two recessive white alleles. There are then two possible outcomes. These are shown in in Figure 3.9.

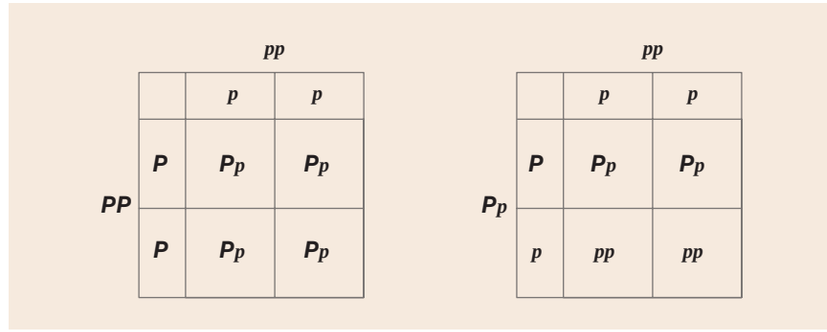


Figure 3.9 *Possible outcomes from a test cross*

So, if we were to carry out the cross and find that any of the offspring had white flowers, we could be certain that the original purple parent was heterozygous. We know this because any white-flowered offspring would need to inherit two recessive 'white' alleles – one from each parent. If all the offspring were purple-flowered, we could be *almost* certain that the purple-flowered plant was homozygous. But because predicted ratios aren't always met in the real world, we couldn't be *absolutely* certain.

How can we tell if an allele is dominant or recessive?

This, again, requires us to look at offspring resulting from a particular cross. Sometimes information is given in a genetic pedigree. Figure 3.10 shows a genetic pedigree of a family over three generations for the trait of 'widow's peak'. In this pedigree:

- squares show males, circles females
- shaded symbols are 'affected' (have widow's peak)
- W – dominant allele for widow's peak
- w – recessive allele for no widow's peak
- a horizontal line between two individuals represents a marriage
- vertical lines show parents/children

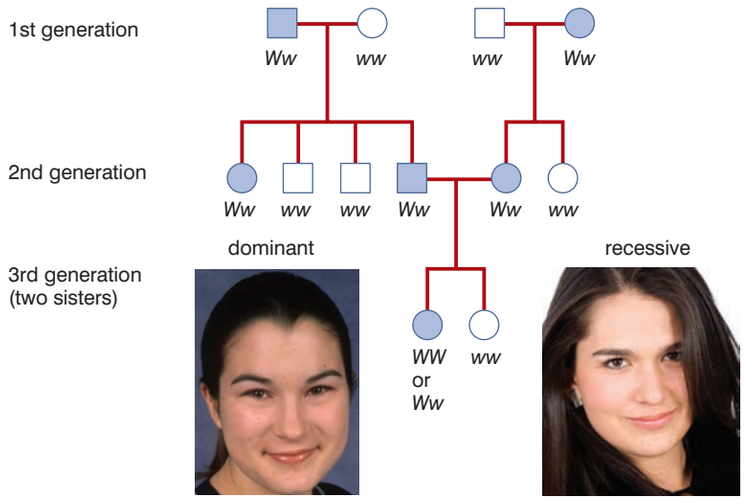


Figure 3.10 *A genetic pedigree for widow's peak*

In this example, all the genotypes are shown, but it is possible to work out genotypes from a pedigree. Look at the sisters in the third generation. Their parents both had widow's peak, but one of the sisters doesn't. Even if you weren't told which was dominant, you could use what we learned in the previous section to work it out. The only way two parents showing one feature (the sisters' parents) can have children showing the alternate feature (the sister with no widow's peak) is if the parents are heterozygous. So they are heterozygous – they have both alleles. But they have widow's peak. This must mean that the widow's peak allele is dominant.

Activity 3.5: How to work out genotypes of individuals in a pedigree

Look at figure 3.11, which is a pedigree showing the inheritance of albinism over three generations in a family.

In this activity we will use:

A to represent the allelle for normal pigmentation

a to represent the allele for albinism

- How does the relationship between individuals 1, 2 and 6 prove that the allele for normal pigmentation is dominant over the allele for albinism?
- Why must the genotypes of all the individuals with albinism be aa?
- From where have the people with albinism inherited each of the a alleles?
- What allele will each of their children inherit from the individuals with albinism?
- What are the genotypes of individuals 3 and 17?

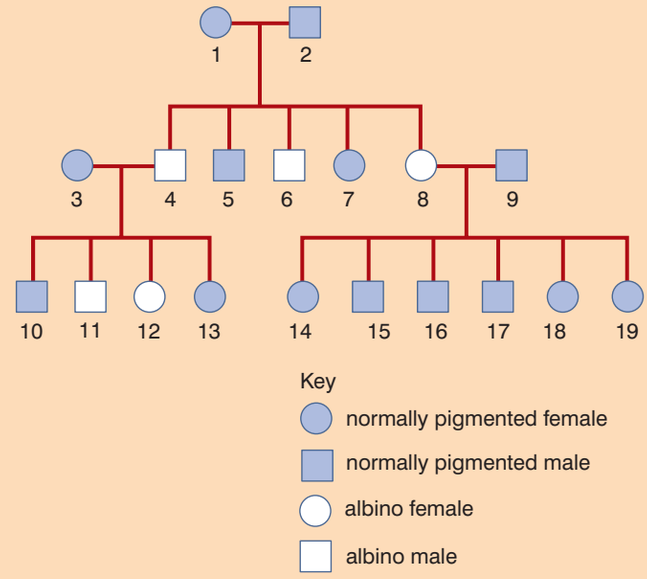


Figure 3.11 *A pedigree for albinism*

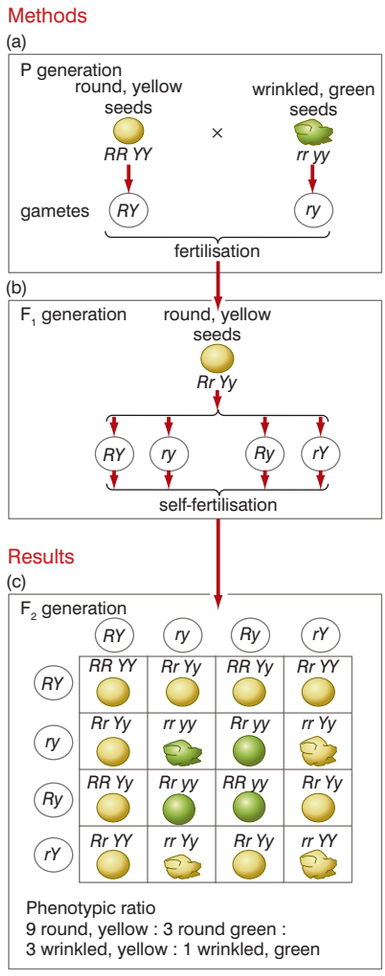


Figure 3.12 *A dihybrid cross*

	AB	Ab	aB	ab
AB	AABB	AABb	AaBB	AaBb
Ab	AABb	AAbb	AaBb	Aabb
aB	AaBB	AaBb	aaBB	aaBb
ab	AaBb	Aabb	aaBb	aabb

Figure 3.13 *How to lay out a Punnett square for a dihybrid cross*

What patterns do we get if we consider the inheritance of two genes at the same time?

This is known as dihybrid inheritance. When Mendel considered the inheritance of two characteristics at the same time, he followed essentially the same procedure as with his monohybrid experiments.

In one investigation, he bred plants that were homozygous for round, yellow seeds with plants homozygous for wrinkled, green seeds.

All the F_1 plants had round seeds which were yellow, showing that these alleles were dominant over the wrinkled and green alleles.

He then allowed these plants to self-fertilise themselves. In the F_2 generation, the other two features re-appeared, but in new combinations.

The four phenotypes that appeared in the F_2 and their proportions were:

- round and yellow 9
- round and green 3
- wrinkled and yellow 3
- wrinkled and green 1

Figure 3.12 shows how the alleles are passed from one generation to the next to bring about this result.

The behaviour of the alleles in gamete formation illustrates Mendel's law of independent assortment.

The F_1 plants produce gametes containing an allele for each feature. But they are not linked in any way. When a gamete is formed containing an R allele, there is a 50% chance that it will also contain a Y or a y. This results in the four different types of gametes formed by the heterozygotes and the 16 possible combinations (some of them the same) in the Punnett square, giving the 9:3:3:1 ratio. Remember this ratio; it is always found in a dihybrid cross where the parents are heterozygous for both traits. Also, if you have to construct a Punnett square for a dihybrid cross, always write both sets of gamete genotypes in the sequence (let's use alleles A and a with B and b) AB, Ab, aB, ab. This will then place the different genotypes in the same location in the square every time. Just think in triangles!

The nine individuals with both dominant alleles form a big triangle and are represented in blue. The three with the first dominant allele only (in our case, A) form a triangle represented in green. Those with the second dominant allele only (B) form a small triangle, shown in pink, and, finally, those with two recessive alleles are tucked away in the bottom right-hand corner. This is illustrated in figure 3.13.

Is there a dihybrid test cross procedure?

There most certainly is! To discover the genotype of a plant whose phenotype shows both dominant features (we will stick with round seeds and yellow seed colour as our example), again a breeding experiment must be carried out. There are more possibilities than in monohybrid inheritance. The plant could be:

- homozygous for both features – **RRYY**
- heterozygous for both features – **RrYy**
- heterozygous for one feature but not the other – **RRYy** or **RrYY**

Following breeding with a double recessive type (rryy) there are the following possible outcomes:

- If the plants produced show all four possible phenotypes, the original was heterozygous for both features.
- If the plants produced all had round, yellow seeds, the original was homozygous for both features.
- If the plants produced all had rounds seeds but some had green and some had yellow seeds, the original was heterozygous for seed colour only.
- If the plants produced all have yellow seeds but some are round and some wrinkled, the original was heterozygous for seed shape only.

Are alleles always simply dominant or recessive?

The short answer to this is no. Sometimes alleles are **codominant**; the two alleles of a gene are both equally dominant and so, in the heterozygote, both are expressed. An example of this is found in the flower colour of snapdragons. This is controlled by a single gene with two alleles:

- **R** – determines red-coloured petals
- **r** – determines white-coloured petals

The possible genotypes are:

- RR – plants with red flowers
- rr – plants with white flowers
- Rr – plants with pink flowers; both alleles still express themselves and some red pigment and some white pigment is produced, resulting in pink flowers

If a red-flowered plant and a white-flowered plant are cross-bred, all the offspring will be heterozygous and have pink flowers. If two heterozygotes are crossed, the same genotype ratio (1:2:1) is obtained as with any monohybrid cross, but instead of a 3:1 phenotype ratio, this is also 1:2:1 (1 red:2 pink:1 white).

This is shown in figure 3.14.

KEY WORD

codominant or **incomplete dominant alleles** *the pattern of inheritance where both alleles of a gene are equally expressed and determine which trait occurs in a heterozygous organism*

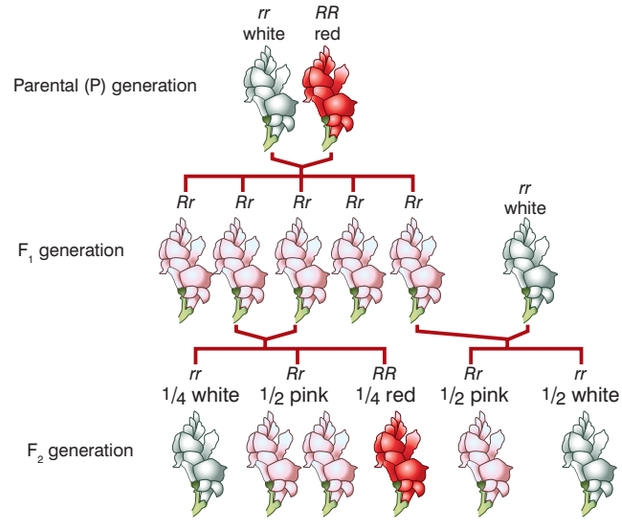


Figure 3.14 *Codominance in snapdragon flower colour*

DID YOU KNOW?

Although the gene may have more than two alleles, because they are alleles of the same gene, **any individual will still only have a maximum of two of the alleles**.

This is because the different alleles are found at the same locus (position) on homologous chromosomes. Because there are only two copies of each chromosome, the person can only have two alleles of the gene.

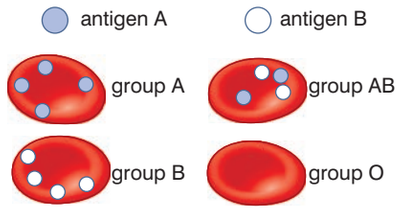


Figure 3.15 *The ABO blood groups*

		male sex cells	
		I^A (1/2)	I^O (1/2)
female sex cells	I^B (1/2)	I^A I^B (1/4)	I^B I^O (1/4)
	I^O (1/2)	I^A I^O (1/4)	I^O I^O (1/4)

Figure 3.16 *How the four offspring of parents with blood groups A and B can all have different blood groups*

Are there always two alleles of a gene?

Again, the short answer is no. Some genes have more than two alleles, and then the pattern of inheritance is a little more complex. We call this situation multiple allele inheritance. However, the basic rules are just the same – alleles can be dominant or recessive or codominant.

An example of multiple allele inheritance occurs in the inheritance of the ABO blood groups. This is an interesting example as it also involves codominance. In the ABO blood grouping system, there are four blood groups, determined by the presence or absence of two antigens (A and B) on the surface of the red blood cells. Figure 3.15 illustrates this.

There are three alleles involved in the inheritance of these blood groups:

- I^A, which determines the production of the A antigen
- I^B, which determines the production of the B antigen
- I^O, which determines that neither antigen is produced

Alleles I^A and I^B are codominant, but I^O is recessive to both. The possible genotypes and phenotypes (blood groups) are shown below.

Genotype	Blood group
I^AI^A, I^AI^O	A
I^BI^B, I^BI^O	B
I^AI^B	AB
I^OI^O	O

It is possible for two parents, with blood groups A and B, to have four children, each with a different blood group! Figure 3.16 shows how:

	Father	Mother	
Parents	I^A I^O	I^B I^O	Both are heterozygous, but for different blood groups.
Sex cells	I^A or I^O	I^B or I^O	Parents can make two types of gametes in equal numbers, each with one allele

Other examples of codominance

When 'red' cattle (homozygous for the red allele) are bred with white cattle (homozygous for the white allele), the offspring are heterozygous and have patches of red and patches of white skin. They are called roan cattle.Two of the alleles that determine our ABO blood group are codominant.

What is the physical basis for these patterns of inheritance?

We began this chapter by pointing out that a gene is a part of a chromosome. To understand the patterns of inheritance we have discussed so far, we must look at how chromosomes behave when gametes are formed. For gametes to be formed, special cells in the sex organs of the organism divide by a process known as **meiosis**. When a cell divides in this manner, there are three key outcomes:

- it produces four 'daughter' cells
- these daughter cells have only half the number of chromosomes of the original cell; they have one chromosome from each **homologous** pair
- the daughter cells show genetic variation

To understand how this happens we need to look at the stages of meiosis. First, if you think carefully, a cell does not normally divide to produce four cells – it produces two. Therefore, meiosis must entail two divisions. We call these meiosis I and meiosis II. Let us first gain some kind of overview of meiosis, by looking at how just one pair of homologous chromosomes behaves through the two divisions. As you can see from figure 3.17, at the start of the process, each chromosome is a double structure; it is made of two **chromatids** held together by a centromere. This is because the DNA in each chromosome replicated prior to meiosis commencing. Before any division takes place, chromatids from different chromosomes in the homologous pair undergo 'crossing over'. In this process, they exchange sections of DNA. After this has taken place, meiosis I follows and the two chromosomes that make up the pair are separated into different cells. In meiosis II, the two chromatids that make up each chromosome are separated into separate cells. Notice that, because of crossing over, none of these chromatids are the same. Look at the combinations of alleles on the chromosomes at the start and at the end. There is genetic variation in the daughter cells, which also have only half the original chromosome number – they are said to have the **haploid** number of chromosomes, unlike the parent cell which had the **diploid** number of chromosomes.

During meiosis, the following things happen to the chromosomes:

- They duplicate; the DNA in each chromosome makes an exact copy of itself and histones associate with it to make another chromosome. The original and the copy remain attached by a centromere and are called not chromosomes but chromatids.
- They 'condense'; when chromosomes are not involved in cell division, they are very long and thin and all the genes can be active. However, they cannot be moved around a cell in this form, so they become much shorter and fatter.
- The chromosomes of a homologous pair (each one by now duplicated) 'find' each other (this is called synapsis and no one is quite sure how it happens) and form a **bivalent**.

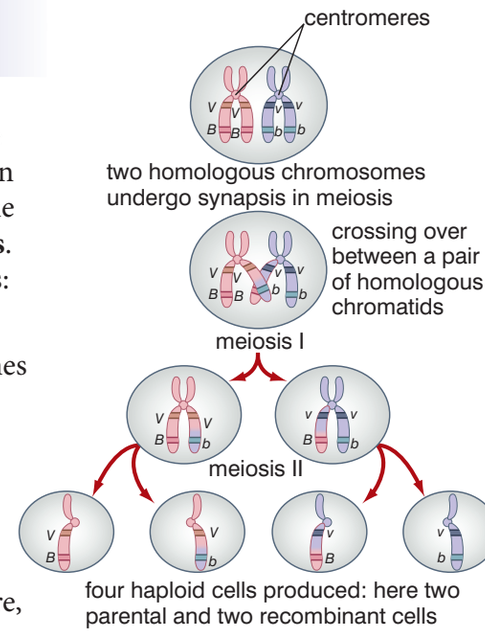


Figure 3.17 *An overview of meiosis.*

KEY WORDS

meiosis *the process by which a cell divides to form haploid gametes*

homologous chromosomes *chromosomes that carry genes for the same feature at the same loci (in the same places)*

chromatid *when a eukaryotic cell divides during meiosis, each of its chromosomes divides into two chromatids*

haploid *a haploid cell, usually a gamete, has a single set of chromosomes instead of homologous pairs*

diploid *a diploid cell has homologous pairs of chromosomes*

bivalent *a pair of homologous chromosomes*

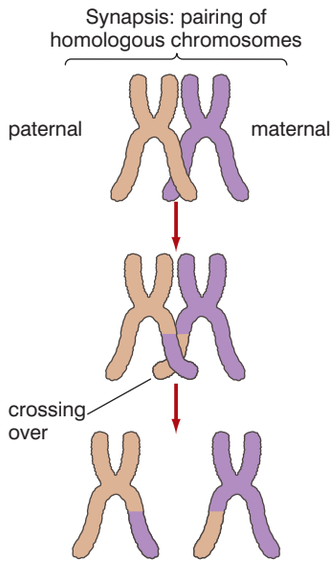


Figure 3.18 *Crossing over*

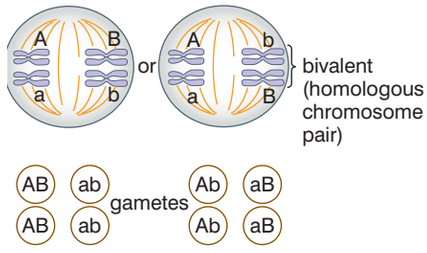


Figure 3.19 *Independent assortment in meiosis*

- Whilst associated in the bivalent, chromatids from different chromosomes undergo crossing over. These chromatids are called non-sister chromatids; the chromatids that make up one chromosome are sister chromatids. In this process, the chromatids exchange equivalent sections of DNA, and all four chromatids in the homologous pair are genetically different – as shown in figure 3.18.
- The chromosomes (or chromatids) are moved around the cell by fibres that make up a spindle.
- This is achieved by the spindle fibres contracting and pulling the chromosomes/chromatids. In the two divisions of meiosis, the chromosomes attach to the spindles differently so that:
  - in meiosis I, whole chromosomes are moved and the chromosomes that make up a homologous pair are separated
  - in meiosis II, the chromatids that make up each chromosome are separated. This is shown in figure 3.19.

It is pure chance how bivalents arrange themselves at metaphase 1. With just two bivalents, there are two possible arrangements and two different sets of gametes. With 23 pairs of chromosomes, there are 2^{22} different combinations. Each bivalent aligns itself independently of the others. This is called independent assortment and is an important source of genetic variation in the gametes produced by meiosis. It explains why alleles of two different genes behave in the way they do in a dihybrid cross.

The main stages of meiosis

Meiosis I: figure 3.20 shows the main stages of meiosis I. It is divided into four phases:

- prophase
- metaphase
- anaphase
- telophase

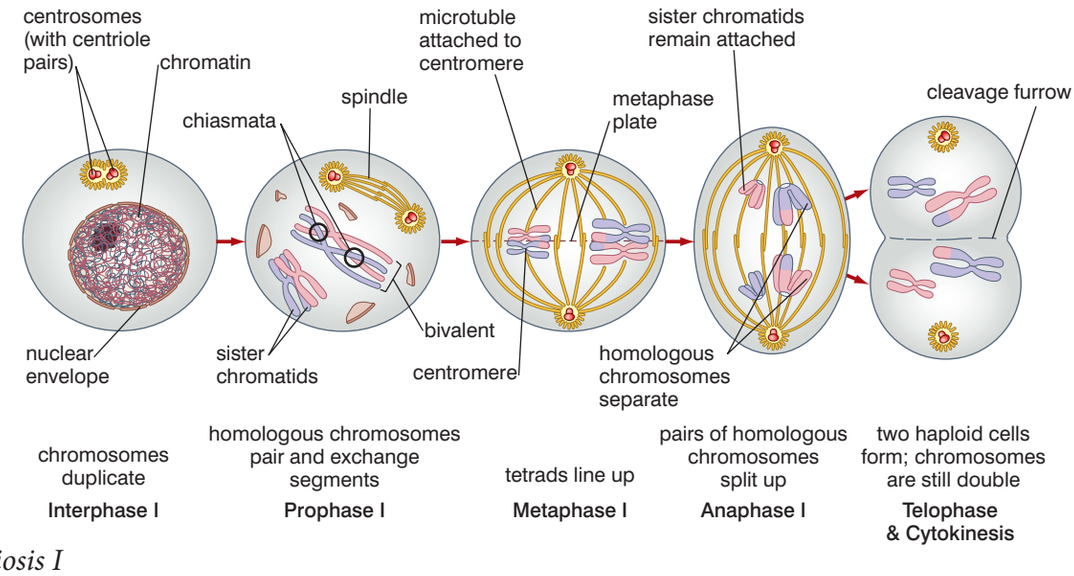


Figure 3.20 *Meiosis I*

After telophase, the cell may enter 'interphase' for a short period, or it may progress straight to meiosis II. The actual division into two cells is called **cytokinesis**.

It is important to note that the cells formed at the end of meiosis I are haploid: each cell contains only one chromosome from each homologous pair. Even though each chromosome comprises two chromatids, it is still only one chromosome and so the cell has half the number of chromosomes of the parent cell.

Meiosis II: Figure 3.21 shows the main stages of meiosis II. It is divided into the same four phases, but there are some important differences:

- there is no crossing over in prophase
- the chromosomes line up side by side in metaphase
- chromatids are separated in anaphase

KEY WORDS

sister chromatid *chromatids from the same chromosome; they have the same alleles in the same sequence*

non-sister chromatid *chromatids from different chromosomes of a homologous pair; although the genes are the same and at the same loci, the alleles may be different*

cytokinesis *the process that leads up to the cell dividing into two during meiosis*

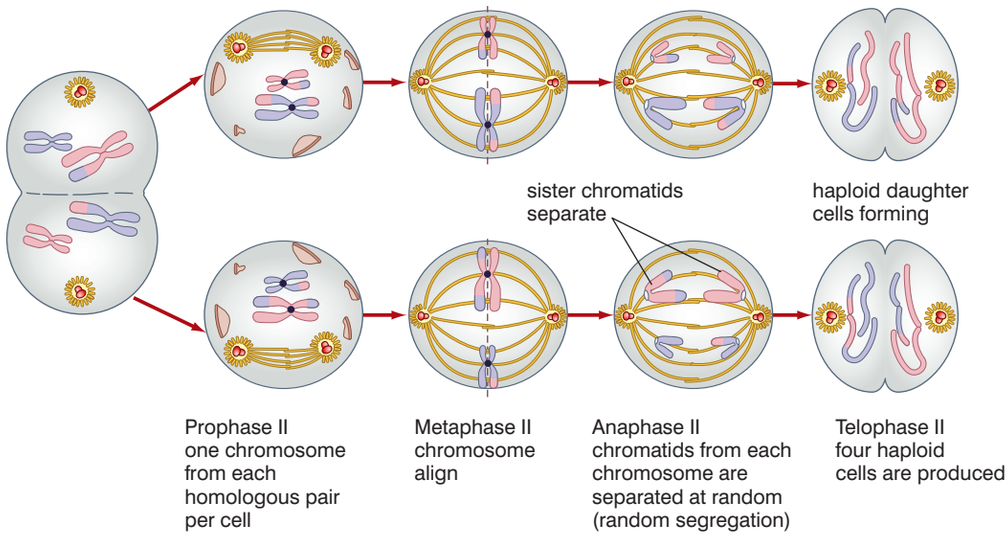


Figure 3.21 *Meiosis II*

What about alleles that don't segregate at gamete formation – genetic linkage

Mendel was very fortunate in his choice of organisms with which to experiment. All the alleles of all the genes involved in his experiments did segregate. But this does not always happen; some genes are always inherited together with other genes – they exhibit linkage. This happens when the genes in question are on the same chromosome. A chromosome is a physical unit as are the genes on it, so when a particular chromosome is passed into a **gamete**, all the genes on that chromosome pass into the gamete and none of them pass into another gamete. The genes are linked and inherited together because they are on the same chromosome.

KEY WORD

gamete *a sex cell*

One of the earliest studies of linkage was carried out by two British geneticists, Bateson and Punnett (who also devised the Punnett square). They investigated the inheritance of flower colour (purple or red) and pollen shape (round or long) in sweet peas. The alleles are:

Did you notice that we have written the genotypes differently?

Because P and L (also p and l) are on the same chromosome (linked) we show the genotype as two sets of this unit – PL/PL (rather than PPLL, which we would write for non-linked genes).

- P – purple (dominant)
- p – red (recessive)
- L – long (dominant)
- l – round (recessive)

If we were to cross individuals heterozygous for two features, then we normally would expect the 9:3:3:1 ratio typical of dihybrid inheritance. But these are linked genes, and, because they are linked, the two genes are inherited as a single unit. Starting from pure-breeding (homozygous) parents which were:

- purple-flowered with long pollen (PL/PL)
- red flowered with round pollen (pl/pl),

We can predict what might happen over two generations using the standard genetic diagram.

Parent genotypes ***PL/PL*** × ***pl/pl***

Gametes ***PL*** ***pl***

F_1 genotypes ***PL/pl*** (self-fertilised)

Gametes male female

PL ***pl*** ***PL*** ***pl***

	PL	***pl***
PL	***PL/PL*** purple, long	***PL/pl*** purple, long
pl	***PL/pl*** purple, long	***pl/pl*** red, round

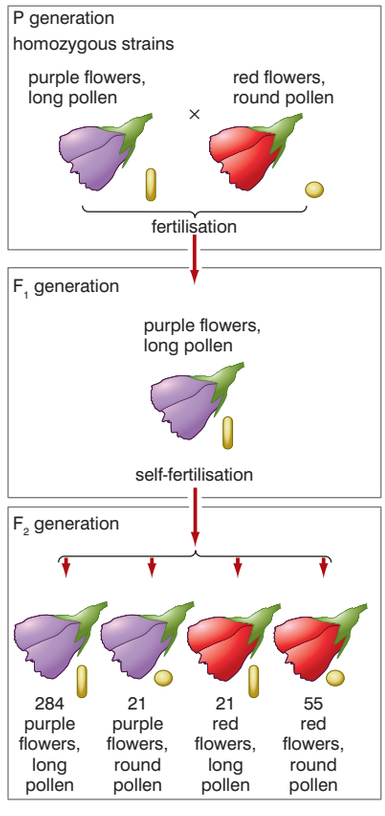


Figure 3.22 *Bateson and Punnett's investigation*

We now predict not a 9:3:3:1 ratio, but a 3:1 ratio of purple-flowered, long-pollen plants to red-flowered, round-pollen plants. Because the two genes are behaving as a single unit, it is like carrying out a monohybrid cross. Because the genes are inherited in this way, we wouldn't predict any plants that had either purple flowers with round pollen or red flowers with long pollen. But the story doesn't end there. We mustn't forget that when these gametes are formed, they are formed by meiosis and that this involves crossing over at prophase I. The consequence of this is some gametes do contain the combination Pl and others contain pL. So we do, in fact, get the four types of offspring from a cross between two plants both heterozygous for both features – but not in a 9:3:3:1 ratio. The procedure and results from Bateson and Punnett's original investigation are summarised in figure 3.22. What we might have expected from a 9:3:3:1 ratio is:

- 215 purple, long
- 71 purple, round
- 71 red, long
- 24 red, round

and from a 3:1 ratio:

- 286 purple, long
- 95 red, round

The reason we do not get either is because the genes are linked, but there is some crossing over between them during prophase of meiosis I. This produces the types we would not expect from linked inheritance. These types are called recombinant types.

Much of the early research on crossing over and recombination was carried out using fruit flies. They are convenient experimental animals because:

- they are small animals with a short life cycle (just two weeks)
- they are cheap and easy to breed and keep in large numbers
- they have only four pairs of chromosomes per cell
- the chromosomes are large and easily observed
- staining reveals dark bands which correspond to particular genes

Using fruit flies in the early 1900s, Thomas Morgan was able to prove, finally, that genes carried on chromosomes are the physical basis of inheritance. One of his students, A H Sturtevant, worked on linkage and crossing over in *Drosophila*. In these experiments, he made predictions about what offspring to expect if there was no crossing over and then counted the number of expected and recombinant types to find the percentage of recombinant types. This percentage of recombinant types is called the crossover value and is a measure of how far apart the genes are on a chromosome. A low crossover frequency indicates that the genes are close together; a high one that they are further apart. This has been used in creating gene maps of chromosomes, where the percentage crossover values are used as 'units of separation' of the genes on the chromosome.

DID YOU KNOW?

The units of separation on a chromosome are sometimes called centimorgans in honour of Morgan's pioneering work on chromosomes and inheritance.

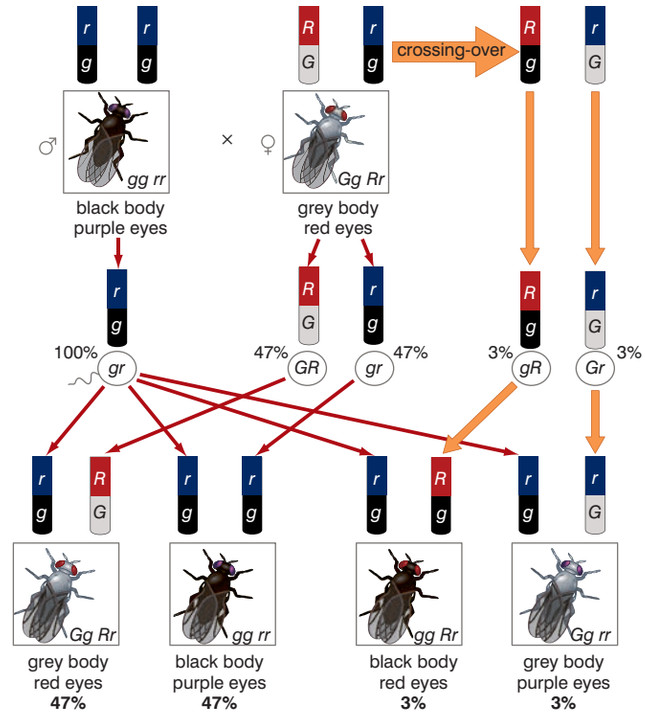


Figure 3.23 *Crossing over in* Drosophila

KEY WORDS

inbreeding *involves breeding animals or plants with close relatives. This can cause problems such as infertility in the resulting offspring*

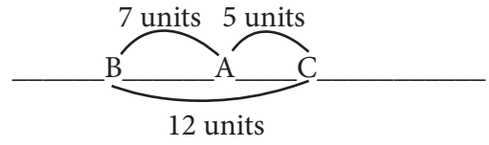
hybrid vigour *the increased vigour or productivity of organisms resulting from cross-breeding different varieties of the same species*

The chance of crossing over occurring between two genes depends on how far apart they are on the chromosome. If they are very close together, then it is unlikely that crossing over will occur between the genes; if they are further apart, it is more likely that crossing over will occur between them and that recombinant types will be formed.

Suppose three genes A, B and C have loci on the same chromosome. From investigations, the crossover values are found to be:

- A and B – 7%
- A and C – 5%
- B and C – 12%

This can only hold true if the genes are arranged as shown below:



Gene mapping has been used to 'track down' genes that cause disease (for example, cystic fibrosis and Huntington's disease) so that the DNA of the gene can be cloned for analysis and research.

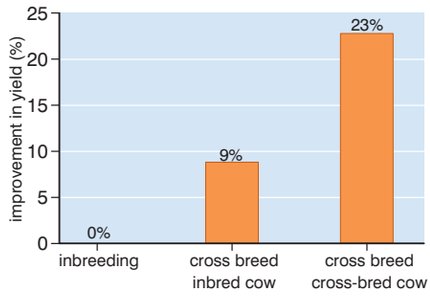


Figure 3.24 *The gains in productivity from hybrid vigour*

How is knowledge of genetics important in cross-breeding and inbreeding crops and stock?

Both cross-breeding and **inbreeding** are aspects of the same process – selective breeding – where organisms are chosen to breed with a specific outcome in mind. In grade 10, you learned about some examples of cross-breeding in Ethiopia. Now we must extend that a little to understand a little more of the genetic principles behind cross-breeding. Cross-breeding is an established breeding method used in sheep and beef cattle breeding to increase overall productivity. It has been used throughout the world and there is a lot of evidence to support the production gains possible from cross-breeding. Commercial cattle farmers may cross-breed animals for two related reasons:

- to take advantage of **hybrid vigour**
- to take advantage of the good qualities of two or more breeds and to combine these qualities to improve market suitability

Hybrid vigour occurs when unrelated breeds or lines (of the same species) are cross-bred. In many cases the offspring from these crosses are more productive (higher milk yields, more beef per carcass) than the average of their parent breeds. The extra performance observed through hybrid vigour is simply the recovery of production losses that occurred through inbreeding in the parental breeds. Hybrid vigour is reduced when animals produced by cross-breeding are mated together.

So what is going on? When a new variety of a species is established, organisms of that type are often bred only with each other. This

is called inbreeding and, whilst it helps to produce a pure line (remember Mendel's pea plants?), it often reduces the productivity of the line. When two lines or varieties are cross-bred, the offspring (the F_1 hybrid) results in an increase in the number of genes that are heterozygous. The 'pure lines' that were used would each be homozygous dominant for the genes which give them their particular characteristics. Crossing the two results in offspring with more dominant alleles, albeit in heterozygous form. However, since the dominant allele in a heterozygote often has the same effect as a dominant allele in a homozygote, this increase in the heterozygosity is what causes the increased vigour of the hybrid. Figure 3.24 shows some of the effects of hybrid vigour in cattle.

In addition to making use of hybrid vigour, cross-breeding can have the advantage of allowing breeds to be chosen for complementary characteristics. For example, cattle produced by cross-breeding dairy and beef breeds can have high milk yields and the ability to produce many calves. However, if mated with large bulls, the offspring of these cattle also grow to large sizes, making them good beef cattle. It would not be possible to achieve both these outcomes with either pure-bred dairy cattle or pure-bred beef cattle. It is important at the outset to choose the cattle carefully – to check that they are likely to produce the desired result.

The same principles can apply in breeding crops. Cross-breeding, natural or planned, has been important in producing many of the high-yielding crop plants we now grow. Figure 3.25A shows a plant breeding station for maize where scientists can test hybrids and their yields. Figure 3.25B shows the healthy and high-yielding 'corn cobs' produced by hybrids.

DID YOU KNOW?

Because it is the result of increased heterozygosity, the term hybrid vigour is sometimes replaced by **heterosis**.

The cattle only produce milk after they have calved. So if we can produce a breed of cattle that produces potentially high beef calves at the same time as producing a lot of milk (intended for these calves) then the cross-breeding will have been successful.

Figure 3.25 *Hybrid vigour in corn (maize)*

What about genes on the sex chromosomes?

More about sex determination

In grade 10 you learned that sex is determined by the X and Y chromosomes. Males have one X chromosome and one Y chromosome, whereas females have two X chromosomes. Because males have two different sex chromosomes, they are called the heterogametic sex, whereas females are the homogametic sex. In addition, they both have 44 (22 pairs) autosomes – non-sex chromosomes.

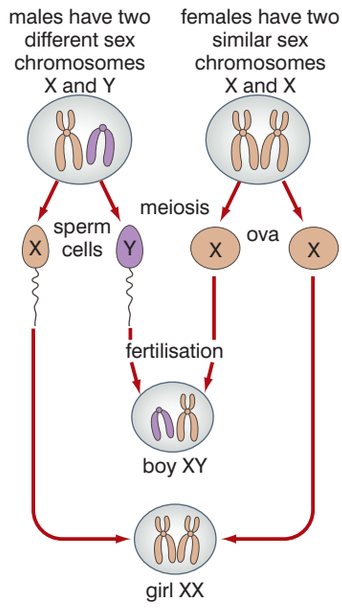


Figure 3.26 *Sex determination in humans*

The **karyotypes** in figure 3.27 show the chromosomes from a human male and a human female.

You also learned that in any family, or in any mating in mammals, the predicted ratio of males to females is 1:1, as shown in figure 3.26. However, although it is the Y chromosome that appears to determine a person's sex, it is, in fact, the action of one gene on this chromosome – the **SRY gene** – that determines the formation of testes.

In the early development of the embryo, a region called the urogenital ridge develops into a 'bi-potential gonad'. This means that the same structure can develop into either ovary or testis.

When the SRY gene is activated, the bi-potential gonad develops into a testis, and the embryo is male. If the SRY gene is absent (or inactivated for some reason), genes on the X chromosome and on the autosomes cause the bi-potential gonad to develop into an ovary, and the embryo is female.

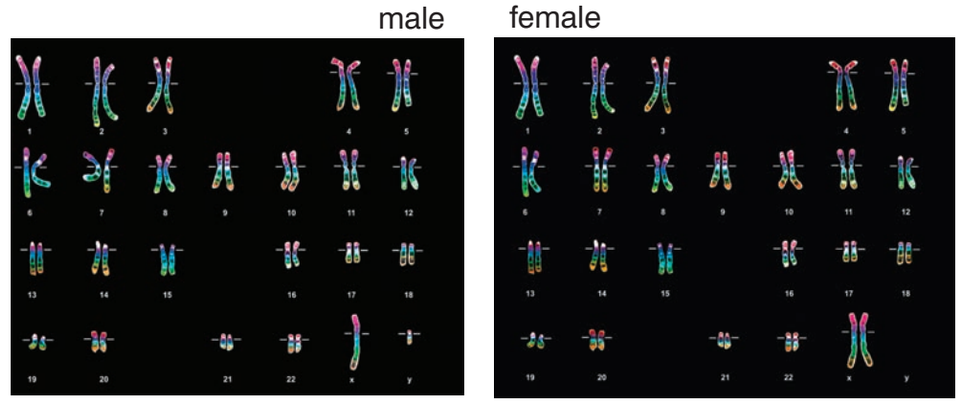


Figure 3.27 *Karyotype of human male and female*

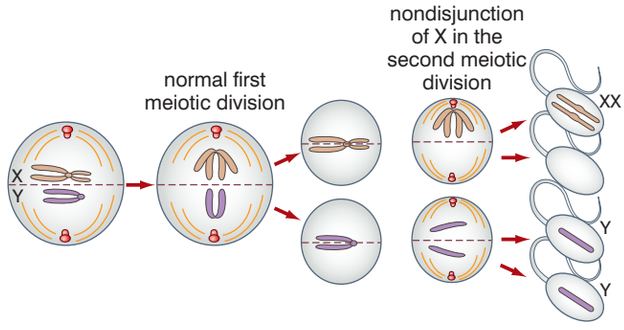


Figure 3.28 *Non-disjunction of the sex chromosomes*

Because it is the presence or absence of the SRY gene that determines sex, individuals with only one X chromosome and no Y chromosome (written X–) develop into females, but with slightly masculinised features. Similarly, individuals with two X chromosomes and one Y chromosome (XXY) develop into males, but with feminised features. These individuals are also sterile. The abnormal number of chromosomes arises as a result of non-disjunction of the sex chromosomes during meiosis. This means that the chromosomes do not segregate properly into the gametes, as shown in figure 3.28. When these abnormal gametes fuse with normal gametes, the abnormal chromosome numbers give rise to the conditions described above. This is summarised in figure 3.29.

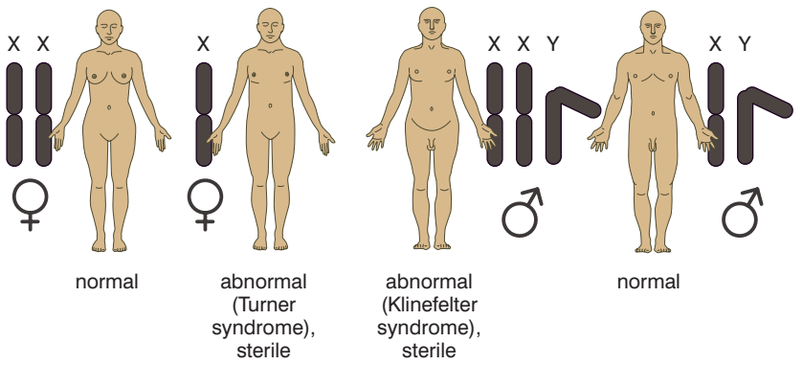


Figure 3.29 *The results of non-disjunction of sex chromosomes*

DID YOU KNOW?

Other systems of sex determination

There are several other systems of sex-determination. In birds it is females who are the heterogametic sex and males the homogametic sex! But they don't have X and Y chromosomes – they have W and Z. Females are ZW and males ZZ. There are also other chromosomal systems, as shown in figure 3.30.

In some reptiles, such as alligators, sex is determined by the temperature at which the egg is incubated. Some snails start out male, then become female! In tropical clown fish, the dominant individual in a group becomes female while the other ones are male, and in blue wrasse fish the reverse. Some species have no sex-determination system – they are hermaphrodite (have both male and female sex organs). Hermaphrodites include the common earthworm and some species of snails.

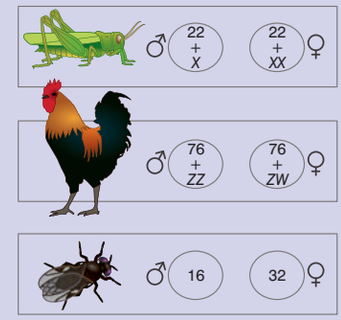


Figure 3.30 *Other systems of sex determination*

Activity 3.6: Making an edible model of DNA!

You will need:

- 2 long pieces of boiled potato
- 12 toothpicks
- 9 pink beans (Thymine)
- 9 yellow beans (Cytosine)
- 9 green beans (Adenine)
- 9 orange beans (Guanine)
- 5 paperclips
- masking tape

Method:

1. Choose one of the base sequences below.
   Sequence 1: T A C G T A T G A A A C -or-
   Sequence 2: T G G T T T A G A A T T
2. Assemble one side of your DNA molecule. A piece of boiled potato will form the sugar-phosphate backbone of the DNA and beans will be the chemical bases (as shown in the list above). Place a bean on the end of a toothpick so that the point of the toothpick goes all the way through. Anchor the toothpick into the boiled potato backbone.
3. Label the backbone. With a marker or pen and masking tape, label your boiled potato backbone 'DNA-1' or 'DNA-2', depending on which sequence you used.
4. Match the chemical base pairs. Place the coloured bean for the matching chemical base on the other end of each toothpick. Remember that A always pairs with T and C always pairs with G!
5. Complete your DNA model. Attach the other backbone so your model looks like a ladder.
6. Twist your DNA model. Carefully twist your DNA molecule so that it looks like a double helix.
7. Label parts of your DNA out of paper clips and tape. Label one of each of the following: Adenine, Thymine, Cytosine, Guanine, and sugar-phosphate backbone. Make sure your chemical base pairs are correct!
8. If your teacher says it's ok – you can eat it!!

KEY WORDS

karyotype *a photograph of all the chromosomes in a cell arranged in homologous pairs*

SRY gene *the dominant gene on the Y chromosome that causes a mammal to develop as a male*

sex-linked *a gene found on one of the chromosomes that determine sex*

The genes on the sex chromosomes

Genes that are found only on the X chromosome or on the Y chromosome are said to be **sex-linked**.

Genes found only on the Y chromosome include those that determine:

- one form of the degenerative condition retinitis pigmentosa (in which eyesight becomes progressively weaker and may lead to blindness)
- one form of deafness

These particular conditions can only be inherited by males, as only males have the Y chromosome.

Genes found only on the X chromosome include those that determine:

- red-green colour blindness
- one form of haemophilia

These conditions can be inherited by females and males as both possess at least one X chromosome.

Many of these conditions are determined by recessive alleles, including both red-green colour blindness and haemophilia. If you think about this carefully, you will see why it is that these conditions are more common in men than in women:

- men only have one X chromosome
- if this chromosome carries the recessive allele for haemophilia, there is no corresponding dominant allele on the Y chromosome to mask its effect
- women have two X chromosomes
- both these need to carry the recessive allele for haemophilia for a woman to suffer from the conditions as, if only one of them did, the dominant allele on the other X chromosome would mask its effects

DID YOU KNOW?

About genes on both the X and Y chromosomes

Even though the X and Y chromosomes are very different, they have regions that are homologous (see figure 3.31). The genes in this region follow the same pattern of inheritance as genes on the autosomes. Most of these genes are concerned with control of metabolic activities in cells.

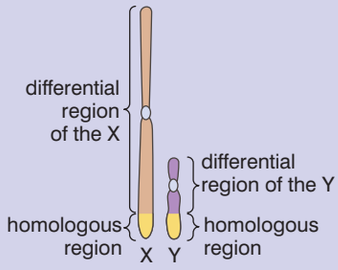


Figure 3.31 *The homologous and differential regions of the X and Y chromosomes*

- a man needs to inherit only one X chromosome with a recessive haemophilia allele to suffer from the condition, whereas a woman must inherit two; this is less likely to happen

Sex-linked features determined by recessive alleles on the X chromosome share the following characteristics:

- they are much more common among males (because females must inherit two chromosomes carrying the recessive allele, whereas males must inherit only one)
- affected males inherit the allele from their mother
- affected females inherit one allele from each parent (so the father will be affected)
- females who are heterozygous for the condition are called carriers
- they may 'skip' a generation and then appear in the males only

Genotypes of sex-linked features include the appropriate sex chromosomes as well as the alleles. For example, for red-green colour blindness, B represents the allele for normal vision and b represents the allele for red-green colour blindness. The possible genotypes and phenotypes are:

- $\mathbf{X^BY}$ – normal male
- $\mathbf{X^bY}$ – affected male
- $\mathbf{X^BX^B}$ – normal female
- $\mathbf{X^BX^b}$ – carrier female (is not colour blind)
- $\mathbf{X^bX^b}$ – affected female

Figure 3.32 shows the inheritance of red-green colour blindness in a family.

If you were not told that this was a sex-linked feature, there are several hints:

- it clearly skips a generation
- it is more common in the males
- the only affected female has an affected father

To determine the genotypes of individuals in a pedigree of a sex-linked feature, begin with a genotype of which you can be certain. This can only be either an affected male (e.g. genotype $\mathbf{X^bY}$ – with the affected X chromosome inherited from his mother) or an affected female (for example, genotype $\mathbf{X^bX^b}$ – each parent has passed on one affected X chromosome).

You can now work back and work forward from this known starting point. For example, what are the genotypes of individuals 11 and 7?

Individual 7 is the mother of individual 15 – an affected male ($\mathbf{X^bY}$). The $\mathbf{X^b}$ chromosome must have come from the mother (individual 7) who is unaffected and so must be $\mathbf{X^BX^b}$.

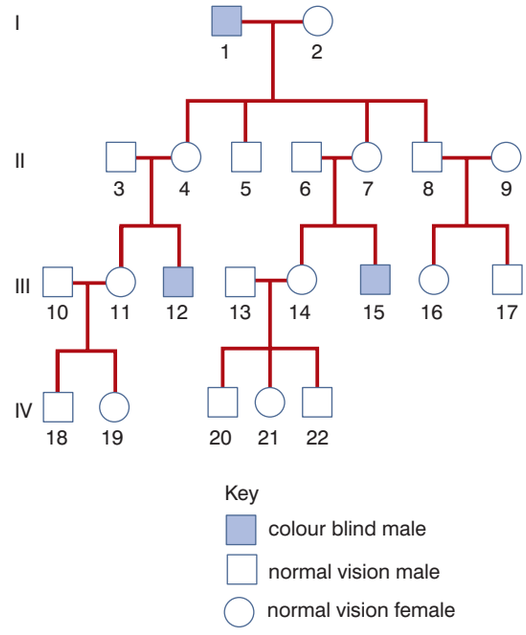


Figure 3.32 *The inheritance of red-green colour blindness in a family*

KEY WORDS

sex-influenced trait *a sex-influenced trait is more likely to occur in one sex but may sometimes occur in the other sex*

sex-limited trait *a sex-limited trait occurs only in one sex and never occurs in the other sex*

What are sex-influenced and sex-limited traits?

Both these are examples of traits that are expressed differently in the two sexes. However, the genes that determine these traits are not carried on the sex chromosomes, so they cannot be said to be sex-linked.

Pattern baldness (often called male pattern baldness) is an example of a **sex-influenced trait**. It is the high concentrations of the male sex hormone testosterone that makes the allele dominant in males. Because of this, males need only inherit one pattern baldness allele and they will go bald (because the allele is dominant in males). It doesn't matter whether the second allele is a baldness allele or a non-baldness allele. Females must inherit two before they go bald (because the allele is recessive in females). Even then the level of baldness in females is minimised by the low level of action of the alleles.

Sex-limited traits are only expressed in one sex. Both males and females have genes that stimulate lactation, but these are only expressed in females. The condition of cryptorchidism (undescended testicles) is genetically determined, but clearly can only ever be expressed in males.

Review questions

Choose the correct answer from A to D.

1. Two parents of genotype Aa are cross-bred. The alleles do not show codominance. What proportion of the offspring will look like their parents?

   A none

   B ¾

   C ¼

   D ½

2. A woman with blood group A and a man with blood group B could potentially have offspring with which of the following blood groups?

   A A

   B B

   C O

   D all blood groups

3. In an organism of genotype Aa, half the gametes carry the A allele and half carry the a allele. This is due to:

   A dominance

   B recessiveness

   C independent assortment

   D segregation

4. The genotype of a homozygote could be:
   A AA
   B aa
   C Aa
   D XX
5. A plant has a genotype AaBb. There is no linkage of the genes. The gametes it will produce are:
   A AB and ab
   B Aa and Bb
   C AA, aa, BB and Bb
   D AB, Ab, aB and ab
6. A tall pea plant with purple flowers (both determined by dominant alleles) is crossed with a short plant with white flowers. There is no linkage of the genes. If the tall, purple-flowered plant is heterozygous for both traits, the offspring will be:
   A 1 purple tall:1 white short
   B 3 purple tall:1 white short
   C 9 purple tall:3 purple short:3 white tall:1 white short
   D 1 purple tall:1 purple short:1 white tall:1 white short
7. Cross-breeding results in:
   A an increase in heterozygosity
   B hybrid vigour
   C an increase in the number of dominant alleles
   D all of the above
8. Which of the following statements concerning multiple allele inheritance is not true?
   A A gene has more than two alleles.
   B An individual will have more than two alleles of the gene.
   C There are more than two alleles in the population.
   D The alleles may be dominant, recessive or codominant.
9. Which of the following is not true of sex limited traits?
   A They are determined by genes on the autosomes.
   B They are expressed in only one sex (male or female).
   C They are carried on the X chromosome.
   D They often result in sexual dimorphism (very different physical appearance in male and female animals).
10. It is characteristic of sex-linked traits that they:
    A occur more frequently in males than in females
    B rarely skip a generation
    C are always determined by genes found on the Y chromosome
    D none of the above

KEY WORDS

DNA (*deoxyribonucleic acid*) *is the molecule that stores genetic information*

histone *the core of a chromosome around which the chromosome's DNA is wrapped.*

chromatin *the loose form taken by a chromosome when the cell is not dividing*

RNA (*ribonucleic acid*) *another molecule that stores genetic information. Genetic information stored as DNA is transcribed into RNA as part of the process for making proteins.*

double helix *describes the structure of a DNA molecule. It consists of two anti-parallel polynucleotide strands*

nucleotide *a component of a nucleic acid molecule. It consists of a phosphate group, a sugar called a deoxyribose (or ribose) and a nitrogenous base*

3.2 Molecular genetics

By the end of this section you should be able to:

- Describe the structure of a chromosome.
- Describe in detail the structure of the DNA molecule.
- Name the four nucleotides that build up the DNA molecule.
- Construct a model of DNA showing the base pair between complementary nucleotides.
- Describe the semi-conservative replication of DNA.
- Describe the significance of some of the uses of gene technology in forensic science (such as genetic fingerprinting).
- Describe how genetic fingerprints are produced.
- Define and give examples of cloning.
- Understand that genes can be cloned and explain in outline how this is achieved.
- Describe, in outline, the procedures involved in genetic engineering and appreciate that whilst there are many advantages that result from the process, there are also some ethical concerns about some of the procedures.

What is a chromosome really like?

It all depends when you look! Chromosomes are made from two chemicals:

- **DNA** (deoxyribonucleic acid) and
- **histones** (a set of globular proteins)

Figure 3.33 shows the way in which the DNA molecule wraps itself around the histone molecules to form a fibre of **chromatin**.

When a cell is not dividing, the chromatin is loosely organised throughout the nucleus as loops of chromatin fibres. Individual chromosomes cannot be distinguished. The 'loose' organisation allows the genes to be active. As a cell prepares to divide, the

Do you remember from grade 11 about globular proteins?

Globular proteins are proteins that have a tertiary structure that is loosely spherical.

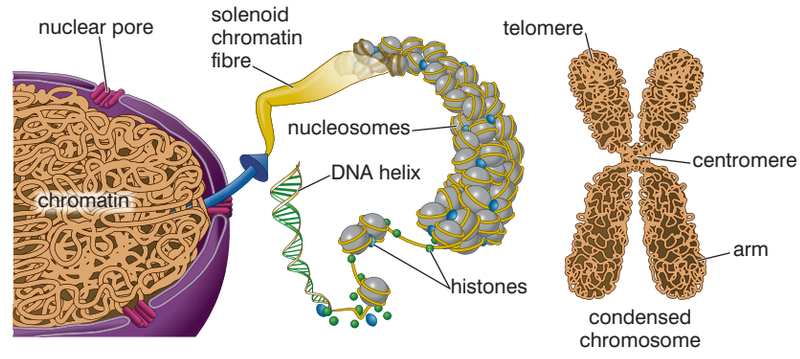


Figure 3.33 *DNA and histones are combined to form chromatin, which is organised into chromosomes.*

chromatin loops (which by now will have duplicated themselves) become compacted or 'condensed' to form a chromosome that is visible (when stained) under a light microscope. The compact state of the chromatin in such a chromosome means that the genes are too tightly packed to be active.

Genes are short sections of DNA within the chromosome. We shall learn more about the structure and action of genes in section 3.3.

How is a molecule of DNA put together?

DNA – Deoxyribo-Nucleic Acid is one of two types of nucleic acids. The other is **RNA** – Ribo-Nucleic Acid. You already know something of the structure of DNA from your grade 10 work on genetics, and your studies of biological molecules in grade 11, but let's recap these basics. Figure 3.34 shows part of a DNA molecule.

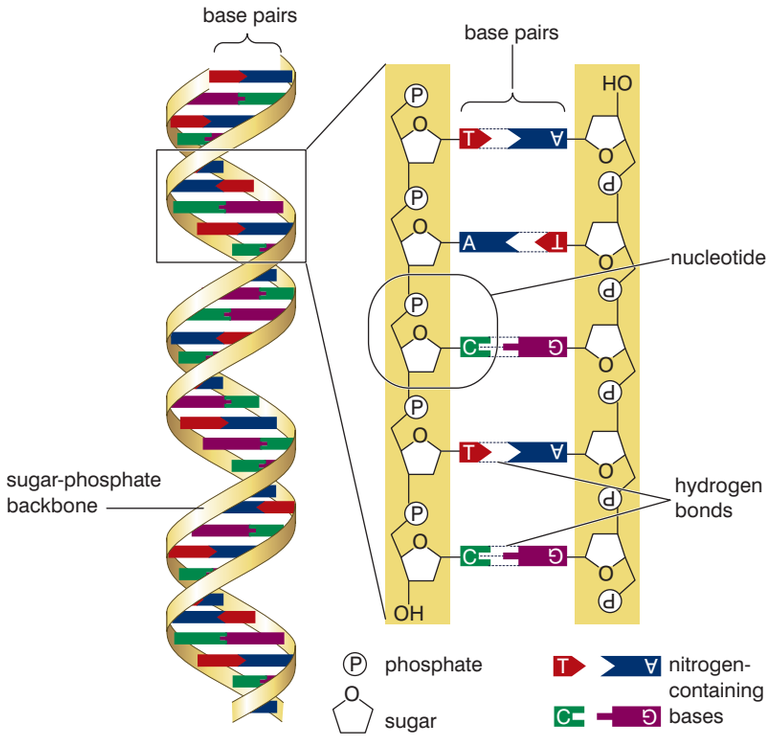


Figure 3.34 *The structure of DNA.*

You can see that it is made of two strands joined together and wound into a **double helix**. If you look carefully, you will see that the structures in one strand are 'upside down' when compared to the same structures in the other. This is because the strands are 'anti-parallel'. The 'start' of one strand is paired with the 'end' of the other strand.

The basic unit of a DNA strand is a **nucleotide**. There are four types of nucleotides. These are:

- Adenine-containing nucleotide
- Guanine-containing nucleotide
- Cytosine-containing nucleotide, and
- Thymine-containing nucleotide (in DNA, or Uracil-containing nucleotide in RNA).

Do you remember from unit 1 about DNA in different cells?

This organisation of DNA with histones into chromosomes is found in all eukaryotic cells. But the molecules of DNA in prokaryotic cells are different in a number of ways:

- they are much smaller
- they are circular, not linear as in eukaryotic cells
- they are not associated with histones to form chromosomes

As you learned in grade 11, all nucleotides have the same three components:

- a phosphate group
- a pentose sugar (deoxyribose in DNA nucleotides and ribose in RNA nucleotides)
- one of four nitrogenous bases – Adenine, Cytosine, Guanine and either Thymine (DNA) or Uracil (RNA)

The structure of a nucleotide is shown in figure 3.35.

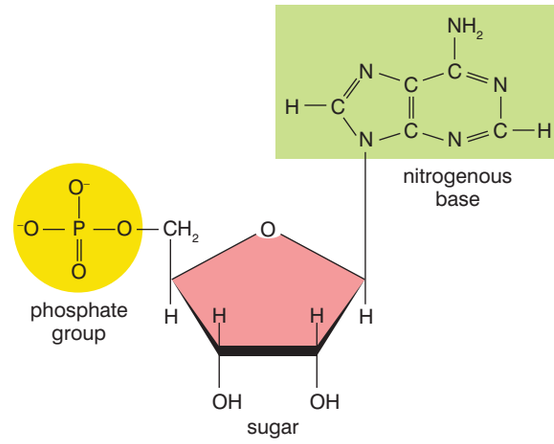


Figure 3.35 *The structure of a nucleotide*

DNA is a huge molecule made from two anti-parallel polynucleotide strands. The nucleotides are held together by bonds between the sugar in one nucleotide and the phosphate group in the next. The base does not take in this linking of the nucleotides in a strand. For this reason, we sometimes say that there is a 'sugar-phosphate backbone' holding each DNA strand together. The nucleotides in one strand are paired with nucleotides in the other according to the base-pairing rule.

This states:

- Adenine-containing nucleotides will always be opposite Thymine-containing nucleotides
- Cytosine-containing nucleotides will always be opposite Guanine-containing nucleotides

Because of this base-pairing rule, all the bases on one strand of a DNA molecule are base-paired to those on the other strand. We say that the sequences of bases on the two strands are complementary.

DNA is a very stable molecule at normal temperatures. The individual hydrogen bonds that hold the two strands together are quite weak, but the sheer number of them in the whole molecule ensures that the two strands stay in position. The bonds that hold the nucleotides together in each strand are much stronger than the hydrogen bonds. The stability of the DNA molecule is important in ensuring that the genetic code – held in the DNA molecule – does not become corrupted in any way.

A word of warning …

Do not confuse DNA *strands* with DNA *molecules*. Each molecule of DNA is made from two strands.

Activity 3.7: Extracting DNA from bananas

You will need:

- A banana, cut into chunks
- 5 g washing up liquid or hand soap
- 2 g salt
- 100 cm^3 tap water
- 100 cm^3 of ice-cold ethanol
- a knife
- a pipette
- a test tube
- a thermometer
- access to a blender
- filter paper, a filter funnel and a beaker
- another 250 cm^3 beaker to act as a water bath

Method:

1. Mix together the washing up liquid, the salt and the tap water and stir **slowly** (try to produce as little foam as possible) until the salt has dissolved. This mixture is called an **extraction buffer**.
2. Blend the chunks in the blender (this is to break open the cells).
3. Add the extraction buffer to the banana and MASH!
4. Set up your water bath so that the temperature of the water is 60°C.
5. Stand the banana and buffer in the water bath for 15 minutes. Try to maintain the temperature at 60°C by adding hot or cold water as necessary.
6. Remove the beaker from the water bath and filter the banana mixture through a fine sieve or coffee filter paper into the other beaker. You should be left with a greenish liquid, which contains the banana DNA.
7. Half-fill a test tube with some of this filtrate.
8. Pour the ice-cold alcohol **slowly** down the side of the test tube. The alcohol will form a transparent layer on top of the banana mixture, as the alcohol is less dense.
9. Where the two liquids meet, the DNA, which was dissolved in the buffer mixture, will precipitate (come out of solution).
10. Remove the DNA from the ethanol/buffer with the pipette and place it in a Petri dish lid or on a tile.
11. Test the DNA with litmus paper to show that it really is deoxyribonucleic acid.

DID YOU KNOW?

Because adenine always pairs with thymine and cytosine with guanine, the amount of adenine in any DNA molecule will always be the same as the amount of thymine. And the amount of cytosine will always equal the amount of guanine. So, if you know the percentage of just one base in a DNA molecule, you can work out the percentage of all the others. Here's how.

Suppose a DNA molecule contains 16% cytosine. It must also contain 16% guanine. That's 32% so far, leaving 68% of the DNA made from adenine and thymine. But as the amounts of these two are equal, there must be 34% of each.

KEY WORDS

DNA helicase *the enzyme that initiates the separation of the polynucleotide strands during DNA replication*

DNA polymerase *the enzyme that initiates the building of a new complementary polynucleotide strand of DNA following separation of the original two strands*

How does the DNA molecule replicate itself?

The ability of a DNA molecule to make an exact copy of itself is the basis of all methods of reproduction and the basis of passing on genetic information from one generation to the next. When cells divide, it is important that the daughter cells formed (unless sex cells are being formed) contain the same genetic information as the parent cell that produced them. To achieve this, DNA must be able to replicate itself exactly.

DNA molecules exist within chromosomes in the nucleus and are surrounded by a 'soup' of free DNA nucleotides – the 'building blocks' with which to build new DNA molecules. Even though they did not know the details, in 1953, Watson and Crick (the discoverers of the structure of DNA) proposed that DNA must replicate semi-conservatively. This means that the DNA molecule replicates in such a way that:

- each new DNA molecule formed contains one strand from the original DNA
- both new DNA molecules formed are identical to each other and to the original molecule

The process involves several enzymes and proteins, but the key stages are as follows:

- Molecules of the enzyme **DNA helicase** break hydrogen bonds and 'unwind' part of the helix of the DNA molecule, revealing two single-stranded regions.
- Molecules of **DNA polymerase** follow the helicase along each single-stranded region, which acts as a template for the synthesis of a new strand.
- The DNA polymerase assembles free DNA nucleotides into a new strand alongside each of the template strands. The base sequence in each of these new strands is complementary to its template strand because of the base-pairing rule, A-T, C-G.
- The processes of unwinding followed by complementary strand synthesis progresses along the whole length of the DNA molecule.
- The result is two DNA molecules that are identical to each other (and to the original molecule); each contains one strand from the original DNA molecule and one newly synthesised strand that is complementary to this.

Activity 3.8

Making a model of DNA can make it easier to understand. Working in small groups, plan and make a model of the DNA molecule. You could use modelling clay, card, paper or anything else you think would work well. You can make a model of the double helix, or make a model which can be used to show how DNA replicates. You might even just choose to make a big poster showing the molecule. Evaluate the models made by your peers and decide which is the most useful for explaining the structure of this important molecule.

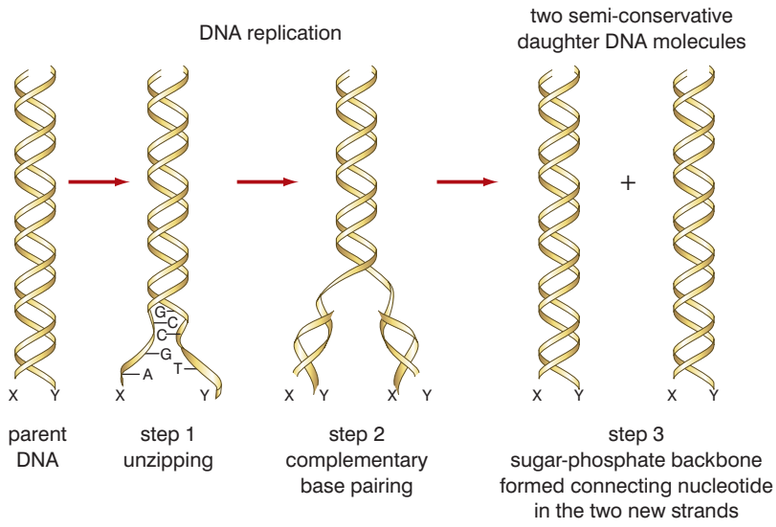


Figure 3.36 *Semi-conservative replication of DNA*

DID YOU KNOW?

Gene cloning means making multiple copies of a gene. There are several ways in which this can be done. The principal methods are divided into two main categories; these are:

- **in vivo cloning** – the gene is introduced into a cell and is copied as the cell divides
- **in vitro cloning** – this does not take place in living cells but the DNA is copied many times over using the **polymerase chain reaction** (**PCR**). This process mimics the natural semi-conservative replication of DNA in a machine called a PCR machine.

There are advantages and disadvantages to both methods of gene cloning. In vitro cloning using the PCR is both quicker and cheaper. Billions of copies of a gene can be made within a few hours at low cost. However, if the gene is to be used by an organism to make a product – for example, by a bacterium to allow it to make insulin – then in vivo cloning delivers the gene already in the organism.

Figure 3.37 *A stem cutting*

KEY WORDS

clone *a clone of an organism is a group of organisms that are genetically identical to each other and to the organism from which they were derived*

genetically modified organism *an organism created using genetic engineering which contains a transferred gene or genes*

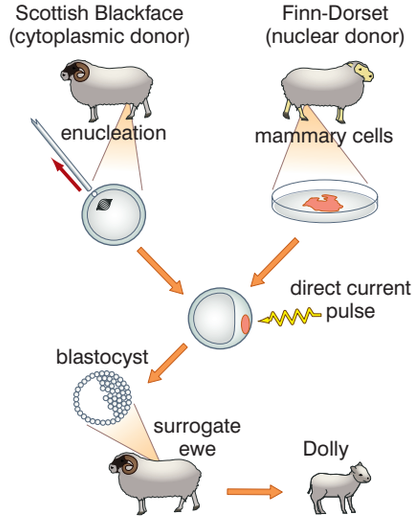


Figure 3.38 *How Dolly the sheep was produced*

How are organisms cloned?

The term **clone** is often applied to whole organisms as well as to genes. A clone of organisms is a group of organisms produced asexually from one parent. The members of the clone are genetically identical to each other and to the parent organism. Plant cuttings are clones and the thousands of plants produced from one parent by micropropagation also represent a clone.

To take a simple 'stem cutting', just cut off a region of a stem near to a bud – as shown in figure 3.37. Remove some of the leaves so that it will not lose too much water. Dip the cut end in some hormone rooting powder and plant the cutting in some compost. Keep the cutting well watered and within a few weeks it will have developed its own root system and be an independent plant. It will be genetically identical to the parent plant the cutting was taken from. If several are taken from one plant, they will form a clone.

Cloning plants by taking cuttings has been practised for thousands of years. More recently the technique of micropropagation made it possible to produce a clone of thousands of identical plants from just one parent plant. Typically, a small section of the growing point of a shoot is taken and sub-divided. These small groups of a few hundred cells are placed in test tubes containing a special medium with hormones that induce root growth. They are then transferred to another medium containing hormones to induce shoot growth. When they have grown sufficiently, the small plantlets are transferred to a compost and grown on. In this way, thousands of identical plants can be produced. Most of the world's bananas are now produced by micropropagation. The reason why it is relatively easy to clone plants is that many more plant cells retain the ability to divide than is the case in animals. You cannot just cut off a piece of animal and place it in a special medium and watch it grow! However, animals have been cloned. The first mammal to be cloned, and still the most famous, was Dolly the sheep.

Dolly's genetic mother was a type of sheep called 'Finn-Dorset'. Dolly was produced by transferring a diploid nucleus to an egg cell that had been enucleated (had its nucleus removed). Once the nucleus had been successfully transferred, the egg cell was stimulated to divide by a small electric current. When development had reached a stage called a blastocyst, the embryo was implanted into a surrogate 'mother' ewe. Seven months later, Dolly was born. She was genetically identical to the Finn-Dorset ewe (female sheep) from whom the genetic material had been obtained. Figure 3.38 summarises these procedures.

What is genetic engineering?

Genetic engineering is a process in which the genome of an organism is altered, usually by having an extra gene from a different organism added. The organism is then a **genetically modified** or a **transgenic** organism. Much of the early work on genetic engineering was done to genetically modify bacteria. This was often

What do you think about cloned humans?

Some biologists believe that, although there are important differences between sheep and humans, the technology and knowledge is now available to clone human beings. Is this acceptable? There are many issues involved here and different people hold very strong views for and against human cloning. At the moment it is illegal throughout the world. Should it stay that way forever, or is that just placing an obstacle in the way of scientific progress?

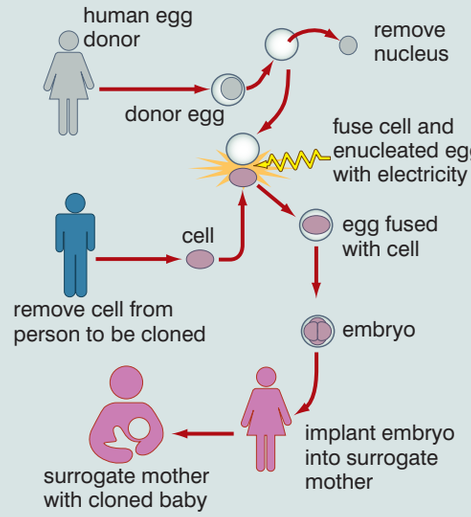


Figure 3.39 *Should this ever be legal?*

done with the aim of altering the bacteria so that they would make a useful product. One of the first of these products to be produced by transgenic bacteria was human insulin. The gene that controls the production of human insulin was extracted from human pancreas cells and transferred to the bacteria. Once modified, the bacteria were then cultured on a massive scale in a fermenter and the insulin harvested and purified before distribution.

KEY WORD

transgenic organism *a genetically modified organism that contains a gene or genes transferred from another organism belonging to a different species*

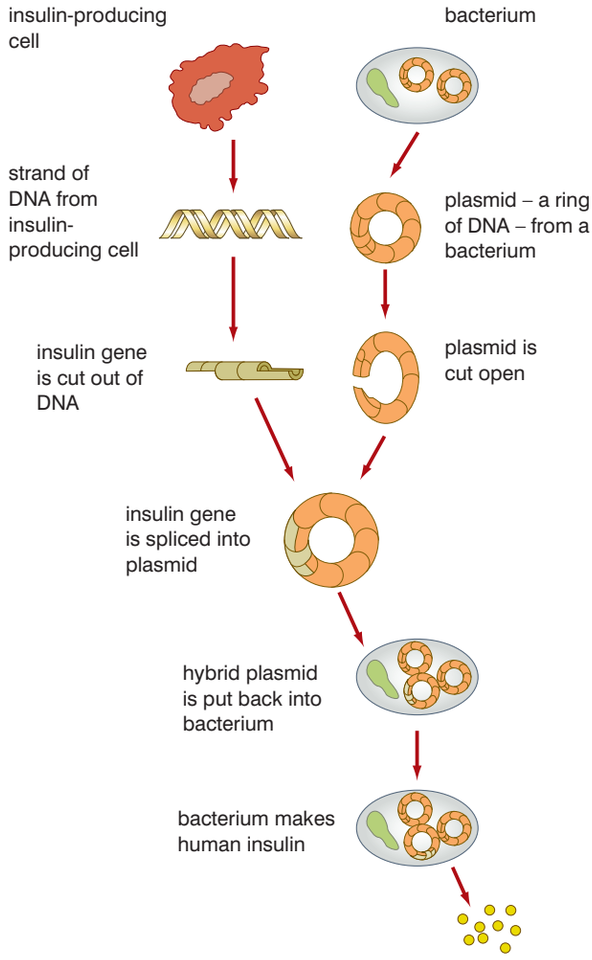


Figure 3.40 *The main steps in genetic engineering*

Activity 3.9

Should human cloning ever be allowed? Set up a debate about this. Have a class vote to measure opinions before the discussions. Plan a speech either explaining why human cloning should be made possible and allowed, or explaining why it should never be allowed. Carry out your debate in small groups and then vote again to see if the views of your class have changed.

Activity 3.10

Chose one recent example of genetic engineering eg golden rice which produces the precursor of vitamin A, bananas and tomatoes which can be engineered to produce a vaccine for hepatitis B, plants which are engineered to produce pesticides in their leaves or are herbicide resistant, using genetic engineering to cure genetic diseases such as SCID or cystic fibrosis.

Find out as much as you can about the case you have chosen, considering both the potential benefits and the problems and produce a presentation about it which you can deliver to the rest of your class.

Figure 3.41 *Genetically modified zebra fish – glofish*

Genetically modified bacteria produce a range of products, including:

- enzymes for the food industry
- thermostable enzymes for washing powders
- human insulin
- human growth hormone
- vaccines (for example, for prevention of hepatitis B)
- bovine somatotrophin (to increase milk yield and muscle development in cattle)

Plants have also been genetically modified so that they:

- are disease resistant
- have an improved yield
- produce a specific product (for example, golden rice is genetically modified rice that produces beta-carotene – important in the formation of vitamin A, which prevents night blindness)

Fewer animals have been genetically modified, but genetically modified salmon and *Tilapia* fish grow bigger and faster than the non-modified fish and could prove to be an important source of protein in some regions of Africa. Other animals have also been genetically modified to produce specific products; this is sometimes called 'pharming'.

Most of the genetic modifications that have been carried out have been with the aim of improving yield of a crop plant or a stock animal, or changing organisms so that they will produce a useful product – like insulin. But some do not fall into this category. The glofish in figure 3.41 literally glow in the dark because they have had a gene added from a bioluminescent jellyfish. It was originally produced as a warning against water pollution – it would only glow in polluted water. Now they are produced to glow in various colours for the pet market.

Genetic engineering has many potential benefits. Some of these are described below:

- Disease could be prevented by detecting people/plants/animals that are genetically prone to certain hereditary diseases, and preparing for the inevitable.
- It may be possible to treat infectious diseases by implanting genes that code for antiviral proteins specific to each antigen.
- Genetically engineered plants and animals can be produced to give increased growth rates and reduced susceptibility to disease. This would reduce the use of fertilisers and pesticides and the chemical pollution that results from their use.
- Animals and plants can be 'tailor made' to show desirable characteristics. Genes could also be manipulated in trees, for example, to absorb more CO_2 and reduce the threat of global warming.

- Genetic engineering could increase genetic diversity, and produce more variant alleles which could also be crossed over and implanted into other species. It is possible to alter the genetics of wheat plants to grow insulin, for example.
- Genetic engineering is a much quicker process than traditional selective breeding. This often took many generations to bring about the desired improvement. A single gene transfer may achieve the same result.

How can gene technology be used in forensic science?

Fingerprints have been used for many years to help place a suspect at the scene of a crime. They continue to provide strong evidence because, with the exception of identical twins, an individual's fingerprints are unique. They do not change throughout life. **Genetic fingerprinting** has nothing to do with actual fingerprints. It is a technique for comparing the DNA of different people. Much of the DNA in the cells of the body is what is known as non-coding DNA. The non-coding DNA is found between genes and contains base sequences that are repeated, sometimes many times over. These repeating sequences of non-coding DNA are called mini-satellites and it is these that form the basis of a genetic fingerprint. The mini-satellites are inherited along with the coding DNA from one or other parent.

The DNA used for analysis can be obtained from a sample of blood (white blood cells could supply the DNA), skin or semen – in fact, from any type of cell that has a nucleus. If the sample does not contain sufficient DNA for analysis, then the amount can be amplified using the polymerase chain reaction.

The main stages in preparing a genetic fingerprint are as follows:

- DNA is isolated from the cells.
- The DNA is cut into fragments using one or more restriction enzymes. The fragments that are obtained are treated with alkali to separate the strands of each DNA fragment.
- The fragments are separated by gel electrophoresis. Smaller fragments (with a lower molecular mass) move further than larger fragments.
- The (invisible) pattern of separated DNA fragments is transferred from the gel to a nylon membrane. The membrane is placed over the gel in a tray of 'flow-buffer' and is held in place by paper towels and a weight. The buffer soaks up through the gel, carrying the fragments of DNA with it. The buffer can pass through the membrane (to be absorbed by the paper towels), but the DNA cannot. It remains in the nylon membrane in the same relative position as it was in the gel.
- A radioactive gene probe is applied to the membrane. This is made of single-stranded DNA (called c-DNA) and binds with base sequences in the mini-satellite regions.

KEY WORD

genetic fingerprinting *a forensic technique that is used to try to solve crimes by matching DNA found at crime scenes with the DNA of suspects*

DID YOU KNOW?

The technique of transferring DNA fragments from the gel to the nylon membrane was devised by Professor E M Southern and is called Southern blotting.

Electrophoresis

Gel electrophoresis is a technique that uses a thick block of gel (jelly-like material) to act as a 'molecular sieve'. Fragments of DNA (or protein molecules) are separated by applying an electrical field across the gel. Because DNA fragments are negatively charged, they move to the positive electrode. The smaller fragments move more quickly than the larger ones and so move futher in the same time.

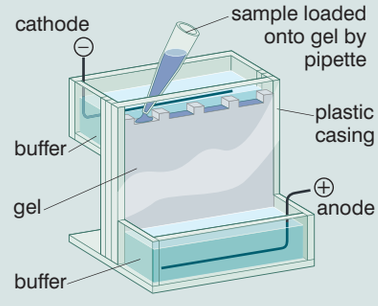


Figure 3.42

- The membrane is placed over a piece of X-ray film to reveal the positions of those fragments that have bound to the probe.

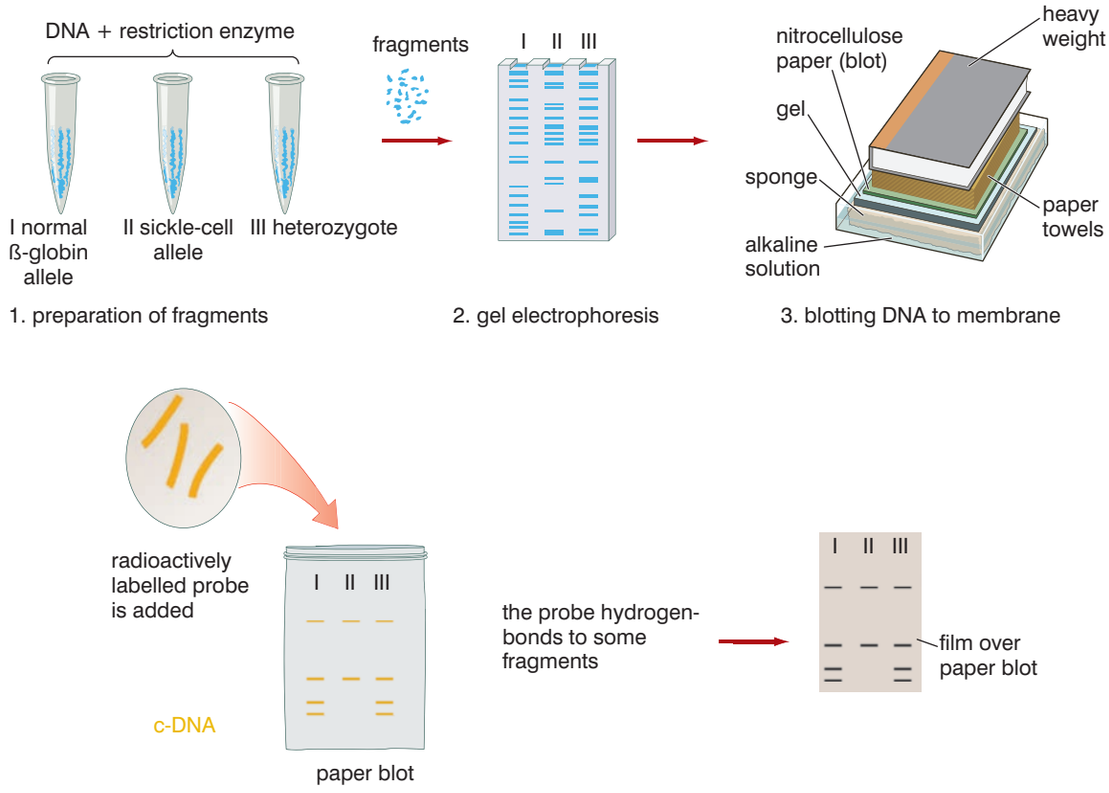


Figure 3.43 *Preparing a genetic fingerprint*

DID YOU KNOW?

The size of DNA molecules is usually measured in kilobase pairs (thousands of pairs of bases). The fragments used in a genetic fingerprint are single stranded, so there are no base pairs. Their size is measured in kilobases.

The chance of two people having the same genetic fingerprint (unless they are identical twins) is about 1 in 1 000 000. This means that a genetic fingerprint can be used to provide strong evidence of involvement in or innocence of a crime.

Look at the fingerprints in figure 3.44 of a person accused of attacking a person, together with the victim's genetic fingerprint.

Clearly the blood on the defendant's clothes has the same DNA as the victim's blood – it must be the victim's blood. So this is strong evidence that the defendant was at least present at the time.

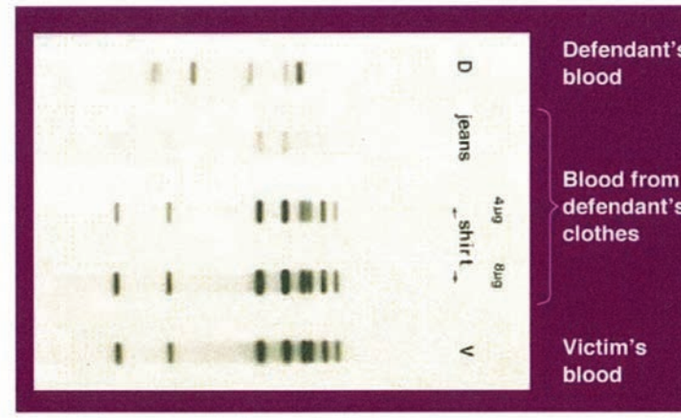


Figure 3.44 *DNA fingerprints from the defendant and victim*

What are the moral and ethical considerations of using gene technology?

Is genetic engineering right or wrong? A debate about right and wrong involves the principles of ethics and morality.

- Morality is our personal sense of what is right, or acceptable, and what is wrong. Morality is not necessarily linked to legality.
- Ethics also involve a sense of right and wrong. However, ethics are not individual opinions. They represent the 'code' adopted by a particular group to govern its way of life.

Many people have passionate views about genetic engineering. Some hold an unshakeable belief in the technology, which they see as something that will bring great benefits to humankind. Other people hold the equally strong belief that genetic engineering is tampering with nature and is likely to cause serious ecological and physiological problems. Some of the issues people are concerned about are discussed below.

- A species is sacrosanct and should not be altered genetically in any way. This is a personal, moral viewpoint. People who take this moral stance usually do so on the basis that the genes from one species would not normally find their way into another species. However, genes have been 'jumping' from one species to another (albeit at a very low frequency) for millions of years.
- Not enough is known about the long-term ecological effects of introducing genetically modified organisms into the field. They may outcompete wild plants and take over an area. This is also a moral viewpoint. The effects of any new crop cannot be determined without field trials. Ten thousand years ago, the early farmers who cross-bred wild wheat plants to produce the forerunner of today's strains could not have known what impact these would have. Does this make it wrong?
- If plants are genetically engineered to be resistant to herbicides, the gene could 'jump' into populations of weeds and other wild plants. This is perfectly true – it could. However, non-genetically modified herbicide-resistant strains of plants already exist. The gene could just as easily jump from these.
- Gene technology might give doctors the ability to create designer babies. It could become possible to obtain a newly fertilised human egg, determine its genotype and ask the parents which genes they would like to be modified. Initially, only genes that cause disease might be replaced. Subsequently, the technology might be used to replace other genes. Most doctors would find this morally and ethically unacceptable. They might consider replacing genes that cause disease but not replacing genes merely to improve a child's image in the eyes of its parents. However, if such practices become possible, who will define for doctors what is ethically acceptable? What will be the dividing line between cosmetic gene therapy and medical gene therapy?

DID YOU KNOW?

Although the human genome project has identified all the base sequences in the human genome, much of this is 'junk' (non-coding) DNA and the exact start and end points of many genes are not yet known.

Activity 3.11

Penicillin was first discovered in a mould growing in a laboratory by Alexander Fleming. This antibiotic has gone on to save millions of lives. It is a great example of biotechnology in action. Find out as much as you can about the history of penicillin and it's manufacture. Make a timeline to help you tell the story.

KEY WORD

penicillin *the first antibiotic to be discovered*

- Using genetic fingerprinting to combat crime will only be useful if there is a genetic database – a file of the genetic fingerprints of everyone in the country, so that a genetic fingerprint found at the scene of a crime could instantly implicate that person. But who will have access to this information? There are concerns that a genetic database would be subject to misuse. If insurance companies had access to the genetic database, they might refuse insurance (or charge higher premiums) to people with an increased risk of, say, heart disease. Employers could (covertly) refuse employment to people because their 'genetic profiles' did not meet particular requirements. A recent ruling from the European court states that the police have no right to hold the DNA of someone unless they have been convicted of a crime.

But you should also consider the fact that biotechnology (including gene technology) is sometimes merely a refinement of less controversial practices. Organic farmers use the naturally occurring soil bacterium *Bacillus thuringiensis* as a non-chemical insecticide. Genetic engineers have extracted a gene from this bacterium and transferred it to cotton plants to make them resistant to attack by insects. Is there any real difference? People have known for centuries that rubbing a certain blue mould onto cuts can stop them turning septic. In 1922, Alexander Fleming discovered **penicillin** in the blue mould *Penicillium*.

Activity 3.12: Different views about the use of DNA technology

Different groups of people have different viewpoints because of their cultural background and their previous experiences. For example, if you have a starving child or a child with a disease that may result in the death of the child unless DNA technology is used (to produce the crops or the drug) you will have a different attitude to a family who has never experienced this situation.

For some in big business the driving force is to make money to satisfy their shareholders. However, shareholders are people who often are concerned about ethical issues so even satisfying the shareholders isn't straightforward.

Other groups, such as animal liberationists, and some religious groups are against the use of animals in biotechnology without considering the benefits that come from such research as they consider that the welfare of the animal is paramount.

Some people's views are based on incorrect knowledge or fear, but others have those views because they have knowledge that the ordinary consumer does not, for example they have seen a research laboratory where they think that animals are not looked after adequately.

Many genetically modified organisms are designed to be food for human consumption. The evaluation of the ethical issues can be decided on the arguments for and against the issues.

Design a poster using the information above to show how:

- a person from a biotechnology company
- a mother in a developing country
- an animal liberationist
- an informed 'man in the street'

might react to an announcement that a sheep that will produce 20% more meat has been developed as a result of genetic engineering.

Review questions

Choose the correct answer from A to D.

1. DNA consists of two polynucleotide strands in which:
   - A the percentage of adenine is the same in each strand
   - B the percentage of adenine is the same as that of thymine in each strand
   - C the percentage of adenine is the same as that of thymine in the whole molecule
   - D the percentage of adenine is 50% of that of thymine in the whole molecule
2. Ligase is an enzyme that:
   - A cuts DNA molecules, leaving sticky ends
   - B joins sticky ends of DNA fragments
   - C copies DNA fragments
   - D separates DNA fragments
3. A gene probe could be:
   - A a short length of single-stranded DNA that has been made radioactive
   - B a tRNA molecule that has been made radioactive
   - C a short length of double-stranded DNA that has been made radioactive
   - D all of the above
4. Viruses and plasmids are examples of:
   - A vectors
   - B transformed bacteria
   - C restriction enzymes
   - D liposomes
5. Which of the following statements about genetic fingerprinting is not accurate?
   - A Genetic fingerprinting involves the analysis of the DNA to identify an individual.
   - B Genetic fingerprinting can be used to identify criminals and also the real parents of a child when the identity is in doubt.
   - C Only coding DNA is used to make a genetic fingerprint.
   - D Genetic fingerprinting has become faster and more detailed over time.
6. In gel electrophoresis of DNA:
   - A the DNA fragments migrate towards the positive electrode and are separated according to their molecular mass
   - B the DNA fragments migrate towards the negative electrode and are separated according to their molecular mass
   - C the DNA fragments migrate towards the negative electrode and are separated according to their electric charge
   - D the DNA fragments migrate towards the positive electrode and are separated according to their electric charge
7. One advantage of genetic engineering over conventional selective breeding is that genetic engineering:
   - A is quicker
   - B has fewer side effects
   - C cannot harm the environment
   - D none of these
8. The best definition of a transgenic organism is:
   - A a bacterium that contains genes from another organism
   - B a plant that has been genetically modified
   - C an animal that has been ‘pharmed’
   - D any organism that has had a foreign gene added to its genome

KEY WORDS

mRNA (messenger RNA) *is a nucleic acid that transmits the genetic code from DNA to ribosome*

transcription *the process that converts genetic information from a DNA code into an mRNA code*

tRNA (transfer RNA) *transfers individual amino acids during translation*

ribosome *the part of a cell that makes proteins*

translation *the process in which the mRNA code is converted into a sequence of amino acids*

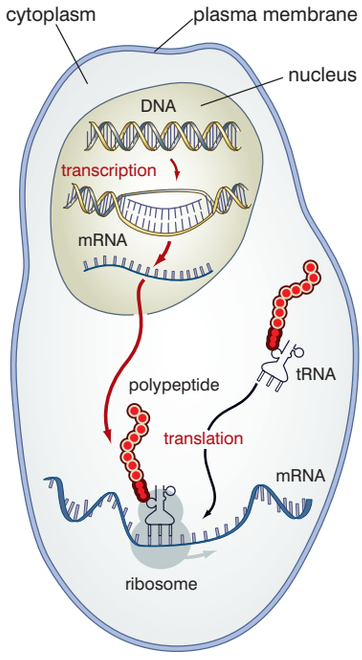


Figure 3.45 *An overview of protein synthesis*

3.3 Protein synthesis

By the end of this section you should be able to:

- Describe how the flow of information in a cell starts from the code on DNA and ends with proteins being synthesised.
- Understand the nature of the genetic code.
- Describe the roles of DNA, mRNA, tRNA and ribosomes in protein synthesis and understand the processes of transcription, translation and gene expression.
- Understand that protein synthesis depends on having a supply of amino acids which, in animals, come from the food they eat.
- Understand the different roles proteins have in cells and in the body.

How does a cell 'know' to make a protein?

The code for a protein is specified by DNA and has to be carried to the ribosomes so that they can assemble the amino acids in the correct sequence to form the protein. However, DNA is a huge molecule and remains in the nucleus at all times. The following events occur:

- The DNA code for the protein is rewritten in a molecule of **messenger RNA** (mRNA); this rewriting of the code is called **transcription**.
- The mRNA travels from the nucleus through pores in the nuclear envelope to the ribosomes.
- Free amino acids are carried from the cytoplasm to the ribosomes by molecules of **transfer RNA** (tRNA).
- The **ribosome** reads the mRNA code and assembles the amino acids carried by tRNA into a protein; this is called **translation**.

Figure 3.45 summarises these processes.

What is the genetic code like?

The genetic code is held in the DNA molecule. As you already know from your studies in grade 10, it is the sequence of bases in the nucleotides of the DNA that makes up a gene that codes for the protein and that each amino acid in the protein is coded for by a triplet (sequence of three) of bases. This gives us a useful definition of a gene:

A gene is a sequence of base triplets in the DNA molecule that carries the code for a protein.

With four different bases to work with (adenine, thymine, cytosine and guanine), there are 64 possible triplet codes, but only 20 amino acids are used to make all the different proteins. What is

the purpose of the other 44 codes? In fact, none of these is spare or redundant.

However, only *one* of the strands of the DNA molecule carries the code for proteins. This is called the coding strand or the sense strand. The other strand is the non-coding or antisense strand.

Most amino acids have more than one code. Only methionine and tryptophan have just one triplet that codes for them; arginine has six. Three of the triplets (TAA, TAG and TGA) do not code for amino acids at all. They are 'stop' codes that signify the end of a coding sequence. Because there is this extra capacity in the genetic code, over and above what is essential, it is said to be a degenerate code.

Besides being a triplet and degenerate code, the DNA code is a non-overlapping code. This means that each triplet is distinct from all other triplets. The last base in one triplet cannot also be the first base (or second base) in another triplet. This is illustrated in figure 3.46.

The genetic code is also a universal code. This means that the triplet TAT is the DNA code for the amino acid tyrosine in a human, a giant redwood tree, a bacterium or in any other living organism.

The 64 DNA triplets and the amino acids they code for are shown in two different ways in figures 3.47A and B. Notice the 'stop' codes.

In this method of representing the genetic code, start with one of the 'biggest' letters in the centre. This represents the first base in the triplet. One of the four medium-sized letters in the next layer out represents the second base and the smallest letters represent the third base in the triplet. Outside that is the name of the amino acid for which the triplet codes.

So, ACC codes for threonine. GGG codes for glycine.

DID YOU KNOW?

Order matters in the genetic code

It is not just the actual bases in a triplet that matter, but also the sequence of bases within that triplet. So, the sequence ATT codes for a different amino acid to TTA.

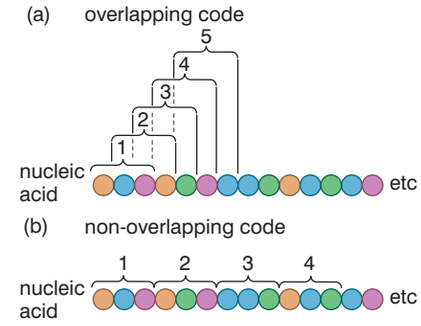


Figure 3.46 *Overlapping and non-overlapping codes*

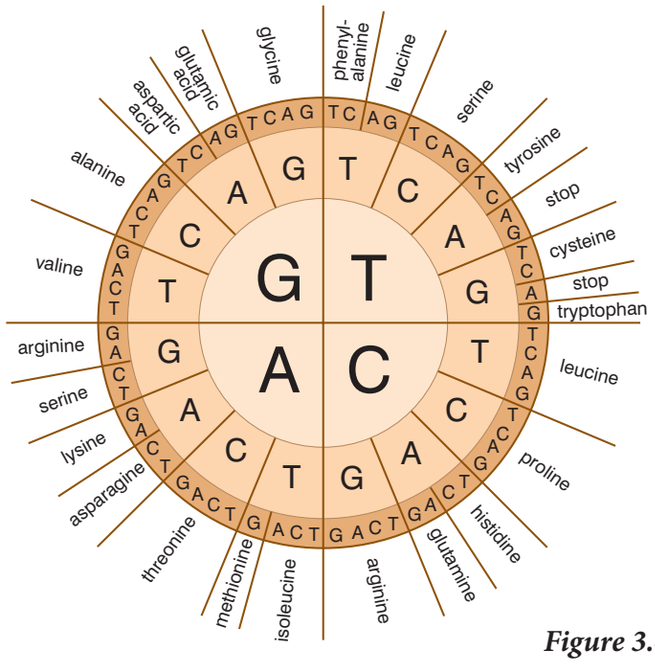


Figure 3.47A *The genetic code*

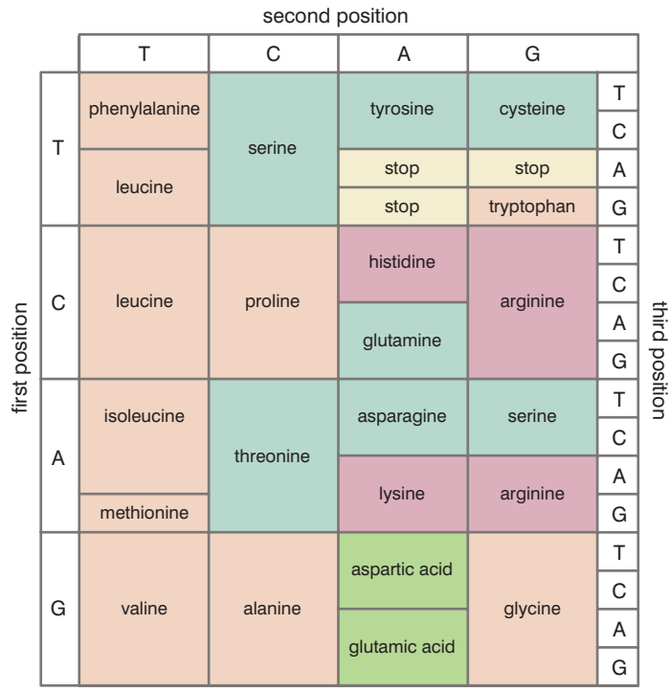


Figure 3.47B *Another way of representing the genetic code*

In this method of representing the genetic code, start with the letters at the left-hand side of the table. These represent the first base in the triplet. They define which row in the table to look in. The letters across the top represent the second base in the triplet and define which column in the table to look in. The letters at the right of the table represent the third base in the triplet and define which line in the row to look in. So, again, A (third row), C (second column) and C (second line) is the code for threonine and GGG the code for glycine.

KEY WORDS

codon *a triplet of mRNA bases that has the code needed to make one protein*

How does transcription take place in eukaryotic cells?

During this process, the coded information in the DNA of one gene is used to synthesise a molecule of mRNA that will carry the code to the ribosomes. mRNA is similar to DNA in that it is built from nucleotides; however, it is different from DNA in a number of ways:

- it is a much smaller molecule
- it is single stranded
- the base thymine is replaced by uracil
- the sugar in the nucleotides is ribose, not deoxyribose

The triplets of bases in mRNA that code for amino acids are called **codons**. The mRNA codons are identical to the DNA triplets that code for specific amino acids, except that U (uracil) is substituted for T (thymine). To form the single-stranded mRNA when transcription takes place, only the antisense strand of DNA is transcribed. This is because the sense strand of this section contains

Activity 3.13

Protein synthesis is complicated. Produce a wall chart showing the stages of protein synthesis. It could be anything from a simple flow diagram to a complex series of images – but it must be clear and help with understanding and revision.

the gene that codes for a protein. However, transcribing this would produce a *complementary* sequence of bases, similar to those in the antisense strand, which would not code for anything.

In eukaryotic cells, transcription takes place in the following way:

- The enzyme DNA-dependent RNA polymerase (RNA polymerase) binds with a section of DNA next to the gene to be transcribed.
- Transcription factors (see later) activate the enzyme.
- The enzyme begins to 'unwind' a section of DNA. RNA polymerase moves along the antisense strand, using it as a template for synthesising the mRNA.
- The polymerase assembles free RNA nucleotides into a chain in which the base sequence is complementary to the base sequence on the antisense strand of the DNA. This, therefore, carries the same triplet code as the sense strand (except that uracil replaces thymine).

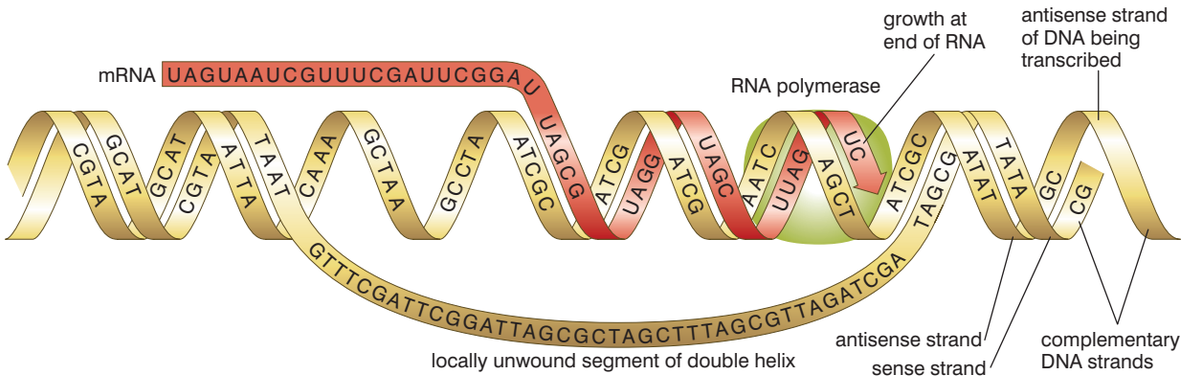


Figure 3.48 *Transcription in eukaryotic cells*

- The completed molecule leaves the DNA; the strands of DNA rejoin and re-coil.

The mRNA molecule now contains the code for the protein that was held in the DNA of the gene.

How does translation take place?

Translation of the mRNA code into a protein depends on the interaction within a ribosome between mRNA and tRNA. All tRNA molecules have the same basic structure. The 'cloverleaf' configuration of the molecule has at one end a triplet of bases called an anticodon. This anticodon will be complementary to one of the mRNA codons. The other end of the tRNA molecule has an attachment site for the amino acid that is specified by the mRNA codon.

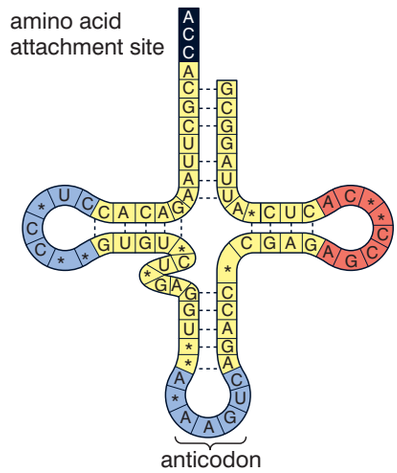


Figure 3.49 *The structure of tRNA*

Ribosomes are made from ribosomal RNA (rRNA) and proteins organised into a large and a small subunit. Within the ribosome, there are three sites that can be occupied by a tRNA molecule, called the A, P and E sites. The following events take place:

- The first two codons of the mRNA enter the ribosome.
- Transfer RNA molecules (with amino acids attached) that have

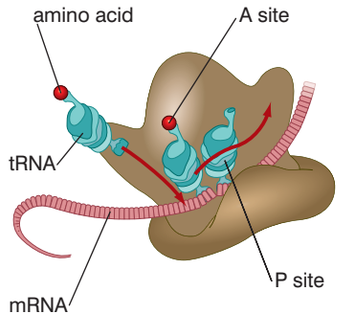


Figure 3.50 *The structure of a ribosome*

complementary anticodons to the first two codons of the mRNA bind to those codons.

- A peptide bond forms between the amino acids carried by these two tRNA molecules and the dipeptide is transferred to the tRNA in the A site.
- The ribosome moves along the mRNA by one codon, bringing the third codon into the ribosome; at the same time the 'free' tRNA exits the ribosome and the tRNA with the dipeptide moves into the P site.
- A tRNA with a complementary **anticodon** binds with the third codon, bringing its amino acid into position next to the second amino acid.
- A peptide bond forms between the second and third amino acids.
- The ribosome moves along the mRNA by one codon, bringing the fourth mRNA codon into the ribosome, and the whole process is repeated until a 'stop' codon is in position and translation ceases.

KEY WORD

anticodon *a triplet on tRNA complementary to a codon in mRNA*

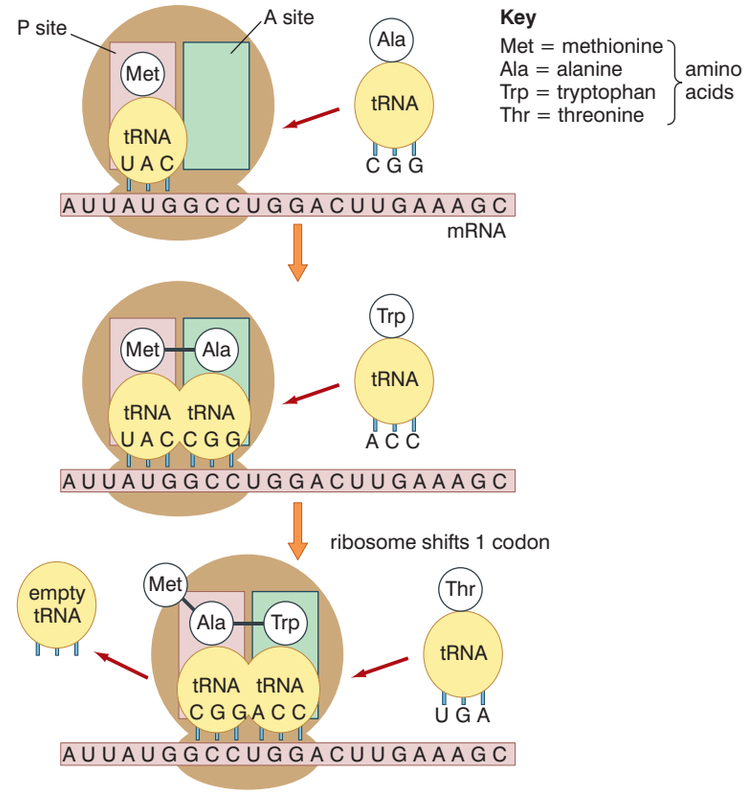


Figure 3.51 *Translation*

The translation of the mRNA code into a protein molecule requires energy. However, this does not come from the hydrolysis of ATP as is usual in a cell, but from the hydrolysis of a similar molecule, GTP – Guanosine Triphosphate. It is hydrolysed to GDP and P_i in the same way as ATP, with the release of a small amount of energy.

How is protein synthesis different in prokaryotic cells?

The process is essentially similar in both types of cells, with DNA being transcribed to mRNA, which is then translated to a polypeptide chain. However, there are some differences and these are linked to the fact that:

- prokaryotic cells do not have a nucleus
- prokaryotic mRNA does not need post-transcriptional processing
- prokaryotes: transcription and translation are coupled; mRNA can be translated by ribosomes at one end of its molecule while it is still being transcribed from DNA at the other end
- eukaryotes: transcription and translation are separated
- transcription occurs in the nucleus
- translation occurs in the cytoplasm
- eukaryotic mRNAs are modified before leaving the nucleus

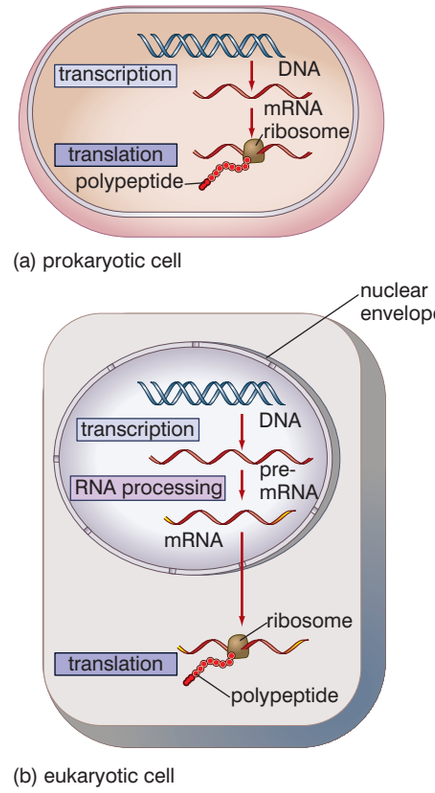


Figure 3.52 *Protein synthesis in prokaryotic and eukaryotic cells*

What becomes of the proteins that are synthesised?

All our proteins are synthesised in the way just described, but all our cells do not synthesise all our proteins as we shall see in the next section. However, we synthesise a vast array of different proteins that we can categorise, broadly, into the types shown in table 3.2.

Table 3.2 *Some of the proteins our body synthesises*

Type of protein	Example	Function of example
Structural	Collagen	Building fibres of cartilage
	Keratin	Building nails and feathers
Enzyme	ATP synthase	Producing ATP from ADP and P_i
	DNA helicase	Unwinding the double helix of DNA
Peptide hormone	Insulin	Control of plasma glucose concentration
	Adrenaline (epinephrine)	Fight or flight response
Antigen	A antigen on red cells	Determine blood group
	CD4	Allows binding of HIV to T-lymphocytes
Antibody	Anti-a antibodies	Causes clotting of red cells with A antigen
	HIV antibodies	Destroys some HIV antigens

To synthesise these proteins continually, our bodies require a constant supply of amino acids. These we obtain from the protein in the foods we eat. The average adult protein requirement per day is about 50 grams. The proteins are hydrolysed to amino acids in our gut and absorbed into the blood plasma by active transport. They are then transported to the cells where they are used to synthesise our proteins.

KEY WORD

amino acid *the 'building block' of proteins; each amino acid has an 'amino' group and a 'carboxyl' (acid) group*

As mentioned earlier, just 20 amino acids are used to make all the different proteins. Some of these can be made in our bodies by a process called transamination. In this process, the amino group of an **amino acid** is removed and transferred to a keto acid. The keto acid then becomes a different amino acid and what was the amino acid becomes a keto acid. Figure 3.53 illustrates this.

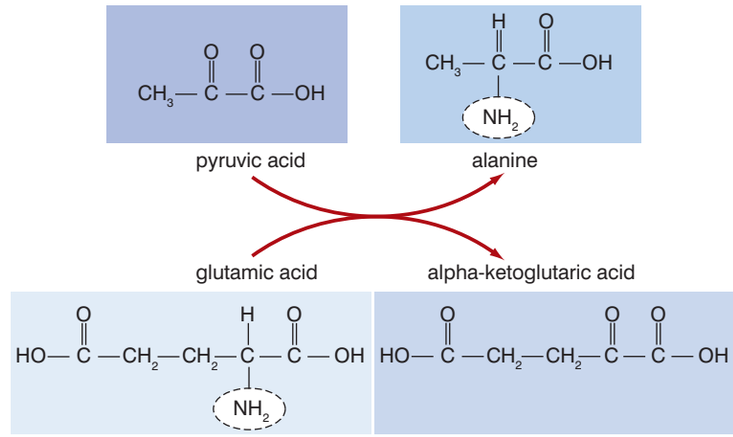


Figure 3.53 *Transamination*

Not all amino acids can be produced by transamination. There are some that we just have to obtain from our food. These amino acids are called essential amino acids (although they are all essential really).

Meat, fish, poultry, eggs and milk are animal sources of protein that provide a good balance of all eight essential amino acids. The best non-animal sources are quinoa, buckwheat, hempseed and amaranth, although these contain lower overall amounts of protein than some cereals (wheat, rice, maize) and nuts and pulses.

What controls gene expression?

The fact that some genes are sex-limited tells us that all genes aren't active all the time. There are more examples of this – the genes that control the colour of your iris are present in all your cells, but all your other cells aren't this colour – just the iris. Somehow, we can control which genes are active where.

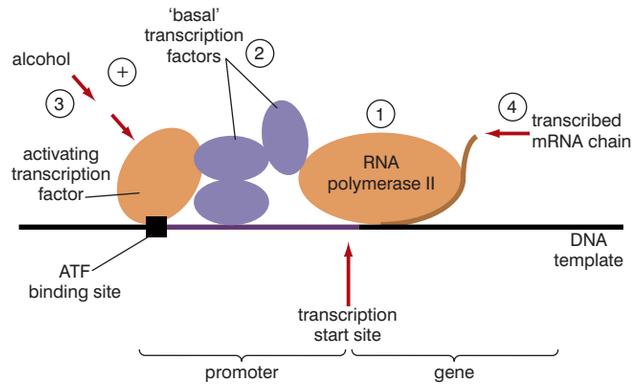


Figure 3.54 *How some transcription factors act*

How are genes switched on?

Very often, genes are switched on by 'transcription factors' that are present in the cell. These transcription factors are usually proteins that bind to a regulatory sequence of DNA near to the gene they influence. They operate in the following way:

- The transcription factors bind to a promoter sequence of DNA near to the gene to be activated.
- RNA polymerase binds to the DNA/transcription factor complex.

- The RNA polymerase is 'activated' and moves away from the DNA/transcription factor complex along the gene.
- The RNA polymerase transcribes the antisense strand of the DNA as it moves along; the gene is now being expressed.

Think about it – where do the transcription factors come from?

If the transcription factors are proteins themselves, then they must be synthesised as a result of gene expression, and some other genes must regulate the expression of these genes. Biologists think that this goes all the way back to the egg cell itself, which is able to synthesise a certain number of transcription factors. These are made once the egg is fertilised to become a zygote and are passed on to the cells formed when the zygote divides. They influence the cells formed and these cells produce other transcription factors, which are, in turn, passed on to the next generation of cells and so on. This 'cascade' or 'hierarchy' of transcription factors results in each cell having only certain transcription factors that can activate certain genes.

DID YOU KNOW?

Some cancers are caused by hormones acting as transcription factors

Oestrogen is a steroid hormone that can diffuse through the plasma membrane of a cell. It binds with a receptor in the cytoplasm. The oestrogen-receptor complex moves into the nucleus and binds with and activates specific genes. In the breasts, and lining of the uterus, the activated genes cause cell division.

Many breast cancers are said to be oestrogen-receptor positive. This means that the cancer cells have oestrogen receptors to which the hormone can bind, causing the same increase in cell division as it does in normal breast tissue. The anti-cancer drug tamoxifen can bind with the oestrogen receptors and the tamoxifen/receptor complex binds with the DNA. However, tamoxifen does not allow transcription factors to bind and so expression of the genes is prevented, and cell division in the cancer is slowed.

How are genes switched off?

Besides transcription factors that promote the expression of genes, other factors can act to repress gene action. One group of substances that does this is known as **short interfering RNA** (**siRNA**). These RNA molecules are unusual because they are very short – only about 21 to 23 nucleotides long – and are double stranded.

They don't act on the gene itself, but they 'interfere with' or 'silence' the mRNA once it has been transcribed from the DNA. This is called post-transcriptional interference. If the mRNA is prevented from translating its codons into amino acids, then the protein for which the gene codes cannot be built. The gene has effectively been silenced.

Biologists think that the action of siRNA is as follows:

- Double-stranded RNA (dsRNA) is produced in the nucleus from a range of genes.
- It is then split into the very short lengths that characterise siRNA by an enzyme called 'Dicer'.

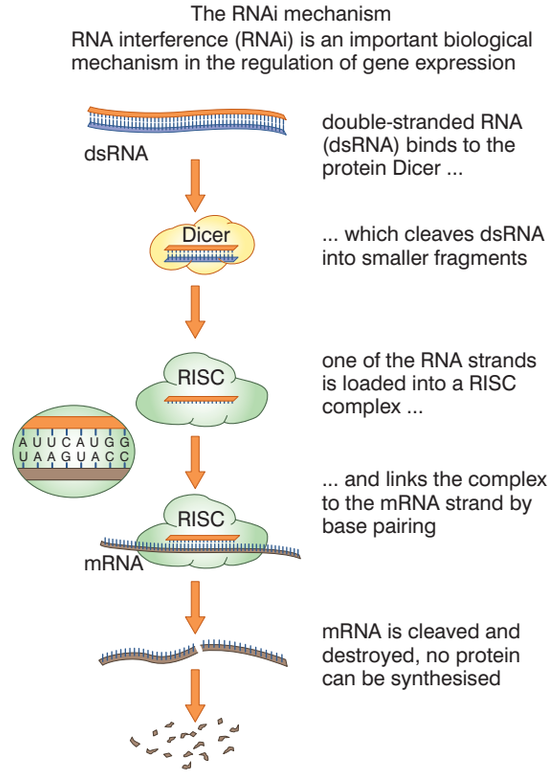


Figure 3.55 *Gene silencing*

KEY WORD

short interfering RNA *a short sequence of RNA which can be used to silence gene expression*

DID YOU KNOW?

Biologists think that siRNAs hold a great deal of promise to treat AIDS and some cancers

Researchers have already shown that they can use siRNA to prevent the replication of HIV in cultures by silencing either some of the genes of the virus or some of the human genes on which it depends.

Other researchers have shown that they can silence genes associated with cancer. If oncogenes could be silenced effectively, then a new treatment for many cancers is possible.

- The antisense strand of the siRNA then binds with a complex of molecules called RISC.
- The siRNA binds with mRNA and allows RISC to degrade/cleave the mRNA into small fragments.

Review questions

Choose the correct answer from A to D.

1. tRNA differs from DNA because it is:
   - A smaller, single stranded and shows no base pairing
   - B smaller, single stranded with thymine replaced by uracil
   - C smaller, single stranded and with deoxyribose instead of ribose
   - D smaller, single stranded and linear in shape
2. The genetic code is:
   - A a triplet code, degenerate and overlapping
   - B a doublet code, degenerate and universal
   - C a doublet code, degenerate and non-overlapping
   - D a triplet code, degenerate and universal
3. The DNA triplet AAT would code for an amino acid carried by tRNA with the anticodon:
   - A AAU
   - B TTA
   - C AAT
   - D UUA
4. In a ribosome, when the two amino acids that are held adjacent to each other form a peptide bond, the tRNA molecules are in the:
   - A A and P sites
   - B A and E sites
   - C E and P sites
   - D none of the above
5. Post-transcriptional modification of mRNA is carried out in order to:
   - A remove exons
   - B remove introns
   - C alter its shape so that it can bind with a ribosome
   - D alter its shape so that it can bind with an amino acid

6. Which of the following statements about transcription factors is correct?
   A They are always produced within cells.
   B They bind with promoter sequences of DNA next to the gene.
   C They are the same in all cells.
   D All of the above.
7. Gene silencing by siRNA is referred to as a form of post-transcriptional repression because:
   A it stops transcription of genes by RNA polymerase
   B it only allows certain genes to be expressed
   C it destroys the mRNA formed by transcription of a gene
   D none of the above
8. Essential amino acids:
   A must be taken in as part of our diet
   B cannot be synthesised by transamination
   C are found in large amounts in quinoa, meat and buckwheat
   D all of the above
9. When comparing protein synthesis in eukaryotic cells and prokaryotic cells it is correct to say that transcription and translation are:
   A separate in both
   B coupled in both
   C separate in prokaryotes and coupled in eukaryotes
   D separate in eukaryotes and coupled in prokaryotes
10. Which of the following statements about transcription is correct?
    A RNA polymerase assembles DNA nucleotides into a single strand.
    B RNA polymerase assembles DNA nucleotides into a double strand.
    C RNA polymerase assembles RNA nucleotides into a double strand.
    D RNA polymerase assembles RNA nucleotides into a single strand.

3.4 Mutations

By the end of this section you should be able to:

- Explain what is meant by the term mutation.
- Describe some of the different types of mutations.
- Describe and explain some of the causes of mutations.
- State the spontaneity of a mutation.
- Describe and explain some of the consequences of mutations.
- Give examples of inheritable mutations.

KEY WORD

mutation *a random change in genetic information*

What are mutations?

A **mutation** is any spontaneous change in the genetic material of an organism. There can be large structural changes involving whole chromosomes or parts of chromosomes, or changes that involve only a single base. The changes involving only a single base are called point mutations, and it is these that we are mainly concerned with.

There are several types of point mutation, in which one of the bases in the DNA sequence of a gene is altered, usually by being copied wrongly when the DNA replicates. The different point mutations are:

- substitution
- addition
- deletions

These mutations occur quite randomly when DNA is replicating and each involves a change to just one base, but the change to the gene can be dramatic and the result can be that the protein the gene should code for is not made at all or a different protein is made.

Substitution

In substitution mutations, one base is replaced by a different base, as shown in figure 3.56.

Figure 3.56 *A substitution mutation*

Guanine replaces thymine in this substitution. The triplet ATT has been changed to ATG (no other triplet is affected). The original triplet, ATT, codes for the amino acid isoleucine. However, the new triplet, ATG, codes for methionine. As a result, a different protein

will be synthesised, which may or may not be significantly different from the original. One different amino acid in a protein does not always make a functional change. If the substitution had been by any base other than guanine, because the DNA code is degenerate, (see figures 3.47A and B) the triplet would still have coded for isoleucine and the same protein would have been synthesised. Effectively, it would still have been the same gene.

Other substitutions can result in a 'stop' triplet, as shown in figure 3.57. In this case transcription ceases when it reaches the stop code and a non-functional mRNA results.

KEY WORD

sickle-cell anaemia *a condition caused by a mutation that affects the structure of the haemoglobin molecules in red blood cells causing the red blood cells to sickle under low oxygen tension*

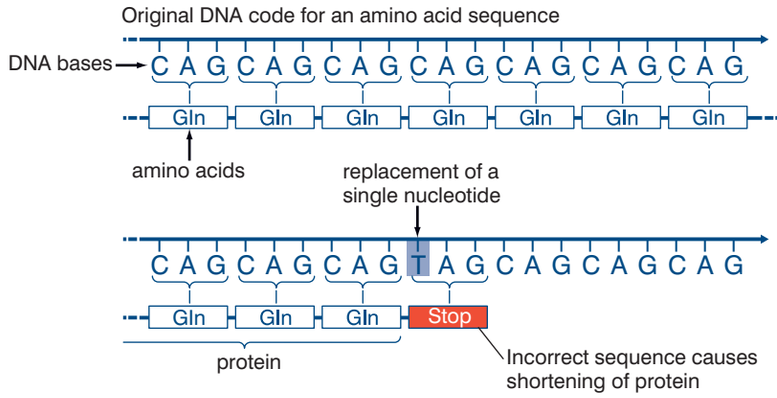


Figure 3.57 *A nonsense substitution.*

DID YOU KNOW?

A substitution of just one base in the sixth triplet of the gene coding for one of the four polypeptides in the haemoglobin molecule alters the triplet from GAG to GTG. This results in the amino acid valine replacing glutamate in the polypeptide chain. The different haemoglobin molecule formed results in the condition known as **sickle-cell anaemia**.

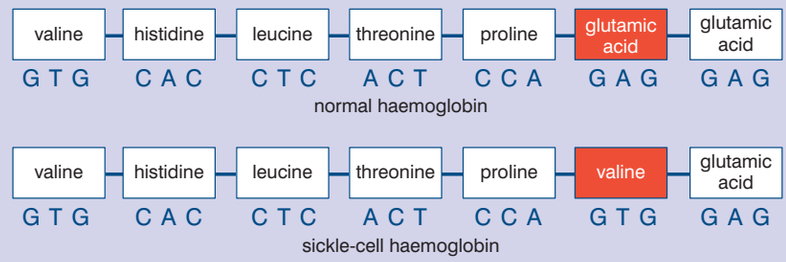
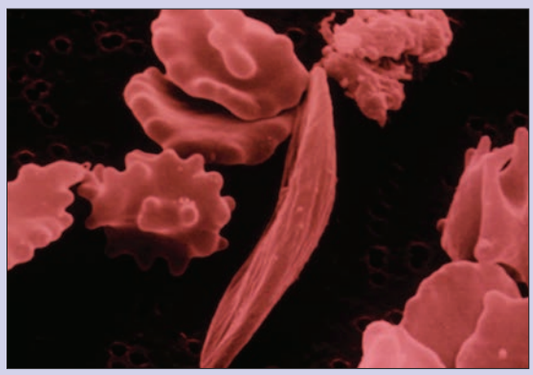


Figure 3.58 *The mutation that causes sickle-cell anaemia*



If a person inherits two copies of the mutated gene, then all of their red blood cells will contain the abnormal haemoglobin that causes the red blood cells to collapse into sickle-shaped cells under conditions of low oxygen concentration. The sickled cells often fracture and stick together and block capillaries.

Figure 3.59 *Sickle-cell anaemia*

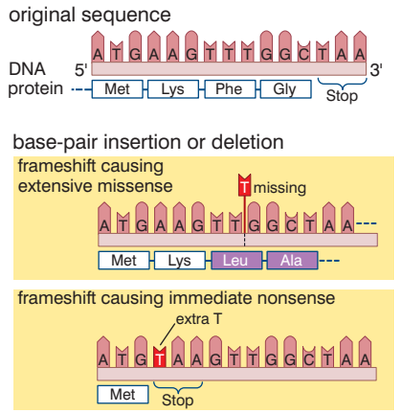


Figure 3.60 *Frameshift mutations*

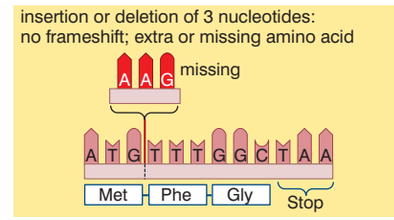


Figure 3.61 *Deletion of an entire triplet*

KEY WORD

deletion mutation *a mutation caused by one DNA nucleotide being omitted from the sequence*

Addition and deletion

In a **deletion mutation** a base is 'missed out' during replication, whilst in additions, an extra base is added. Both these are more significant mutations than substitutions. Substitutions affect just one triplet and, because the DNA code is degenerate, may well have no overall effect – the same protein may still be produced. This can never be the case with additions and deletions.

The reason for this is that they do not just alter the triplet in which the mutation occurs. Because there is one fewer or one extra base, the whole sequence after the point of the mutation is altered. We say that there has been a frameshift and these are frameshift mutations. A totally different mRNA is produced (if one is produced at all) and a non-functional protein or no protein at all.

Sometimes, a whole triplet is missed out or inserted. This will result in either one extra or one fewer codon in the mRNA. In turn, this will lead to one extra or one fewer amino acid in the polypeptide chain.

Another way of thinking about frameshifts

Look of this sequence of letters:

THEMANWASHOTANDRANFORHISHAT

If we give this a 'reading frame' of three letters, it becomes:

THE MAN WAS HOT AND RAN FOR HIS HAT

and it makes sense. But if we take out the S at the end of WAS (a deletion mutation), it becomes:

THE MAN WAH OTA NDR ANF ORH ISH AT

In other words it no longer makes sense. In genetic terms it is **mis-sense** coding

What causes point mutations?

Mutations occur spontaneously and randomly – they are accidents that occur when DNA is replicating. Mistakes happen. Mutations are rare events, which is quite surprising when you consider that each cell contains 6×10^9 (six billion) base pairs that might mutate! Biologists estimate that mutations arise at the rate of 1 in 50×10^6 (one in fifty million) base pairs. This means that each new cell will have, on average, 120 mutations. This sounds rather worrying, but you should remember two things:

- most of these mistakes (mutations) are detected and repaired, and
- because 95% of our DNA is non-coding, most mutations are unlikely to affect coding genes.

The rate of mutation can be increased by a number of factors including:

- carcinogenic chemicals, for example, those in tobacco smoke
- high-energy radiation, for example, ultraviolet radiation, X-rays

What are the consequences of gene mutations?

There are a number of factors that influence the answer to this, but, really, two important ones:

- which cells, and
- which genes?

Mutations that occur in a normal body cell (a non-sex cell) will have one of four possible consequences:

- It will be completely harmless.
- It will damage the cell.
- It will kill the cell.
- It will make the cell cancerous, which might kill the person.

Whichever of these is the case, the mutation will affect no other person; it will not be passed on to the next generation. However, if the mutation occurs in a sex cell, or a cell that will divide to give rise to a sex cell, then it may be passed on to the next generation.

Mutations in different genes will obviously produce different effects, but two types of genes are really important. Genes called proto-oncogenes and tumour suppressor genes play important roles in regulating cell division and preventing the formation of a **tumour**. When proto-oncogenes mutate, they often become active oncogenes, which stimulate the cell to divide in an uncontrolled manner. Ordinarily, some growth factor would be necessary to make the cell divide.

Tumour suppressor genes recognise uncontrolled cell division and act to suppress cell division. If these genes mutate and become inactive, a tumour will form as uncontrolled cell division continues.

KEY WORDS

tumour *a tumour is a mass of cells created when cell replication gets out of control. Tumours cause the disease cancer*

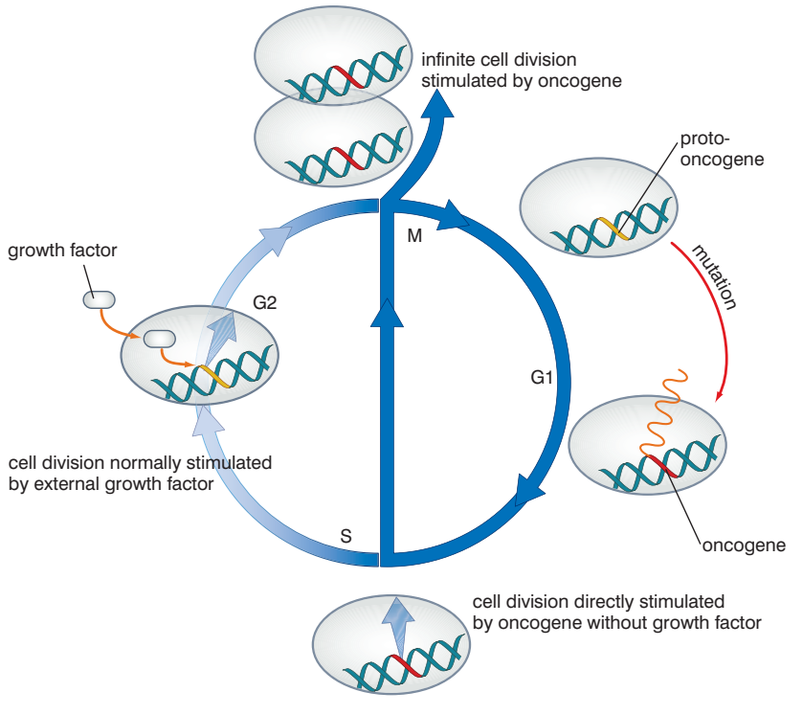


Figure 3.62 *How a tumour starts*

Can mutations benefit an organism?

So far, we have talked only about how mutations produce harmful effects, but mutations are the raw material of evolution. It is the only process that creates new genes. Crossing over, segregation and random assortment in meiosis together with random fusion in fertilisation reshuffle existing genetic material, but only mutation produces new genetic material.

If a mutated allele gives an organism an advantage then Natural Selection will act so that frequency of that allele increases with successive generations. As it does the numbers of the organism with the mutated allele will also increase, at the expense of those without it.

Mutations in the DNA of bacteria can give them resistance to a specific antibiotic, such as penicillin or ampicillin. These mutations arise spontaneously, as do all mutations. They only give the bacterium an advantage if the particular antibiotic is actually being used. Being resistant to streptomycin is no advantage if penicillin is being used. But being resistant to penicillin in an environment where penicillin is widely used confers a considerable advantage to the organisms. In 1947, just four years after penicillin was used widely in the USA, the first penicillin-resistant bacterium was found – it was a bacterium called *Staphylococcus aureus*. Today over half the infections caused by *Staphylococcus aureus* are caused by penicillin-resistant types.

KEY WORDS

antibiotic resistance *the evolution of strains of bacteria that are not affected by antibiotics. It is caused by the overuse of antibiotics*

Bacteria can also 'swap' **antibiotic resistance** genes with each other. Most of the mutant genes that confer resistance are found in the plasmids – the 'extra' small circular pieces of DNA that are separate from the main bacterial DNA. They can transfer these plasmids to other bacteria by:

- conjugation – the plasmid passes through a special 'conjugation' tube from one bacterium to another
- transduction – a virus carries the plasmid from one to another
- transformation – the plasmid is absorbed from a dead bacterium

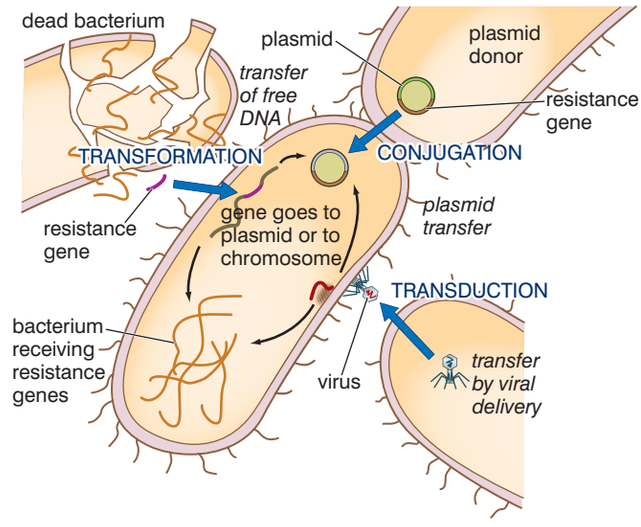


Figure 3.63 *Transfer of antibiotic resistance between bacteria*

Chromosome mutations

Chromosome mutations occur when there is any change in the arrangement or structure of the chromosomes. They occur most often during meiosis at crossing over in prophase 1. There are several different mutation types that result in a change in the structure of a chromosome. They are much bigger events than point mutations and usually result in the death of a cell. They may also affect the whole organism. For example, if essential parts of the DNA are affected by chromosomal mutations, a foetus may be aborted.

Inversion

This occurs when an area of DNA on a chromosome reverses its orientation on the chromosome. Just one inversion on chromosome 16 can cause leukemia. An inversion that leads to an embryo having too few or too many copies of genes, can cause the embryo to miscarry, fail to grow, or be born with substantial medical problems.

Deletion

With this cause of mutation, a decrease in the number of genes occurs due to the deletion of a large section of a chromosome. Deletion can result in a variety of genetic disorders, such as Prader-Willi syndrome. This results from a malfunction of the hypothalamus (a small endocrine organ at the base of the brain), which plays a crucial role in many bodily functions, including hunger and satiety, temperature and pain regulation, fluid balance, puberty, emotions and fertility.

Insertion

This type of mutation describes an increase in the number of genes caused when an unequal crossover happens during meiosis. The chromosome may become abnormally long or short and stop functioning as a result.

Duplications

When genes are duplicated it results in them being displayed twice on a single chromosome. This is usually harmless as the chromosome still has all its genes. However, duplication of the whole chromosome is more serious. Having three copies of **chromosome 16**, known as trisomy 16, leads to babies being born with a range of medical issues, such as poor foetal growth, muscular and skeletal anomalies, congenital heart defects and underdeveloped lungs.

Chromosome non-disjunction

When homologous chromosomes do not separate successfully to opposite poles during meiosis, the result is one of the gametes lacking a chromosome and the other having an extra chromosome. If this happens with **chromosome 21**, Down's syndrome results. Those with the condition will have 47 chromosomes in every cell

KEY WORDS

Chromosome 16 *one of the 23 pairs of chromosomes in humans. It spans about 90 million base pairs and accounts for nearly 3% of DNA in cells*

Chromosome 21 *one of the 23 pairs of chromosomes in humans. It is the smallest of the chromosomes*

Activity 3.14

Mutation is very important. It can cause genetic diseases, but it is also needed for natural selection and evolution to take place. Work in a group, discuss all aspects of mutation. Develop a poster using a large spider diagram to show everything you have discussed Include with simple facts about mutation and what causes it in one area of the diagram, positive benefits of mutation in another and the damaging aspects of mutation in a third area. Think of inventive ways to highlight these different regions of your diagram so it is easy for others to see them.

(because they have three copies of chromosome 21) as opposed to 46 like normal. Down's syndrome is characterised by mental retardation, heart defects and stunted growth.

Translocations

A piece of one chromosome is transferred to another non-homologous chromosome. This type of chromosome mutation is often responsible for chronic myelogenous leukemia.

These chromosomal mutations are illustrated in figure 3.64.

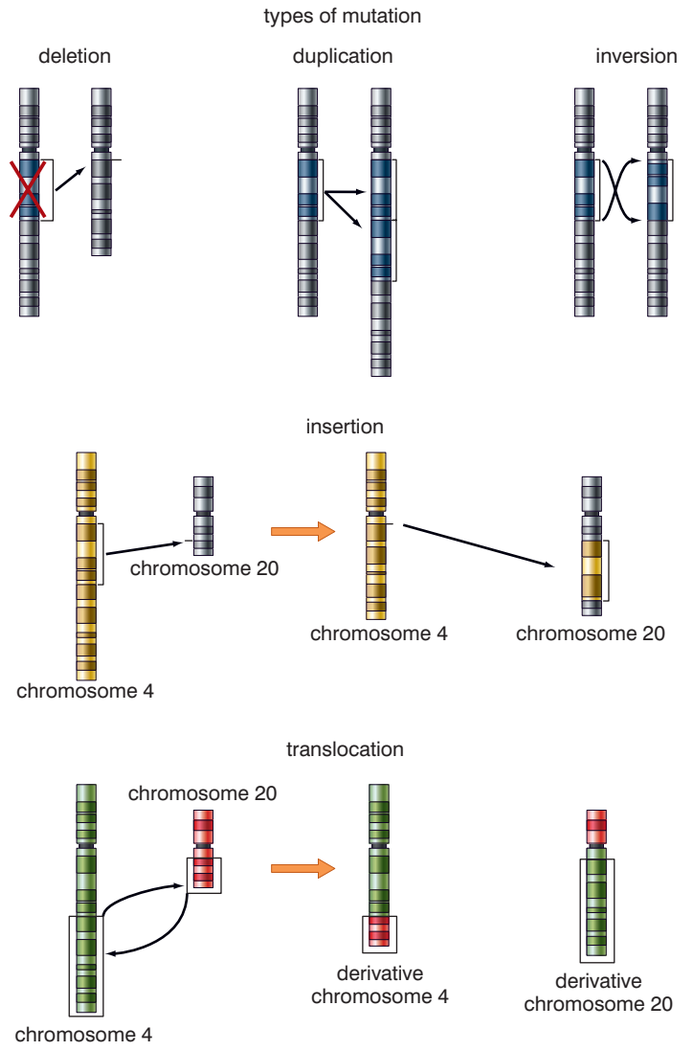


Figure 3.64 *Chromosomal mutations*

Review questions

Choose the correct answer from A to D.

1. Which of the following is an example of a chromosomal mutation:
   A a base duplication
   B a base insertion
   C a translocation
   D none of these
2. Which of the following is a frameshift mutation?
   A point replacement
   B Inversion
   C Insertion
   D substitution
3. The only source of new genetic material during evolution is:
   A crossing over
   B segregation
   C random assortment
   D mutation
4. The increase in bacterial resistance to penicillin is due to:
   A mutation
   B natural selection
   C the increased use of penicillin
   D a combination of all the above
5. If a substitution occurs in the DNA of an organism, which of the following will also occur?
   A The mRNA will also be altered.
   B All the triplets after the mutation will be altered.
   C All the triplets before the mutation will be altered.
   D A frameshift will occur.

Summary

In this unit you have learnt that:

- Genes are sections of DNA in a chromosome that determine a particular feature.
- Alleles are different 'versions' of a gene (for example, pea plants have purple and white alleles of the gene for flower colour).
- Homologous chromosomes carry alleles of the same genes at the same loci.
- Dominant alleles are expressed in the homozygote and in the heterozygote; recessive alleles are only expressed in the homozygote.
- Some alleles are codominant; both alleles are expressed in the heterozygote.
- In multiple allele inheritance, there are more than two alleles of a gene in the population as a whole, but any individual still has only two alleles.

- Meiosis produces four haploid cells that show genetic variation; the variation is a result of:
  - crossing over in prophase I
  - independent assortment of the chromosomes at anaphase I and anaphase II
- In dihybrid inheritance, a cross between two individuals heterozygous for both traits produces a 9:3:3:1 ratio in the offspring, if the genes are not linked.
- Some genes show linkage and are inherited as though they were a single unit; this is because their loci are on the same chromosome.
- Crossing over in meiosis produces recombinant types in the offspring; the frequency of these recombinant types can be used to measure how far apart the genes are on the chromosome.
- Gender, in humans, is determined by the X and Y chromosomes; males have the genotype **XY** whilst that of females is **XX**.
- Some conditions are determined by alleles carried on the sex chromosomes; these are called sex-linked conditions.
- Most sex-linked conditions are determined by recessive alleles on the X chromosome; males are affected more frequently than females by these because they need only inherit one X chromosome with the recessive allele whilst females must inherit two.
- Cross-breeding and inbreeding are both important techniques in agriculture; cross-breeding results in hybrid vigour (heterosis) and can be used to combine desirable traits in one variety, whilst inbreeding is used to establish pure lines.
- The DNA molecule is a double helix in which the base sequence on the sense strand is complementary to the base sequence on the antisense strand.
- The genetic code is a triplet, degenerate, non-overlapping and universal code.
- When compared with DNA, mRNA is smaller, single stranded (not double stranded), contains ribose (not deoxyribose) and contains uracil instead of thymine.
- The genome of an organism is the complete set of genetic information in that organism.
- A transgenic organism has had genes from a different type of organism (usually a different species) added to its genome.
- Restriction enzymes cut DNA at specific sequences, called restriction sites, to leave overlapping, sticky ends.

- A gene is inserted into a plasmid using a ligase enzyme.
- If insufficient DNA is obtained, the amount can be amplified using the polymerase chain reaction.
- Genetically modified organisms can be used to manufacture specific products to benefit humans (for example, insulin, bovine somatotrophin and vaccines).
- Other organisms have also been genetically modified to produce increased yields.
- In genetic fingerprinting:
  - a DNA sample is cut into fragments by restriction enzymes
  - the fragments are denatured by separating the two strands
  - the fragments are separated by gel electrophoresis and transferred to a nylon membrane by Southern blotting
  - a radioactive gene probe is added to the membrane and the pattern of complementary sequences is revealed using X-ray film
- In the transcription of the DNA in a gene RNA polymerase uses RNA nucleotides to build the single-stranded mRNA molecule that has a base sequence complementary to the strand of DNA being transcribed.
- During translation of mRNA into a polypeptide chain, tRNA molecules with anticodons complementary to the mRNA codons inside the ribosome bind to the mRNA; their amino acids form a peptide bond and one of the tRNA molecules leaves and the process is repeated.
- The proteins produced have a variety of functions: they may be structural proteins, enzymes, peptide hormones, antigens and antibodies, for example.
- Transcription factors are necessary to activate genes; these are proteins that bind with the promoter regions next to a gene and allow RNA polymerase to transcribe the gene.
- Molecules of short interfering RNA (siRNA) can 'silence' genes by degrading the mRNA transcribed from the genes.
- siRNA has the potential to treat conditions such as AIDS by preventing replication of HIV, and cancers by silencing genes that enhance cell division.
- Point mutations are spontaneous changes in a single base on the DNA molecule.
- Substitutions replace one base with another; because the code is degenerate, there may be no change in the amino acid coded for.
- Deletions and additions both cause a frameshift; these mutations alter all the DNA triplets after the point of mutation and change all the amino acids after this point also.

- High-energy radiation and carcinogenic chemicals increase the rate of mutation.
- If proto-oncogenes mutate to become active oncogenes, they will stimulate the cell to divide in an uncontrolled manner.
- If tumour suppressor genes mutate and fail to regulate cell division, a tumour may form.
- Mutations can be inherited; if a mutation is beneficial the frequency of the mutated allele will increase in successive generations.

End of unit questions

1. (a) Describe the structure of the DNA molecule. You may use a diagram to help if you wish.

   (b) Describe three ways in which a molecule of mRNA is different from DNA.

   (c) Describe two ways in which a molecule of tRNA is different from mRNA.

2. A sequence of bases on a strand of DNA is:

   A T T C C C G C T A A A C A G

   (a) What is the sequence of bases of the mRNA molecule that could be formed from this strand?

   (b) Use this sequence to explain what is meant by:

   (i) a deletion mutation

   (ii) a substitution mutation

3. Protein synthesis is divided into two stages: transcription and translation.

   (a) Describe how transcription takes place in a eukaryotic cell.

   (b) Describe three ways in which protein synthesis in a prokaryotic cell differs from protein synthesis in a eukaryotic cell.

4. Flower colour in pea plants is controlled by a single gene with two alleles. The allele for purple flowers is completely dominant over the allele for white flowers.

   (a) Explain what is meant by the following terms:

   gene

   allele

   dominant

   (b) How could you find the genotype of a purple-flowered plant of unknown parents? Explain your answer.

5. Andalusian fowl can have plumage with have three distinct colours:

   - black
   - white
   - blue

   In breeding experiments, the following results were obtained:

Parents	Black x White	Blue x Blue
Offspring	All blue	1 black : 2 blue : 1 white

   (a) Suggest an explanation for these results. Use evidence from the crosses to support your explanation.

   (b) If a blue fowl were bred with a white fowl, what offspring would you expect? Explain your answer.

6. The pedigree in figure 3.65 shows the inheritance of red-green colour blindness in one family over four generations.

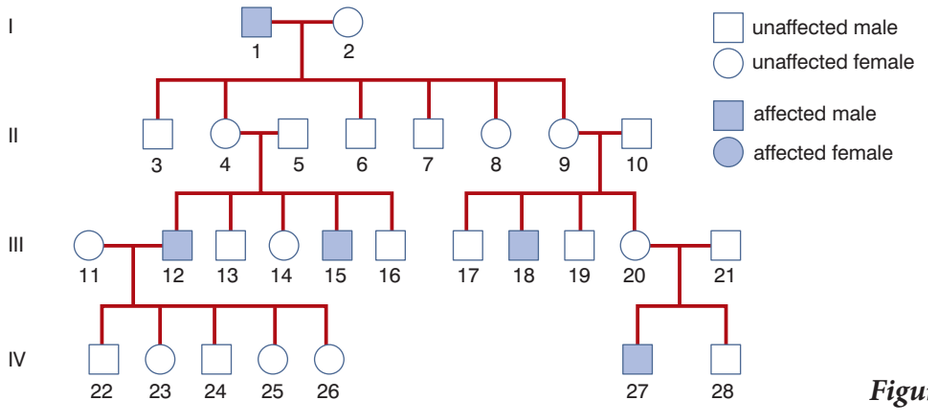


Figure 3.65

   (a) What evidence in the pedigree suggests that red-green colour blindness is:

   (i) sex-linked

   (ii) recessive?

   (b) Give the number of *one* individual who is a carrier. Give reasons for your answer.

   (c) If individual 18 were to marry a female with red-green colour blindness, what would be the genotypes of:

   (i) their sons

   (ii) their daughters

   Explain your answers.

7. (a) Outline the main stages of meiosis I.

   (b) In maize:

   - the allele for yellow seeds is dominant to that for colourless seeds
   - the allele for smooth seeds is dominant to that for wrinkled seeds

A plant heterozygous for both traits was crossed with a plant homozygous for both recessive alleles. The offspring were:

- coloured, smooth – 48%
- colourless, wrinkled – 48%
- coloured, wrinkled – 2%
- colourless, smooth – 2%

(i) How do these results support the idea that these genes are linked? Give reasons for your answer.

(ii) Draw a genetic diagram to show the results you would expect from a cross between two plants heterozygous for both traits. Assume no crossing over takes place.

8. The graph in figure 3.66 shows the change in the percentage of bacteria that cause pneumonia resistant to penicillin in the USA between 1986 and 2001.

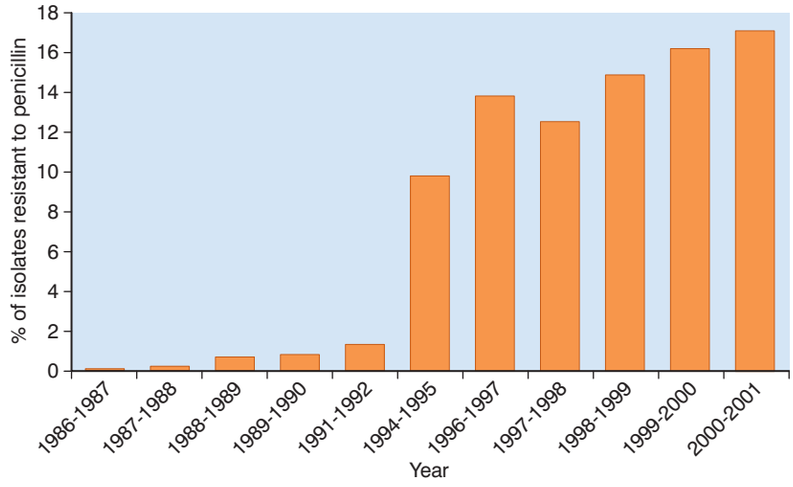


Figure 3.66

(a) (i) Describe the trend shown in the graph.

(ii) Suggest an explanation for the trend you have described.

(b) Describe three ways in which bacteria can transfer antibiotic resistance from one bacterium to another.

9. Mary and Bob have three children. However, Bob suspects that the third child is not his, but is the child of another man called Larry. All the individuals have genetic fingerprints taken. Figure 3.67 shows these genetic fingerprints.

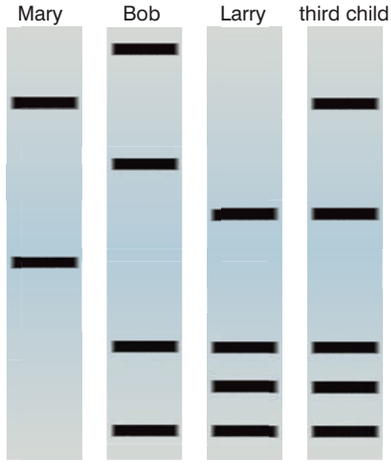


Figure 3.67

(a) Describe how a genetic fingerprint is made.

(b) Was Bob justified in his suspicions? Explain your answer using information from the genetic fingerprints.

10. (a) Insulin is a peptide hormone containing 51 amino acids. It is produced in the islets of Langerhans in the pancreas.

    (i) How many bases would there be in the mRNA that controls insulin production? Explain your answer.

    (ii) Outline how insulin is produced in cells in the islets of Langerhans.

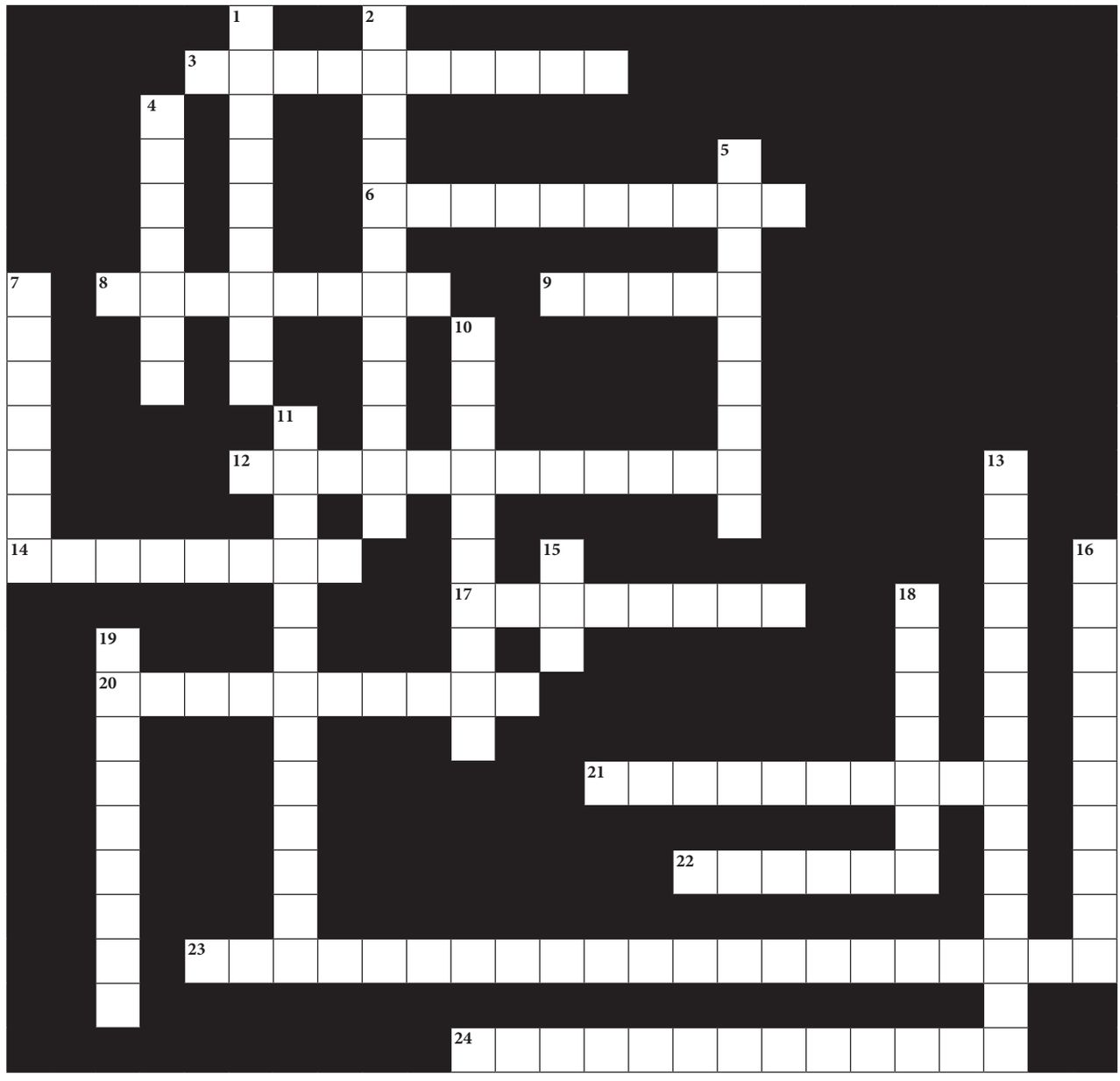
    (b) People who suffer from type I diabetes must inject themselves regularly with insulin. Today, this insulin is made by genetically modified bacteria.

    (i) Describe the main steps in genetically modifying bacteria.

    (ii) Gene technology has attracted much debate. Give two ethical concerns that some people have and suggest how these concerns might be eased.

Copy the crossword puzzle below into your exercise book (or your teacher may give you a photocopy) and solve the numbered clues to complete it.

Classical genetics



Across

3. The structure that holds two chromatids together (10)
6. When a gene cannot be expressed in either male or female, it is said to be … (3–7)
8. The allele that expresses itself in the heterozygote is … (8)
9. A feature controlled by a gene is sometimes called a … (5)
12. An organism carrying both dominant and recessive alleles for a feature is said to be … (12)

14. A genetic cross involving two features at the same time is a … cross (8)

17. The alleles an organism posseses for a particular feature (8)

20. Chromosomes with the same genes at the same loci are said to be … (10)

21. Genes that are carried on the X chromosome show… (3–7)

22. A version of a gene (6)

23. Mendel's law of … states that one feature is inherited independently of another (11, 10)

24. A way of showing in a genetic cross how different gametes can combine (7, 6)

Down

1. The allele that is not expressed in the heterozygote is … (9)

2. How genetic material is exchanged between homologous chromosomes in prophase I of meiosis (8, 4)

4. A cell with two sets of chromosomes is … (7)

5. A procedure to find if an organism showing the dominant feature is homozygous or heterozygous (4, 5)

7. A cell with only one set of chromosomes is … (7)

10. An organism carrying two dominant or two recessive alleles for a feature is said to be … (10)

11. When the expression of a gene is affected by the gender of the person, it is said to be … (3–10)

13. The type of inheritance shown by the ABO blood group alleles (8, 6)

15. Genes are made of this (3)

16. If both alleles express themselves in the heterozygote, they are said to be … (10)

18. Alleles for two different features on the same chromosome show … (7)

19. They physical expression of a genotype (9)

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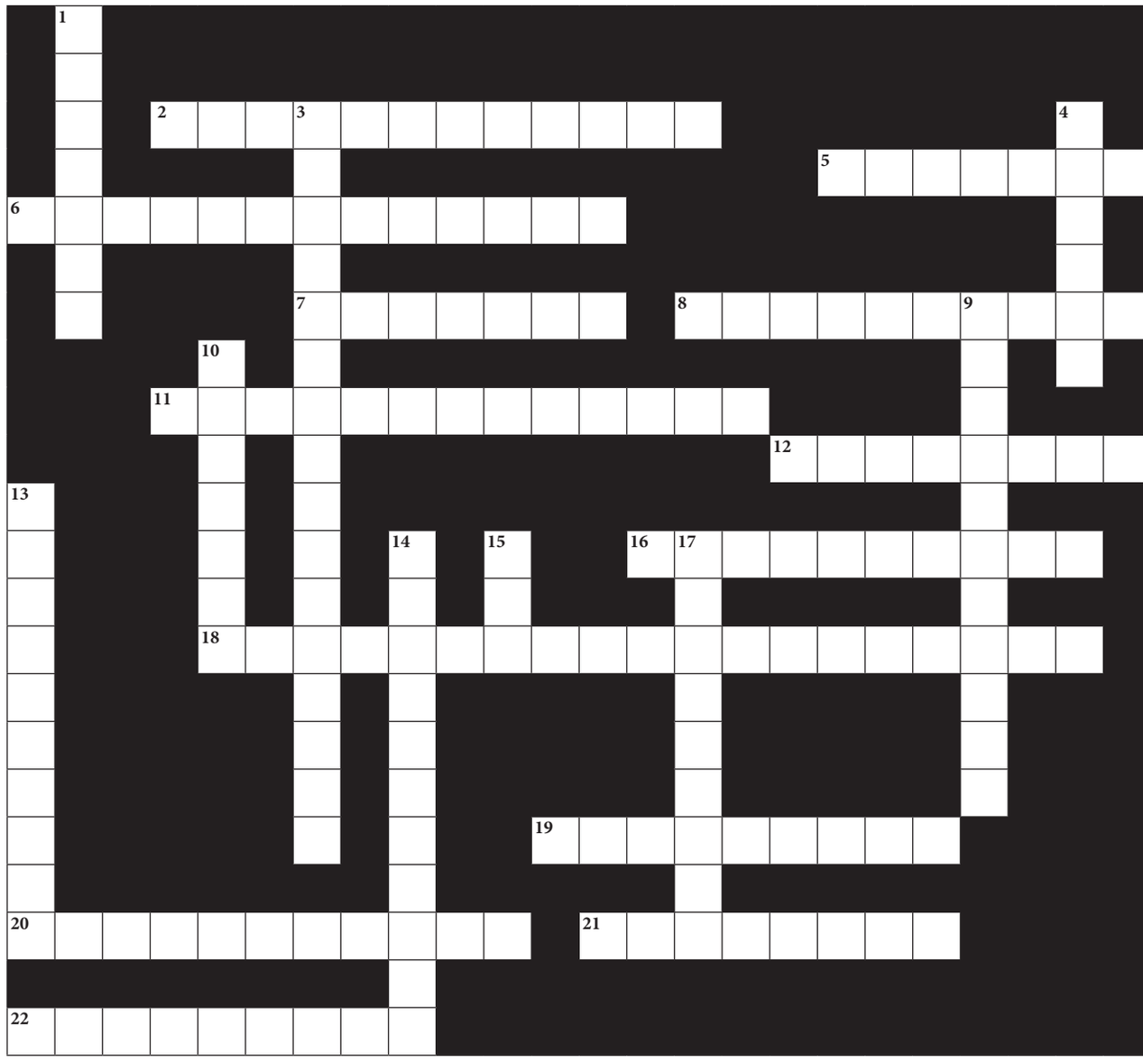
Molecular genetics



Across

2. A mutation in which one base is replaced by another (12)
5. A small, circular piece of DNA found in bacteria (7)
6. The sequence of bases on one strand of DNA is … to the sequence on the other strand (13)
7. Taking cuttings is a traditional example of this process (7)
8. The enzyme which assembles nucleotides into a new DNA strand is DNA … (10)
11. Rewriting the genetic code from DNA to mRNA (13)

12. A permanent genetic change (8)
16. The building block of a nucleic acid (10)
18. A protein that initiates transcription of a gene (13, 6)
19. The type of RNA that carries the genetic code from DNA to a ribosome (9)
20. Converting the code in mRNA into a sequence of amino acids (11)
21. The enzyme which 'unzips' a DNA molecule is DNA … (8)
22. The type of DNA that does not code for any feature and is used in a genetic fingerprint (9)

Down

1. The protein associated with DNA in chromosomes (7)
3. The type of replication shown by DNA (4–12)
4. This enzyme helps two pieces of DNA to anneal (6)
9. This type of enzyme cuts a DNA molecule at a specific base sequence (11)
10. The three bases that code for an amino acid form a … (7)
13. Addition and deletion are this type of mutation (10)
14. This rule states that, in DNA, A will always be opposite T and C opposite G (4, 7)
15. The polymerase chain reaction (acronym) (3)
17. Because the genetic code is the same in all organisms, it is said to be … (9)