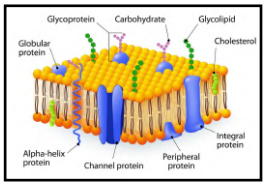
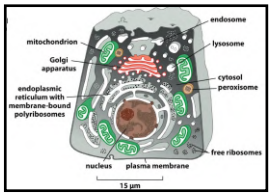
The Cell (W1)

The Cell (L1) - MCQ ONLY



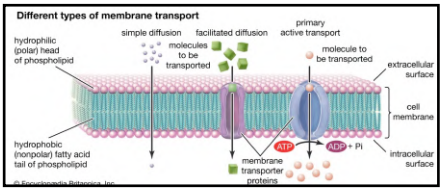


Cells

- Specialised functions, comprised of plasma membrane and internal cytoplasm
- Fluid = **cytosol**. **Cytoplasm** = everything inside plasma membrane
- **Membranous organelles**: nucleus, mitochondria, lysosomes, peroxisomes, endoplasmic reticulum, Golgi apparatus, vesicles
- **Non-membraneous components**: ribosomes, cytoskeleton, centrioles, flagella
- All membranes are different - components of membrane are different

Compartmentation

- Keep cell content separate from environment
- Controlled interaction with environment
- Membranes have **selective permeability** to polar and charged molecules via specific membrane transporters
- Different types of membrane transport:
  - **Simple diffusion (passive)**
  - **Facilitated diffusion (passive)**
  - **Primary active transport** (directly uses energy from ATP)
    - Membrane transporter proteins facilitate this
  - **Secondary active transport** (leverages the energy stored in an existing ion gradient)

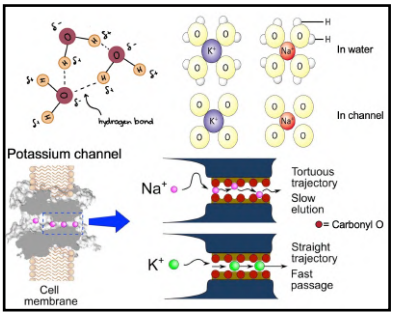


Which will readily enter the cell?

- Na+ and K+ ions can readily enter the cell with **specialised channels**
- K+ enters more easily than Na+, even though it is bigger
- Cations interact with water mainly - hydrates cations (hydration cell)

Hydration Cell

- Na+ and K+ surrounded by 4 water molecules
- **Na+**: **tortuous trajectory**, **slow** elution through channel
- **K+**: **straight trajectory**, **fast** passage through channel
- **C=O** in channels interact with ions. **K+ (but not Na+) coordinates better with** amino acid backbone **(C=O)** carbonyl **oxygens** in the **channel**
- Distance between C=O in channels is the same in channels, but due to K+ size, it can **interact more strongly with C=O groups** in channels.
- Na+ tries to bind to many carbonyls and moves around a lot
- K+ transport is about 1000x faster than Na+ transport through channels

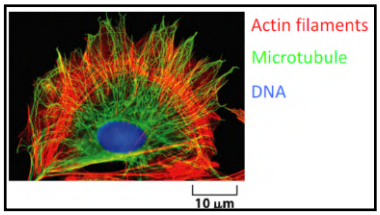


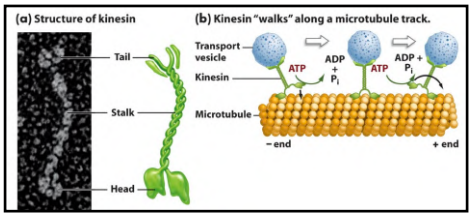
Specificity in binding

- Between macromolecules (proteins, lipids, carbohydrates, nucleic acid)
- Between a macromolecule and a small molecule e.g. an enzyme binding to its substrate
- Matching of functional groups enables specific interactions
  - Hydrogen bond, electrostatic interaction, hydrophobic interaction
- Collectively: strong interactions

The Cytoskeleton

- Network of protein filaments
- Grow/shrink to determine **cell shape**, **structure**, **organises** cell contents, **move** material within cell, and contributes to **cell movement**
- Composed of:
  - **Microfilaments** (6nm, **actin**)
    - Cell **shape** and **movement**, cortex of cell
  - **Intermediate** filaments (8-10nm)
    - Provide **mechanical strength** and cell structural integrity
  - **Microtubules** (25nm, **tubulin**)
    - Intracellular **transport**, **positioning** of **organelles**, cell **shape** and division





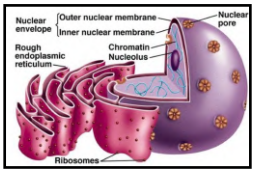
Motor proteins

- **Motor proteins** move themselves (and other things) along the cytoskeleton
- **Myosin** (motor protein associated with microfilaments (actin)), **kinesin** and **dynein** (associated with microtubules)
- Structure of Kinesin: head, stalk and tail
- **Kinesin** "walks" along a microtubule track, requires ATP
  - Moves from the negative end to the positive end (**anterograde movement**, cell body to cell periphery)
- **Dynein**: **retrograde movement**, cell periphery to cell body, positive end to negative end

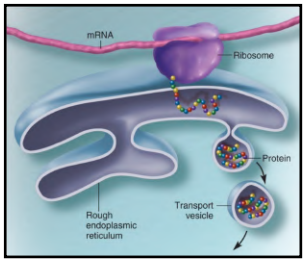
The nucleus

- Largest organelle
- Most cells have one nucleus
  - Some cell types are **anuclear** (mature RBCs) or **multinucleate** (skeletal muscle cells)
- Stores most of the cells genetic information (DNA) - 46 chromosomes (23 dad, 23 mum)
  - As **chromatin** composed of **linear DNA and proteins**
  - **Nucleoli** - **rRNA synthesis** and **ribosome biogenesis**

Nuclear envelope



- Double membrane around nucleus - perforated by **nuclear pores** formed by rings of proteins.
- **Selective molecular trafficking** - back to nucleus, cytoplasm, exocytosis
- **Outer nuclear membrane** and **Inner nuclear membrane**
- **Perinuclear** space in-between membranes, **connected with endoplasmic reticulum**
- **Rough ER** and **ribosomes** connected to nuclear envelope
- Nucleolus inside **nucleoplasm**



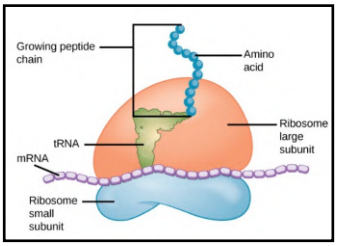
Endoplasmic reticulum

- System of channels (cisternae: flat sacks) enclosed by membranes
- Continuous with outer membrane of nuclear envelope
- **Rough ER**: covered in ribosomes
  - Produces **phospholipids** and **proteins** of the **plasma membrane**
  - Synthesises proteins that are packaged in other organelles or **secreted** from cell
- **Smooth ER**: no ribosomes
  - Synthesises **fats** and **lipids**, **steroid hormones**
  - **Detoxifies alcohol** and **other drugs**
  - **Calcium storage** (especially in muscle = sarcoplasmic reticulum)

Function of endoplasmic reticulum

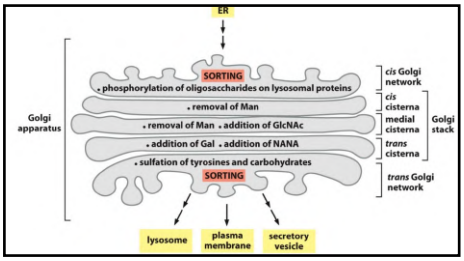
- mRNA translated into proteins by ribosomes and packaged into transport vesicle

Ribosomes: protein-production (translation) (no membrane)



- Ribosomes: comprised of rRNA and proteins
- Protein-production (translation) - no membrane; Macromolecular complex
- Found free in cytoplasm, or on membranes (RER, nuclear envelope) or in organelles (nucleus, mitochondria)
- "Read" coded genetic messages (mRNA) and joins amino acids to form proteins, specific by the code
- tRNA reads codon which is connected to amino acid
- Produces growing peptide chain
- Ribosome small subunit (40S) binds mRNA at the 5′-end and scans in the 5′ to 3′ direction to locate the initiation codon
- Large subunit (60S) catalyses formation of peptide bonds that create the protein
- Eukaryotic ribosomes are 80S ribosomes

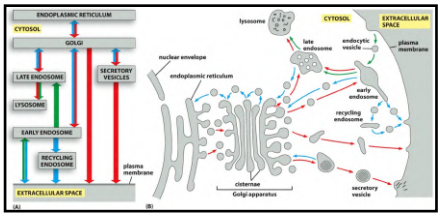
Golgi Apparatus



- Sorting
  - Phosphorylation of oligosaccharides on lysosomal proteins (cis Golgi network)
  - Removal of Man (cis cisterna)
  - Removal of Man and addition of GlcNAc (medical cisterna)
  - Addition of Gal and addition of NANA (trans cisterna)
  - Sulfation of tyrosines and carbohydrates (trans Golgi network)
- **Sorting** into **lysosome, plasma membrane, secretory vesicles**
- System of cisternae: synthesise **carbohydrates** and puts "finishing touches" on proteins (**PTMs**)
- Receives newly synthesised proteins from rough ER (cis)
- Adds **carbohydrates/sulfates** to some (glycosylation/sulfation)
- Packages them into membrane-bound vesicles (trans)

Vesicles

1. Protein formed by ribosomes on rough ER
2. Protein packaged into **transport vesicle** which **buds** from ER (clathrin-coated transport vesicles)
   - **Clathrin-coated vesicles** (CCVs) are vesicles that transport proteins and nutrients **between organelles** and throughout cells and plasma membrane
3. Transport vesicles **fuse** into clusters that unload protein into **Golgi complex**
4. Golgi complex **modifies protein structure** (PTMs)
5. **Golgi vesicle** containing finished protein is formed
6. **Secretory vesicles** release protein by exocytosis at plasma membrane



Vesicle transport (endomembrane system)

- Rough ER bud transport vesicles with proteins. Packaged and modified in Golgi
  - Secretory vesicle pathway and exocytosed
  - Vesicles form **early endosome**, then **late endosome** and then **lysosome**
  - **Recycling** of endosome, return back to Golgi apparatus and then back to ER
- **Endocytotic vesicle**: Form early endosome, late endosome eventually lysosome, or recycled
- **Exocytosis**: constitutive (continuous) regulated (needs signal)
- **Endocytosis**: big things (**phagocytosis**), little things (**pinocytosis**), can be highly specific (receptor-mediated)

Lysosomes and peroxisomes

- A **lysosome** is a membrane-bound cell organelle that contains **digestive enzymes**
  - Digestion of proteins, nucleic acids, complex carbohydrates, phospholipids and other substances
- **Peroxisomes** are small, membrane-enclosed organelles that contain enzymes involved in a variety of **metabolic reactions**, including several aspects of energy metabolism - contains the reducing enzyme **catalase** and usually some **oxidases**
  - Use hydrogen peroxide (H_2O_2 -> H_2O + O_2) - oxidises organic molecules
  - Neutralise free radicals, catabolise some amines (e.g. purines)

Proteosomes and autophagosomes

- Clear old/damaged proteins and organelles - cell recycle components
- **Proteosomes**: digest proteins
  - Contain enzymes that break down "tagged" (with **ubiquitin**) proteins into short peptides and amino acids
- **Targeted protein** (folded) is tagged by **ubiquitin** on a **Lysine** residue
- Protein is **unfolded in proteasome** (large protease complex) and **degraded** by protease
- **Autophagosomes**: carry **damaged cell components** to **lysosomes** for degradation
  - Fuse with lysosome, where contents are degraded

Mitochondria

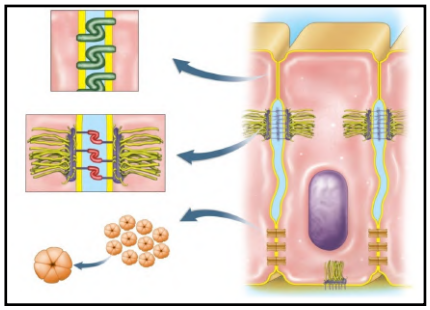
- **Inter-membrane space** between **outer and inner membrane**
- **mtDNA** and **ribosomes** within **matrix**
- ATP synthase particles in matrix - converts ADP to ATP by H+ influx from inter-membrane space
  - Membrane-bound enzyme use protons to convert ADP to ATP
  - Energy from organic molecules is extracted and drives protons across inner membrane which powers ATP synthase
- Surrounded by double membrane
  - **Inner membrane highly folded** = **cristae**
  - Inside cristae = **matrix**
    - Matrix contains ribosomes, enzymes used for ATP synthesis, mtDNA (small circular DNA)

Brief summary

- Nucleus: location of main genome, site of most DNA/RNA synthesis
- ER: continuous membrane throughout cell, Ca2+ storage, protein/lipid synthesis and processing
- Golgi apparatus: series of flattened membranes; involved in protein secretion and sugar linkage
- Vesicles: exocytosis/endocytosis
- Lysosomes: sacs containing hydrolytic enzymes
- Peroxisomes: contains enzymes for H2O2 metabolism
- Proteosomes and autophagosomes: digest/remove old proteins/organelles
- Mitochondria: site of energy-yielding oxidation reactions, has own circular DNA

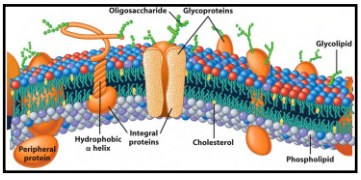
Cells interact with other cells

- **Tight junctions**
  - **Cell-adhesion** proteins attached to **plasma membrane**
- **Desmosomes**
  - Cadherins attach to **cytoskeleton,** cell-cell adhesion
- **Gap junctions**
  - **Pores connecting** cells **cytoplasm**
- Tight junctions: seal gap between cell (prevent leakage, in or out)
- Desmosomes: very strong - hold cells together
- Gap junctions: direct communication between cells



Cells interact with extracellular fluid (ECF) and other body fluid compartments

- The role of membranes that surround cells/organelles = **selectively** keep stuff in or out
- Within plasma membrane: peripheral protein, integral proteins, glycoproteins, cholesterol, glycolipid

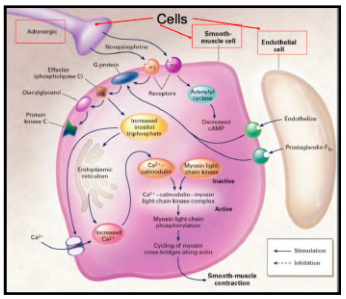


Swell (W2)

Swell (L1) - MCQ ONLY

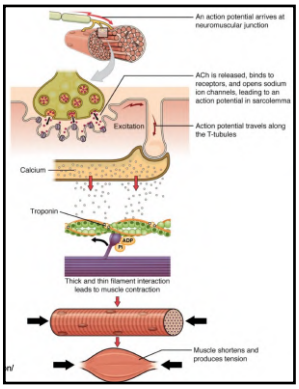
Muscle

- **Skeletal** muscle
  - Striated, tubular, multinucleate, voluntary, rapid contraction, fatigue easily
- **Smooth** muscle
  - Non-striated, spindle, uninucleate, involuntary, slow contraction, low fatigue
- **Cardiac** muscle
  - Striated, branched, uninucleate, involuntary, rapid contraction, low fatigue



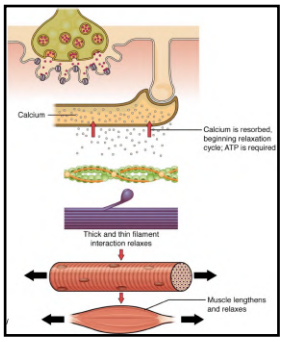
Maintenance of vascular smooth muscle contraction

- Adrenergic receptors release **norepinephrine** which act on **alpha receptors**.
- Alpha receptors **inhibit adenylyl cyclase** which **decreases cAMP**
- Alpha receptors activate G protein which **activates phospholipase C** which **increases cytosolic IP3**
- IP3 results in the **sarcoplasmic reticulum releasing Ca2+**
- Ca2+ binds to **calmodulin**. This complex binds to **MLCK** and **activates**
- Myosin light-chain phosphorylation results in smooth-muscle contraction



Muscle contraction

- An action potential arrives at **neuromuscular junction**
- **ACh is released**, binds to receptors, and **opens sodium ion channels**, leading to an action potential in the **sarcolemma** (plasma membrane of muscle cells)
- Action potential travels along the **T-tubules**
- **Sarcoplasmic reticulum releases Ca2+ ions**
- Thick and thin filaments interaction leads to muscle contraction
- Muscle shortens and produces tension



Muscle relaxation

- **Calcium is reabsorbed** back into the sarcoplasmic reticulum, beginning relaxation cycle - **ATP** is required
- Thick and thin filament interaction relaxes
- Muscle lengthens and relaxes

Cells are different

- Endothelial cell - line blood vessels and control exchange between blood and tissues
- Smooth muscle cell - heterogenous - control diameter, stiffness and movement of walls in “hollow” organs (e.g. vascular, GI, bronchial, urogenital)
- Adrenergic nerves - control involuntary actions (e.g. circulation), release neurotransmitters (adrenaline, noradrenaline, dopamine)… cause cellular responses

Endoplasmic Reticulum

- Smooth ER (no ribosomes)
  - Synthesise lipids, detoxifies alcohol and other drugs, **calcium storage**
- Endoplasmic reticulum: non-excitable cells
- Sarcoplasmic reticulum: **excitable cells**

Proteins have many functions

- Proteins as **receptors** — specificity of binding
  - Binding (alpha1 and alpha2) and signalling (G protein)
- Proteins as **enzymes** — specificity of catalysis