GENETICS

Genetic terminology

1. Trait
- Any characteristic that can be passed from parent to offspring
2. Heredity
- Passing of traits from parent to offspring
3. Genetics
- Study of heredity

Genetic terminology cont'd

4. Alleles
- Two forms of a gene i.e. dominant and recessive
5. Gene
- A gene is a sequence of nucleotides in DNA which is concerned with synthesis of RNA

Genetic terminology cont'd

6. Genotype
- Gene combination for a trait
7. Phenotype
- The physical feature resulting from a genotype

MENDEL'S LAWS

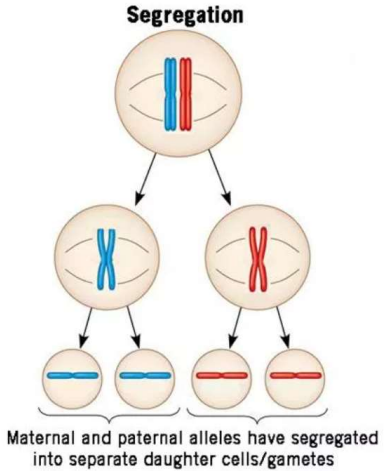
- Inheritable factors or genes are responsible for all heritable characteristics
- Phenotype is based on genotype
- Each trait is based on two genes, one from the mother and the other from the father

Mendel's law of segregation

- During the formation of gametes (ova and sperms), the alleles for each gene segregate from each other such that each gamete formed carries only one allele for each gene
- Alleles for a trait are then recombined at fertilization, producing the genotype for the traits of the offspring

Mendel's law of dominance

- In a cross of parents that are pure for contrasting traits, only one form of the trait will appear in the next generation
- All the offspring will be heterozygous and express only the dominant trait

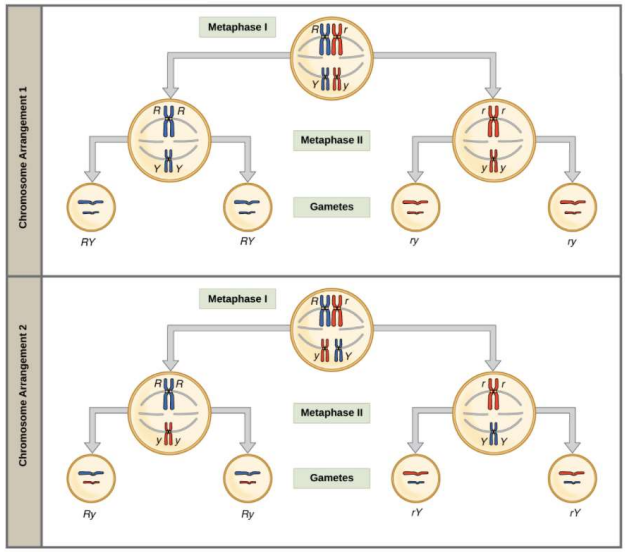


Mendel's law of independent assortment

- Alleles for different traits are distributed to sex cells and (offspring) independently of one another

DNA, Genes and Chromosomes

1. Genetic material of both eukaryotes and prokaryotes is DNA (deoxyribonucleic acid).
2. DNA has two chains, each made of nucleotides composed of a deoxyribose sugar, a phosphate group and a base.
3. The chains form a double helix

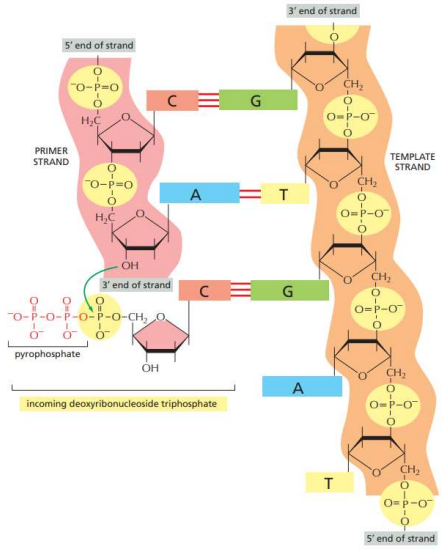


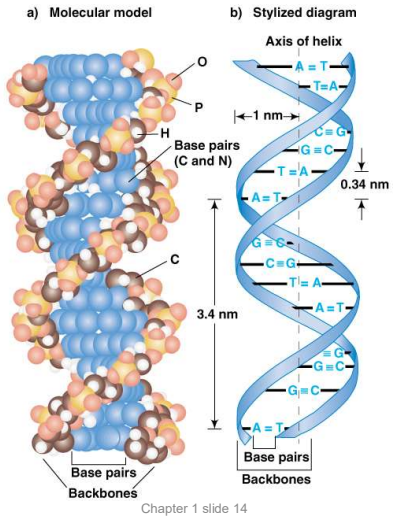
DNA

- There are four bases in DNA
  - A - adenine
  - G - guanine
  - C - cytosine
  - T - thymine
- In RNA, U (uracil) replaces T

A = T G ≡ C

T = A C ≡ G





DNA cont'd

- The sequence of bases determines the genetic information.
- Genes are specific sequences of nucleotides that pass traits from parents to offspring.

Chromosomes

- Genetic material in cells is organized into chromosomes
- Eukaryotes generally have:
  - i. Linear chromosomes in their nuclei, with different species having different numbers of chromosomes.
  - ii. DNA in organelles (e.g., mitochondria) that is usually a circular molecule.

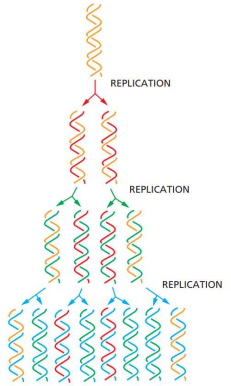
DNA replication cont'd

- Because each of the two daughters of a dividing cell inherits a new DNA double helix containing one original and one new strand the DNA double helix is said to be replicated "semiconservatively."

DNA REPLICATION

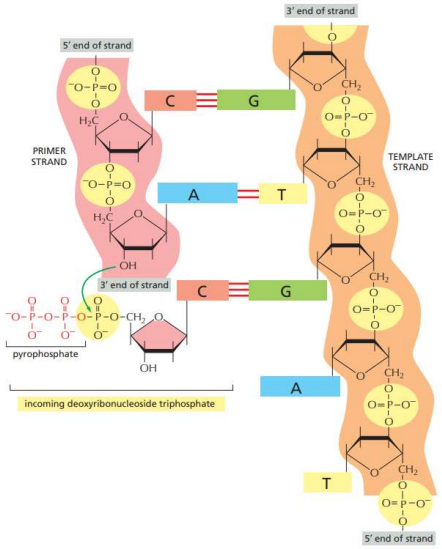
- During DNA replication inside a cell, each of the two original DNA strands serves as a template for the formation of an entire new strand.

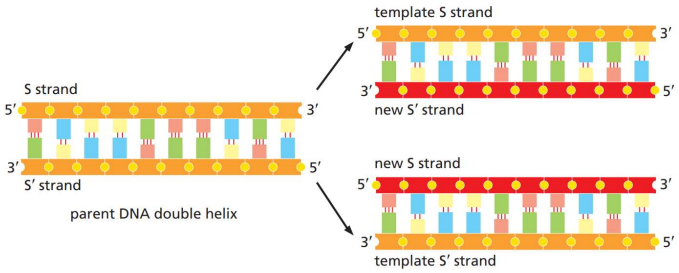
DNA replication cont'd



DNA replication cont'd

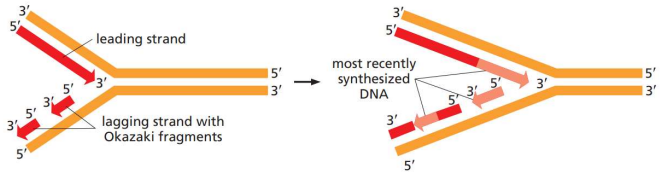
- **DNA replication requires the separation of the DNA helix into two template strands, and entails the recognition of each nucleotide in the DNA template strands by a free (unpolymerized) complementary nucleotide**





DNA Replication cont'd

- **DNA replication takes place at a Y-shaped structure called a replication fork.**
- **A self-correcting DNA polymerase enzyme catalyzes nucleotide polymerization in a 5′-to-3′ direction, copying a DNA template strand 3′ to 5′ with remarkable fidelity.**

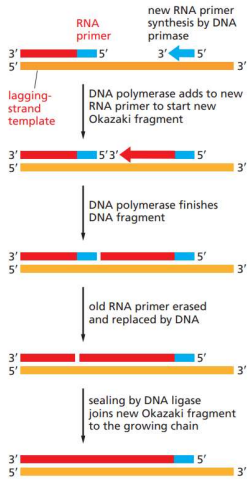


DNA Replication cont'd

- **Because the self-correcting DNA polymerase cannot start a new chain, these lagging-strand DNA fragments are primed by short RNA primer molecules that are subsequently erased and replaced with DNA.**

DNA Replication cont'd

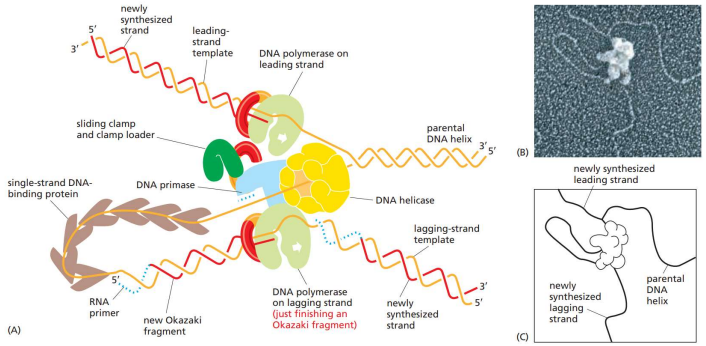
- **Since the two strands of a DNA double helix are antiparallel, this 5'-to-3' DNA synthesis can take place continuously on only one of the strands at a replication fork (the leading strand).**
- **On the lagging strand, short DNA fragments must be made by a "backstitching" process.**



DNA Replication cont'd

- DNA replication requires the cooperation of many proteins.

1. DNA polymerase and DNA primase to catalyze nucleoside triphosphate polymerization
2. DNA helicases and single-strand DNA-binding (SSB) proteins to help in opening up the DNA helix so that it can be copied



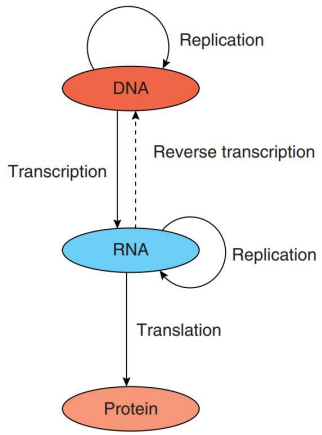
DNA Replication cont'd

3. DNA ligase and an enzyme that degrades RNA primers to seal together the discontinuously synthesized lagging strand DNA fragments
4. DNA topoisomerases to help to relieve helical winding and DNA tangling problems.

EXPRESSION OF GENE

- Gene expression is the process by which a gene produces its product (protein)
- Production of proteins requires two steps

1. Transcription
2. Translation



Central dogma: the flow of genetic information.

Transcription cont'd

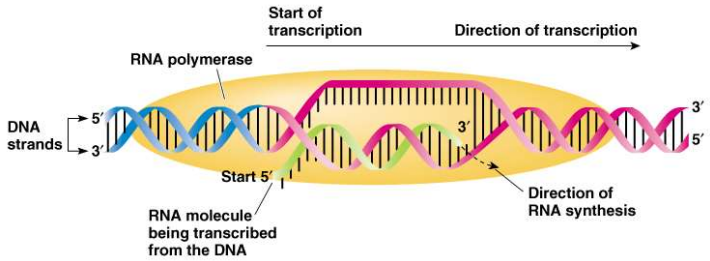
2. One of the two strands of the DNA double helix then acts as a template for the synthesis of an RNA molecule
3. The nucleotide sequence of the RNA chain is determined by the complementary base-pairing between incoming nucleotides and the DNA template

TRANSCRIPTION

- Transcription is the process by which RNA in a cell is made by DNA transcription

1. It begins with the opening and unwinding of a small portion of the DNA double helix to expose the bases on each DNA strand.

Transcription cont'd



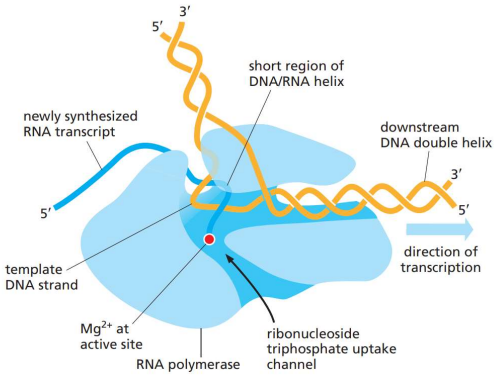
Transcription cont'd

4. When a good match is made (A with T, U with A, G with C, and C with G), the incoming ribonucleotide is covalently linked to the growing RNA chain in a reaction catalyzed by RNA polymerase.

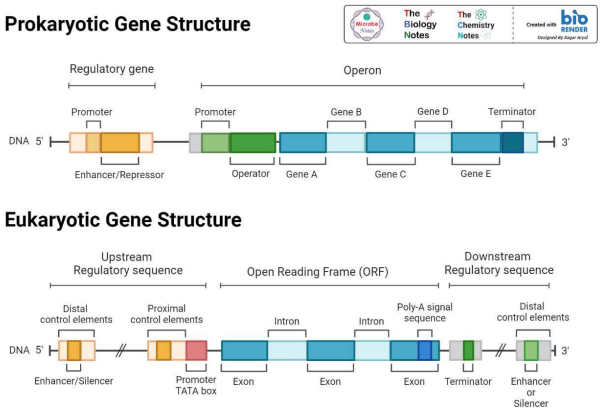
Transcription cont'd

5. RNA polymerase initiates transcription at a promoter, synthesizes the RNA by chain elongation, stops transcription at a terminator, and releases both the DNA template and the completed mRNA molecule.

Transcription cont'd



Transcription cont'd



Transcription cont'd

- In eukaryotic cells, the process of transcription is much more complex, and there are three RNA polymerases—polymerase I, II, and III.

Transcription cont'd

- There are four main classes of RNA

1. Messenger RNAs – mRNA
2. Transfer RNAs - tRNA
3. Ribosomal RNAs - rRNA
4. Small nuclear RNAs - snRNA

Transcription cont'd

- RNA polymerase II synthesizes eukaryotic mRNA.
- For many genes, RNA, rather than protein, is the final product, these genes are usually transcribed by either RNA polymerase I or RNA polymerase III.
- RNA polymerase I makes the ribosomal RNAs

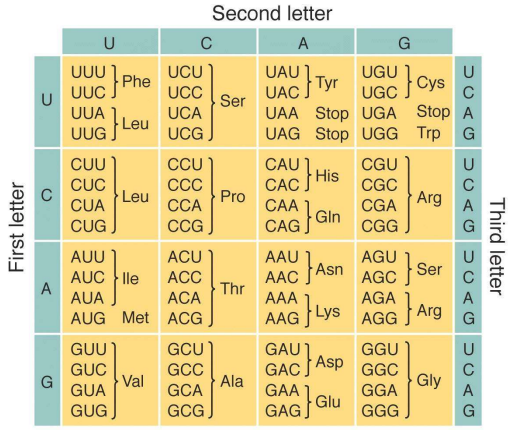
TRANSLATION

- Translation is the process by which genetic message carried by mRNA from the DNA is converted in the form of a polypeptide chain having specific sequence of amino acids

Translation cont'd

- Genetic code
- The genetic code (codons) is formed by three nucleotides (triplet) base sequences in mRNA.
- The codons are formed of four nucleotide base (A, G, C and U)
- These four bases produce 64 different combinations of three base codons

Genetic code cont'd



Genetic code cont'd

- Of the 64 codons, the 61 codons code for 20 amino acids found in proteins
- Three codons (UAA, UAG and UGA) are termination codons which act as stop signals in protein synthesis.
- The codons AUG and sometimes GUG act as initiating codons.

Genetic code cont'd

Standard genetic code

1st base	2nd base U		2nd base C		2nd base A		2nd base G		3rd base
U	UUU	(Phe/F) Phenylalanine	UCU	(Ser/S) Serine	UAU	(Tyr/Y) Tyrosine	UGU	(Cys/C) Cysteine	U
	UUC		UCC		UAC		UGC		C
	UUA	(Leu/L) Leucine	UCA		UAA	Stop (*Ochre*)	UGA	Stop (*Opal*)	A
	UUG		UCG		UAG	Stop (*Amber*)	UGG	(Trp/W) Tryptophan	G
C	CUU		CCU	(Pro/P) Proline	CAU	(His/H) Histidine	CGU	(Arg/R) Arginine	U
	CUC		CCC		CAC		CGC		C
	CUA		CCA		CAA	(Gln/Q) Glutamine	CGA		A
	CUG		CCG		CAG		CGG		G
A	AUU	(Ile/I) Isoleucine	ACU	(Thr/T) Threonine	AAU	(Asn/N) Asparagine	AGU	(Ser/S) Serine	U
	AUC		ACC		AAC		AGC		C
	AUA		ACA		AAA	(Lys/K) Lysine	AGA	(Arg/R) Arginine	A
	AUG[A]	(Met/M) Methionine	ACG		AAG		AGG		G
G	GUU	(Val/V) Valine	GCU	(Ala/A) Alanine	GAU	(Asp/D) Aspartic acid	GGU	(Gly/G) Glycine	U
	GUC		GCC		GAC		GGC		C
	GUA		GCA		GAA	(Glu/E) Glutamic acid	GGA		A
	GUG		GCG		GAG		GGG		G

Characteristics of genetic code

1. Universality, i.e. same codons are used to code for the same amino acids in all the living organisms with a few exceptions
2. Specificity, i.e. a particular codon always codes for the same amino acid, e.g. AUG is the codon for methionine.

Translation cont'd

- The translation of the nucleotide sequence of an mRNA molecule into protein takes place in the cytosol on a large ribonucleoprotein assembly called a ribosome.

Characteristics of genetic code cont'd

3. Non-overlapping, i.e. the genetic code is read from a fixed point as a continuous base sequence
4. Degenerate, i.e. one amino acid is coded by more than one codons. The codons that designate the same amino acid are called synonyms.

Translation cont'd

- Each amino acid used for protein synthesis is first attached to a tRNA molecule that recognizes, by complementary base-pair interactions, a particular set of three nucleotides (codons) in the mRNA.

Translation cont'd

- As an mRNA is threaded through a ribosome, its sequence of nucleotides is then read from one end to the other in sets of three according to the genetic code

Translation cont'd

- During this phase, aminoacyl-tRNAs each bearing a specific amino acid bind sequentially to the appropriate codons in mRNA through complementary base-pairing between tRNA anticodons and mRNA codons.

Translation cont'd

- To initiate translation, a small ribosomal subunit binds to the mRNA molecule at a start codon (AUG) that is recognized by a unique initiator tRNA molecule.
- A large ribosomal subunit then binds to complete the ribosome and begin protein synthesis

Translation cont'd

- Each amino acid is added to the C-terminal end of the growing polypeptide in four sequential steps: aminoacyl-tRNA binding, followed by peptide bond formation, followed by two ribosome translocation steps.

Translation cont'd

- Elongation factors use GTP hydrolysis both to drive these reactions forward and to improve the accuracy of amino acid selection.
- The mRNA molecule progresses codon by codon through the ribosome in the 5' to 3' direction until it reaches one of three stop codons.

Post-translational modifications

- The proteins synthesized in translation are, as such not functional.
- Many changes take place in the polypeptides during or their synthesis

Translation cont'd

- A release factor then binds to the ribosome, terminating translation and releasing the completed polypeptide.

Post-translational modifications

- Post-translational modification include

1. Proteolytic degradation
2. Covalent modifications (Phosphorylation, hydroxylation and glycosylation).

THE CELL CYCLE

- A cell reproduces by performing an orderly sequence of events in which it duplicates its contents and then divides in two
- This cycle of duplication and division is known as the cell cycle
- It is the essential mechanism by which all living things reproduce.

The cell cycle cont'd

- Chromosome duplication occurs during S phase of the cell cycle, whereas most other cell components are duplicated continuously throughout the cycle

The cell cycle cont'd

- Cell division usually begins with duplication of the cell's contents, followed by distribution of those contents into two daughter cells

The cell cycle cont'd

- During M phase, the replicated chromosomes are segregated into individual nuclei (mitosis), and the cell then splits in two (cytokinesis)

The cell cycle cont'd

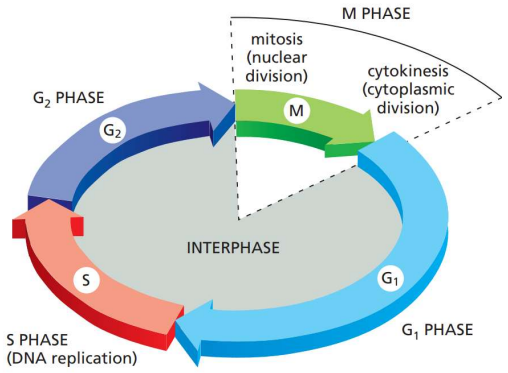
- S phase and M phase are usually separated by gap phases called G1 and G2, when various intracellular and extracellular signals regulate cell-cycle progression.

CELL DIVISION

- Cell division is the process by which a cell reproduces itself.
- There are two types of cell division

1. Mitosis
2. Meiosis

The cell cycle cont'd



MITOSIS

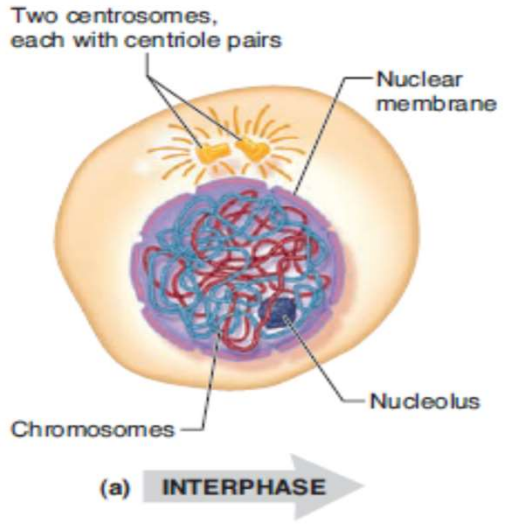
- One cell with the diploid number of chromosomes divides into two identical cells, each with the diploid number of chromosomes.
- This necessary for the growth of the organism and for repair of tissues

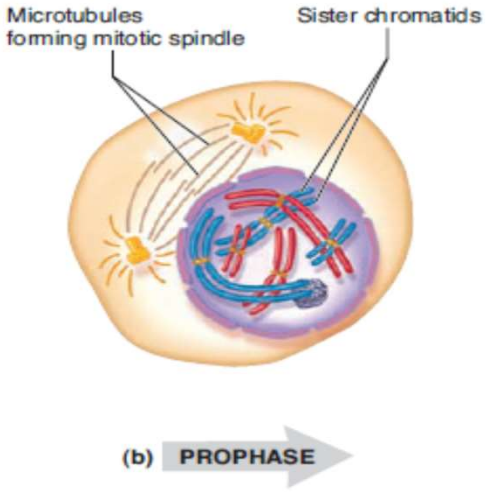
Interphase

- Chromosomes are in the nucleus,
- Chromosomes are less tightly compacted
- Chromatids joined in pairs as sister chromatids
- A pair of centrosomes in one pole of the cell, each with a pair of centrioles.
- Chromosomes (DNA) replicate to double the chromatin number

Prophase

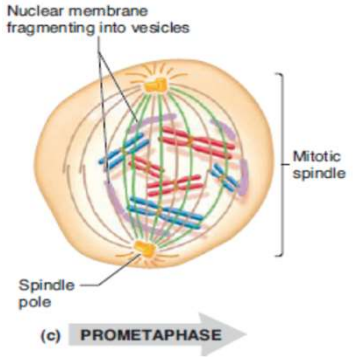
- Nuclear membrane begins to dissociate into small vesicles.
- Chromatids condense and become visible
- Formation of the mitotic spindle.
- Centrosomes move to opposite poles
- The nucleolus disappears.

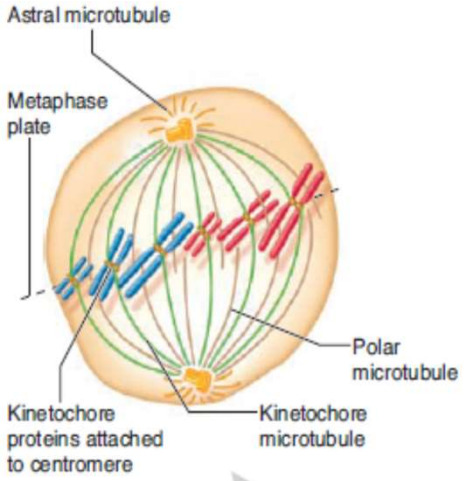




Early metaphase

- The spindle fibers interact with the sister chromatids.
- Sister chromatid pairs are “captured” and firmly attached to the spindle fibres.





Metaphase

- The pairs of sister chromatids align themselves along the equator
- Each pair of sister chromatids is attached to both spindle poles by spindle fibres.

Anaphase

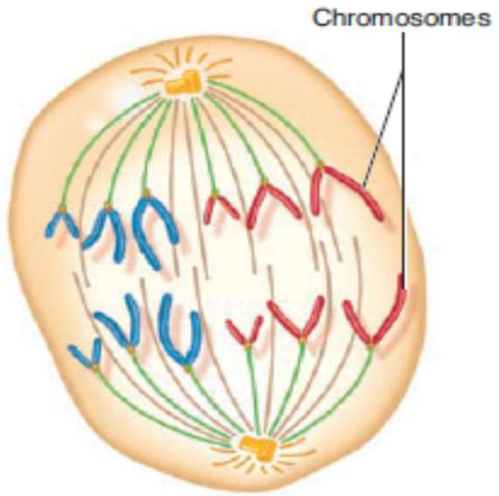
- The centromeres holding the two sister chromatids break and let free the chromatids
- The sister chromatids of each pair are separated
- Each chromatid, now becomes an individual chromosome linked to only one of the two poles.

Anaphase cont'd

- There are now two sets of chromosomes moving to either of the poles.
- This involves a shortening of the kinetochore microtubules

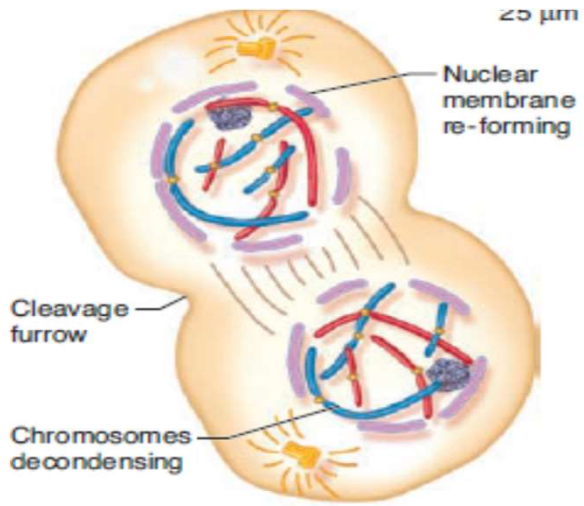
Telophase

- The chromosomes have reached their respective poles and decondense.
- The nuclear membrane reforms to produce two separate nuclei with the same diploid number of chromosomes.
- The nucleolus also reappear in either nucleus.



Cytokinesis

- Formation of cleavage furrow in the cell membrane to segregated the two nuclei into separate daughter cells.
- Also segregation of cell organelles into the two daughter cells.



MEIOSIS

- **In meiosis, one cell with the diploid number of chromosomes divides twice to form four cells, each with the haploid number (half the usual number) of chromosomes**
- **Meiosis results in the formation of gametes, which are egg and sperm cells.**
- **Read about meiosis**