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# General Physiology

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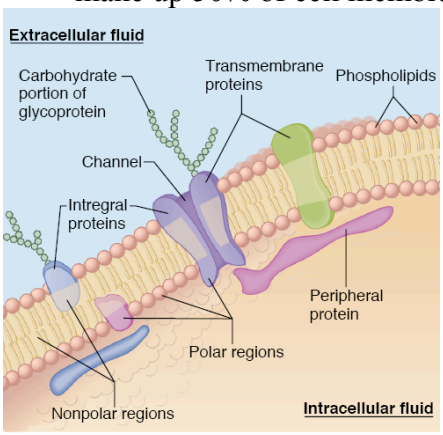
# Cell Membrane

- Made of
  - Phospholipids
  - Proteins
  - Cholesterol - Found in eukarocytes ie cells with nuclei
- Cell membrane = 7.5nm thick semi permeable structure

## Lipid Bilayer

- Fluid rather than solid
- Phospholipids have:
  - eg phospha-tidyl-choline & phospha-tidyl-ethanol-amine
  - Hydrophilic head
    - Water soluble
    - Exposed to aqueous exterior & interior
  - Glycerol backbone
  - Fatty acid tails –
    - Hydrophobic
    - Meet in middle of cell membrane
- Proteins can be either:
  - Integral – ie pass through bilayer eg ion channels
  - Peripheral = straddling

  ↳ make up 50% of cell membranes mass






## Function of CM Proteins

1. **Structural**
2. Carriers for **facilitated diffusion** ( ie down electrochemical gradient)
3. Pumps for ion **active transport**
4. **Ion channels** (diffusion down electro- or chemical gradient or both; eg K-"leak" channels)
5. **Receptors** for chemical messengers ( ie hormones , neurotransmitters , autacoids…)
6. **Enzymes**
7. **Glycoproteins** involved in AB processing or *anti*coagulation ( eg the mucopolysaccharide glycocalyx of the endothelium which repels clotting factors + PLT's → helps prevent blood from clotting in *intact* blood vessels)

## Underlying CM

- Basement membrane or basal lamina
- Made up of:

  - Collagens
  - Laminins
  - Fibronectins
  - Proteoglycans
- Function to bind cells & regulate development & growth

# Intercellular Connections

- 2 main types:
  - adhesive type connections
  - transfer type connections

## Adhesive type Connections

- tight junctions:
  - aka zona occludens
  - attachements between cell membrane at apical margins
  - differ in leakiness:
    - tight = impermeable eg distal renal tubule for water, BBB, bladder
    - leaky = paracellular permeable eg prox renal tubule, small intestine, liver
  - help maintain cell polarity & prevent movement of proteins in plane of CM
    ↳ is a protein inserted into apical CM will stay there
- zonula adherens:
  - lies below tight junction ie almost a continuous structure
  - contains cadherins
  - acts as site for attachments of cellular microfilaments
- desmosomes:
  - patches of apposed thickenings of membranes of adjacent cells
- hemidesmosomes:
  - attach cells to underlying basal lamina
  - attached intracellular to filaments
  - contain integrins (not cadherins)
- focal adhesions:
  - also attach to basal laminae
  - labile
  - associated with actin filaments inside cell
  - have role in cell movement

## Transfer Type Connections

- GAP junctions:
  - Six subunit protein connections
  - Between cells which are apposed
  - Form low electrical resistance channels
  - Permit intercellular communication
    ↳ eg current flow & electrical coupling between myocardial cells via ions, aa, sugars
  - @GAP junction Intercellular space narrows from 25 ⇒ 3nm
  - diameter of junctions regulated by:
    - pH
    - voltage
    - Intracellular calcium

# Transport Across Cell Membranes

- Water, ions, substances can cross cell membrane by:
  - Bulk flow:
    - Aka ultrafiltration
    - Eg fluid movement between capillaries & interstitium 2nd to Starlings forces
    - If bulk flow of solvent then also drags some solute
      ↳ = solvent drag
  - Exocyotosis & endocyotosis
  - Diffusion:
    - Down gradients though:
      - Directly through membrane
      - Through protein channels:
        - Voltage
        - Ligand gated
  - Carrier mediated diffusion
    - ie where protein binds & carries
    - facilitated diffusion = when item moved along their gradient (chem or electrical) no energy is needed eg GLUT transporters
  - Active transport
    - Primary –
      - hydrolysis of ATP
      - uniports = transport 1 substance
      - symports = need to bind more than 1 substance for movement to occur
      - antiports = exchange one for another
    - Secondary active
    - Counter-transport

## Exocytosis/Endocytosis

**Exocytosis**

- Vesicle containing material sent to cell membrane
- Fusion with CM
- Ca dependant exocytosis
- 2 pathways:
  - nonconstitutive pathway =
    - aka regulated pathway
    - protein from Golgi enter secretory granules
    - process of prohormones to hormones occurs before exocytosis
  - constitutive pathway =
    - prompt transport of proteins to cell membrane in vesicles with no processing

**Endocytosis**

- = reverse of exocyotis
- different methods:
  - phagocytosis =
    - cell eating
    - material makes contact with CM which then invaginated
    - invagination pinched off ⇒ engulfed material in vacuole with intact CM
  - pinocytosis =
    - cell drinking
    - vesicles much smaller
    - substance ingested in solution
  - clathrin mediated endocytosis =

        - where protein clathrin accumulates in CM
        - clathrin forms a geometric array that sorrounds endocytotic vesicle
        - GTP binding protein dynamin involved at neck
        - When vesicle formed clathrin falls off & is recycled
        - Responsible for internalisation of many receptors & ligands bound to them eg LDL, nerve growth factor
    - Caveolae =
        - Areas rich in cholesterol & sphingolipids
        - Caveolin found in CM (similar to clathrin)
        - Dynamin also involved
    - Nonclathrin/noncaveolar endocyotosis

## Diffusion

- Usually down chemical =/- electrical gradient ie no energy needed
- Summarized by Fick's equation

$$J = -D.A.\frac{(\Delta c)}{(\Delta x)}$$

J = net rate of diffusion

D = diff coefficient and is ~ sol / √mw (Graham's Law)

A = area

c = concentration

x = thickness of membrane

## Osmosis

- = diffusion of solvent molecules into a region with higher conc of a solute to which the membrane is impermeable
- osmotic pressure = pressure necessary to prevent solvent migration into its compartment
- osmotic pressure =

$$p = \frac{nRT}{V}$$

n = number of particles
R = gas constant
T = temp
V = volume

- ∴ if T held constant: p ∝ number of particles/unit of volume

## Gibbs-Donnan Effect

- definition:
    - semipermeable membrane separates 2 solutions
    - 1 solution contains non diffusible charged species
    - THEN the distribution of all other diffusible univalent cations & anions across the membrane is altered in predictable manner ie at equilibrium the conc ratios are equal
- More complex for divalent ions due to protein binding
- NET effect:
    - On side of non-diffusible ion = more ions
    - ∴ if situation is intracellular ⇒ osmotic movement of water into cell ⇒ cell rupture
        - ↳ eg –ve change intracellular protein
        - ↳ this process opposed by Na/K/ATPase

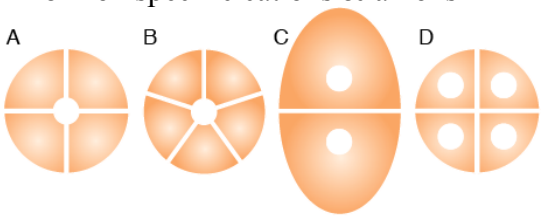
**importance of Gibbs-Donna effect**

- maintain & stabilise cell volume:
    - balance of:

        - intracellular: non diffusible proteins & inorganic phosphates
        - ECF: non diffusible Na – due to Na/K/ATPase pumping it out & low membrane permeability
    - = Double Donnan effect
    - if Na/k/ATPase stops working ⇒ influx of Na & water ⇒ cell rupture
- contribution to plasma oncotic pressure:
    - equilibrium ⇒ alteration distribution of other ions across CM
    - ⇒ small NET ↑ in ions in plasma
    - ⇒ ↑↑plasma oncotic pressure in capillary blood ie 15 to 25mmHg
- contributes to resting membrane potential:
    - small effect
    - small amount of:
        - intracell: ↑cations
        - ECF: ↑anions

## Ion Channels

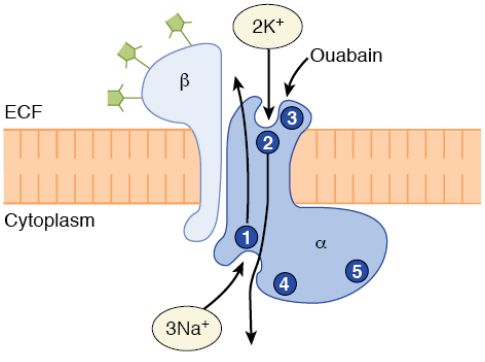
- Channels exist
    - specific for K+, Na+, Ca,+ Cl-
    - non specific cations & anions






- 
- A = K channels – mostly tetramers
- B = Ach receptor. Each subunit contributes to channel
- C = Cl- channels = dimers with intracellular pore in each subunit
- D = tetramers with intracellular channel in each subunit

## Na/K/ATPase






- Na-K Pump
- = enzyme which catalyses the hydrolyses of ATP ⇒ ADP
- = heterodimer made of:
    - α subunit =
        - MW ~ 100K
        - Transport of Na/K

    - Spans cell membrane x10
    - Amino-carboxyl terminals intracellular
  - ß subunit =
    - MW ~55K
    - Glycoprotein
- Movement of Na & K major energy process of body:
  - Cells – 24% energy used
  - Neurons – 70% energy used
- both subunits extend thru CM
- separation of subunits kills pump
- when Na binds to α subunit ⇒ ATP also binds and converted to ADP
- energy used to extrude 3 Na, and move 2 K into cell or each ATP
- actively inhibited by ouabain
  ↳ related to digitalis glycosides
- found in all parts of body

**Functions**

- functions include:
  - genesis & maintainence of RMP
  - stability of cell volume
  - transport of substances across membranes (primary & secondary active)
  - hydrogen in secretion in kindey
  - signal transduction

**Regulation**

- ↑intracellular Na
- 2nd messengers produced in cells eg cAMP, DAG, arachidonic acid derivates
- thyroid hormones ⇒ ↑activity & ↑number of Na/K pumps
- aldosterone ⇒ ↑number of pumps
- dopamine – inhibits pump in kidneys ⇒ natriresis
- insulin ⇒ ↑activity

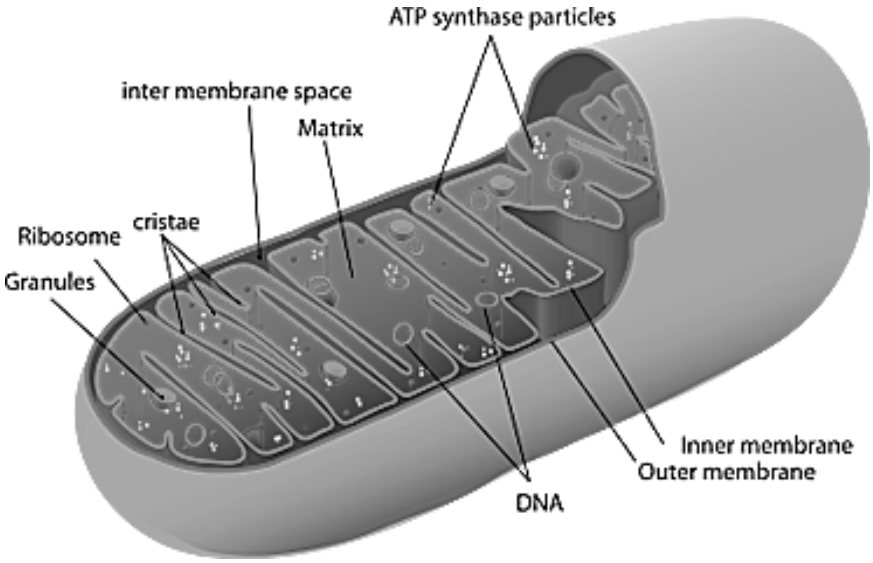
### Secondary Active Transport

- = active transport of Na coupled to transport of other substances
- eg Na/K/ATPase creates an elec-chem gradient by pumping Na out of cells into ECF:
  - eg mucosal cells of small intestine: symport which transports glucose only if Na also attached and moves at same time
  - myocardium- NCX pump

# Organelles

## Mitochondria

- mitochondria have own genome & ability to manufacture own RNA & proteins
- their ribosomes = 70S type (30S & 50S) ie same as bacteria
  ↳ rest of cell has 80S ribosomes




**Structure**

- 1-10um
- outer membrane:
  - encloses whole organelle
  - contains several integral proteins = porins
  - porins form large aqueous channels which allow passage of movement of molecules up to 5000D
- intermembrane space:
  - between outer & inner membrane
  - chemically equivalent to cells cytosol
  - contains cytochrome-c
- inner membrane:
  - no porins
  - controlled permeability via transporter proteins
  - proteins have diff functions:
    - proteins carrying out oxidative reactions of resp chain
    - ATP synthase – makes ATP in matrix
    - Transport proteins
    - Protein import machinery
- Cristae:
  - Formed by folded inner membrane
  - Vastly ↑s surface area for ATP production
  - Cells which more active eg mm have more cristae
- Matrix:
  - Space enclosed by inner membrane
  - Impt in ATP production
  - Contains highly conc mixture of
    - hundreds of enzymes
    - mitochon ribosomes (70S)
    - tRNA
    - several copies of DNA genome
  - major function of enzymes =
    - oxidation of pyruvate & Fas
    - citric acid cycle

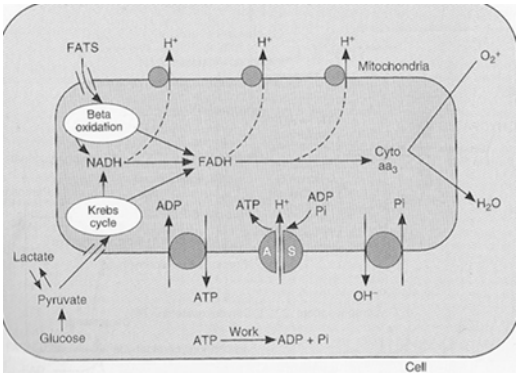
**Function**

- main = ATP production which needed for cellular metabolism
- other functions:
  - cell signalling
  - apoptosis

- cellular differentiation
- cell growth

**Oxidative Phosphorylation - Mitcochondria Energy Production**

- mitochon found in high conc in cells with high metabolic demands eg myocardium (23% of cell), brown fat (neonate)
- exercise ↑s numbers
- OP = production of ATP associated with oxidation by the flavoprotein cytochrome system in mitochondria



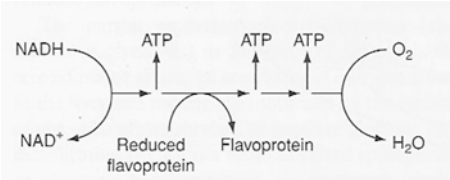
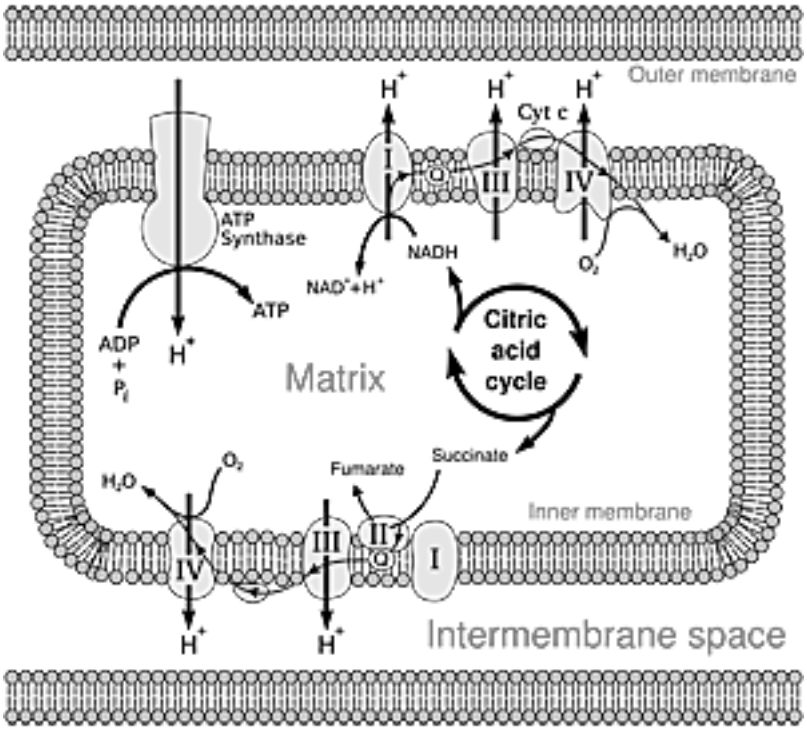




**Figure 12.6** *Outline of oxidative phosphorylation*

- ATP formed in electron transfer chain:
  - Substrate diffuses into mitochon cytoplasm
  - Hydrogen removed by a dehydrogenase
  - NAD carries hydrogen to respiratory chain
  - Hydrogen ionises and protons pass along series of carrier molecules across insulating membrane (inner membrane of mitochondria – forms cristae)
  - Movement of protons creates a electrochemical gradient for transport of protons from intermediate space back into matrix ⇒ this drives a reversible ATPase in inner membrane (ATP synthase)
  - ATp synthase: ADP + Pi ⇒ ATP
  - @end:
    - ATP produced
    - Reduction of O2 to water – catalysed by cytochrome oxidase
      ↳ cyanide inhibits this oxidase ∴ inhibits OP in mitochon
      ↳ O2 required to oxidise NADH




- Eg's of carrier molecules in electron transfer chain
  - Flavoprotein
  - Cytochromes A, A3, B, C, C1
  - Ubiquinone
  - Several iron sulphide proteins
- OP depends on:
  - Adequate supply of ADP - +ve feedback loop eg ↑ATP utilisation ⇒ ↑ADP ⇒ ↑OP
  - Rate of delivery of fats, lactate, glucose to interior of mitochon
  - Availability of O2:
    - Pasteur point = 1-2mmHg ie point below OP cannot occur
- ∴ cardioresp works in harmony to ensure o2 reaches cells
  - defined by oxygen flux equation:

    $DO_{2body} = CaO_2 \times CO$
- lack of oxygen causes:
  - nothing to scavenge H+ at end of transfer chain
  - transfer chain ceases
  - build up of reduced compounds ⇒ inhibits TCA cycle ⇒ inhibition of glycolysis

    ↳ but glycolysis continues as lactate dehydrogenase removes reduced compounds

## Endoplasmic Reticulum

- complex system of tubules in cytoplasm
- tubule walls made of membrane
- rough ER =
  - ribosomes (granules) attaches to cytoplasmic side of membrane
  - involved in protein synthesis:
    - folding polypeptide chains
    - form S-S bonds
- smooth ER =
  - attached ribosome absent (but free ribosomes in cytoplasm)
  - dunction:
    - site of steroid synthesis
    - detoxification processes

- sarcoplasmic reticulum = impt role in skeletal & cardiac mm functioning

### Ribosomes

- eukaryotes =
  - 80S – 60S & 40S subunits
  - 22-32nm
  - site of protein synthesis
  - contain
    - many proteins &
    - at least 3 ribosomal RNAs
  - ribosomes attached to ER synthesize proteins for eg
    - hormones for secretion
    - proteins seregated in lysosomes
    - proteins in cell membranes
  - free ribosomes in cytoplasm:
    - protein in Hb
    - protein in mitochondira
- Golgi apparatus involved in processing proteins found in ribosomes

# Cell Receptors & Secondary Messengers within Cells

- Extra-cellular ligands = 1st messangers
- Intracellular mediators = 2nd messangers

**Types of receptors:**

| | **Type 1** Ligand-gated ion ch's (*ionotropic*) | **Type2** G-prot coupled (*metabotropic*) | **Type3** Kinase-linked | **Type4** Nuclear |
|---|---|---|---|---|
| Location | membrane | membrane | membrane | intracellular |
| Effector | ion channel | Ch or enzyme | enzyme | gene transcription |
| 2nd msgr | -- | c-AMP/c-GMP<br>IP3 / DAG | -- | -- |
| Coupling | direct | G-prot | direct | via DNA |
| E.g.'s | n-AchR<br>$GABA_A$<br>NMDA | m-AchR<br>adrenoceptors<br>opioid R's | Insulin<br>growth factor<br>Cytokine r's<br>EPO | steroid, thyroid H receptors |
| Time | millisec's<br>(Fast synaptic) | seconds | hrs | hrs |
| Structure | oligomeric assembly of subunits around central pore | Monomeric with 7 transmembrane helices | Single trans-membr helix linking EC R domain to IC kinase domain | Monomeric str with separate R and DNA binding domains. |

## Type 1 - Ionotropic

- See prev notes on NaKATPase & ion channels

## Type 2: G Proteins & P Protein Coupled Receptors (GPCRs)

- GPCR = monomer compromising 7 membrane spanning segments
- One of intracellular loops = larger & interacts with G protein
- ∴ GPCR couple to intracellular effector systems via a GP
  ↳ G Protein 100: 1 GPCR (amplification system)
- G proteins =
  - membrane proteins coupled to specific receptors
    ↳ aka metabotropic receptors
  - non selective workhorses for GPCR they are couple to.
    ↳ = go between from receptor (selective) to effector (enzyme or ion channel)
- GP consist of 3 subunits:
  - Alpha –
    - bound to GDP
    - possesses intrinsic GTPase activity
  - Beta
  - Gamma
- Process of activation:
  - Ligand bind to GPCR ⇒ GDP on alpha subunit is exchanged for GTP
  - Alpha subunit separates from combined ß & gamma subunit
    ↳ ß & gamma subunit tightly bound to membrane
  - Alpha-GTP complex free to activate an effector eg membrane enzyme or channel
- Activation terminated
  - when bound GTP hydrolysed to GDP
    ↳intrinsic GTPase ability of alpha subunit is upregulated when bound to target protein
  - alpha (& bound GDP) then reattach with beta-gamma subunits
- 1400 combinations of alpha, beta, gamma combinations to control different effectors
- complex activation process ⇒ slower onset than ionotropic receptors eg GABA, n-ACH = milliseconds

**Targets of GPs**

G protein can activate:

- adenylate cyclase (AC) or Guanylate cyclase (GC) ⇒ c-AMP or c-GMP formation
- phospholipase C (PLC) on inner surface of CM

**c-AMP**

- = cyclic adenosine 3'5'monophosphate
- cAMP = physiologically active
- c-AMP formed from ATP by adenylyl cyclase
- inactivated by conversion to 5'AMP by phosphodiesterase
  ↳ can be inhibited by methylxantines eg theophylline

**c-GMP**

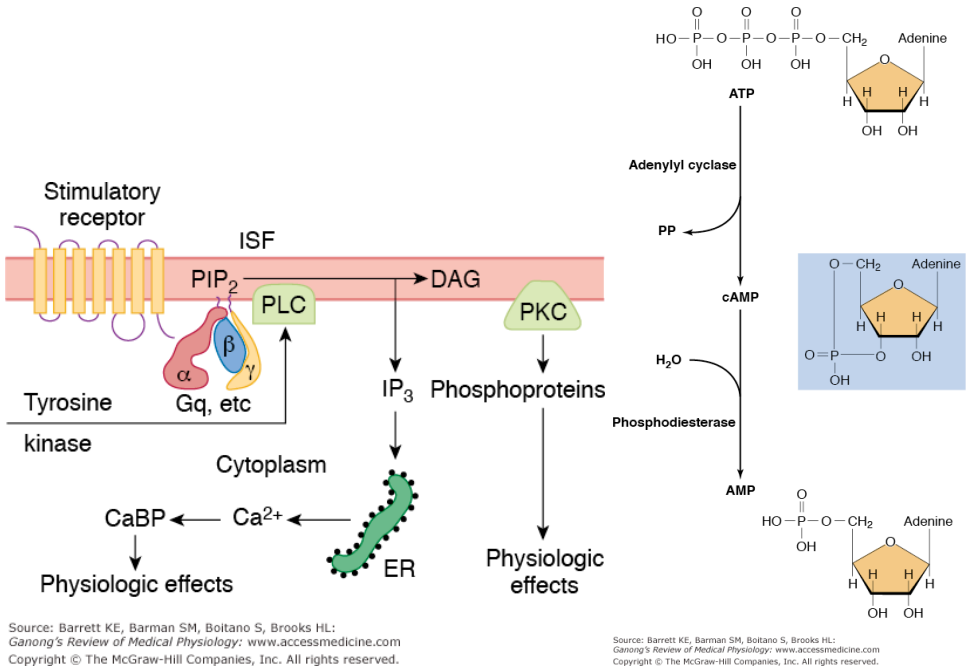
- = cyclinc guanosine monophosphate
- impt in vision
- guanylate cyclases = family of enzymes which catalyse formation of cGMP

**PLC**

- catalyse hydrolysis of membrane lipid PIP2 to

- inositol phosphate (IP3) or
- diacylglycerol (DAG)

- IP3 – diffuses to ER where binds to IP3 receptor
  ↳ = ligand gated Ca channel
- DAG – stays in cell membrane where it activates protein kinase C






**Types of G Proteins**

- **Gs** : → ↑ AC(or GC) → ↑ c-AMP eg of substances causing Gs activation:
  - ADH ,
  - adrenalin(beta receptors) ,
  - adenosine (A2 ) ,
  - ANP ,
  - glucagon ,
  - histamine(H2)
- **Gi**: → ↓ AC (or GC)→ ↓c-AMP
  - angiotensin (AT2) ,
  - adenosine (A1),
  - alpha-2 and
  - opioid receptors.
- **$G_q$**:→ ↑ PLC → IP3 + DAG eg noradrenaline (alpha1) , histamine H1 ,
- **Gt**: → stim c-GMP phosphodiesterase in photoreceptors
- **Go**: → involved in gating of ion ch's , ↑ concentration in brain

## Type 3 – Kinase linked

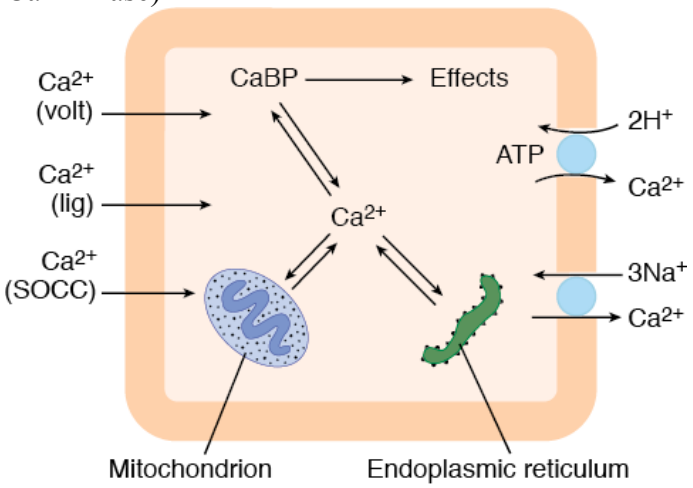
- Eg
  - insulin like growth factor 1 (IGF-1)
  - Epigermal growth factor (EGF)
- Single membrane spanning domain
- Intracellular tyrosine kinase domains
- Ligand binds to tyrosine kinase receptor⇒
  - Dimerization of 2 similar receptors
  - ⇒ partial activation of intracellular tyrosine kinase domains

- ⇒ cross phosphorylation to fully activate each other
- ⇒ production of transcription factors

## Type 4 – Nuclear Receptors

## Intracellular Calcium as a 2nd Messenger

- Free Ca2+ conc in cytoplasm = rest 100nmol/L
- Ca conc in ECF = 1,200,000 nmol/L
  ↳ ie marked inwards conc gradient
- ∴ most of intracellular Ca stored at v high conc in ER & other organelles
- Ca can enter cell by variety of methods:
  - Down gradient
  - Ligand gated or voltage gated channels
  - Stretch channels
- Secondary messengers ⇒ ↑intracell Ca conc by:
  - Ca release from intracellular stores
    - IP3 –
      - major 2nd messenger with this effect
      - IP3 receptor on ER
  - ↑ed entry Ca into cells
    - SOCCs (store-operated Ca channels)
      - Transient release Ca from internal stores ⇒ opening SOCC on cell membrane
      - Influx of Ca replenishes & refills ER
- Movement of Ca out of cell against conc gradient:
  - Active transport – membrane Ca ATPase
  - 2nd Active transport –
    - NCX (3 Na in for each Ca out)
    - Driven by Na gradient
- Movement of Ca into internal stores via action SERCA pump (sarcoplasmic or endoplasmic reticulum Ca ATPase)



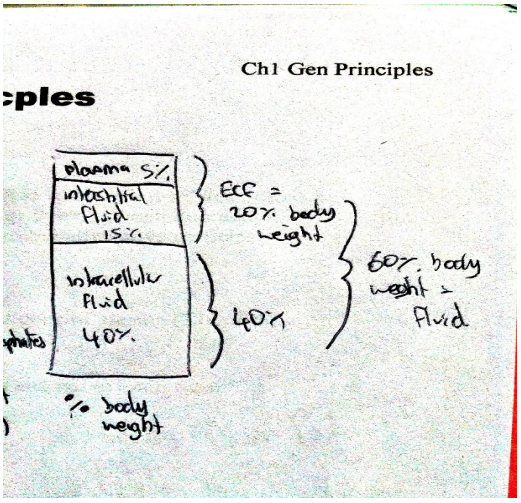
# General Prinicples

## Definitions

- **Osmolarity** : = no of osmoles of solute per *litre* of solvent:
  - altered by temp changes + vol of solute
- **Osmolality**: = no of osmoles of solute per *kg* of solvent:
  - independent of T changes or vol of solute
- **Tonicity**:
  - = the *effective* osmolality of a solution.
  - = to the sum of the [ ]'s of the solutes which have the capacity to exert osmotic force across the membrane concerned.

## Intracelluar Fluid (ICF) & Extracellular (ECF)

- ICF cannot be measure directly
- Derived from TBW – ECF
- TBW measured by dilution principle using Deuterium oxide (D20 = a heavy water)
- ECF measured with inulin
- TB Water = 60% of total body weight
- body water can be further subdivided via simple or complex models:
  - complex (60% broken down into)
    - ICF = 55%
    - ECF = 45% which broken down into
      - 20% interstitial
      - 7.5% intravascular
      - 7.5% bone
      - 7.5% dense CT
      - 2.5% transcellular fluid eg CSF, urine in bladder etc
  - simple (% = breakdown of 60%) (bracketed = fraction of 60%)
    - 40% ICF (2/3)
    - 20% ECF (1/3)
      - 5% plasma (1/4)
      - 15% interstitial (3/4)
- ∴ 70kg person:
  - TBW = 42litres
  - ICF = 28litres
  - ECF = 14 litres:
    - 3.5 litres plasma
    - 10.5 litres interstitial fluid




ECF = majority Na & Cl
ICF = majority:

- K (most ~150mmol/L)
- Misc phosphates
- Protein
- (small amount Na)

Other Body Weights

- weights:
  - 60% fluid
    - intracellular - 40%
    - extracellular - 20%
  - 17% protein
  - 15% fat
  - 7% mineral

## Control of Cell Volume

- H20 can cross CMs freely ∴ could lead to:
  - Change ECF tonicity
  - Change in cell volume

  ↳but doesn't
- Cell contain sig conc of anions which non-diffusable

  ↳ proteins & organic phosphates
- Creates Donnan effect across CM ⇒ intracellular anions drawing water into cell ⇒ cell rupture if nt counterbalanced!
- Counterbalance =
  - Donnan effect in opposite direction set up by Na in ECF
  - Na in ECF effectively non diffusible due to Na/K/ATPase pump & ↓ed Na CM permeability

↳ = double Donnan effect ⇒ stable cell volume
↳ reliant on Na/K/ATPase

## Changes to Tonicity

- Acute change in ECF tonicity ⇒ acute change in cell volume
- Adaptation can occur with time:
  - Cell adapt to minimise disruption caused by change in ECF tonicity
  - Done by changing intracellular solute content

    ↳ie lose or gain solute to minimise volume changes
- Eg ECF hypertonicity:
  - ⇒ IC dehydration
  - cell will gain solute from ECF or ↑production of own solute

## Mole

- = gram molecular weight of a substance
- 1mol NaCl = 23g + 35.5g = 58.5g

## Water

- H20 has a dipole moment:
  - o2 pulls away electrons from the hydrogen atoms ⇒ slightly polar
  - allows water to dissolve variety of charged atom & molecules
  - allows H20 – H20 bonding via Hydrogen bonds
- hydrogen bond network causes:
  - high surface tension
  - high heat vaporisation & heat capacity
  - high dielectric constant

## Electrolytes

- eg NaCl = molecules which dissociate in water to:
  - Na+ = cation
  - Cl- = anion
- Tend not to reasociate in water due to elec charge

## pH & Buffering

- pH = logarithm to the base 10 of the reciprocal of the H+ concentration
  ↳= -ve log of H+ conc
- water = pH 7
- gastric acid = 2
- pancreatic enzyme = 8
- buffer = substance which has ability to bind or release H+ in solution thus normalising pH of solution
- isohydric principle = all buffer pairs in homogenous solution are in equilibrium with same H+ conc

## Tonicity

- = osmolality of a solution relative to plasma
- solution which same osmolality as plasma = isotonic
- hypertonic = greater osmolality than plasma
- all solutions which initially isosmotic with plasma would remain isotonic but solutes diffuse into cells/metabolised ↳ie same osmotic pressure or freezing point depression
  - 0.9% saline = remains isotonic – as net movement of osmotically active particles
  - 5% gluc =
    - isotonic initially
    - gluc then metabolised ⇒ hypotonic solution
- Na+, Cl- & HCO3- provide most impt contribution to osmolal conc of plasma (270 of the 290mOsm/L)

## Non ionic Diffusion

- Some acids/bases can cross membrane in undissociated form and not in ionic form
- ∴ move across as undissociates and then dissociate
- = non ionic diffusion

# TransMembrane Potential

## Concentration of Ions

- resting cell membrane potential = -70mV

| Ion | Inside Cell | Outside Cell | Equilibrium Potential mV |
|---|---|---|---|
| Na+ | 15 | 150 | +60 |
| K+ | 150 | 5.5 | -90 |
| Cl- | 9 | 125 | -70 |
| Ca | 100nanomol | 2.2-2.5 (1.15-1.3) | |
| Mg | 10mmol | 0.75-1mmol | |
| HCO3 | 10 | 20-30 | |
| pH | 7.1 | 7.4 | |

- Na:
  - Concentration & elec gradient is inward
  - ∴ expect slow gain of intracellular Na
- K:
  - Conc gradient outward
  - Elec gradient inward
  - But conc gradient is greater ∴ expect slow outward movement
- Cl-:
  - Conc gradient inward
  - Elec gradient neutral

## Genesis of Membrane Potential

- Na,K, ATPase:
  - Uses ATP to pump K back into cell
  - Keeps intracellular Na low
  - 3Na out; 2 K in ⇒ ∴contributes to membrane potential
    ↳= electrogenic pump

## Resting Membrane Potentials

- skeletal mm -90mV; threshold -70mV
- cardiac mm -80mV; threshold -65mV
- Neurones -70mv; threshold -55mV
- Cardiac pacemaker cells -60mV
- smooth mm – wandering baseline but average -50mV

# Energy Production

- large amounts of energy released when high energy phosphate compound bonds are hydrolysed
- also see low energy phosphates
- ATP = most impt high energy phosphate:
    - ATP ⇒ ADP ⇒ AMP
      ↳all steps create energy

## Oxidation

- Oxidation =
    - combination of a substance with O2 or
    - loss of a hydrogen or
    - loss of electrons

  ↳opposite = reduction
- reduction reactions:
    - NAD+ ⇒ NADP+ ⇒ NADH ⇒ NADPH
- Oxidative phosphorylation:
    - Energy from a proton gradient across mitochondrial membrane
    - Flavoprotein-cytochrome systems creates H+ movement from inner to outer lamella of mitchondria
    - Return movement of proton down proton gradient ⇒ ATP
- 90% o2 consumption in basal state = mitochondrial
  ↳80% this coupled to ATP synthesis