Chemical Signaling

How is chemical signaling used?

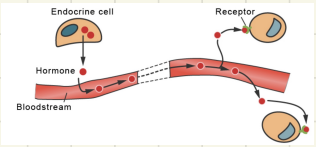
C2.1.2 — Signaling by bacteria in quorum sensing

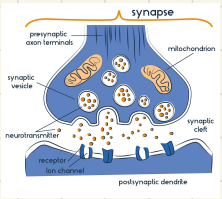
Quorum sensing => a change in the behavior of a colony when its population density reaches a certain threshold

- More cells = more chemical messenger molecules
- @ certain density, enough molecules have been received to cause change in activity
  - ↳ Ex: bioluminescence in Vibrio fischeri and mutualism w/ bobtail squid. The bacteria allow squid to create luminescent proteins. But this only happens when there is a min. amount.

C2.1.5 — Local / distant effect of signaling molecules

- Hormones can have effects over large distances (travel through blood to get to cells)
- Neurotransmitter produce localised effect between 2 neurons





3 steps of chemical signaling:

1. Reception => cell detects signaling molecule from outside/inside the cell
2. Transduction => Signaling molecule binds to the receptor protein, causing a conformational change
3. Response => signal causes a specific chemical response

Types of chemical signals

C2.1.3 — Hormones, neurotransmitters, cytokines, Ca^{2+} => signaling chemicals

Hormones

Endocrine glands => secrete hormones into the bloodstream throughout the body

- Target cell have receptor proteins
- May have a long effect time
  - ↳ Ex.:
    1. insulin
    2. glucagon
    3. testosterone
    4. estrogen

Neurotransmitters

- Synaptic transmission (between nerves)
- Isolated to just that nerve junction
- Short effect time
- Removal from synapse
  - ↳ Ex:
    1. acetylcholine
    2. dopamine
    3. serotonin

Cytokines

Cytokines => proteins that act as chemical messages within cells / between nearby cells

- Can have multiple effects depending on binding site
  - ↳ Ex:
    1. Interferon
    2. erythropoietin

Calcium ions

before muscle contraction can even begin, Ca^{2+} have to shift a fiber covering actin out of the way.

1. Muscle fibres => calcium ions bind to a protein on actin to allow myosin heads to attach
2. Neurons => causes the release of neurotransmitters from the presynaptic neuron

C2.1.4 — diversity of hormones ⁝ neurotransmitters

- Evolved separately many times (many form/functions)
- Similarities:
  a) Small
  b) Soluble
  c) Have shape compatible w/ receptor

Hormones:

1. Steroids: hydrophobic — internal receptors
2. Amines: hydrophilic — external receptors
3. Peptides

considered hormones bc. of the way that they work ⁝ where they come from
NOT
bc of structure

Neurotransmitters:

1. Amines
2. Amino acids
3. Esters
4. Gases

most: hydrophilic ⁝ bind on cell surface

considered neurotransmitters bc. of the way that they work ⁝ where they come from
NOT
bc of structure

What are receptors ? how they help.

C2.1.1 – Receptors = proteins w/ binding site

Signaling molecules => ligands

Protein receptor => ligand - binding site

when ligand binds to receptor protein's binding site, protein undergoes a conformational change.

May cause:

1. change in gene expression
2. kick off series of cellular responces

Ligand = specific to protein

Ligand remains unchanged, does not undergo conformational change

Ligand may remain bound to protein 4 long time.
↳ cellular responce lasts.

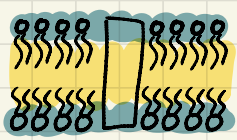
C2.1.6 – transmembrane / intracellular receptors

Transmembrane => in plasma membrane

Intracellular => in cytoplasm / nucleus

CAN the chemical signaling molecule even enter the cell? This dictates a LOT about type of receptor protein needed

- CAN enter cell: (they themselves = hydrophobic)
  a) Receptor protein = in cytoplasm/nucleus
  b) Intracellular
  c) Surface of receptor = covered in hydrophilic amino acids (dissolved)
- CANNOT enter the cell
  a) Receptor protein on plasma membrane
  b) Transmembrane
  c) Hydrophilic / hydrophobic amino acids
     (hydrophilic: out of membrane; hydrophobic: inside membrane)



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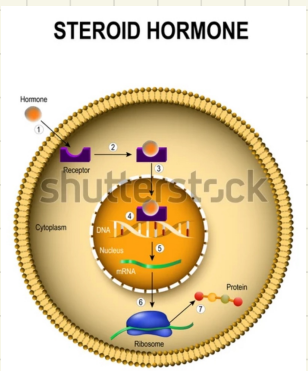

C2.1.7 – Initiation of signal transduction by receptors

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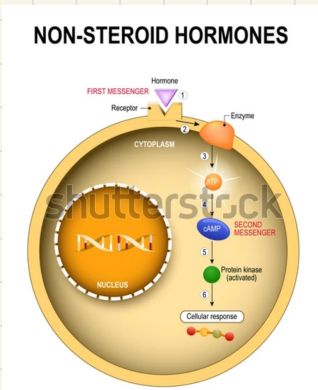


Transduction pathway => sequence of interactions initiated by the ligand binding to the receptor

1. Intracellular pathway => ligand enters the cell, binds to receptor, complex regulates gene expression
   - Together, they enter nucleus
2. Transmembrane pathway => ligand binds with receptor, receptor changes shape, produces secondary messenger molecules, causes changes within cell

Second messenger: Molecules inside cells that relay signals received by cell-surface receptors

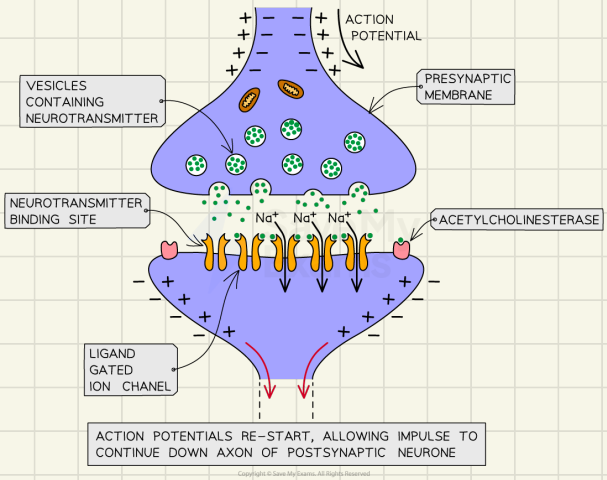
Different extracellular receptors!

C2.1.8 – Transmembrane receptors for neurotransmitters ⁝ membrane potential

1. Neurotransmitters are released from the presynaptic neuron
2. They travel through the synaptic gap
3. They bind to receptors on the postsynaptic neuron (temporarily)
   Called ligand-gated sodium ion channels
4. Causes sodium ion channels to open
5. Sodium enters the cell via facilitated diffusion (Na^+)
6. Changes membrane potential [− → +]
7. The products = absorbed back to presynaptic membrane, recycled ⁝ packaged into vesicles ready to be used again

These steps can also happen between neuron ⁝ muscle

→ acetylcholine = common messenger including between neurons ⁝ muscle fibers



C2.1.9 — Receptors that activate G proteins

GPCR => G-protein coupled receptors

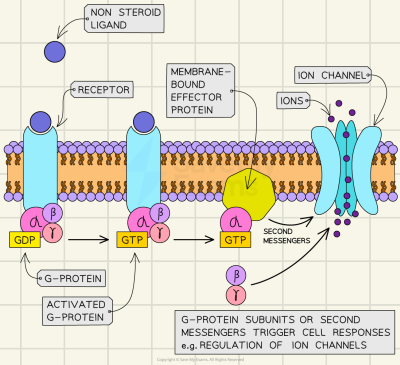
- Transmembrane receptor proteins

for example...
- Dopamine
- pheromones
- Serotonine
- Oxytocin

GDP => guanosine diphosphate

GTP => guanosine triphosphate

- Posta:
  1. When GDP = bound to a G protein, it is inactive
  2. When ligand binds to receptor, the GPCR changes shape
     ! makes contact w/ G-protein (which is composed of α,β,γ subunits bound to a GDP molecule)
  3. This contact prompts GDP to be replaced by GTP.
  4. This causes the G-prot. to activate, disassemble and cause changes within the cell
     i) α ! GTP bind and activate enzymes
     ii) β ! γ bind and activate ion channels
  5. The GTP, α,β,γ subunit detach from GPCR ! can attach to other proteins → This is why they are called second messengers

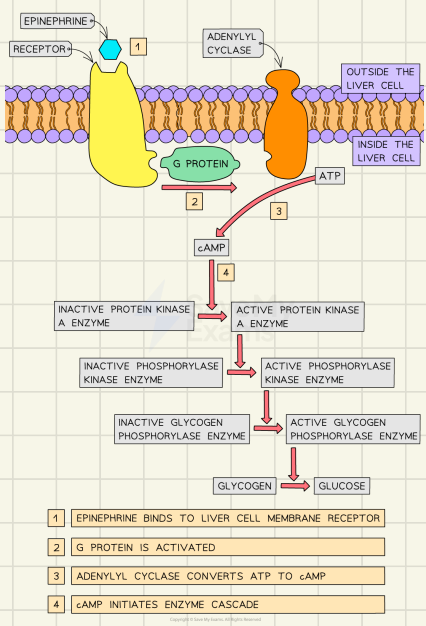


C2.1.10 — Epinephrine (adrenaline) receptors

- Epinephrine = adrenaline — key rol on fight/flight
- Hormone produced by adrenal glands
  - On kidneys
- Binds w/ a G protein (through a transmembrane receptor)
  - Causes ATP to be converted into a secondary messenger molecule called cyclic AMP (cAMP)
    - Amplifies effect
    - Produces glucose [This is why glucose levels sky rocket during stressful scenarios]

→ Ex. hydrolysis of glycogen → glucose

ligand cannot enter cell



C2.1.11 — Receptors w/ tyrosine activity

Kinase => special type of enzyme that phosphorylates molecules by removing a phosphate group from ATP & adding it to a molecule

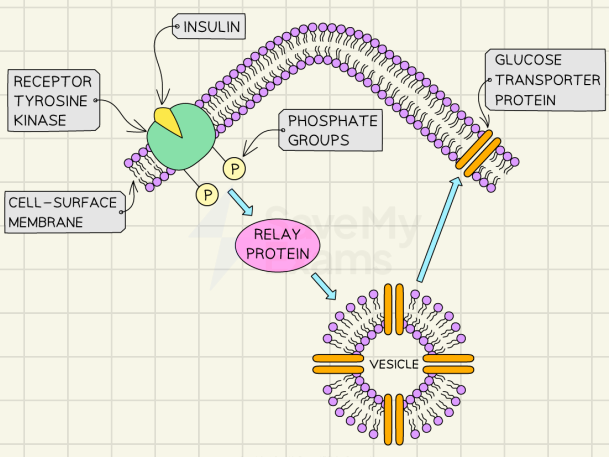
- Take out phosphate from ATP & place it on another molecule

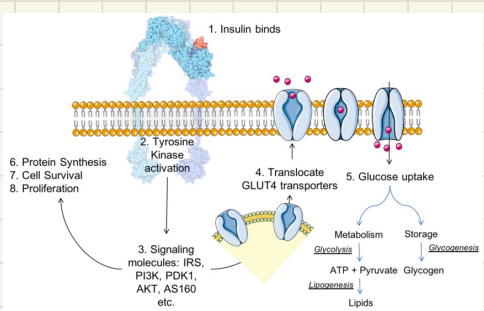
Tyrosine Kinase => enzyme that transfers a phosphate group from ATP to tyrosine (amino acid) in a protein

Secreted by pancreas when glucose levels = too high

Whole Point of insulin: Promote glucose uptake by cells to decrease glucose levels within bloodstream

- Ex: binding of insulin to the transmembrane receptor protein
  1. Insulin binds to tyrosine kinase receptor (TKR)
     a) TKR has an α unit that can be found in extracellular space & β domain in intracellular space
        i. The Tyrosine Kinase enzyme = found within β domain
  2. Conformational change of transmembrane protein
  3. Tyrosine Kinase (on β) become autophosphorylated
  4. Causes Tyrosine Kinase to add phosphate groups onto proteins (phosphorylation of other proteins)
  5. Causes a conformational change to proteins that are embeded on vesicles
  6. Vesicles => fuse with cell membrane
     a) Glucose transporters = inserted into membrane
        i. Glucose can diffuse into cell w/ more ease [+ channel proteins that allow this to happen]





How do dif. intracellular receptors work?

C2.1.12 — Intracellular receptors ⁝ gene expression

- Some hormones = hydrophobic ⁝ can enter cell
  1. They bind to intracellular receptor
  2. Hormone-receptor complex moves to nucleus
  3. Complex attaches to DNA ⁝ changes gene expression
     - ↳ Can:
       - a) promote transcription / translation
       - b) Inhibit transcription / translation

} Can mean many dif. things BUT directly impacts genetic expression

Steroid hormones:

C2.1.13 — effect of oestradiol ⁝ progesterone on target cells

→ responsible for female sexual characteristics

Oestradiol / oestrogen

brain:

releases hormone (GnRH)

hypothalamus] gland

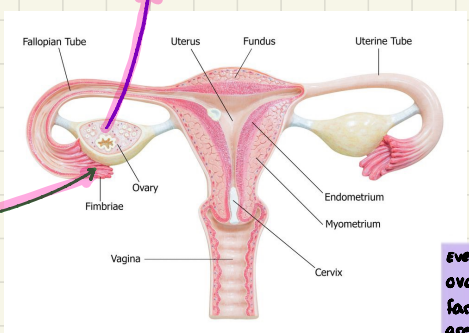
pituitary] gland

Prompts pituitary gland to release 2 hormones: LH ⁝ FSH

travel through blood and act on tissue found in ovaries

oestradiol travels to hypothalamus, enters cells, binds to receptors ⁝ causes more GnRH to be secreted ↳ ∴ more of everything

{ ovary produces eggs. These are surrounded by cells called follicles. ↳ when acted upon by pituitary hormones (LH / FSH), they secrete oestradiol

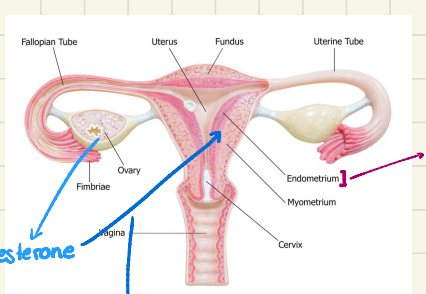


Even if brain ⁝ ovaries are far apart, they are connected by hormone that can enter cells.

"Positive feedback loop"

→ responsible for maintenance of endometrial lining

Progesterone



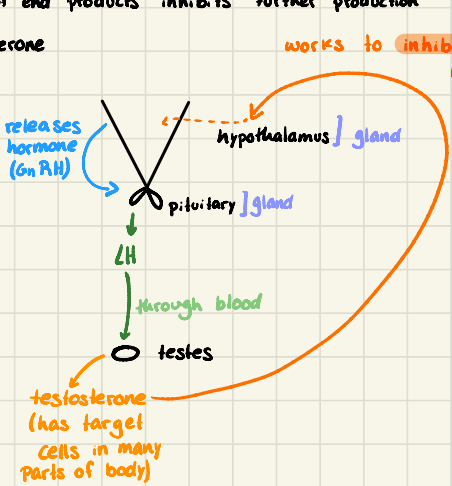
→ where embryo would implant ∴ important that these cells have a lot of nutrients

progesterone travels through blood to these cells, enters, bind to receptors that can intensify nutrient value of lining

Some pathways = homeostasis ... others, extreme responses

C2.1.14 – cell signaling throug (+/-) feedback

- Negative feedback loop
  - ↳ Maintaining stable conditions / ranges
  - ↳ Increasing [ ] of end products inhibits further production
    - Ex: testosterone



- Positive feedback loop
  - ↳ Final product triggers more production of product
    - Ex: calcium induced calcium release in muscle contractions