Genetics & Inheritance – Genetic Basis for Variation I

1. Introduction

Organisms inherit genetic information from their parents. To appreciate how characteristics or conditions are passed on in a family, it is important to understand the basic laws of inheritance.

Gregor Mendel was the first person to describe the manner in which traits are passed on from one generation to the next. By experimenting with pea plant breeding, Mendel developed the principles of inheritance that described the transmission of genetic traits, before anyone knew genes existed. However, not all organisms pass their genes on the same way as the pea plant and therefore Mendel's principles of inheritance only explain the most basic phenomena of inheritance. Other than Mendelian inheritance, you will also learn of non-Mendelian inheritance (e.g. autosomal linkage, epistasis), as well as how the environment plays a role in determining the phenotype of an organism. Statistical tests, such as the chi-squared test, which allow us to test the significance of differences between observed an expected results of genetic crosses will also be covered.

2. Learning Outcomes

u. Explain the terms: *locus, allele, dominant, recessive, codominant, incomplete dominance, homozygous, heterozygous, phenotype, genotype* and *linkage*.
v. Explain how genes are inherited from one generation to the next via the germ cells or gametes.
w. Explain how genotype is linked to phenotype.
x. Use genetic diagrams to solve problems in dihybrid crosses, including those involving codominance, incomplete dominance, multiple alleles, sex linkage, autosomal linkage and epistasis.
y. Use genetic diagrams to solve problems involving test crosses.
z. Explain the meaning of the terms linkage and crossing-over and explain the effect of linkage and crossing-over on the phenotypic rations from dihybrid crosses.
bb. Explain how the environment may affect the phenotype (including how the diet affects the differentiation of honey bees and how temperature affects fur colour of Himalayan rabbits).

3. References

Campbell, N.A. and Reece, J.B. (2008). Biology, 9th edition. Pearson.

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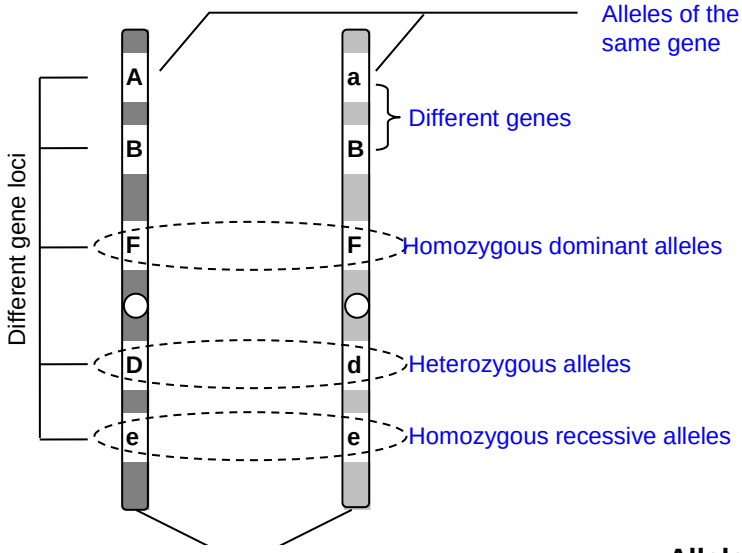
4. Common Terms to Understand

Notes to self

Term	Explanation
Homologous chromosome	Recall: A diploid organism (2n) has 2 sets of chromosomes, one set from each parent. Homologous chromosomes are **similar in size, shape, position of centromere** and **staining pattern**. Homologous chromosomes have the **same genes** that determine a certain trait **at corresponding loci**. e.g. blood group. However, the genes may be of **different alleles** which give rise to different observed trait (**phenotype**), e.g. blood group A, B, O.
Locus	The **position of a gene on a chromosome**.
Gene	A gene is an ordered sequence of DNA nucleotides located at a particular locus on a particular chromosome that encodes a specific functional product, i.e. a protein or RNA molecule.
Allele	An allele is one of a number of **alternative forms of a gene**, each possessing a unique nucleotide sequence, only one of which can occur at a given locus. The differences in the nucleotide sequences of each allele, when translated may produce a different gene product which results in various phenotypes. Alleles are usually represented by the same letter of the alphabet with **upper case for dominant alleles** and **lower case for recessive alleles** (e.g. A and a respectively).
Homozygous	The diploid condition in which the **alleles at a given locus** on a pair of homologous chromosomes are **identica**l, e.g. AA or aa.
Heterozygous	The diploid condition in which the **alleles at a given locus** on a pair of homologous chromosomes are **different**, e.g Aa.



Alleles on homologous chromosomes

Genotype

Genotype refers to the **combination of alleles**, situated on **homologous chromosomes at corresponding loci** (such as "Aa", "aa" or “AA”). The genotype determines a specific trait of an organism.

Phenotype

Phenotype refers to the **characteristic (trait)** of an organism that is expressed or observed.

These characteristics may arise from the **interaction between the genotype (i.e. the alleles on the homologous chromosomes) and the environment** in which the organism develops. Hence, the environment may alter the appearance of the organism.

For example, while Himalayan rabbits can produce black fur, the black fur is only produced on parts of the body that are cool enough. Heat from other warmer parts of the body result in white fur (Page 8).

Dominant allele

The allele that shows its phenotype regardless of whether it is homozygous or heterozygous.

In cases involving heterozygotes, it is said that the **expression of the gene product of the dominant allele masks the effect of the gene product expressed by the recessive allele**.

Recessive allele

The allele that shows its phenotype only in the presence of another identical recessive allele (homozygous recessive).

In cases involving heterozygotes, the **effect of the gene product of the recessive allele is masked by the effect of the gene product expressed by the dominant allele**.

Cross	The mating of two organisms.
Self-fertilisation	Crossing of an organism with itself. This term is used for plants and not animals. Self-fertilisation over many generations can produce a pure line.
Test cross	Cross between an individual of unknown genotype or a heterozygote and a **homozygous recessive individual**: unknown genotype X homozygous recessive OR heterozygous X homozygous recessive Offspring ratios can be used to deduce the genotype of the unknown, and/or the linkage relationships of its heterozygous loci.
Pure breed / True breed	When an organism is **homozygous** for the traits concerned.
F_1 generation (First filial)	The offspring of the **cross** between a **homozygous dominant** organism and **homozygous recessive** organism. Genotype of F_1 generation is **heterozygous**.
F_2 generation (Second filial)	The offspring produced by crossing two F_1 organisms.
Wild type	The typical genotype found in a natural population of that species. While this term is much used by *Drosophila* geneticists, it is best avoided.
Codominance	When two different dominant alleles of the same gene are **both expressed** and **influence the phenotype.** This results in a **heterozygote's** phenotype that is **different** from the **phenotypes of both homozygotes** and thus **more than two phenotypes possible**. e.g. alleles $\mathbf{I^A}$ and $\mathbf{I^B}$ of the human ABO blood group system are codominant, the heterozygote phenotype is blood group AB while the blood group of the homozygous dominant is either A or B.
Incomplete dominance	The situation in which the phenotype of heterozygotes is intermediate between the phenotypes of individuals homozygous for either allele.
Linkage	Two or more **genes on same chromosome** that **do not assort independently** in meiosis and are thus **inherited together**. Genes closer together less likely to cross-over and exchange alleles between homologous chromosomes.

5. Labelling Conventions for Alleles

Notes to self

(a) Alleles are usually represented with **upper case** for **dominant allele** and **lower case** letter for **recessive allele**.

The choice of the letter can be based on either the dominant trait or the mutant trait. For example:

R (round seed) and **r** (wrinkled seed)
D (tall) and **d** (dwarf)

An **apostrophe** is added to the lower case letter if the upper and lower cases of the letter look similar, e.g. **C** and **c'**, **W** and **w'**.

Avoid upper and lower case versions which are difficult to distinguish when handwritten, e.g. c, o, s, u, v, w, x and y.

(b) When there are **multiple alleles** of the same gene, the gene should be allocated an uppercase letter and each allele an appropriate **superscript**.

For example, representation of the different alleles for human blood groups where:

I represents the gene
A, B and **o** represent alleles

The alleles are therefore indicated as $\mathbf{I^A}$, $\mathbf{I^B}$ and $\mathbf{I^o}$ (note that the superscript 'o' is lowercase to denote its recessive represents allele for blood group O.

(c) For **sex-linked** (X-linkage), the sex chromosomes XX and XY should always be indicated and the dominant or recessive alleles of particular genes should be indicated by appropriate superscript of uppercase and lowercase letters.

For example:

In the transmission of haemophilia, $\mathbf{X^HX^h}$ designates a female carrier.
$\mathbf{X^HY}$ denotes a normal male and $\mathbf{X^hY}$ a haemophiliac male.

(d) For genes with codominant alleles, a distinguishing letter of the alphabet will be added as a superscript.

For example:

ABO blood group system in humans where $\mathbf{I^A}$ and $\mathbf{I^B}$ are codominant.

6. From Genotype To Phenotype

Notes to self

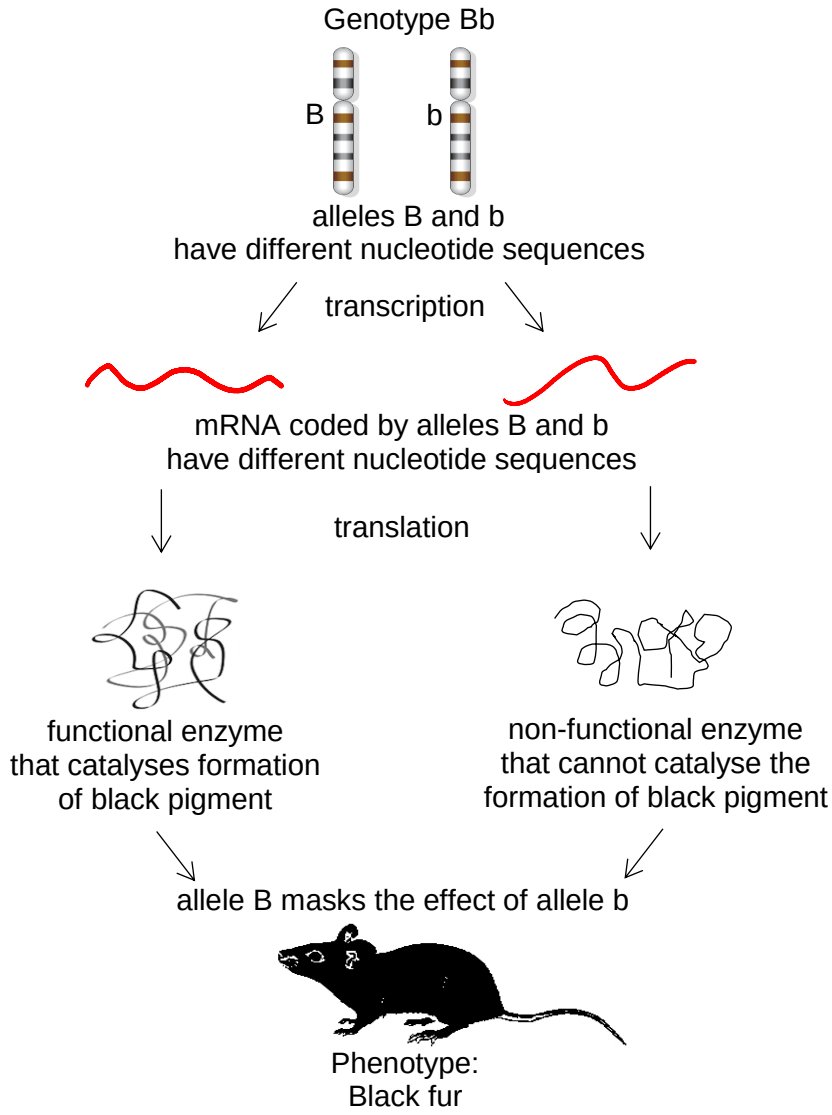
The **genotype** of an organism is its **genetic makeup** which is the combination of alleles situated on corresponding loci on homologous chromosomes. The genotype determines a trait or phenotype observed.

While the genotype is genetic information, **phenotype** is the **expression** of that information that results in a **trait** that can be observed. For example, in the case of seed shape in pea plants, the genotypes RR and Rr will result in plants that produce round seeds (phenotype). The genotype rr will result in plants that produce wrinkled seeds (phenotype)

As learnt previously (DNA and Genomics), nucleotide sequences determine gene product, such as proteins. The link between genotype and phenotype is closely tied to the Central Dogma theory.

For example, the inheritance of coat colour in mice:
The presence of the dominant allele B results in black fur while the presence of 2 copies of the recessive allele b results in white fur.

The diagram below shows how the genotype Bb in a mouse determines the observed phenotype:



7. Environmental Factors & Phenotypic Variation

Notes to self

The phenotype of an individual is determined by the combination of alleles (genotype).

Phenotypic variation may result from the interaction of genotype and environment.

Environment may modify or limit the expression of gene(s). e.g. a shortage or lack of food or necessary nutrients such as mineral salts or vitamins will lead to reduce growth in size or mass and possibly height of individuals. Lack of vitamins may also lead to serious health problems such as deficiency in vitamin A results in night blindness.

Environment factors that may **trigger or switch on certain genes** which are always present in the genome:

(a) Temperature

Example 1:
Temperature affects the **coat colour of Himalayan rabbits**. The Himalayan rabbit has a white body with black ears, nose, feet and tail. Only in parts of the body that are cool enough (e.g. the extremities) does black fur grow. This is because heat (from the body) prevents the development of the black pigment. If the fur on the back is shaved and an ice-pack is fixed on the rabbit's back, left in position for weeks and kept cold, black hair begins to develop beneath the ice-pack.

Example 2:
Nile crocodiles have **temperature-dependent sex determination**, which means the sex of their hatchlings is determined by the average temperature during their incubation period. If the temperature inside the nest is below 31.7°C, or above 34.5°C, the offspring will be female. Males can only be born if the temperature is within that narrow range.

(b) Food & Nutrition

Example:
Larvae of honey bees fed with royal jelly become queen bees capable of reproducing and living a long time. But female larvae fed with beebread and honey instead have slower development and become worker bees which are sterile and short-lived.

Example:
Phenylketonuria (PKU) is an autosomal (non-sex linked) recessive genetic disorder characterised by a deficiency in the enzyme phenylalanine hydroxylase. This enzyme is necessary to metabolise the amino acid phenylalanine to the amino acid tyrosine. When phenylalanine hydroxylase is deficient, phenylalanine accumulates and is converted into a toxic substance.

Left untreated, this condition causes problems with brain development, leading to progressive mental retardation and seizures. However, PKU is one of the few genetic diseases that can be controlled by diet. **A diet**

low in phenylalanine is very effective treatment illustrating how an environmental factor such as diet can be manipulated to modify the resultant phenotype of a particular genotype.

Notes to self

(c) UV light

Example:
The human skin contains melanocytes which are melanin-producing cells located in the bottom layer of the skin's epidermis. When exposed to UV light more melanins are produced. The color of the melanin is dark and it absorbs and blocks the UV-B light from passing the skin layer. More exposure to UV light results in darker colour skin.

(d) Photoperiod

Example:
Wavelength of light and duration of light exposure may affect flowering, growth and germination of seeds of the plants. Long-day plant flowers when the day length exceeds their critical photoperiod. These plants typically flower in the northern hemisphere during late spring or early summer as days are getting longer. Conversely, short-day plants flower when the day lengths are less than their critical photoperiod.

Environment **effect** is usually **greater on polygenes**. Polygenic inheritance occurs when one characteristic is controlled by two or more genes. Examples of human polygenic inheritance are height, skin color and weight. The frequency of the phenotypes of these traits generally follows a normal **continuous variation** distribution pattern.

Environment may induce **mutation affecting phenotype** such as over exposure to UV light may cause chromosomal damage that triggers skin cancer. Chemicals such as asbestos and carcinogens in cigarette smoke may cause cancer cells formation.

8. Monohybrid Cross & The Law of Segregation

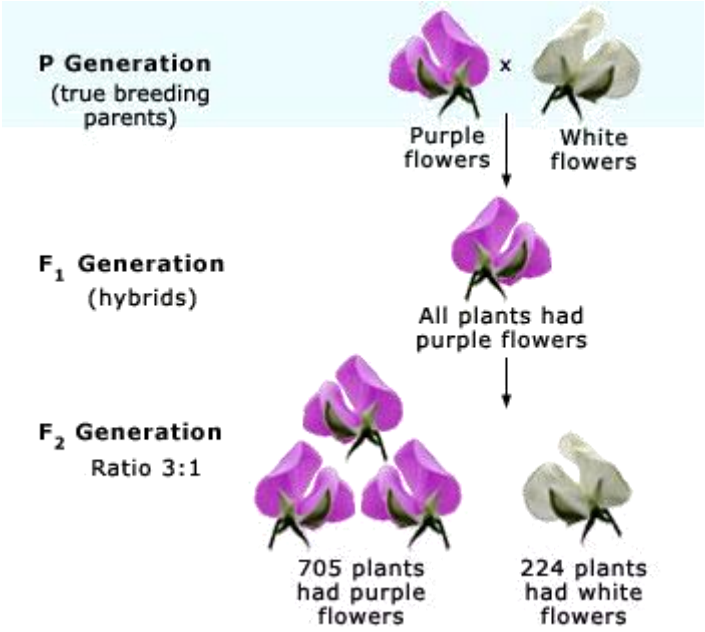
Notes to self

Monohybrid crosses involve genetic crosses that study the inheritance of **ONE** characteristic controlled by a **SINGLE gene**.

For example:

Gregor Mendel conducted **crosses** between **pure-breeding** plants which had different characteristics e.g. purple flowers vs white flowers. Crossing of two varieties with contrasting traits is known as **hybridisation**.

- Such a cross is a **monohybrid cross**, as it tracks the inheritance of a **single characteristic**, in this case, flower colour.
- The pure-breeding parents belong to the **P** (**parental) generation**, their hybrid offspring are the **F_1 (first filial) generation.**
- Allowing the F_1 hybrids to self-pollinate produces an **F_2 (second filial) generation.**



Monohybrid cross: Mendel's flower-colour experiment.

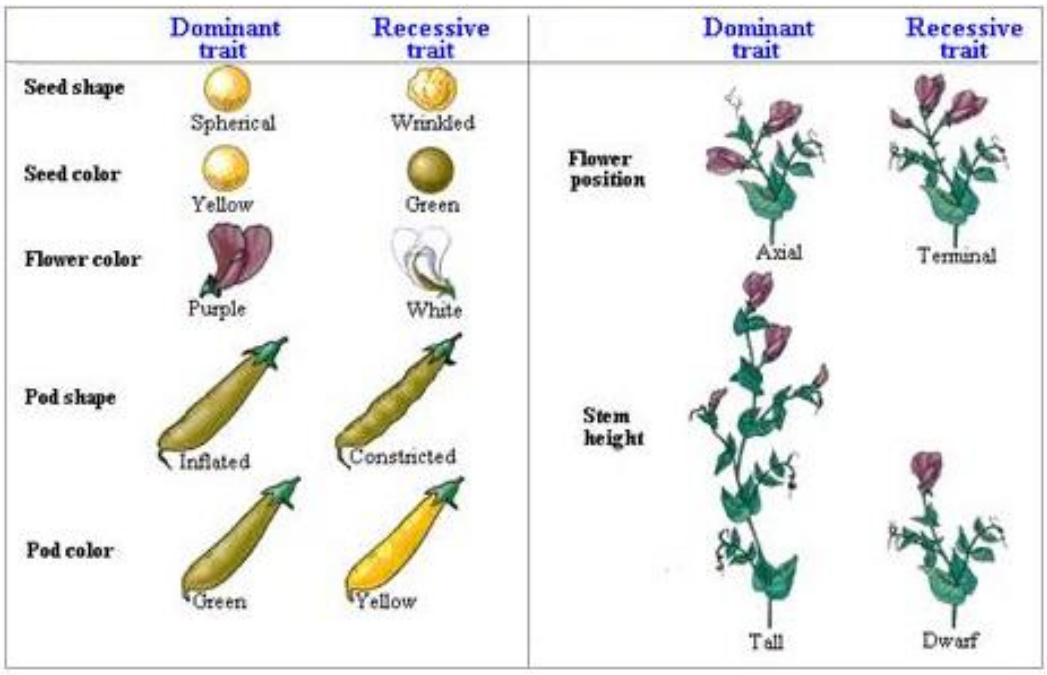
Results of the monohybrid cross involving flower colour:

- In the F_1 generation, plants produced only purple flowers. No white flowers were produced.
- In F_2 generation, ratio of **3 purple-flowered plants to 1 white-flowered plant**.
  This **3:1** ratio is known as the **monohybrid ratio**.

(Note: refer to page 14 for the genetic diagram to understand how the 3:1 ratio is obtained for a monohybrid cross)

In addition to flower colour, Mendel also studied 6 other pairs of contrasting characteristics:

Notes to self



Pairs of contrasting characteristics Mendel studied.

Like his monohybrid cross involving flower colour, Mendel also obtained the ratio of approximately 3:1 for the dominant to recessive characteristic in the F_2 generation for the monohybrid crosses involving each of the these 6 pairs of contrasting characteristics.

Character	Dominant vs. recessive trait	F_2 generation Dominant form	Recessive form	Ratio
Flower color	Purple X White	705	224	3.15:1
Seed color	Yellow X Green	6022	2001	3.01:1
Seed shape	Round X Wrinkled	5474	1850	2.96:1
Pod color	Green X Yellow	428	152	2.82:1
Pod shape	Inflated X Constricted	882	299	2.95:1
Flower position	Axial X Terminal	651	207	3.14:1
Plant height	Tall X Dwarf	787	277	2.84:1

Results of the F_2 generation obtained by Mendel from different monohybrid crosses.

Notes to self

Mendel's conclusions:

- In each organism, there is a pair of "factors" that controls the appearance of a given characteristic.
- F_1 generation obtained **one** "factor" from each parent (the gamete that emerge from meiosis carried a single copy of a "factor").

  The separation of the pair of parental factors during meiosis, so that only one "factor" is present in one gamete, is called:

  Mendel's first law - Law of segregation.
- In a heterozygote such as F_1 which has two unlike factors for a characteristic, the one that is expressed is dominant while the one that is masked is recessive. e.g. white flower is a **recessive** characteristic since the trait did not appear in the phenotype though the allele was present.

The "factors" determining characteristics are now known as **GENES**.

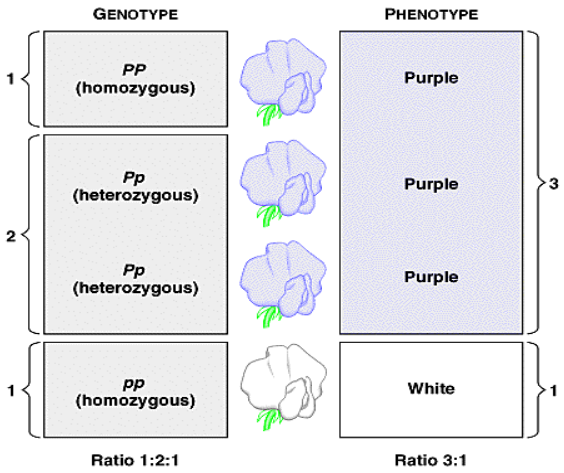
Each pollen grain and egg has one flower colour gene, so the plant formed by fertilisation has two copies of the flower colour gene.

This gene may be one of two distinct types or **ALLELES**; e.g. one allele, **P**, is for purple while the other allele, **p'**, is for white.

A diploid plant may have 2 of the same or 2 different alleles:

- An organism having **a pair of identical alleles** for a character is **homozygous** e.g. true-breeding pea plant for purple flowers (**PP**) and true-breeding pea plant with white flowers (**p'p'**).

- The purple F_1 hybrids with **two different alleles** (**Pp'**) are **heterozygous**.
  In a **heterozygote**, one allele may mask the presence of another.
  Therefore, the allele that shows itself in the phenotype is the **dominant allele**. The allele that is **masked** is the **recessive allele**.
  The allele **P** is dominant over **p'**. So a plant heterozygous for the flower colour gene with **Pp'** is purple. Allele **P** is expressed resulting in purple flower. Allele **p'** for white flower is masked.

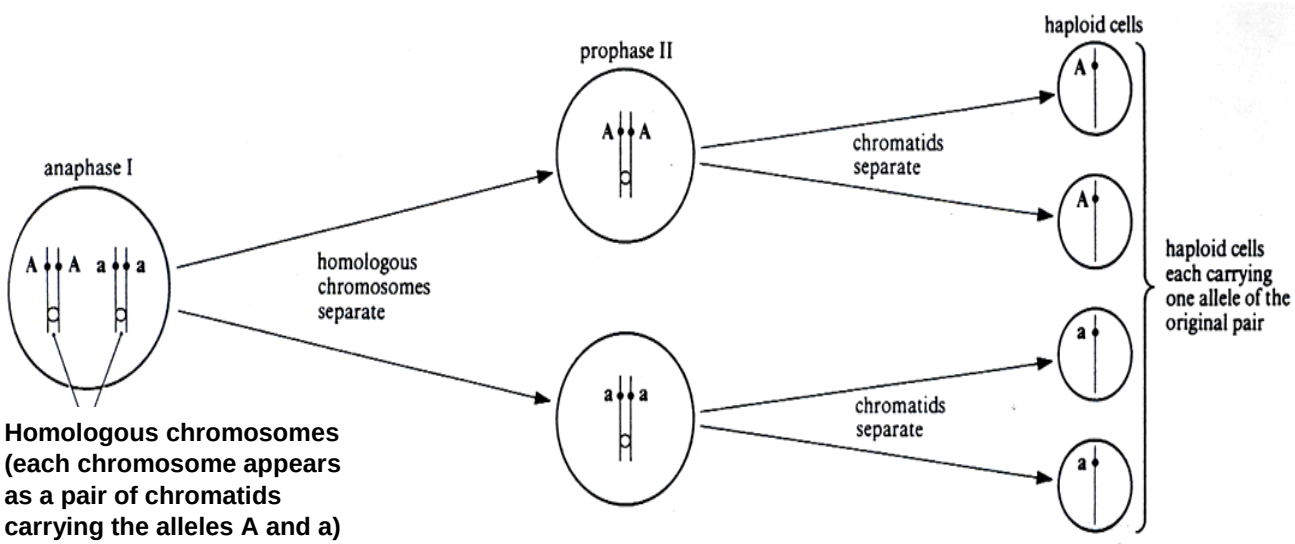


Pictorial representation of the phenotypic and genotypic results of the cross between two flowers

Mendel's First Law – Law of Segregation

The alleles separate from one another during meiosis to form gametes.

Note:
This is not the same as the Law of Independent Assortment that you will learn later.



Mendel's Law of Segregation:
alleles A and a are separated
after the separation of homologous chromosome during meiosis

Drawing a Genetic Diagram to Represent a Monohybrid Cross

Notes to self

Let: **P** represent the dominant allele for purple flowers
p' represent the recessive allele for white flowers

Parental phenotype	Purple flowers	X	White flowers
Parental genotype	PP	X	p'p'
Meiosis, Gametes	(P)		(p')
Fertilisation			
F_1 genotype	Pp'		
F_1 phenotype	Purple flowers		

F_1 selfing

F_1 phenotype	Purple flowers	X	Purple flowers
F_1 genotype	Pp'	X	Pp'
Meiosis Gametes	(P) (p')		(P) (p')

Fertilisation

Gametes	(P)	(p')
(P)	PP Purple flower	Pp' Purple flower
(p')	Pp' Purple flower	p'p' White flower

F_2 genotypes	PP Pp' Pp'		p'p'
F_2 genotypic ratio	3 P_	:	1 p'p'
F_2 phenotypic ratio	3 purple flowers	:	1 white flower

Note:

- All gametes need to be circled
- Phenotypes always need to be linked to genotypes either in the Punnett square and in the ratio outcomes of the cross
- Important **phenotypic ratios** in **complete dominance** monohybrid cross:
  - Pp X Pp → 3 : 1 (dominant phenotype : recessive phenotype)
  - PP X Pp/pp → All dominant phenotype
  - Pp X pp → 1 : 1 (see test cross on page 16)

Test Cross

Notes to self

A test cross can be conducted **to reveal the genotype of an organism that exhibits the dominant trait**.

- For instance, there are 2 possible genotypes for purple flowers: PP (homozygous dominant) or Pp' (heterozygous).
- **Test cross** is a cross with an individual expressing the **homozygous recessive trait(s)**.

- Cross the organism with an individual expressing the **homozygous recessive trait**, e.g. the white-flowered parent, to ascertain the true genotype of the parent exhibiting the dominant trait.

Q. **A plant produces purple flowers. How would you determine if the plant is homozygous dominant or heterozygous. Show your answer in the form of a genetic diagram.**

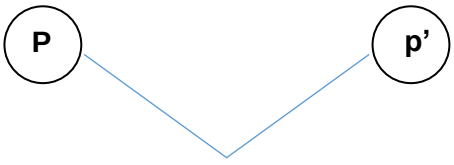
2 Possible Scenarios:

1) Between a homozygous dominant parent (purple flowers) and a homozygous recessive parent (white flowers)
2) Between a heterozygous parent (purple flowers) and a homozygous recessive parent (white flowers)

Scenario (1)

Let: **P** represent the dominant allele for purple flowers

p' represent the recessive allele for white (recessive)

Parental phenotype	Purple flowers	X	White flowers
Parental genotype	PP	X	p'p'
Meiosis Gametes			
Fertilisation			
Offspring Genotype	Pp'		
Offspring Phenotype	All plants with purple flowers		

Scenario (2)

Notes to self

Parental phenotype	Purple flowers	X	White flowers
Parental genotype	Pp’	X	p’p’

Meiosis
Gametes

Fertilisation

Gametes	P	p’
p’	Pp’ purple flower	p’p’ white flower

Offspring genotypic ratio	1	Pp’	:	1 p’p’
Offspring phenotypic ratio	1 purple flower		:	1 white flower

Conclusion:

Parent producing purple flowers crossed with parent producing white flowers:

- If offspring phenotypic ratio is all plants with purple flowers, parent producing purple flowers is homozygous dominant.
- If offspring phenotypic ratio is 1 plant producing purple flowers : 1 plant producing white flowers, parent producing purple flowers is heterozygous.

9. Dihybrid Cross & Law of Independent Assortment

Dihybrid crosses involve genetic crosses that study the inheritance of **TWO** different characteristics controlled by a **TWO different genes**.

Mendel also performed experiments with plants that differed in **two** characters – i.e. he performed **dihybrid crosses**. The purpose of this experiment was to see if the two traits were inherited independently.

For example, Mendel used pea shape (smooth or wrinkled) and pea cotyledon colour (yellow or green) as the characteristics.

- Yellow is dominant (**Y**) and green is recessive (**y’**).
- Round is dominant (**R**) and wrinkled is recessive (**r**).
- True breeding plants with yellow-round seeds (**YYRR**) were crossed with true breeding plant with green-wrinkled seeds (**y’y’rr**).

Drawing a Genetic Diagram to Represent a Dihybrid Cross

Notes to self

Let: **Y** represent the dominant allele for yellow seed
y' represent the recessive allele for green seed
R represent the dominant allele for round seed
r represent the recessive allele for wrinkled seed

Parental phenotype: Yellow, round seed X Green, wrinkled seed

Parental genotype: **YYRR** X **y'y'rr**

Meiosis
Gametes: **YR** **y'r**

Fertilisation

F_1 genotype: Yy'Rr

F_1 phenotype: Yellow and round seed

F_1 selfing

F_1 phenotype: Yellow, round seed X Yellow, round seed

F_1 genotype: Yy'Rr X Yy'Rr

Meiosis
Gametes: **YR** **Yr** **y'R** **y'r** | **YR** **Yr** **y'R** **y'r**

Fertilisation

		Gametes			
		YR	**Yr**	**y'R**	**y'r**
Gametes	**YR**	YYRR Yellow, round seed	YYRr Yellow, round seed	Yy'RR Yellow, round seed	Yy'Rr Yellow, round seed
	Yr	YYRr Yellow, round seed	YYrr Yellow, wrinkled seed	Yy'Rr Yellow, round seed	Yy'rr Yellow, wrinkled seed
	y'R	Yy'RR Yellow, round seed	Yy'Rr Yellow, round seed	y'y'RR Green, round seed	y'y'Rr Green, round seed
	y'r	Yy'Rr Yellow, round seed	Yy'rr Yellow, wrinkled seed	y'y'Rr Green, round seed	y'y'rr Green, wrinkled seed

F_2 genotypic ratio: 9 Y_R_ : 3 Y_rr : 3y'y'R_ : 1 y'y'rr

F_2 phenotypic ratio: 9 Yellow, round seed : 3 Yellow, wrinkled seed : 3 Green, round seed : 1 Green, wrinkled seed

Notes to self

Conclusion:

When a **9: 3: 3: 1** F_2 phenotypic ratio is obtained in a dihybrid cross, this indicates that the alleles of each character are inherited independently of one another. This means that the two alleles for seed colour **segregate independently** of the two alleles for seed shape i.e. whether **Y** or **y** is inherited in offspring is **independent** of whether **R** or **r** is inherited.

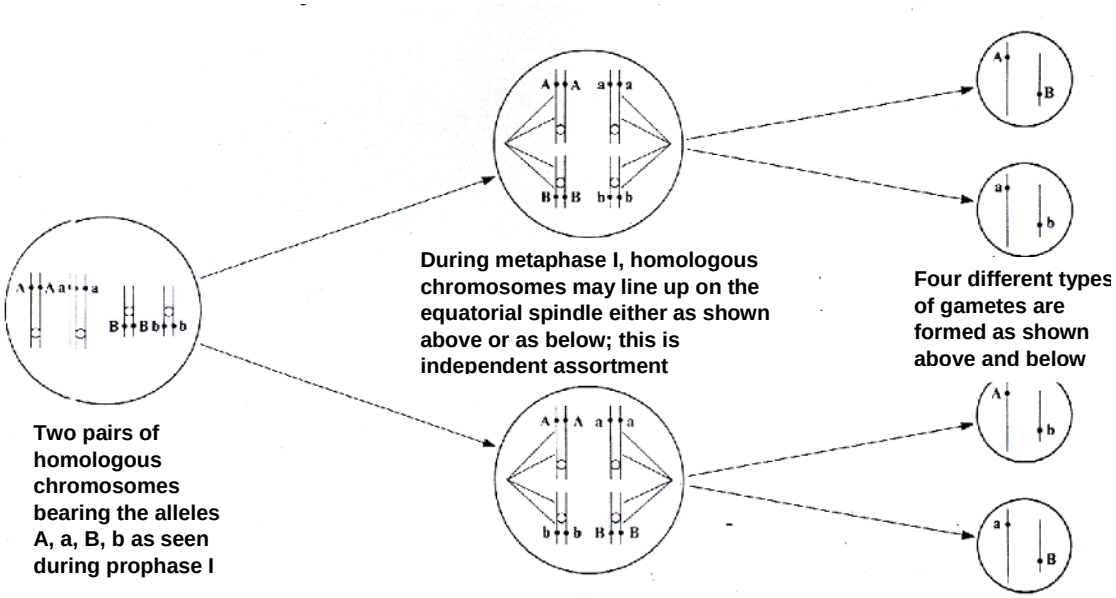
Law of Independent Assortment

The alleles of different genes on different pairs of chromosomes ***assort independently*** of each other.

This is because:

- Alignment of each homologous pair along the metaphase plate is independent of other pairs of homologous chromosomes during metaphase I

This gives rise to different recombination of paternal and maternal chromosomes and therefore different combination of alleles in the gametes as shown in the figure below:



Mendel's Law of Independent Assortment

Q. When do alleles not segregate independently from each other?

Notes to self

Q. True-breeding flies that have long wings and dark bodies are mated to true-breeding flies with short wings and tan bodies. All the F_1 have long wings and tan bodies. The F_1 are allowed to mate and the outcome is:

88 tan, long
32 dark, long
28 tan, short
12 dark, short

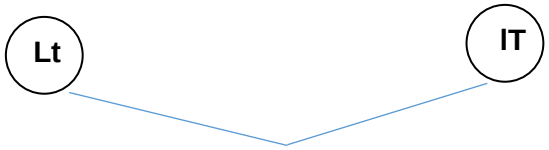
Which alleles are dominant? _____

Show the ratios of the genotypes and phenotypes obtained in all the crosses described above.

Let: **L** represents the dominant allele for long wing
l represents the recessive allele for short wing
T represents the dominant allele for tan bodies
t represents the recessive allele for dark bodies

Parental phenotype	Long wing, dark body	X	Short wing, tan body
Parental genotype	LLtt	X	llTT

Meiosis
Gametes



Fertilisation
F_1 genotype LlTt
F_1 phenotype Long wing tan body

F_1 selfing

F_1 phenotype	Long wing, tan body	X	Long wing, tan body
F_1 genotype	LlTt	X	LlTt

Meiosis
Gametes

Fertilisation

Notes to self

		Gametes			
		LT	**Lt**	**IT**	**It**
Gametes	**LT**	LLTT Long wing, tan body	LLTt Long wing, tan body	LlTT Long wing, tan body	LlTt Long wing, tan body
	Lt	LLTt Long wing, tan body	LLtt Long wing, dark body	LlTt Long wing, tan body	Lltt Long wing, dark body
	IT	LlTT Long wing, tan body	LlTt Long wing, tan body	llTT Short wing, tan body	llTt Short wing, tan body
	It	LlTt Long wing, tan body	Lltt Long wing, dark body	llTt Short wing, tan body	lltt Short wing, dark body

F_2 genotypic ratio 9 L_T_ : 3 L_tt : 3 llT_ : 1 lltt

F_2 phenotypic ratio 9 Long wing, tan body : 3 Long wing, dark body : 3 Short wing, tan body : 1 short wing, dark body

Q. What is the result of the test cross of the flies with the genotype LlTt?

(Recall: test cross refers to a cross with a homozygous recessive individual i.e. **LlTt X lltt**)

Parental phenotype Long wing, tan body X Short wing, dark body
Parental genotype LlTt X lltt

Meiosis
Gametes **LT** **Lt** **IT** **It** **It**

Fertilisation

Gametes	**LT**	**Lt**	**IT**	**It**
It	LlTt Long wing, tan body	Lltt Long wing, dark body	llTt short wing, tan body	lltt short wing, dark body

Genotypic ratio 1 LlTt : 1 Lltt : 1 llTt : 1 lltt
Phenotypic ratio 1 long wing tan body : 1 long wing dark body : 1 short wing tan body : 1 short wing dark body

Note: Important ratios in **complete dominance dihybrid cross**

Notes to self

- When both individuals are heterozygote for both genes are crossed
  e.g. LlTt X LlTt → offspring phenotypic ratio **9 : 3 : 3 : 1**

- When an individual heterozygote for both genes is test crossed
  e.g. LlTt X lltt → offspring phenotypic ratio **1 : 1 : 1 : 1**

10. Other Allelic Interactions

a. Multiple Alleles

Condition where a single characteristic appears in several different forms as it is controlled by **three or more alleles**, of which any *two* may occupy the *same locus* on homologous chromosomes.

Example 1: Control of ABO blood group in humans

- Inheritance of blood group in humans is controlled by an **autosomal** gene.
- Blood group with gene locus represented by the symbol **I** with 3 alleles: $\mathbf{I^A}$, $\mathbf{I^B}$ and $\mathbf{I^o}$.
- $\mathbf{I^A}$ and $\mathbf{I^B}$ are dominant to $\mathbf{I^o}$.
- $\mathbf{I^A}$ and $\mathbf{I^B}$ are codominant (which means that both alleles are **equally expressed** in the phenotype).

Genotype	Phenotype	Genotype	Phenotype
I^OI^O	Type O	I^BI^O	Type B
I^AI^O	Type A	I^BI^B	Type B
I^AI^A	Type A	I^AI^B	Type AB

Example 2: Coat colour of rabbit

A multiple allele system determines coat colour in the rabbit. There are four alleles of the c gene – wild type ***C*** (grey), chinchilla $\boldsymbol{c^{ch}}$ (silvery grey), Himalayan $\boldsymbol{c^h}$ (white with black extremities such as ears, feet, nose and tail) and albino ***c***.

The wild type allele called agouti is completely dominant over the other three alleles; the chinchilla allele is partially dominant over Himalayan and albino alleles, and the himalayan allele is completely dominant over albino. The dominance relations can be summarized as:

$$\boldsymbol{C > c^{ch} > c^h > c}$$

Pair of alleles can be combined with each other to make six different kinds of heterozygotes.

b. Codominance

Notes to self

In codominance, *both alleles* of a gene are *equally* expressed in the phenotype of a heterozygote.

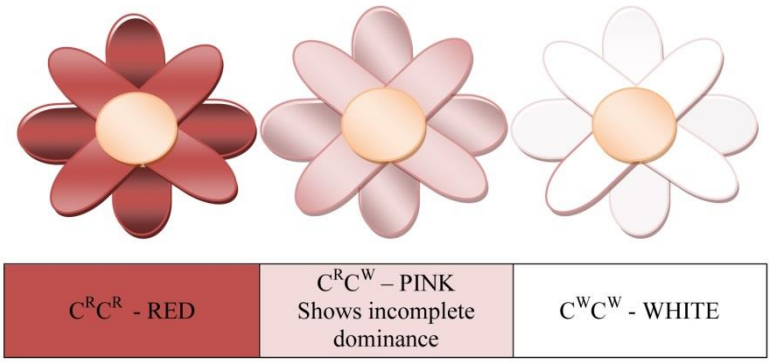
Example 1: The blood group system in human, where I^A and I^B is codominant. Four blood groups possible - A, B, AB and O.

Note:
- Codominance results in more than two traits for a particular gene
- The effects of both alleles can be detected in the phenotype of heterozygote
- Genotypic and phenotypic ratio in **codominant** monohybrid cross involving a heterozygote crossing with heterozygote:
  e.g. I^AI^B X $I^AI^B \rightarrow I^AI^A : 2\ I^AI^B : I^BI^B \rightarrow$ **1 : 2 : 1**

c. Incomplete Dominance

Incomplete dominance results in an **intermediate** expression of a trait in heterozygous individuals.

For instance, in primroses, snapdragons, and four-o'clocks, red or white flowers are homozygous while pink ones are heterozygous. The pink flowers result because the single "red" allele is unable to code for the production of enough red pigment to make the petals dark red.



Note:
- Genotypic and phenotypic ratio in **incomplete dominance** monohybrid cross involving a heterozygote crossing with heterozygote:
  e.g. C^RC^W X $C^RC^W \rightarrow C^RC^R : 2\ C^RC^W : C^WC^W \rightarrow$ **1 red : 2 pink : 1 white**

d. Lethal Alleles

A lethal allele is an allele that causes death of an organism which is homozygous for that allele.

Organisms carrying these alleles are disadvantaged through impaired biochemical or physical functioning.

Example:
In chickens, Dominant allele (C) in chickens is responsible for profound developmental changes that result in aberrant forms called 'creepers'. These birds have short, crooked legs. Homozygous genotype (CC) is lethal.

Monohybrid cross involving lethal alleles:
Let **C** represent allele for creeper chicken.
Let **c'** represent allele for normal chicken

Parental phenotypes	Creeper	X	Creeper
Parental genotypes	Cc'	X	Cc'

Meiosis

Gametes: **C** **c'** **C** **c'**

Fertilisation

Gametes	**C**	**c'**
C	**CC** **Dies**	**Cc'** **Creeper**
c'	**Cc'** **Creeper**	**c'c'** **Normal**

Offspring genotypes	CC	Cc'	Cc'	c'c'
Offspring phenotypes	(Dies- no phenotype)	Creeper	Creeper	Normal
Offspring phenotypic ratio		2 creeper	:	1 normal

A **2:1 phenotypic ratio** is obtained instead of the 3:1 phenotypic ratio because the CC homozygous embryos die.

Note:
Such a deviation from the standard Mendelian ratios indicates that the gene of interest may be a lethal gene.

Q. Wild mice have grey-colored fur, known as agouti. Some mice have yellow fur.

Crossing yellow mice produces offspring in the ratio of 2 yellow: 1 agouti

Show the cross between two yellow mice in the space below.

(Note: you need to determine which if the dominant allele codes for yellow or agouti fur.)

Let **A** represent the allele for yellow fur.
Let **a** represent allele for agouti fur.

Parental phenotypes	Yellow fur	X	Yellow fur
Parental genotypes	Aa	X	Aa
Meiosis Gametes	(A) (a)		(A) (a)

Fertilisation

		Gametes	
		(A)	(a)
Gametes	(A)	**AA** **Dies**	**Aa** **Yellow fur**
	(a)	**Aa** **Yellow fur**	**aa** **Agouti fur**

Offspring Genotypes:	AA	Aa	Aa	aa
Offspring phenotypes:	(Dies- no phenotype)	Yellow fur	Yellow fur	Agouti fur

Offspring phenotypic ratio: 2 yellow fur : 1 agouti fur

e. Sex Linkage

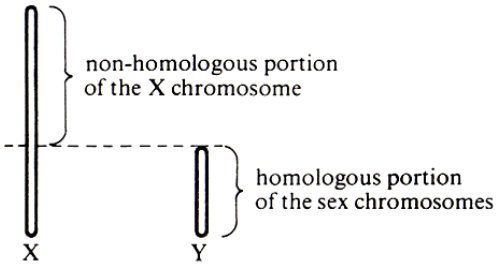
Notes to self

Sex linkage refers to genes that are carried on the sex chromosomes.

This results in a characteristic being expressed mainly in one sex.

In humans, sex linkage usually refers to **genes carried on the X chromosome** (**X-linkage**).

In the case of heterogametic chromosomes, there is a portion of the X chromosome for which there is no homologous region on the Y chromosome (as the Y chromosome is smaller than the X chromosome). .



Homologous and non-homologous regions of the sex chromosomes.

Characteristics determined by genes carried on the non-homologous portion of the X chromosome therefore appear in males even if they are recessive (as there is no dominant allele to mask the effect of the recessive allele).

Hence, these characteristics are **sex-linked**.

Sex-linked characteristics can be detected by their unique pattern of inheritance:
- the male offspring will only obtain these features from their mothers
- daughters get their sex-linked features from both parents

Example 1: Red-green color blindness – sex-linked, recessive condition

Let: $\mathbf{X^B}$ represent the female chromosome carrying the normal allele for colour vision.
$\mathbf{X^b}$ represent the female chromosome carrying the allele for colour blindness.
Y represent the male chromosome.

Genotype	Phenotype
$\mathbf{X^BX^B}$	Normal female
$\mathbf{X^BX^b}$	Normal female (carrier)
$\mathbf{X^BY}$	Normal male
$\mathbf{X^bY}$	Colour-blind male

Note: A carrier refers to the heterozygous female with normal phenotype.

Example 2: Haemophilia - sex-linked, recessive condition.

Let: X^H represent the female chromosome carrying the normal allele for blood clotting.
X^h represent the female chromosome carrying the allele for haemophilia.
Y represent the male chromosome.

Genotype	Phenotype
X^HX^H	Normal female
X^HX^h	Normal female (carrier)

Note:

- You need to know that haemophilia and colour blindness are sex-linked and recessive conditions.
- Males always inherit X chromosome thus the X-linked disease from his mother, since his Y chromosome is from his father.
- The recessive allele is exchanged from one sex to the other at each generation. This means that the father passes it to his daughters, who become carriers. The daughters may in turn pass it to their sons, who will be colour-blind or haemophilic.
- Homozygous recessive females can only arise from a cross if both parents carry a copy of the recessive allele.
- For humans, the males are **heterogametic** (sex chromosomes are not the same, i.e. XY) while the females are **homogametic** (sex chromosomes are the same, i.e. XX). However, this may not always be the case for other organisms, such as birds and some reptiles. In these organisms, the males are homogametic (sex chromosomes are ZZ) while the females are heterogametic (sex chromosomes are ZW).

Reciprocal cross

A reciprocal cross is used to determine if a particular characteristic is sex-linked. In a reciprocal cross, 2 separate crosses are conducted using the same characteristic but the sexes are reversed.

For example:
Cross 1: A true-breeding normal female crossed with colour-blind male
Cross 2: A true-breeding colour-blind female crossed with normal male

Analysing the phenotype of the offspring enables one to determine if the characteristic is sex-linked:

If the offspring phenotypic ratios of the reciprocal crosses are different, it shows that the colour blindness is sex-linked. If colour blindness is not sex-linked, the results of the reciprocal cross will be the same.

Cross 1

Parental phenotypes	normal female	X	colour-blind male
Parental genotypes	X^BX^B	X	X^bY

Meiosis
Gametes

Fertilisation

Gametes	X^b	Y
X^B	X^BX^b **Normal female**	X^BY **Normal male**
X^B	X^BX^b **Normal female (carrier)**	X^BY **Normal male**

Offspring genotypic ratio	1 X^BX^b	:	1 X^BY
Offspring phenotypic ratio	1 normal female	:	1 normal male

Cross 2

Parental phenotypes	colour-blind female	X	normal male
Parental genotypes	X^bX^b	X	X^BY

Meiosis
Gametes

Fertilisation

Gametes	X^B	Y
X^b	X^BX^b **Normal female (carrier)**	X^bY **Colour blind male**
X^b	X^BX^b **Normal female (carrier)**	X^bY **Colour blind male**

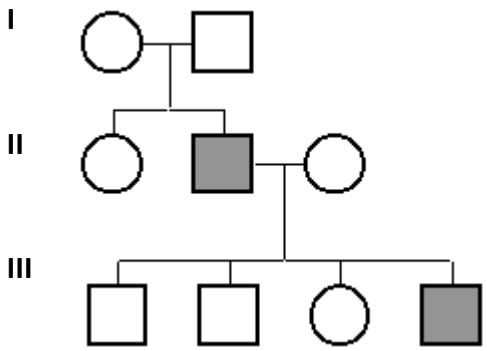
Offspring genotypic ratio	1 X^BX^b	:	1 X^bY
Offspring phenotypic ratio	1 normal female	:	1 colour-blind male

The offspring phenotypic ratio of both crosses are different, colour blindness is therefore sex-linked.

11. Pedigree Analysis

Notes to self

A pedigree is a diagram of family relationships that uses symbols to represent people and lines to represent genetic relationships. These diagrams make it easier to visualise relationships within families, particularly large extended families. Pedigrees are often used to determine the mode of inheritance (dominant, recessive, etc.) of genetic diseases. A sample pedigree is below.



Example of a pedigree.

In a pedigree, squares represent males and circles represent females. Horizontal lines connecting a male and female represent mating. Vertical lines extending downward from a couple represent their children. Subsequent generations are therefore written underneath the parental generations and the oldest individuals are found at the top of the pedigree.

If the purpose of a pedigree is to analyse the pattern of inheritance of a particular trait, it is customary to shade the symbol representing all individuals that possess this trait.

In the pedigree above, the grandparents had two children, a son and a daughter. The son had the trait in question. One of his four children (male) also had the trait.