

Inheritance

A-Level Biology 9700 · Topic 16 revision notes

Everything from the 5 lessons of this topic on a few pages: the key idea of each lesson, the diagram to remember, the points to learn and the traps examiners set. Read it, cover it, test yourself.

1. Meiosis and genetic variation

2. Monohybrid and dihybrid crosses

3. The chi-squared test

4. Genes, proteins and phenotype

5. Gene control

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1 Meiosis and genetic variation

Syllabus 16.1

A **diploid ($2n$)** cell has two complete sets of chromosomes, one set from each parent; a **haploid (n)** cell has one set. The two chromosomes of a **homologous pair** have the same genes at the same loci (but possibly different alleles), the same length and the same centromere position. Gametes must be haploid so that fertilisation restores the diploid number instead of doubling it each generation, so they are made by **meiosis**, a **reduction division**. In **meiosis I** homologous chromosomes pair up and are separated; in **meiosis II** sister chromatids are separated, giving **four haploid cells**. Gametes differ genetically because of **crossing over** between non-sister chromatids in prophase I, **independent assortment** (random orientation) of homologous pairs at metaphase I and of sister chromatids at metaphase II, and then **random fertilisation**.

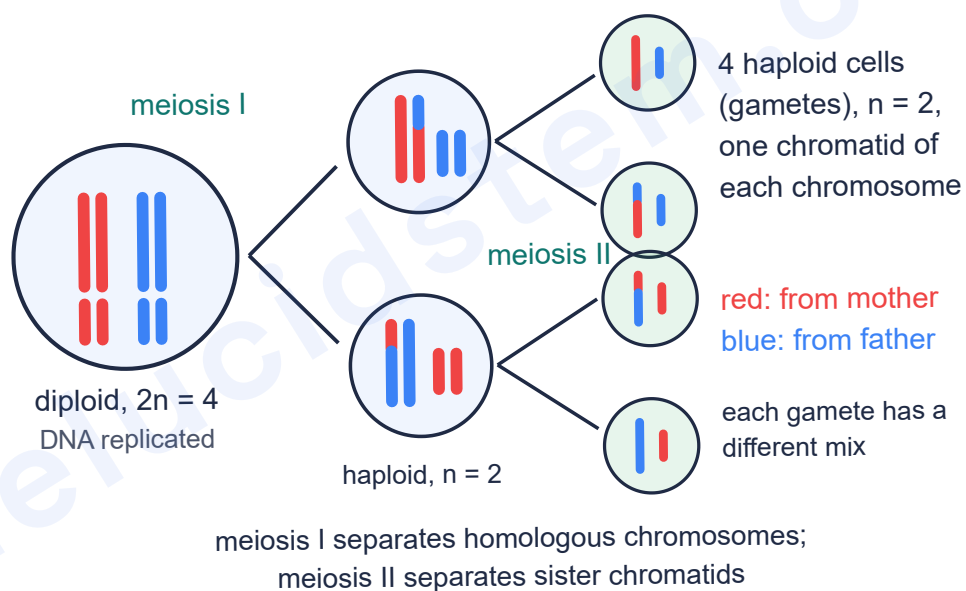


Fig. 1: meiosis in a cell with two homologous pairs ($2n = 4$) makes four genetically different haploid cells

Pairs, then chromatids.

- ✓ **Meiosis I** separates homologous chromosomes: $2n$ becomes n .
- ✓ **Meiosis II** separates sister chromatids, as in mitosis.
- ✓ **Crossing over:** non-sister chromatids, prophase I, chiasmata.
- ✓ **Combinations:** 2^n gametes; random fertilisation multiplies them.

Watch out!

Do not mix up the two anaphases. In **anaphase I** whole **homologous chromosomes** separate (each still has two chromatids); in **anaphase II** the **sister chromatids** separate, just as in mitosis. The chromosome number halves in meiosis I, not meiosis II.

Crossing over happens between **non-sister** chromatids of a **homologous pair**, in **prophase I**. Sister chromatids are identical copies, so swapping between them would change nothing.

2 Monohybrid and dihybrid crosses

Syllabus 16.2

A **gene** is a length of DNA at a fixed position, its **locus**, coding for a polypeptide; **alleles** are different versions of it. The **genotype** is the alleles present (**homozygous** if the two are the same, **heterozygous** if different) and the **phenotype** is the observable feature. A **dominant** allele is expressed in the heterozygote; a **recessive** one only when homozygous; **codominant** alleles are both expressed. In a **genetic diagram**, write parental phenotypes and genotypes, gametes (one allele of each gene per gamete), a Punnett square, then offspring genotypes, phenotypes and ratio. A monohybrid cross of two heterozygotes gives 3 : 1; a dihybrid cross of two double heterozygotes gives **9 : 3 : 3 : 1** if the genes assort independently. A **test cross** with a homozygous recessive reveals an unknown genotype. **Autosomal linkage** (genes on the same chromosome) and **epistasis** (one gene affecting the expression of another) change the expected ratios.

parents: carrier mother $X^H X^h$ × unaffected father $X^H Y$

F8 gene on the X chromosome; H normal, h haemophilia (recessive)

		female gametes	
		X^H	X^h
male gametes	X^H	$X^H X^H$ normal female	$X^H X^h$ carrier female
	Y	$X^H Y$ normal male	$X^h Y$ haemophiliac male

each son has a 1 in 2 chance of haemophilia;
each daughter has a 1 in 2 chance of being a carrier

Fig. 1: a sex-linked cross for haemophilia; alleles are written as superscripts on the X chromosome

One allele per gene per gamete.

- ✓ **Layout:** phenotypes, genotypes, gametes, Punnett square, offspring, ratio.
- ✓ **Codominant and sex-linked alleles** are written as superscripts.
- ✓ **Test cross:** with the homozygous recessive; offspring mirror the gametes.
- ✓ **Linkage:** few recombinants; **epistasis:** one gene masks another.

Watch out!

Write a full genetic diagram: **parental phenotypes, parental genotypes, gametes (one allele of each gene), Punnett square, offspring genotypes and phenotypes, ratio.** For sex-linked genes always attach the allele to the X, and give the Y no allele.

Linkage means two genes on the **same chromosome**; sex linkage means one gene on the **X chromosome**. Do not use the words interchangeably.

3 The chi-squared test

Syllabus 16.2

The **chi-squared (χ^2) test** compares **observed (O)** numbers in each category with the **expected (E)** numbers predicted by a genetic ratio. Start with a **null hypothesis**: there is no significant difference between observed and expected results, and any difference is due to chance. Calculate E from the total and the ratio, then $\chi^2 = \sum (O - E)^2 / E$ (the formula is provided). Find the **degrees of freedom** = number of categories - 1, and compare χ^2 with the **critical value at $p = 0.05$** from the table. If χ^2 is **less than** the critical value, the difference is **not significant** and the null hypothesis is accepted; if it is **greater**, the difference is **significant** (probability less than 0.05 of arising by chance), so the null hypothesis is rejected and something else, such as linkage or epistasis, may be operating.

test cross AaBb $\times$ aabb, 200 offspring, expected 1 : 1 : 1 : 1

phenotype	O	E	O - E	(O - E) ² / E
AB (dominant both)	56	50	+6	0.72
Ab	44	50	-6	0.72
aB	47	50	-3	0.18
ab (recessive both)	53	50	+3	0.18

$$\chi^2 = \sum (O - E)^2 / E$$

1.80

degrees of freedom = 4 - 1 = 3; critical value at $p = 0.05$ is 7.82

1.80 is below 7.82: not significant, the data fit 1 : 1 : 1 : 1

Fig. 1: a worked chi-squared test for a dihybrid test cross

Five steps, every time.

- ✓ **State** the null hypothesis: no significant difference.
- ✓ **Expected** numbers = total $\times$ fraction for each class.
- ✓ **Degrees of freedom** = number of classes - 1.
- ✓ **Compare** with the critical value at $p = 0.05$, then conclude.

Watch out!

Always use the actual **numbers** of offspring for O and E, never percentages or ratios. And E does not have to be a whole number: $100 \times 3/4 = 75$, but $50 \times 3/4 = 37.5$ is fine.

A non-significant result does not prove the hypothesis is true; it means the data are **consistent with** it. Say "the difference is not significant" rather than "there is no difference".

4 Genes, proteins and phenotype

Syllabus 16.2

A gene's **base sequence** determines the **amino acid sequence** of a polypeptide, which determines how it folds and so its **function**; the protein's activity then produces the **phenotype**. The **TYR** gene codes for **tyrosinase**, which converts tyrosine to melanin; a recessive allele gives a non-functional enzyme and **albinism**. The **HBB** gene codes for β -globin; a single base substitution replaces glutamic acid with valine, giving HbS, which forms fibres at low oxygen and causes **sickle cell anaemia**. The **F8** gene on the X chromosome codes for clotting **factor VIII**; a recessive allele causes **haemophilia**. The **HTT** gene codes for **huntingtin**; a dominant allele with too many CAG repeats causes **Huntington's disease**. In peas, the dominant allele **Le** codes for a functional enzyme that makes active **gibberellin** (GA₁), which causes **stem elongation**; **lele** plants make a non-functional enzyme and are dwarf.

gene	protein made	mutant allele	phenotype
TYR	tyrosinase	recessive, no working enzyme	albinism (no melanin)
HBB	β -globin of haemoglobin	codominant; one base change, glu $\rightarrow$ val	sickle cell anaemia
F8	factor VIII (clotting)	recessive, on the X chromosome	haemophilia (slow clotting)
HTT	huntingtin (in neurones)	dominant, extra CAG repeats	Huntington's disease

gene $\rightarrow$ amino acid sequence $\rightarrow$ protein shape $\rightarrow$ function $\rightarrow$ phenotype

Fig. 1: Four human genes, the proteins they code for and the phenotype of the mutant allele

Follow the chain.

- ✓ **TYR** tyrosinase, albinism; **HBB** β -globin, sickle cell.
- ✓ **F8** factor VIII, haemophilia (X-linked); **HTT** huntingtin, dominant.
- ✓ **Le** codes for the enzyme $GA_{20} \rightarrow GA_1$; lele plants are dwarf.
- ✓ **Every answer:** bases, amino acids, shape, function, phenotype.

Watch out!

Link every step: **gene** $\rightarrow$ **base sequence** $\rightarrow$ **amino acid sequence (primary structure)** $\rightarrow$ **folding and shape** $\rightarrow$ **protein function** $\rightarrow$ **phenotype**. Marks are lost when an answer jumps straight from "mutation" to "disease".

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5 Gene control

Syllabus 16.3

Structural genes code for proteins with a function in the cell, such as enzymes; **regulatory genes** code for proteins, such as repressors and transcription factors, that control the expression of other genes. An **inducible enzyme** is made only when its substrate is present (β -galactosidase in *E. coli*); a **repressible enzyme** is made until its product builds up and switches its synthesis off (the enzymes that make tryptophan). In the **lac operon**, the regulatory gene **lacI** codes for a **repressor** that binds the **operator**, so RNA polymerase cannot bind the **promoter** and the structural genes **lacZ**, **lacY** and **lacA** are not transcribed. **Lactose** binds the repressor, changing its shape so it leaves the operator, and the genes are transcribed. In eukaryotes, **transcription factors** are proteins that bind to DNA and increase or decrease the rate of transcription. **Gibberellin** binds a receptor and causes **DELLA proteins** to be broken down; DELLA proteins normally inhibit transcription factors, so their removal lets transcription of growth genes begin.

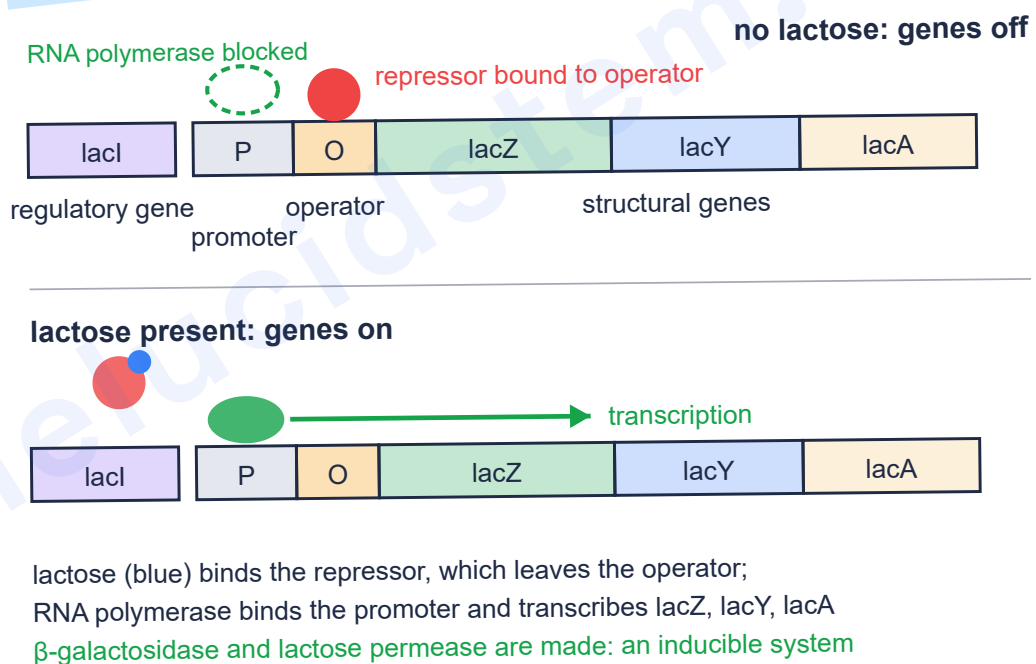


Fig. 1: the lac operon of *E. coli* with and without lactose

Who binds what.

- ✓ **Repressor** binds the operator; **RNA polymerase** binds the promoter.
- ✓ **Lactose** binds the repressor; an inducible system.
- ✓ **Transcription factors** are proteins that raise or lower transcription rate.
- ✓ **Gibberellin** causes DELLA breakdown, freeing transcription factors.

Watch out!

The repressor binds the **operator**, not the promoter, and lactose binds the **repressor**, not the DNA. The repressor is coded for by the **regulatory gene lacI**, which is not one of the structural genes.

Gibberellin does not bind to DNA and is not a transcription factor itself. It acts indirectly: it causes the **breakdown of DELLA**, and that frees the transcription factors.