F215 Control, genomes and environment

Unit 5: Cellular control and variation

DNA and Protein Synthesis

DNA comprises the monomers, **nucleotides**, which themselves comprise the deoxyribose sugar and phosphate group (making the sugar-phosphate backbone) and nitrogenous bases: adenine which has an affinity for thymine, and cytosine for guanine. DNA contains thousands of **genes** which are lengths of DNA coding for polypeptides. DNA has a **triplet code**, whereby every three bases codes for one **amino acid** at protein synthesis

During **transcription** a single-stranded (RNA) copy of a gene to be *expressed* is produced, called **mRNA** (messenger RNA) which contains the appropriate coding for a gene. The **coding strand** of DNA is identical to the mRNA strand, and the **template strand** (used to create the mRNA) is complementary to the coding strand. The DNA double helix unwinds and unzips, as with replication, and **RNA polymerase** builds the mRNA strand from the template strand

The next step is **translation**, which uses the mRNA strand to express a protein. Each **codon** triplet on the mRNA corresponds to a complementary **anticodon** on a **tRNA** (transfer RNA) molecule. These tRNA molecules carry specific amino acids with them, also. As the mRNA strand enters the **ribosome**, beginning with AUG, the tRNA with the complementary anticodon (UAC) binds to the site, bringing with it the right amino acid (in this case methionine). When the next one comes along, matching the second codon on the mRNA strand, a **peptide bond** forms between the two amino acids, and the previous tRNA dissociates. This continues, forming a long **polypeptide** chain

Mutations

DNA **mutations** can occur at any time during DNA replication, by mitosis or meiosis. There are several types:

- **substitutions** (or **point mutations**) involve one base pair replacing another – only one pair changes
- **insertions** and **deletions** involve either introducing an extra base pair or removing a base pair from the sequence, which causes a **frameshift** (alteration in the entire sequence, so all of the triplet codes move)

Point mutations tend to be **silent mutations**, which have no effect on the actual coding. For example, the codons CTA and CTT both code for the same amino acid, so the mutation changing the 'A' to a 'T' is silent

Many mutations can be **neutral**, where despite a change in the coding, the effects are neither beneficial or harmful to the organism; but some can be **positive** (beneficial) or **negative** (harmful)

Apoptosis

The term **apoptosis** refers to literally 'programmed cell death' and it is a series of biochemical events leading to the tidy death of a cell in a way which does not harm neighbouring cells, as opposed to **cellular necrosis** which is the improper or unexpected death of cells which proves harmful in most cases

1. enzymes break down the cell's cytoskeleton
2. cell surface membrane creates folds and the bits that stick out are called **blebs**
3. chromatin from within the nucleus condenses and the nuclear envelope breaks down, and the DNA breaks into separated **nuclear fragments** which disperse among the cell
4. the cell packages all of its contents into vesicles
5. the vesicles are taken up by **phagocytes** and cellular debris is disposed of without harming neighbouring cells

Apoptosis is usually induced by signals from other cells, including **cytokines** of the immune system, and hormones such as **nitric oxide**, which induces apoptosis by making mitochondrial membranes more permeable to hydrogen ions, breaking down the carefully balanced chemiosmotic gradient which had been established

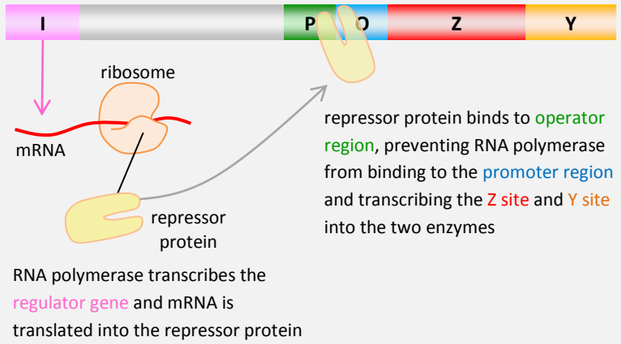
Cells with damaged DNA (or mutations) may not respond at all to these signals, and therefore may not undergo apoptosis, which can lead to the development of **tumours**. These are able to break away from their initial sites and enter the blood or lymph systems (this is called **metastasis**) where they can form **secondary cancers**

Apoptosis is particularly important during development when mitotic divisions are important. Generally, a cell will undergo 50 mitotic divisions on average before apoptosis takes place

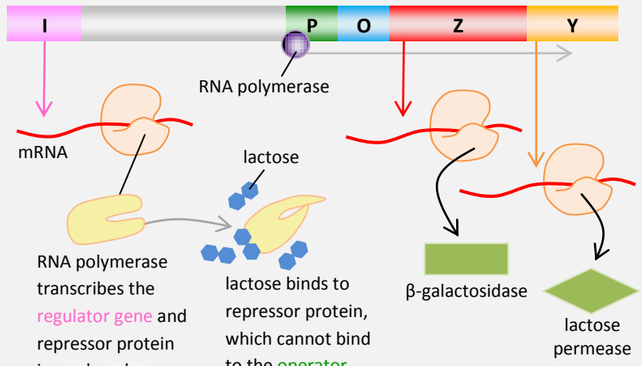
The *lac* Operon

The bacterium *E. coli* requires two enzymes, **lactose permease** (to transport lactose into the bacterial cell) and **β-galactosidase** (to break down lactose into galactose and glucose), in order to respire the carbohydrate **lactose**. Interestingly, when *E. coli* grows in environments lacking lactose, the bacteria do not produce these two enzymes, as they are unnecessary, but when it is present, the two enzymes are in abundant supply

The ***lac* operon** is a DNA **operon** (length of DNA comprising **structural genes**, in this case the Z and Y sites, and **control sites**, in this case the **regulator gene**, **promoter region** and **operator region**). Whether lactose is present or not, the regulator gene always expresses the **repressor protein**



When lactose is *absent* (left), the repressor protein is able to bind itself to the operon to the promoter region, also covering part of the operator region. This means that the enzyme **RNA polymerase** is prevented from binding to the operon at the operator region, and so cannot transcribe the Z and Y genes (which code for the two enzymes).

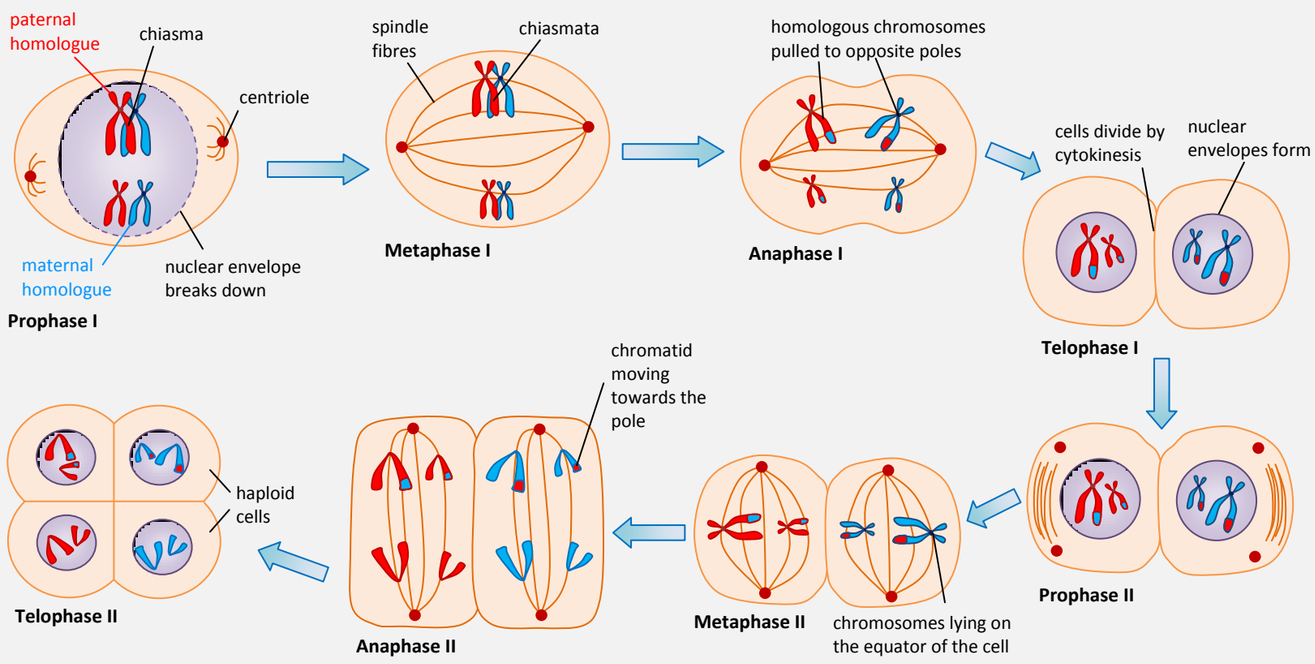


When lactose is *present* (right), the repressor protein is produced as normal, but lactose binds to sites on the protein molecule, which causes the shape of the repressor protein to change. Therefore it cannot bind to the operon, and so RNA polymerase is able to attach at the operator region and transcribe the mRNA for both lactose permease and β-galactosidase

The obvious benefit of the *lac* operon is that energy and resources are not wasted producing enzymes which have no use

Meiosis

The process to produce **gametes** (sex cells) is **meiosis**. Two gametes will fuse at fertilisation to form a **zygote** where chromosomes from each **haploid** parent cell (containing half the number of adult chromosomes, *n*) become one nucleus in the daughter cell (a **diploid** cell, 2*n*)



Meiosis and Variation

- **prophase I** – chromosomes shorten and fatten (**supercoil**) and come together in homologous pairs to form a **bivalent**, and the chromatids wrap around each other at points called **chiasmata** where they may break and swap various sections of DNA
- **metaphase I** – centromeres attach to the spindle fibres and bivalents arrange themselves along the equator
- **anaphase I** – one of each homologous pair is pulled by the spindle to opposite poles of the cell by the centrioles
- **telophase I** – the nuclear envelope reforms around the chromosomes at each pole and the cell begins **cytokinetic** division
- **prophase II** – nuclear envelope breaks down again, chromosomes supercoil and spindle fibres begin to form
- **metaphase II** – chromosomes arrange themselves on the equator of each cell and are attached to the spindle by their centromeres
- **anaphase II** – the centromeres divide and chromatids are pulled to opposite poles by the spindle fibres and randomly segregate
- **telophase II** – a **tetrad** of four haploid cells is formed as cells divide by cytokinesis and nuclear envelopes reform

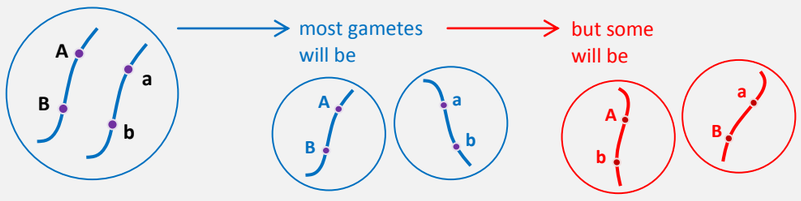
Meiosis introduces genetic variation in four main ways:

- through **crossing over** during prophase I where chromosomal pairs line up and chiasmata appear as they wrap around each other tightly, breaking down the ends of the chromatids so that **non-sister** chromatids can swap **alleles** with each other
- through **genetic reassortment** (random distribution of chromosomes at meiosis I and segregation of chromatids at meiosis II)
- through random **mutation**
- through random fertilisation (only one sperm of 300 million actually will fertilise the egg cell and contribute to the DNA)

Genetics

The **genotype** of an organism refers to the precise *genetic makeup* in terms of the **alleles** it contains. The **phenotype** is the observable characteristic which is the outcome of those alleles. Alleles can be either **dominant** (whereby only one allele is necessary for the trait to be expressed) or **recessive** (whereby both are needed). Those with the same alleles for a phenotype are described as **homozygous**

Alleles can be **codominant** when different alleles share dominance, and when both present they both contribute towards the phenotype, such as in cattle: red poll cattle and white shorthorn can have *roan* calves (a mixture of the two). A **dihybrid cross** can be used to show this. During this, the **F_1 hybrid** shows the possible genotypes of the first generation of offspring. Most linked genes are found on the **autosomes** (chromosomes not responsible for determining sex), but some are **sex-linked genes**



Take this example, where most gametes will have the *AB* or *ab* alleles. However, due to crossing over during prophase I (meiosis I), some alleles can be shuffled between chromosomes, and so some gametes may be *Ab* or *aB*, which are **recombinant genes**

One of the genes for coat colour in cats is sex-linked on the X chromosome. The allele **C^O** gives orange fur, while **C^B** gives black fur. The two are codominant, and when both are present a cat's fur appears tortoiseshell.

We know male cats cannot be tortoiseshell because the alleles are linked to genes on the X chromosome, so in order to be tortoiseshell, a cat needs to have two X chromosomes to have both C^O and C^B – which is not possible for males, as they are heterogametic (have different sex chromosomes, XY) – only possible in females, who have two X chromosomes to be tortoiseshell

Let's see what happens if we do a cross between an orange-coated male and a tortoiseshell female cat:

parental phenotype	orange male	x	tortoiseshell female
parental genotype:	XC^O, Y	x	XC^O, XC^B
gamete opportunities:	**XC^O** (**Y**)	x	**XC^O** **XC^B**
F_1 genotypes:	XC^OXC^O + XC^OXC^B + XC^OY + XC^BY		

		Tortoiseshell female	
		XC^O	**XC^B**
Orange male	**XC^O**	XC^O XC^O	XC^O XC^B
	Y	XC^O Y	XC^B Y

The table and the above cross demonstrates that the cross will produce males around half the time and females equally. Half of those males will have an orange coat, and the others black; we can also tell that half the potential females would have an orange coat (**C^OC^O**) and half would be tortoiseshell (**C^OC^B**)

Alternatively to hybrid crosses, a **family pedigree** can be drawn to work out the genotypes of particular individuals within a family. An example might be to look at a family of sufferers of *DMD* (Duchenne muscular dystrophy), a condition which occurs where there is a mutation or improper expression of the **dystrophin** gene (associated with the X-chromosome)

Epistasis

Epistasis is different from codominance: this is where one gene masks or suppresses the expression of another. With **recessive epistasis**, if the first gene is not expressed (due to recessive alleles), the second gene *cannot* be expressed (whether it is dominant or recessive):

- when the genotype is *AABB*, both genes will be expressed as the first is dominant, as is the second
- when the genotype is *Aabb*, the first is expressed only as the second is recessive
- when the genotype is *aabb* or *aaBB*, neither are expression as the first one must be expressed for the second to be

With **dominant epistasis**, if the first gene is expressed, it masks the second gene, so it cannot be expressed:

- when the genotype is *aaBB*, the second gene only is expressed as it is not masked by the first gene
- when the genotype is *AAbb* or *AABB*, the first gene only is expressed, as it masks the second regardless of its status
- when the genotype is *aabb*, neither of the two are expressed (an alternative route, usually)

Epistasis can work in a complementary fashion, whereby gene *A* codes for an enzyme which makes a precursor molecule which is needed by enzyme *B* to produce a desired molecule

Population Genetics and Genetic Variation

Variation can be **continuous** (non-categorical, such as height or body mass) or **discontinuous** (categorical, such as gender). Whilst both can be influenced by multiple alleles, we know that discontinuous variations must behave in an epistatic way if multiple alleles affect a phenotype. Many characteristics will have **environmental influences** as well as biological bases

The **biological species concept** suggests that a **species** is a group of organisms which can successfully interbreed to produce fertile offspring and are reproductively isolated from other organisms. The **phylogenetic species concept** suggests a species is a group of organisms which share similar physiological, behavioural, adaptive and embryological features, and occupy a similar ecological niche

Genetic drift occurs when the frequency of alleles within a population changes over time. This can lead to the elimination of an allele from a population altogether, and can contribute towards the extinction of a species or the introduction of a new species. Because we observe phenotype and not genotype, it is difficult to study alleles, we need to know genetic mechanisms involved

The **Hardy-Weinberg principle** suggests that the frequency of alleles in a population remains stable over time provided the population is large in size, there is no migration, little mutation and genetic drift and that no particular genotypes are advantageous. It comes with two formulae which can be used (where p = dominant alleles and q = recessive alleles)

- Within a population, the frequency of alleles is calculated using: $p + q = 1$
- Within a population, the frequency of genotypes is calculated using: $p^2 + 2pq + q^2 = 1$

frequency of homozygous dominant | frequency of heterozygous dominant | frequency of homozygous recessive

Natural and Artificial Selection

Natural selection is the driving force of evolution, which is the result of **selection pressures** in the wild on organisms. By the laws of natural selection, advantageous phenotypes are passed onto offspring, allowing greater survival chances in competitive environments. **Artificial selection** involves the use of man-made selection pressures to produce 'favourable' organisms

Artificial selection to create the modern dairy cow:

- quantity and quality of milk produced by cows and the progeny of bulls can be measured and recorded
- elite cows may be given hormones to produce many eggs, and favourable bulls' sperm are used for insemination
- eggs are fertilised **in vitro** (test tube) and embryos implanted into a surrogate mother
- can be cloned and divided to produce even more favourable offspring

Artificial selection to create modern **bread wheat**:

- a wild einkorn (*AA*) and a wild goat grass (*BB*) are crossed many times to produce a hybrid (*AB*)
- hybrid is unable to produce gametes, given its genotype, until a random **polyploidy** (doubling of the diploid nucleus) – *AABB*
- this emmer wheat (*AABB*) is crossed with another wild grass species (*CC*) to produce a hybrid (*ABC*) which again is unable to produce gametes, until a further random polyploidy to produce a **hexaploid** fertile bread wheat (*AABBCC*)
- due to continuous artificial selection techniques, the characteristics of this modern crop are constantly improving