Chapter 1 —> Cell biology

1.1 introduction to cells

Magnification: Magnification = ruler measurement / real life measure

Cell theory:

1) all living things are composed of cells
2) The cell is the smallest unit of life
3) Cells only arise from pre-existing cells

Challenges to the cell theory:

Striated muscle —> are very long —> 300 mm
—> multi-nucleated with continuous plasma membrane
—> not conform to standard view of the cell as autonomous unit
Aseptate fungal hyphae —> very large
—> cytoplasm is continuous so challenges idea of discrete cells
—> multi-nucleated
Giant algae (Acetabularia) —> single-celled organism
—> Gigantic in size (5-100 mm)
—> Complex in form
—> Single nucleus (challenges idea large organism->many cells

Functions of life:

- **M**etabolism —> All the enzyme-catalysed reaction in a cell / organism
- **R**esponse —> Responding to and interacting with the environment
- **H**omeostasis —> The maintenance and regulation of internal cell condition
- **G**rowth —> Growing and changing size / shape
- **E**xcretion —> The removal of metabolic waste
- **R**eproduction —> Producing offsprings either sexually or asexually
- **N**utrition —> Feeding by either synthesis of organic molecules or absorption

Unicellular organisms are the smallest organisms capable of independent life
—> paramecium and scenedesmus are two examples

Surface are to volume ratio:

- Larger SA:V ratio —> cell more efficient
—> diffusion pathways are shorter so faster metabolism
—> concentration gradient easier to generate
—> heat lost more quickly
- To maximise SA:V ratio —> cells divide
—> cells compartmentalise
—> cells create inner membranes
- Villi in intestinal tissue and alveoli in the lungs (microvilli) have a large SA:V ratio

Emergent properties:

- Arise from the interaction of component parts
- Atoms —> molecules —> cells —> tissues —> organ —> organ system —> organism

Gene expression and differentiation:

- Each cell contains the entire set of genetic instructions of the organism and have the same identical genome
- In embryonic stem cells the entire genome is active
- Totipotent , pluripotent , multipotent , unipotent
- Newly formed cells receive signals which deactivate genes
- Active genes —> euchromatin / inactive genes —> heterochromatin (condensed)
- The fewer the active genes, the more specialised the cell is
- 220 distinct highly specialised cell types in humans
- Stem cells —> are self-renewable —> can continuously divide and replicate
  —> Potency —> have the capacity to differentiate into specialised cell types
  —> can be used as a viable therapeutic option to replace non-stem cells

Stargardt's macular dystrophy:

- Causes progressive vision loss to the point of blindness
- recessive genetic condition (photoreceptor cells degenerate)
- Retinal stem cells are injected into the retina and become functional replacing dead cells

Parkinson's disease

- Degenerative disorder of the central nervous system caused by death of dopamine-secreting cells in the midbrain (dopamine is a neurotransmitter, for smooth movements)
- Typically exhibit tremors, rigidity, slowness of movement and postural instability
- Treated by replacing dead nerve cells with living, dopamine-producing one

Leukemia:

- Cancer of blood or bone marrow —> high levels of poorly-functioning white blood cells
- Hematopoetic stem cells harvested and then chemotherapy
- HSCs transplanted back and differentiate into white blood cells

Stem cell sources:

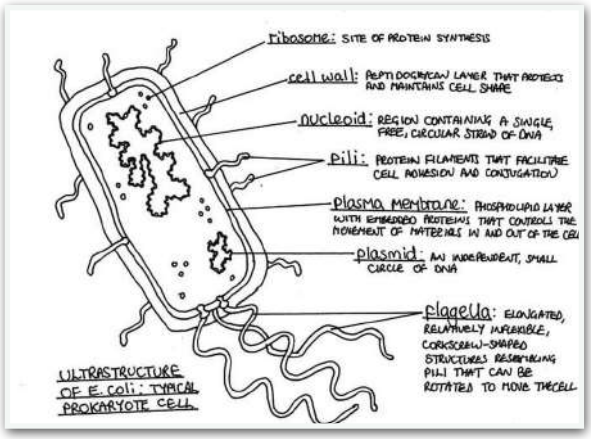
Embryo —> almost unlimited growth potential and totipotent
—> high risk of tutor development
—> kills an embryo
—> less chance of genetic damage
—> not genetically identical to the patient
Cord blood —> easily obtained but in limited quantity
—> reduced potential
—> low risk of tumour
—> limited capacity to differentiate
—> low chance of genetic damage
—> fully compatible
Adult —> Difficult to obtain and with reduced potential
—> low risk of tumour
—> limited capacity to differentiate
—> may be genetic damage
—> fully compatible

Artificial stem cell techniques

- Somatic cell nuclear transfer —> Involves the creation of embryonic clones by fusing a diploid nucleus with an enucleated egg cell —> more embryos are created by this process then needed
- Nuclear reprogramming —> Inducing a change in the gene expression profile of a cell in order to transform it into a different cell type —> as it uses oncogenic retroviruses and transgenes and this increases the risk of health consequences (ex. cancer)

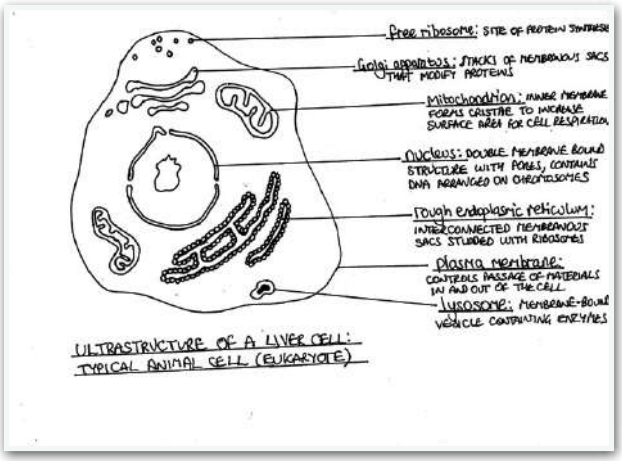
1.2 Ultrastructure of cells

- Resolution —> the shortest distance between two point that can be distinguished
- Ultrastructure —> a structure specimen that are at least 0.1nm in their smallest dimension



Ultrastructure of a prokaryote (E. Coli)

- Prokaryotes —> organisms with no nucleus
- Archaebacteria —> found in extreme environments (ex. Extremophiles)
- Eubacteria —> traditional bacteria including most known pathogenic forms
- Binary fission —> a form of asexual reproduction used by prokaryotic cells



Ultrastructure of an eukaryote (Liver cell)

-eukaryotes are organisms whose cells contain a nucleus

-Are compartmentalised by membrane-bound structures (organelles)

- Divided into four distinct kingdoms:

—> Protista —> unicellular organisms

—> Fungi —> have a cell wall made of chitin and have an heterotrophic nutrition

—> Plantae —> have a cellulose cell wall and obtain nutrition autographically

—> Animalia —> no cell wall and obtain nutrition via heterotrophic ingestion

Organelles:

- Ribosomes —> site of polypeptide synthesis
- Cytoskeleton —> provides internal structure and mediates intracellular transport
- Plasma membrane —> semi permeable and selective barrier surrounding the cell
- Nucleus —> Stores genetic material as chromatin; nucleolus is site of ribosome assembly
- ER —> transports materials between organelles (smooth for lipids and rough fo proteins)
- Golgi apparatus —> sorting, storing and modification and export of secretory products
- Mitochondrion —> site of aerobic respiration
- Peroxisome —> catalyses breakdown of toxic substances and other metabolites

- Centrosome —> radiating microtubules form spindle fibres and contribute to cell division
- Chloroplast —> site of photosynthesis
- Vacuole —> maintains hydrostatic pressure
- Cell wall —> provides support and mechanical strength; prevents excess water uptake
- Lysosome —> breakdown / hydrolysis of macromolecules

Electron microscopy:

- Use beams focused by electromagnets to magnify and resolve microscopic specimens
- TEM —> Transmission…—> high resolution cross-sections of objects
- SEM —> Scanning… —> display enhanced depth to map the surface of objects in 3D
- Much higher range of magnification and resolution in respect to light microscope, but cannot display living specimens in natural colours

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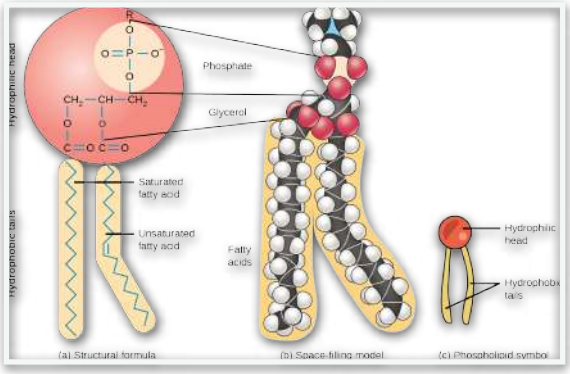
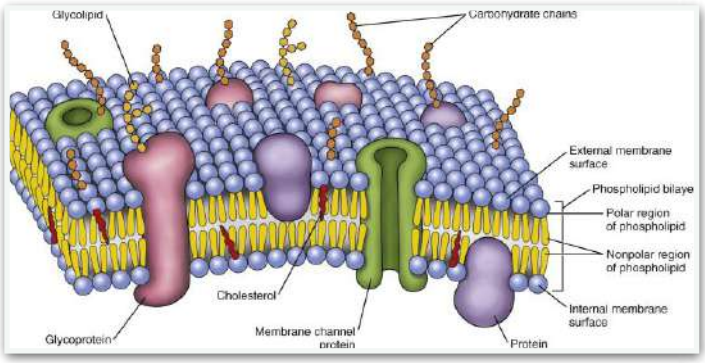
1.3 Membrane structure

Phospholipids:



Phospholipid bilayer:



- Phospholipids arrange spontaneously into a bilayer with the hydrophobic tail regions facing inwards, so shielding from the surrounding polar fluids (are amphipathic)
- The bilayer is held together by weak hydrophobic interactions between the tails
- Individual phospholipids can move within the bilayer —> creates fluidity and flexibility, so allowing spontaneous breaking and reforming of the membrane for endo/exocytosis

T.R.A.C.I.E.

- **T**ransport —> Protein channels and pumps
- **R**eceptors —> Peptide-based hormones
- **A**nchorage —> Cytoskeleton attachments and extracellular matrix
- **C**ell recognition —> MHC proteins and antigens
- **I**ntercellular joinings —> Tight junctions and plasmodesmata
- **E**nzymatic activity —> Metabolic pathways

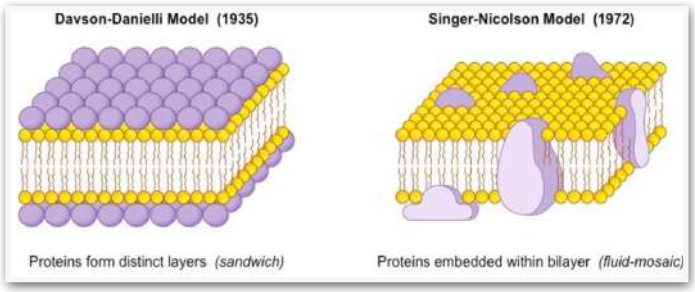
- Integral proteins —> permanently attached to the memb. and typically transmembrane
- Peripheral proteins —> temporarily attache by non-covalent interactions and on one side

Cholesterol:

- It makes phospholipids pack more tightly and regulates the fluidity and flexibility
- Absent in plant cells as they are already supported by a rigid cell wall made of cellulose
- Is a steroid and is amphipathic (has both hydrophilic and hydrophobic regions)
- Restricts the movements of phospholipids (fluidity) and avoids crystallisation of the tails

Singer - Nicholson fluid mosaic:

- According to this model, proteins were embedded within the lipid bilayer
- From 1972 —> most preferred model



Davson - Danielli:

- a protein lipid sandwich (trilaminar —> 3 layers)
- Membrane proteins were discovered to be insoluble in water —> proteins would not be able to form a uniform and continuous layer around the outer membrane surface
- Fluorescent antibody tagging —> showed membrane proteins were mobile and not fixed —> membranes from two different cells tagged with red and green and colours mixed
- Freeze fracturing caused rough surfaces, so proteins had to be also trans-membrane

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1.4 Membrane transport

- The phospholipid bilayer is selectively permeable and there are many ways to go through
- Movement across may occur actively or passively

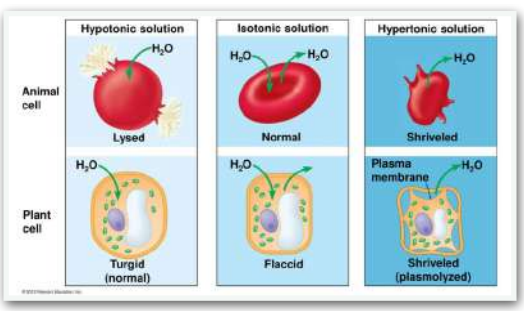
Passive transports:

Diffusion:

- The passive net movement of particles from areas of high concentration to areas of low conc.
- Small and non-polar molecules will be able to freely diffuse across cell membranes
- Affected by —> concentration gradient
  - —> surface area
  - —> length of diffusion pathways
  - —> temperature
  - —> molecular size

Osmosis:

- Diffusion but in water
- Water is considered the universal solvent
- Aquaporins —> integral proteins that speed up water diffusion
- Osmotic control —> fluid introduction (rehydration)
  - —> eye drops / wash
  - —> organs for transport
  - —> keeping areas of damaged skin moist



Facilitated diffusion:

- The passive use of carrier and channel proteins to move large and polar molecules in the direction dependent on the concentration gradient
- Carrier proteins —> Integral glycoproteins which bind a solute and undergo a conformational change to translocate the solute across the membrane
  —> can bind to only correct solutes such as with enzymes and substrates
  —> much slower rate of transport than channel protein —> 1000 molecule x ‘’
- Channel proteins —> integral lipoproteins which contain a pre via which ions may cross
  —> are ion-selective and may be gated to regulate certain passages of ions
  —> only move molecules along a concentration gradient
- Potassium channels —> integral proteins with hydrophilic inner pore —> potassium ions move
  —> are typically voltage-gated and cycle between an opened and closed conformation depending on the transmembrane voltage

Primary + Secondary transport:

- Primary active transport requires ATP and uses energy from the hydrolysis of ATP to move molecules across the membrane against their concentration gradient
- Secondary active transport uses energy in the form of concentration differences of a second solute

Active transport:

- Uses energy to move molecules against a concentration gradient —> the energy may come from ATP or indirectly coupling transport with another molecule that is moving along its gradient
- Involves the use of carrier proteins —> a specific solute will bind to the protein pump on one side of the membrane —> hydrolysis of ATP causes a conformational change in the protein pump —> the molecule is translocated across the membrane and released

Sodium-Potassium pumps:

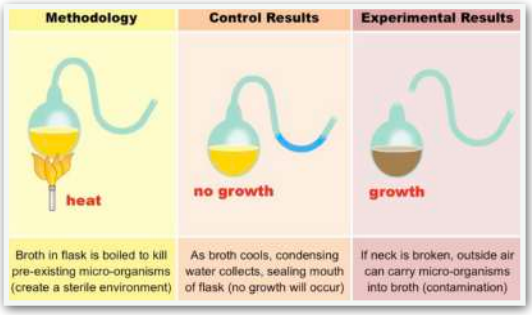
- An integral protein that exchanges 3 sodium ions with two potassium ions
- Three sodium ions bind to intracellular sites on the protein —> a phosphate from hydrolysis of ATP is transferred to the pump —> the pump undergoes a conformational change translocating sodium across the membrane —> the phosphate group is released causing the protein to go back to the original conformation

Vesicles

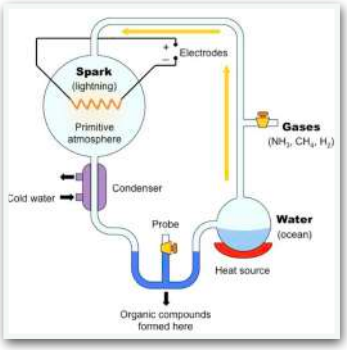
- Move materials within cells (usually ER —> Golgi apparatus —> Lysosome or cell membrane)
- Endocytosis —> taking in of large external substances by forming a vesicle
  —> Phagocytosis —> solid
  —> Pinocytosis —> liquid
- Exocytosis —> release of large substances in a vesicle
  —> constitutive secretion —> occurs continuously
  —> regulated secretion —> response to a trigger

1.5 Origin of cells

Biogenesis:



1) Cells are highly complex structures and no mechanism has been found for producing cells from a simpler subunit
2) All known examples of growth are a result of cell division
3) Viruses do not consist of cells and can't survive outside
4) The genetic code is universal
5) Pasteur's Experiment



Abiogenesis:

1)Non-living synthesis of simple organic molecules
2)Assembly into more complex polymers —> deep-sea thermal vents gave the conditions
3)Certain polymers formed capacity to self-replicate —> RNA instead of DNA
4)Formation of membranes —> phospholipids naturally assembled
5)Miller-Urey experiment

Endosymbiotic theory:

1) Eukaryotic cells are believed to have evolved from early prokaryotes that were engulfed by phagocytosis —> the prokaryotic cell remained undigested and contributed to the cell
2) Plasma membrane enfolded —> nucleus created
3) Mitochondria, chloroplasts —> endosymbionts

Evidence for endosymbiotic theory:

- Own DNA
- 70s ribosomes as prokaryotes
- Double membrane
- Susceptible to antibiotics
- Transcribe and translate DNA
- Same size as bacteria
- Arise only from pre-existing

1.6 Cell division

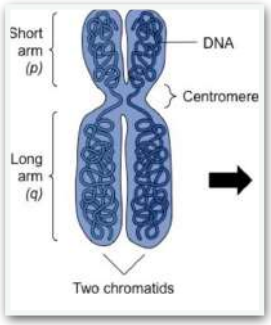
Why replication (mitosis):

- Growth —> organisms increase their size by increasing number of cells
- Asexual reproduction —> just for certain eukaryotic organisms
- Tissue repair —> new cells created to replace dead or damaged cells
- Embryonic development —> zygote uses mitosis to become an embryo

Interphase:

- G1 —> increase the volume of cytoplasm, centrosomes move to opposites, nuclear membrane dissolves, organelles duplicate and nutrients are obtained
- S —> DNA is replicated
- G2 —> equal to G1 —> cell finishes growing and prepares for cell division

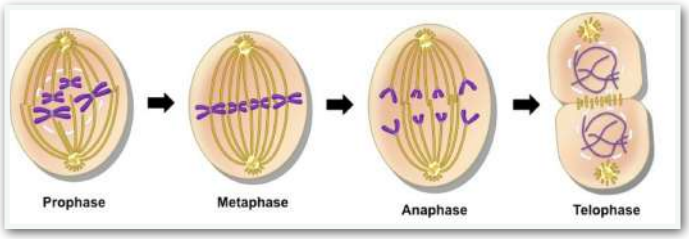
Chromosomes:



- DNA is temporarily packaged into a tightly wound and condensed chromosome prior to division (supercoiling)
- In this way it is easy to be segregated, however is inaccessible to transcriptional machinery

PMAT:

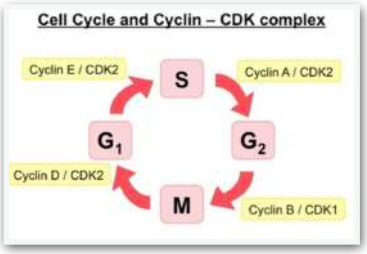
- Prophase —> DNA supercoils
  —> centrosome move to opposites
  —> nuclear membrane dissolves
- Metaphase —> sister chromatids line up as spindle fibres contract (equator)
- Anaphase —> separation sister chromatids
  —> chromatids now chromosomes
- Telophase —> spindle fibres disappear
  —> chromosomes decondense
  —> nuclear membranes reform



Cytokinesis:

- The division of the cytoplasm
- Animal cells —> A ring of contractile proteins at the equator pulls the plasma membrane inward —> cleavage furrow —> when reaches the center —> pinches off and two cells are formed —> centripetal as from outside to inside
- Plant cells —> vesicles migrate to the centre of the cell
  —> vesicles form tubular structures
  —> cell plate continues forming until full existing cell wall
  —> centrifugal as from inside to outside

Cyclins:



- Are needed to tell cells to progress to the next stage (cell cycle)
- Bind to enzymes called cyclin-dependent kinases (CDK)

Tumours and Cancer:

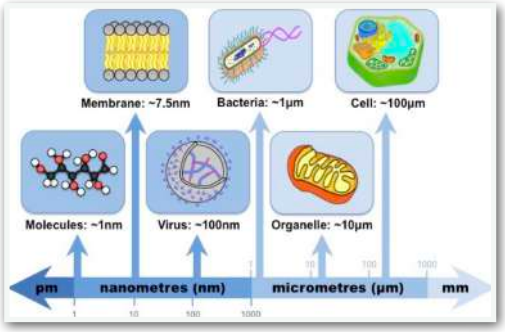
- Tumour —> abnormal growth of tissue resulting from uncontrolled cell division
- Cancer —> a malignant tumour
- Mutagens —> agents that cause gene mutation
  —> chemicals —> carcinogens
  —> biological —> viruses
  —> short-wave ultraviolet light and high energy radiation
- Oncogenes —> control cell cycle and cell division
- Proto-oncogenes —> code for proteins that stimulate the cell cycle and promote cell growth
- Tumour suppressor genes —> code for proteins that repress the cell cycle progression
- Metastasis —> tumour expands from primary tumour and creates secondary tumours

1. Extra

Microscopes:

- Are scientific instruments that are used to visualise objects that are too small to see naked eye
- Light microscopes —> uses lenses to bend light and magnify images
  —> Can be used to view living specimens in natural colour
  —> chemical dyes and fluorescent labelling used to see specific structures
- Electron microscopes —> uses electromagnets to focus electrons —> greater magn. and resol.
  —> can be used to view dead specimens in monochrome
  —> TEM —> generates a cross-section
  —> SEM —> maps in 3D

Cell scale:



Classification of kingdoms:

Property	Monera	Protista	Fungi	Plantae	Animalia
Nucleus	No	Yes	Yes	Yes	Yes
Cell organisation	Unicellular (mostly)	Unicellular (mostly)	Unicellular and multicellular	Multicellular (mostly)	Multicellular (mostly)
Cell wall	Yes (peptidoglycan)	Sometimes	Yes (chitin)	Yes (cellulose)	No
Nutritional class	Autotrophic; heterotrophic	Autotrophic; heterotrophic	Heterotrophic	Autotrophic	Heterotrophic
Mode of nutrition	Absorption	Absorption; Ingestion	Absorption	Absorption (mostly)	Ingestion (mostly)
Example	Archaea; Eubacteria	Protozoa; Algae	Yeasts; Moulds; Mushrooms	Mosses; Ferns; Flowers	Insects; birds; fish

Phospholipids:

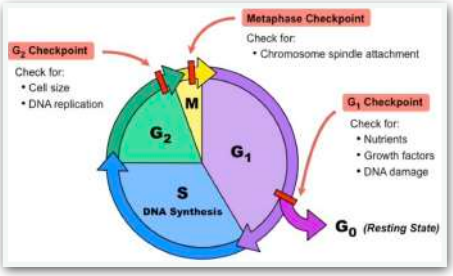
- May vary in the length and relative saturation of the fatty acid tails
- Shorter fatty acid tails will increase fluidity as they are less viscous

Transport:

- Co-transport —> coupled transport of two distinct molecules
  —> symport —> molecules transported in the same direction
  —> antiport —> molecules in opposite directions

Checkpoints:

- Cell cycle checkpoints are mechanisms that ensure the fidelity and continued viability of mitotic division in cells



Cell death:

	Necrosis (uncontrolled cell death)	Apoptosis (programmed cell suicide)
Size	Cellular swelling	Cellular shrinkage
	Many cells affected	One cell affected
Uptake	Cell contents ingested by macrophages	Cell contents ingested by neighbouring cells
	Significant inflammation	No inflammatory response
Membrane	Loss of membrane integrity	Membrane blebbing, but integrity maintained
	Cell lysis occurs	Apoptotic bodies form
Organelles	Organelle swelling and lysosomal leakage	Mitochondria release pro-apoptotic proteins
	Random degradation of DNA	Chromatin condensation and non-random DNA degradation

Normal vs Cancer cells: