SYSTEM COMMUNICATION

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C2.1.2	Cell signalling by bacteria in quorum sensing
C2.1.3	Hormones, neurotransmitters, cytokines and calcium ions as examples of functional categories of signalling chemicals in animals
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C2.1.14	Regulation of cell signalling pathways by positive and negative feedback

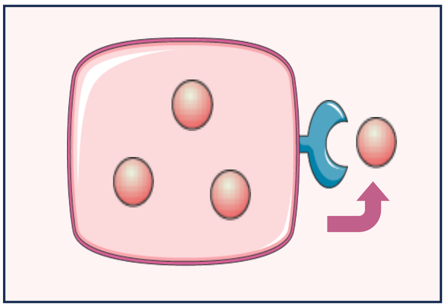
CELL SIGNALLING

Cell signalling describes the transmission of chemical signals between interacting cells. The process begins with a signalling molecule called a **ligand**, which is released by a communicating cell. The ligand binds to a *specific* **receptor** with a complementary binding site. This induces a conformational change in the receptor and triggers a cellular response – such as changes to gene expression, cell division and enzyme regulation.

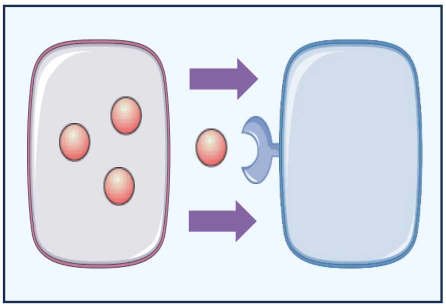
Cell signalling can involve the transmission of a signal over a range of distances in order to elicit a response:

- **Autocrine** signalling involves stimulation of the *same cell* that released the ligand (e.g. T cell activation)
- **Paracrine** signalling occurs when ligands stimulate a *neighbouring cell* (e.g. synaptic transfer in neurons)
- **Endocrine** signalling involves releasing ligands in the *bloodstream* to target distant cells (e.g. hormones)

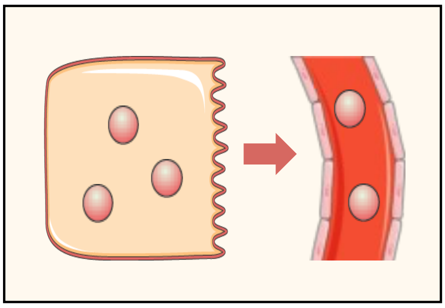
Some ligands are transferred between members of a species (**pheromones**) or distinct species (**allelopathy**)



Autocrine (e.g. cytokine)



Paracrine (neurotransmitter)



Endocrine (hormones)

SIGNALLING MOLECULES

A wide variety of signalling chemicals may be used to communicate messages between specific target cells:

- **Hormones** are chemical messengers that are released into the bloodstream to act on distant tissues
- **Neurotransmitters** are chemicals released by nerve cells to transmit signals across a synaptic cleft
- **Cytokines** are molecules released by cells to coordinate immune activity (and regulate the cell cycle)
- **Calcium ions** act as a signalling chemical *within* cells – may trigger contraction (muscles) or exocytosis

Signalling molecules possess **different chemical structures** based on the properties of the target receptor. Hormones can be either amines, peptides (<50 amino acids), proteins (>50 amino acids) or steroids (lipids). Neurotransmitters consist of amino acids or amines (small), peptides or esters (larger) and certain gases.

Hormone (endocrine cells)	Amine	Peptide	Protein	Steroid
	Melatonin Adrenaline	ADH Oxytocin	Insulin Glucagon	Estrogen Progesterone

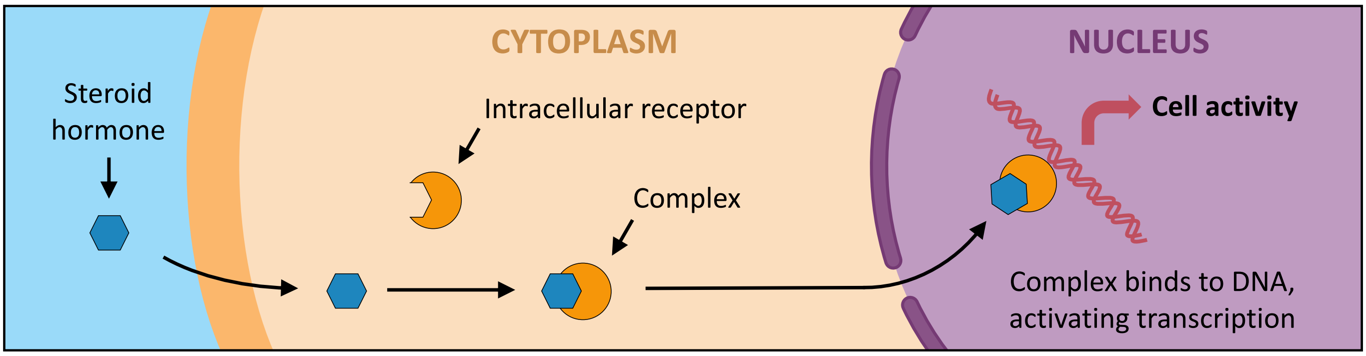
Neurotransmitter (nerve / neuron)	Amine	Amino Acid	Peptide	Gas
	Dopamine Serotonin	Glutamate Glycine	Endorphin Opioids	Nitric oxide Carbon monoxide

SIGNALLING PATHWAYS

Cellular signalling pathways will invariably involve three basic stages: **reception** → **transduction** → **response**
When a ligand binds to a specific receptor (**reception**), the chemical signal is converted into a cellular signal (**transduction**) which initiates a targeted change in expression or metabolic activity within a cell (**response**). Signal pathways differ depending on whether a ligand binds to an intracellular or transmembrane receptor.

INTRACELLULAR RECEPTORS

Lipophilic (fat-soluble) ligands such as **steroid hormones** can freely diffuse across the plasma membrane and enter a target cell. They bind to receptors within the cytoplasm or nucleus of the cell and then form a receptor-hormone **complex** that binds directly to DNA to control gene expression (regulates transcription).



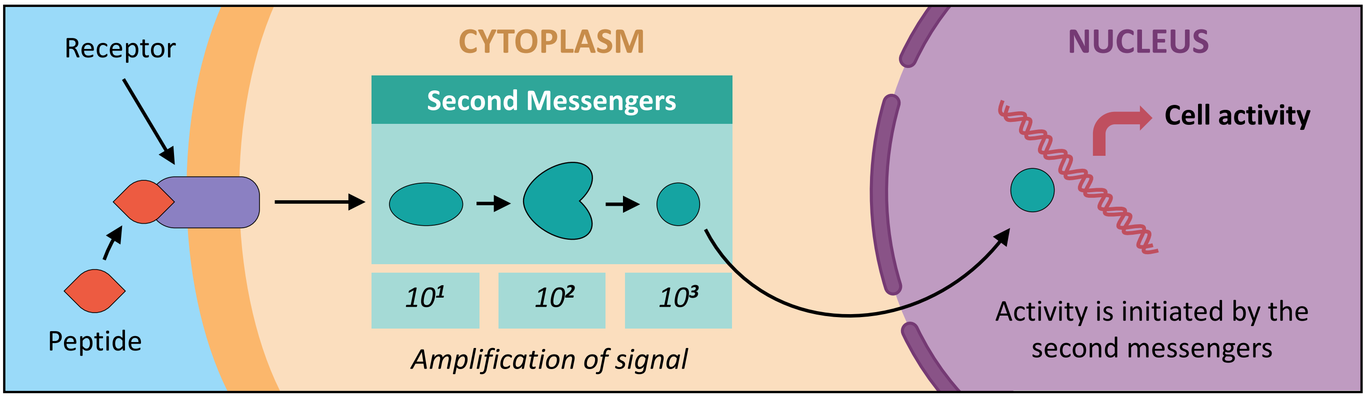
An example of lipophilic steroids are the sex hormones produced by the gonads (oestradiol / progesterone).

Oestradiol binds to intracellular receptors within the hypothalamus of the brain, and forms a complex that acts to regulate the expression of gonadotropin releasing hormone (GnRH). This acts on the pituitary gland to stimulate the release of FSH and LH, which in turn are responsible for the control of the menstrual cycle.

Progesterone binds to intracellular receptors within the endometrial cells that form the uterine lining. The complex formed controls the expression of a growth factor and functions to thicken the endometrial lining.

TRANSMEMBRANE RECEPTORS

Hydrophilic ligands such as **peptide hormones** cannot diffuse across the plasma membrane and will remain outside of the target cell. They bind to receptors that have hydrophobic amino acids on their surface, which allows the receptor to be embedded within the plasma membrane (transmembrane). An activated receptor acts to stimulate intracellular molecules called **second messengers**, which initiates a cascade of reactions in the cell (e.g. can activate or inhibit enzymes). The use of second messengers allows for signal amplification.



The activation of transmembrane receptors can initiate different effects within a target cell, including the activation of G proteins, the phosphorylation of intracellular proteins and changes to membrane potential.

Ligand-Gated Ion Channels

Ligand-gated ion channels undergo a conformational change upon the binding of a neurotransmitter to the transmembrane receptor. This results in the opening of an ion channel in the receptor that allows positively charged ions to diffuse into the cell and change the voltage across the plasma membrane (depolarisation). **Acetylcholine** is an example of a neurotransmitter responsible for muscle contractions and neural activity.

G-Protein Coupled Receptors

G-protein coupled receptors (GPCRs) form a complex with G proteins anchored to the internal surface of the cell membrane. When a ligand binds to the receptor, GDP detaches from the G protein and is replaced by GTP. This causes the G protein to dissociate into two subunits that diffuse laterally along the membrane and interact with other membrane proteins or second messengers in order to initiate a wide variety of cell responses. **Adrenaline** binds to GPCRs to trigger the conversion of ATP into *cyclic AMP* (second messenger).

Receptor Tyrosine Kinases

Receptor tyrosine kinases are transmembrane enzymes that catalyse the phosphorylation of proteins. This phosphorylation is achieved using phosphate groups from ATP and will change the shape and activity of the protein. **Insulin** binds to a receptor tyrosine kinase and triggers the movement of vesicles embedded with glucose transporters to the plasma membrane – this results in the increased uptake of glucose by the cell.

SIGNALLING OVERVIEW

Receptor	Ligand	Cellular Effect
Intracellular receptor	Oestradiol	Changes gene expression (regulates GnRH secretion)
Gated ion channel	Acetylcholine	Changes local membrane potential (depolarisation)
G-protein coupled receptor	Adrenaline	Activates second messenger (cAMP) for fight or flight
Receptor tyrosine kinase	Insulin	Causes movement of vesicles with glucose transporters

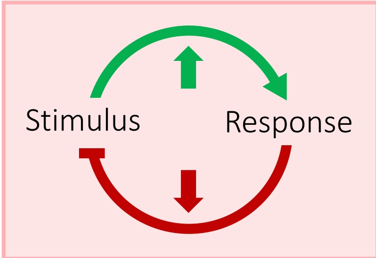
FEEDBACK SYSTEMS

Cell signalling pathways are commonly regulated by feedback loops – which are either positive or negative. Homeostatic processes are coordinated by negative feedback loops, making these systems more common.

Negative Feedback

Negative feedback involves a response that is the **opposite** of a stimulus (it functions to reduce the detected change so as to restore equilibrium). Examples of body processes that involve negative feedback loops include:

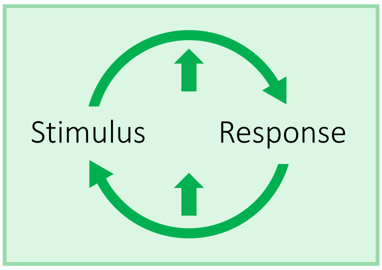
- Thermoregulation (*thyroxin* increases metabolic rate to produce heat)
- Blood glucose regulation (*insulin* and *glucagon* control glucose levels)
- Osmoregulation (*ADH* will retain water when the body is dehydrated)



Positive Feedback

Positive feedback involves a response that acts to **reinforce** the stimulus (it functions to augment a detected change in order to amplify its effect). Examples of body processes that involve positive feedback loops include:

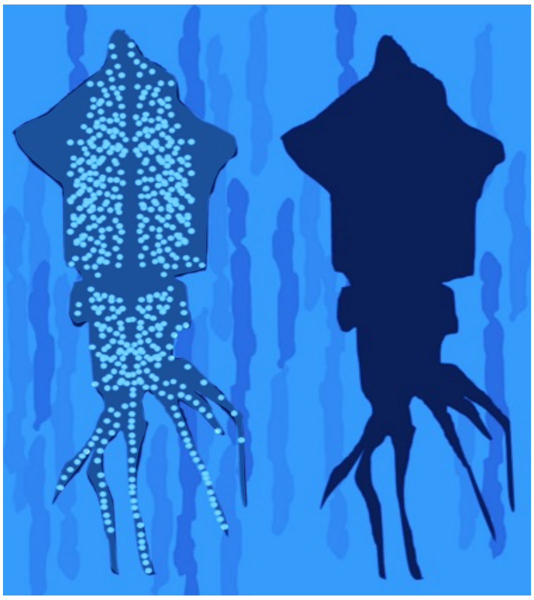
- Blood clotting (platelets release *clotting factors* that recruit platelets)
- Cell division (activation of CDKs may trigger the production of *cyclins*)
- Childbirth (contractions produce *oxytocin* which causes contractions)



QUORUM SENSING

Bacterial colonies may communicate with ligands using a process known as quorum sensing. This involves the regulation of a cell activity according to **population density**. Individual bacterial cells will release ligands (autoinducers) that trigger transcriptional changes when a threshold is reached. As the bacteria aggregate, more ligand is released into the environment. At a certain concentration, a coordinated change in activity is triggered within the entire population as a result of synchronised gene expression occurring in all bacteria.

Quorum sensing can allow certain types of bacteria to achieve **bioluminescence**. *Vibrio fischeri* releases an autoinducer that binds to intracellular receptors in nearby cells. When enough receptors are activated as a consequence of high ligand levels, transcription is activated. This results in the expression of the enzyme luciferase, which will catalyse a luminescent reaction.



Vibrio fischeri bacteria are found inside certain squid species (such as bobtail squids) and forms a mutualistic relationship. The bacteria aggregate on the underside of the squid and act to make a squid appear less visible against the bright surface when viewed from underneath (i.e. it provides camouflage). The bacteria in turn benefit by gaining access to compounds produced by the squid's metabolic activity (e.g. amino acids).

PLANT SIGNALLING

Plants possess signalling chemicals called **phytohormones**. These molecules include hydrophilic compounds that are transported via the vascular tissues (xylem and phloem), as well as gaseous molecules that can be dispersed via the air to exert allelopathic effects on other plant species (e.g. ethylene causes fruit ripening).