REVISION GUIDE

Cells that *talk to each other*

Chemical signalling

A bacterium counts its neighbours, a liver cell hears a hormone and a nerve opens a channel, all with the same trick: a ligand fits a receptor, and the cell does something. Follow the signal from the outside of the cell to the response.

13 chapters · a dry lab

The interactive guide, with every animation:

biologybybradford.com/guides/ib-biology-c2-1-chemical-signalling

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By the end you can

- [ ] Describe receptors as proteins with binding sites for specific ligands C2.1.1
- [ ] Explain quorum sensing in Vibrio fischeri C2.1.2
- [ ] Compare hormones, neurotransmitters, cytokines and calcium ions C2.1.3
- [ ] Give the chemical groups of hormones and neurotransmitters, and say why so many are used C2.1.4
- [ ] Contrast localized and distant effects of signalling chemicals C2.1.5
- [ ] Distinguish transmembrane receptors from intracellular receptors C2.1.6
- [ ] Explain how a receptor starts a signal transduction pathway C2.1.7
- [ ] Explain how the acetylcholine receptor changes the membrane potential C2.1.8
- [ ] Describe how receptors activate G proteins C2.1.9
- [ ] Outline the action of adrenaline, with the G protein and cAMP C2.1.10
- [ ] Explain how insulin acts through a tyrosine kinase receptor C2.1.11
- [ ] Explain how intracellular receptors change gene expression C2.1.12
- [ ] Describe the effects of oestradiol and progesterone on target cells C2.1.13
- [ ] Distinguish positive from negative feedback, with an example of each C2.1.14

Tick each one when you can do it without the book.

01 A lock that *only one key* opens

C2.1.1 HL RECEPTORS AS PROTEINS WITH BINDING SITES FOR SPECIFIC SIGNALLING CHEMICALS

Cells in a body are surrounded by thousands of different chemicals, and each cell has to respond to the right ones and ignore the rest. It does this with **receptors**. A receptor is a protein with a **binding site** whose shape and charge fit one particular signalling chemical, called a **ligand**.

When the ligand binds, the receptor changes shape, and this starts a response inside the cell. Binding is reversible, and it depends on concentration: more ligand means more receptors occupied (see the dry lab). A cell that has no receptor for a ligand does not respond to it, however much is around. The cells that do are its **target cells**.

KEY POINTS

- A **ligand** is a signalling chemical; a **receptor** is a protein with a binding site that fits it.
- Binding changes the receptor's **shape** and starts a response.
- Only **target cells**, with the right receptor, respond.

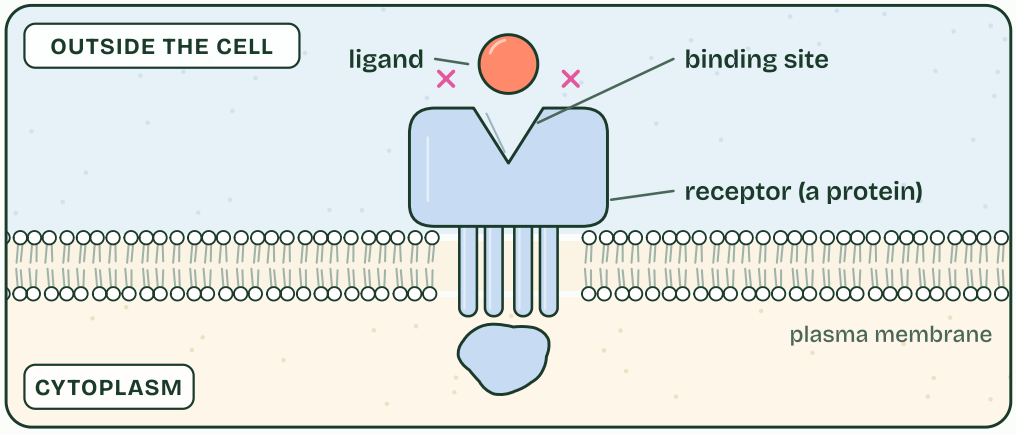
KEY TERMS

receptors
Proteins with a binding site for a specific signalling chemical. Binding makes the receptor change shape, which starts a response in the cell.

binding site
A region on a protein with a shape and chemistry that fit one particular molecule.

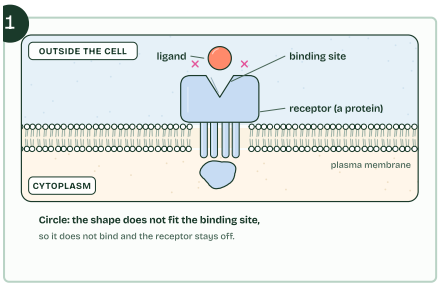
ligand
A signalling chemical that binds to a receptor.

target cells
The cells that have receptors for a particular signalling chemical and so respond to it.

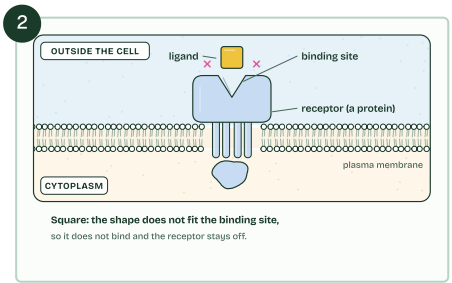


Circle: the shape does not fit the binding site,
so it does not bind and the receptor stays off.

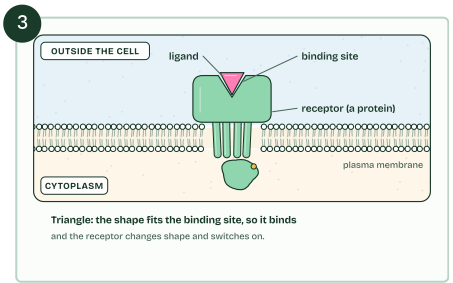
SWITCH IT 3 SETTINGS



Circle



Square



Triangle

PREDICT

Three ligands, a circle, a square and a triangle, are added to a receptor with a triangular binding site. Which one will switch the receptor on?

(A) The circle, because it is the smallest and so reaches the site first

(B) The triangle, because its shape fits the binding site

(C) All three, because any molecule that touches a receptor binds

(D) None, because a receptor only responds to molecules made inside the cell

Decide before you look. Answer on page 36.

C2.1.2 HL CELL SIGNALLING BY BACTERIA IN QUORUM SENSING

02 Bacteria that *count each other*

Signalling is not only for animals. Bacteria are single cells, but many act together once there are enough of them, and they work out when by releasing a signalling chemical and sensing how much of it there is. This is **quorum sensing**.

The marine bacterium *Vibrio fischeri* lives in the light organ of the Hawaiian bobtail squid, which feeds it and in return uses the light to hide its shadow from predators below. Each bacterium makes a small signalling molecule, an **autoinducer**, which diffuses out of the cell. In open water it disperses and its concentration stays low, so the cells do not glow. Packed together in the light organ, the autoinducer builds up. At a threshold concentration it binds to receptors in the bacteria, which switch on the genes for the light-producing enzyme luciferase. Lit cells also make more autoinducer, which is a positive feedback that switches on the whole population together.

Other bacteria use the same idea to decide when to form a biofilm or release toxins, which is why quorum sensing matters in medicine. A different set of bacteria, those of the human gut, also exchange chemical signals with each other and with the body, though the course asks only for *Vibrio fischeri*.

KEY POINTS

- Each cell releases an **autoinducer**. The more cells, the higher its concentration.
- At a **threshold** it binds receptors and switches on genes, here for light.
- It lets a population act together only when it is **big enough** to matter.

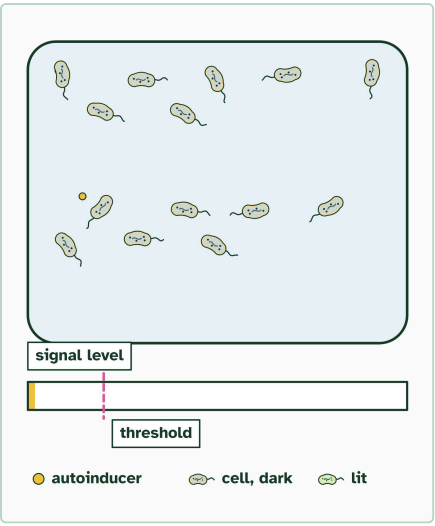
KEY TERMS

quorum sensing
The way bacteria detect their population density by the concentration of a signalling molecule they release, and switch genes on or off together when it passes a threshold.

ANIMATION · BACTERIA COUNTING EACH OTHER

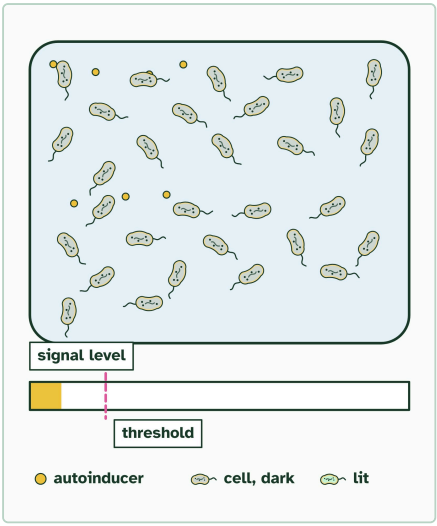
5 MOMENTS

1 14 CELLS, DARK



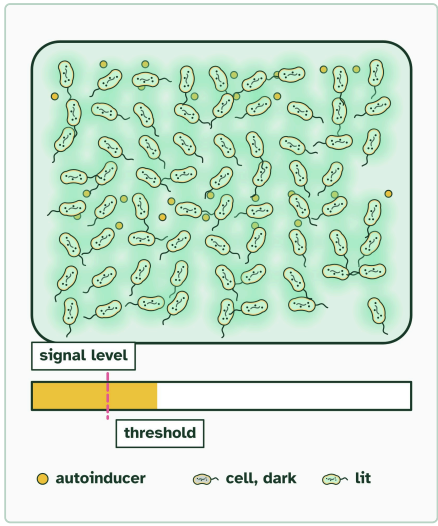
A few **Vibrio fischeri** cells in seawater. Each releases a little of a signalling molecule, an **autoinducer**, but it drifts away. The cells stay dark.

2 30 CELLS, DARK



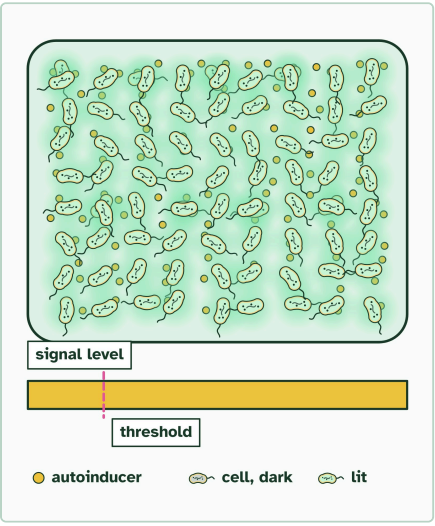
The cells divide, and more of them are making the autoinducer.

3 70 CELLS, LIGHT ON



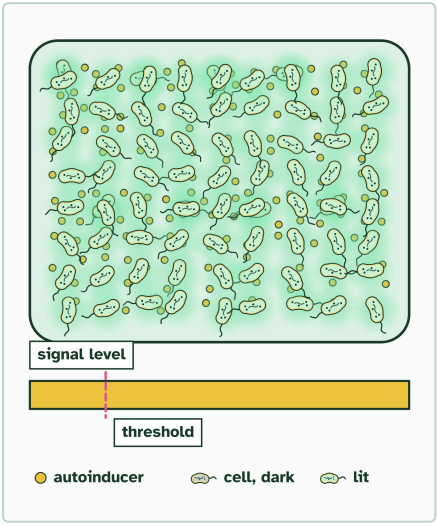
The molecules now arrive faster than they drift away, so the **concentration builds up**. Each cell is measuring how many cells are around it.

4 80 CELLS, LIGHT ON



At a **threshold** concentration the signal binds receptors in every cell and switches on the genes for light: **quorum sensing**.

5 80 CELLS, LIGHT ON



Lit cells make even more autoinducer, so the whole population switches on together. Move the slider to start with more or fewer cells.

Watch it move, and change it as it runs: biologybybradford.com/guides/ib-biology-c2-1-chemical-signalling#quorum

PREDICT

A single Vibrio fischeri cell in a large volume of seawater is given the genes for light. Will it glow?

(A) Yes, because the genes for light are always switched on in every cell

(B) No, because the autoinducer it makes spreads out and never reaches the threshold

(C) Yes, because bacteria need only one cell to make a signal

(D) No, because it cannot make the autoinducer by itself

Decide before you look. Answer on page 36.

C2.1.3 HL C2.1.5 HL CATEGORIES OF SIGNALLING CHEMICALS; LOCALIZED AND DISTANT EFFECTS

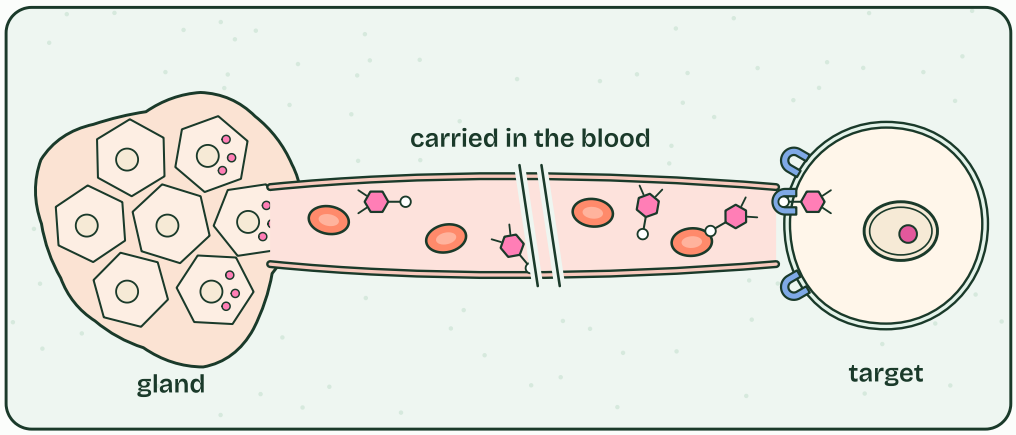
03 Four ways to *send a message*

Animals use four main categories of signalling chemical, and they differ in where they are made, how far they travel and how long they last.

Hormones are made by endocrine glands and carried by the blood to target cells anywhere in the body, so their effects are distant and slow, and often last for hours or longer. **Neurotransmitters** are released by a neuron and diffuse across a synaptic gap, about 20 nm wide, to the next cell. They act very locally, within milliseconds, and are quickly removed. **Cytokines** are small proteins released by immune and other cells that change the behaviour of nearby cells, and sometimes distant ones, to coordinate a defence. **Calcium ions** are released from stores inside a cell into the cytoplasm and are a signal within and between cells.

KEY POINTS

- **Hormones:** in the blood, distant, slow, long-lasting.
- **Neurotransmitters:** across a synaptic gap, local, fast, brief.
- **Cytokines:** immune signals, nearby or in the blood.
- **Calcium ions:** a signal inside cells.

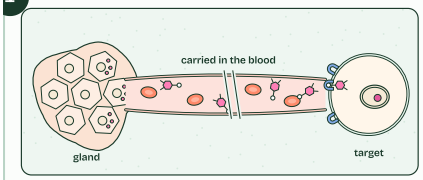


Hormones: made by endocrine glands and carried by the blood,
so they reach target cells anywhere in the body. Slow, and long-lasting.

SWITCH IT

4 SETTINGS

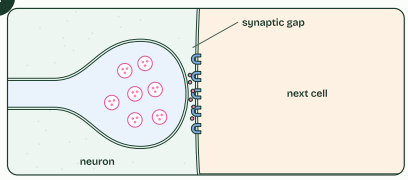
1



Hormones: made by endocrine glands and carried by the blood, so they reach target cells anywhere in the body. Slow, and long-lasting.

Hormone

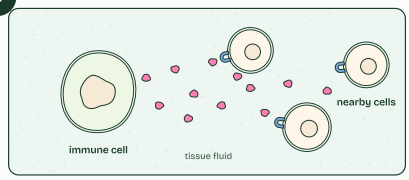
2



Neurotransmitters: released by a neuron into a gap about 20 nm wide and gone in milliseconds. Fast, and very local.

Neurotransmitter

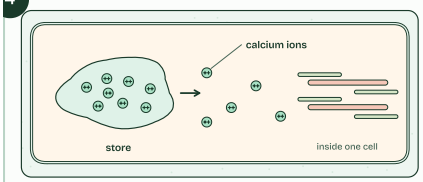
3



Cytokines: small proteins made by immune and other cells. They act on nearby cells and some travel in the blood, to organize a defence. Medium range.

Cytokine

4



Calcium ions: released from stores into the cytoplasm. They signal inside a cell, for example to start muscle contraction or secretion.

Calcium ions

PREDICT

Which signalling chemical would be the best choice for a message that has to reach every muscle in the body, and last for several minutes?

(A) A neurotransmitter, because it is the fastest

(B) A hormone, because it travels in the blood to all target cells and lasts

(C) Calcium ions, because they cross the cytoplasm in one cell

(D) A cytokine, because it acts only on its neighbours

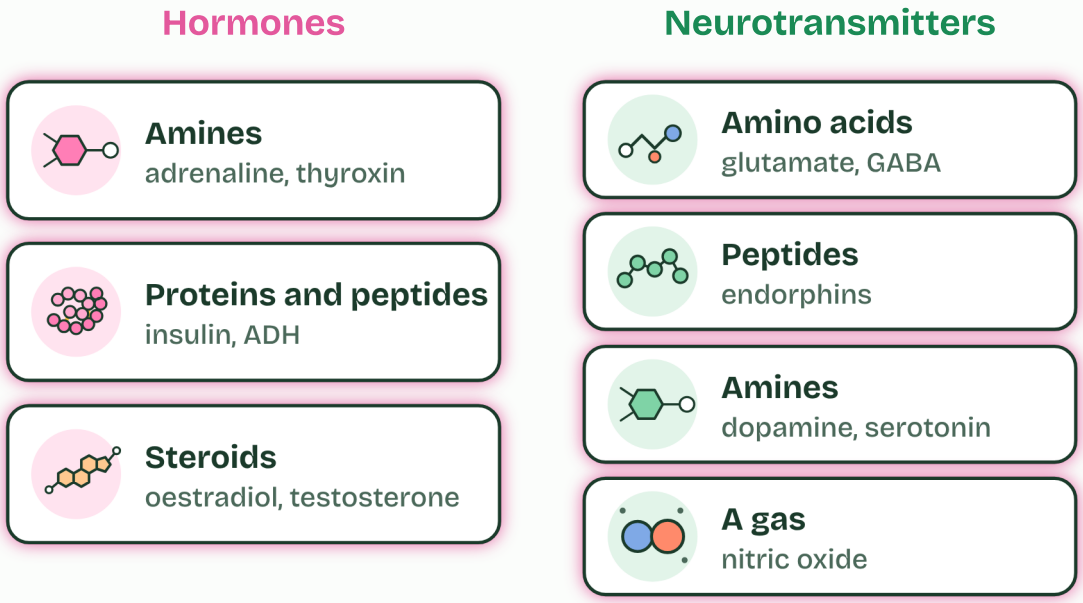
Decide before you look. Answer on page 36.

04 Why so *many kinds* of chemical?

C2.1.4 HL CHEMICAL DIVERSITY OF HORMONES AND NEUROTRANSMITTERS

Hormones and neurotransmitters are not one family of molecule. **Hormones** include **amines** such as adrenaline and thyroxin, **proteins and peptides** such as insulin and ADH, and **steroids** such as oestradiol and testosterone. **Neurotransmitters** include **amino acids** such as glutamate and GABA, **peptides** such as endorphins, **amines** such as dopamine and serotonin, and even a gas, nitric oxide.

A wide range of chemicals gives a wide range of messages. Each chemical needs only its own receptor, so thousands of signals can use the body at once without confusion. Their chemistry gives different properties: a peptide is made quickly on ribosomes and stored in vesicles, so it can be released at once; a steroid passes through membranes and its effect lasts; a small amine or a gas is made and removed quickly, which suits a fast synapse. Tap each group to read an example.



Amines small molecules made from one amino acid in a few enzyme steps. Adrenaline (water-soluble, acts at the membrane) and thyroxin (lipid-soluble, acts inside the cell).

Steroids lipids made from cholesterol. They pass through the phospholipid bilayer, so they bind receptors inside the cell and change gene expression. Their effects last longer.

Peptides short chains of amino acids. Endorphins reduce the sensation of pain.

Nitric oxide (NO) a small gas made by an enzyme and not stored in vesicles. It diffuses straight out of one cell and into the next, where it acts inside the cell.

Proteins and peptides chains of amino acids made on ribosomes and stored in vesicles ready to release. Water-soluble, so they act through receptors in the plasma membrane.

Amino acids glutamate excites many neurons, and GABA inhibits them. They are taken up again from the synaptic gap.

Amines made from amino acids. Dopamine is involved in reward and movement, serotonin in mood and sleep.

WATCH OUT

Some course documents say the gas neurotransmitter is **nitrous oxide**. The signalling molecule is **nitric oxide**, NO. Nitrous oxide, N_2O, is laughing gas.

05 Receptor *at the door* or *inside the house*

C2.1.6 HL TRANSMEMBRANE RECEPTORS AND INTRACELLULAR RECEPTORS

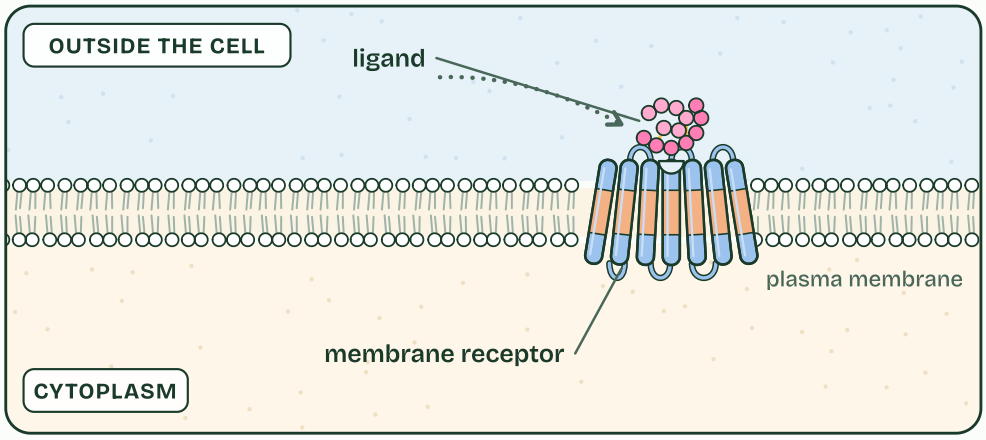
Where a receptor sits depends on whether its ligand can get through the plasma membrane. The bilayer has a hydrophobic core, so it blocks water-soluble ligands but lets lipid-soluble ligands through.

A ligand that is **hydrophilic**, such as a peptide hormone or adrenaline, cannot enter, so it binds a **transmembrane receptor**: a protein that spans the membrane. The part outside, with the binding site, and the part inside are made mostly of hydrophilic amino acids, which are in contact with water. The part that crosses the bilayer is made of **hydrophobic** amino acids, which are at home in the lipid core. Binding on the outside changes the shape of the protein, and the signal passes through the membrane without the ligand entering.

A ligand that is **hydrophobic**, such as a steroid hormone, diffuses through the bilayer and binds an **intracellular receptor** in the cytoplasm or nucleus. This receptor has no membrane-spanning part, so it is a water-soluble protein with a pocket that fits the ligand.

KEY POINTS

- **Hydrophilic ligand** cannot cross the membrane: it binds a **transmembrane receptor**.
- The receptor has **hydrophilic** parts in the water and a **hydrophobic** part in the bilayer.
- **Hydrophobic ligand** (a steroid) crosses the membrane: it binds an **intracellular receptor**.



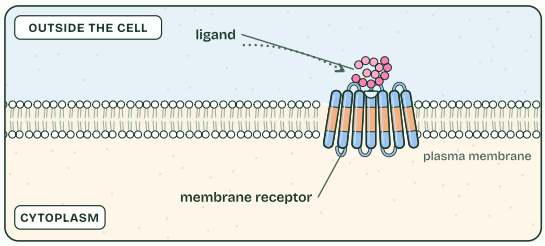
Water-soluble ligand: cannot cross the bilayer.
It binds the outside of a transmembrane receptor.

hydrophilic amino acids hydrophobic amino acids

SWITCH IT

2 SETTINGS

1

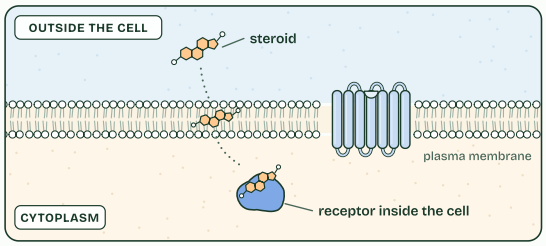


Water-soluble ligand: cannot cross the bilayer.
It binds the outside of a transmembrane receptor.

hydrophilic amino acids hydrophobic amino acids

Peptide or amine

2



Lipid-soluble ligand (a steroid): crosses the bilayer
and binds an intracellular receptor.

Steroid

PREDICT

Which sentence correctly describes the part of a transmembrane receptor that lies in the lipid bilayer?

(A) It is made mostly of hydrophilic amino acids, which are attracted to the fatty acid tails

(B) It is made mostly of hydrophobic amino acids, which are at home in the lipid core

(C) It is made mostly of nucleotides, which pass the signal on

(D) It is a gap, a pore through which the ligand passes into the cell

Decide before you look. Answer on page 36.

06 One ligand, a *chain of events*

C2.1.7 HL INITIATION OF SIGNAL TRANSDUCTION PATHWAYS BY RECEPTORS

A ligand that binds a receptor on the outside of a cell never has to enter. Instead, the binding switches the receptor on, and the receptor starts a **signal transduction pathway**: a series of steps in which one molecule activates the next, until the cell does something.

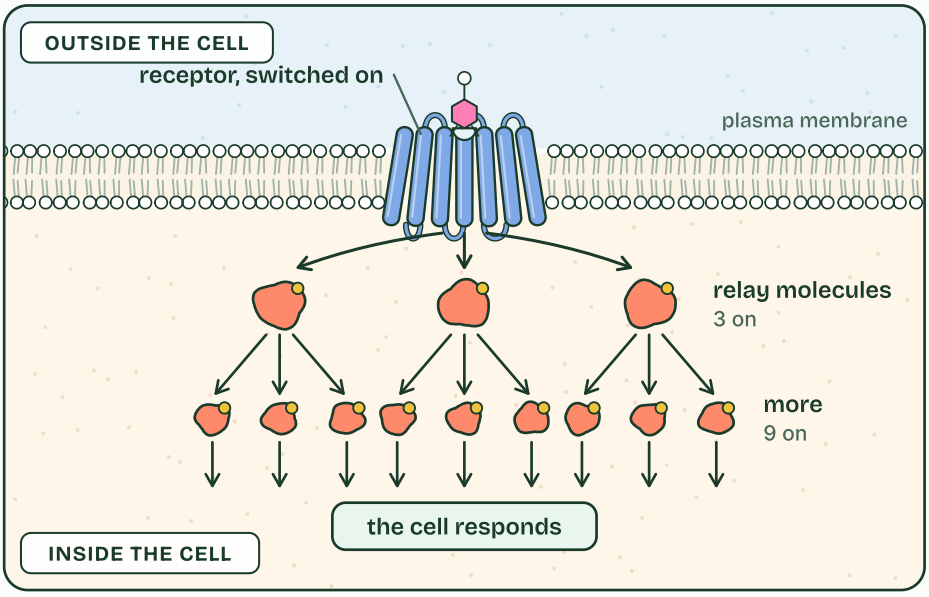
Each step can switch on many molecules of the next, so the pathway **amplifies** the signal: one ligand molecule can lead to thousands of enzyme molecules at work. The response may be an enzyme switched on, a channel opened, a gene read, or a change in the shape of the cell. The same few types of pathway are used again and again, in different cells, with different results. The next four chapters follow the examples the course asks for.

KEY POINTS

- Binding **switches the receptor on**, which starts a **pathway** of steps inside the cell.
- Each step activates **many** of the next: the signal is **amplified**.
- The pathway ends in a **response**: an enzyme, a channel or a gene.

KEY TERMS

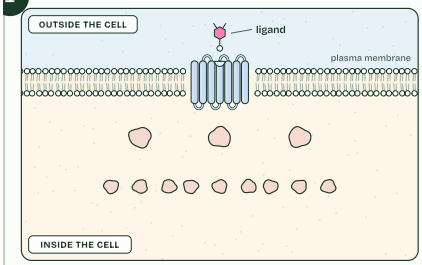
signal transduction pathway
A sequence of molecular events inside a cell that passes a signal from a receptor to the cell's response.



STEP BY STEP

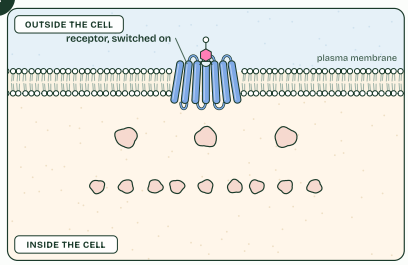
5 STEPS

1



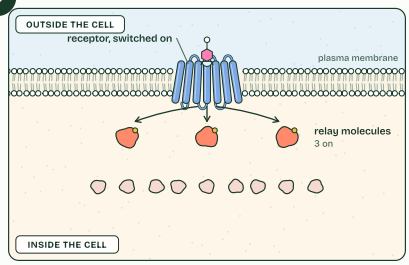
The **ligand** arrives at its receptor in the plasma membrane.

2



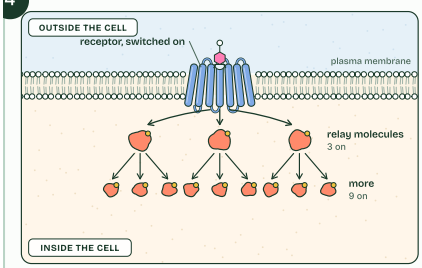
It binds, and the receptor changes shape: it is **switched on**.

3



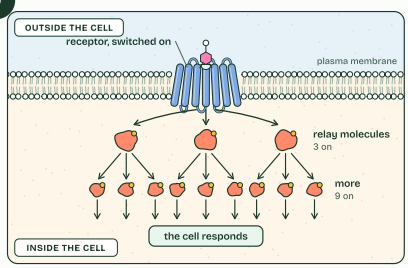
The receptor activates several **relay molecules** inside the cell.

4



Each of those activates several more: the signal is **amplified**.

5



The pathway ends in a **response** by the cell.

PREDICT

A single molecule of a hormone binds to a single receptor, yet the cell makes millions of glucose molecules. What best explains this?

(A) The hormone enters the cell and makes the glucose itself

(B) Each step of the pathway switches on many molecules of the next step, so the signal is amplified

(C) The receptor makes a new molecule of hormone each time it binds

(D) The hormone is changed into glucose by the receptor

Decide before you look. Answer on page 36.

C2.1.8 HL TRANSMEMBRANE RECEPTORS FOR NEUROTRANSMITTERS AND CHANGES TO MEMBRANE POTENTIAL

07 A receptor that is *also a gate*

Some receptors need no pathway at all, because the receptor is itself an ion channel. The **acetylcholine receptor** in the membrane of a muscle fibre or a neuron is a protein with a central pore that is closed at rest. Acetylcholine is released by the presynaptic neuron, crosses the synaptic gap and binds the receptor. The receptor changes shape and the channel opens.

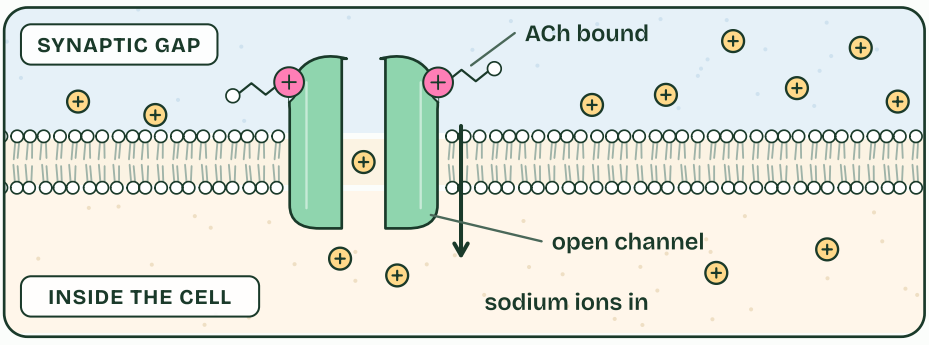
With the channel open, **positively charged ions**, mostly sodium, diffuse into the cell down their concentration gradient. The inside of the cell, which was negative (about −70 mV at rest), becomes less negative: the membrane **depolarizes**. If the change reaches the threshold in a neuron, an **action potential** starts and travels along the axon (see the C2.2 guide, and its films of the synapse and the action potential).

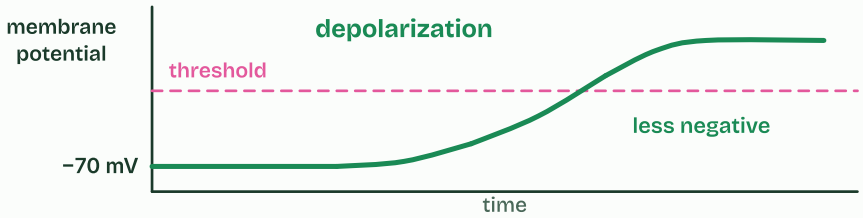
KEY POINTS

- The **acetylcholine receptor** is a **ligand-gated ion channel**: binding opens the pore.
- **Positive ions** (sodium) diffuse in, and the membrane **depolarizes**.
- It may then trigger an **action potential** or a contraction.

KEY TERMS

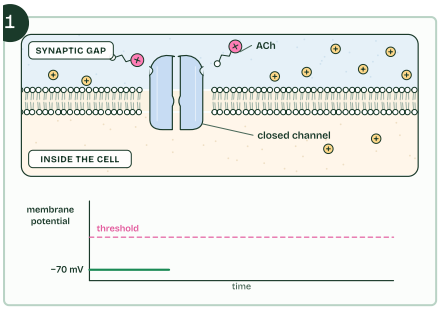
depolarizes
Becomes less negative inside, so the voltage across the membrane moves toward zero.





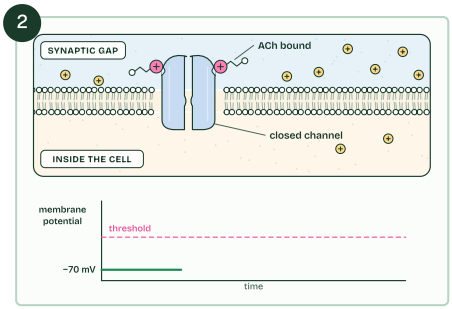
STEP BY STEP 5 STEPS

1



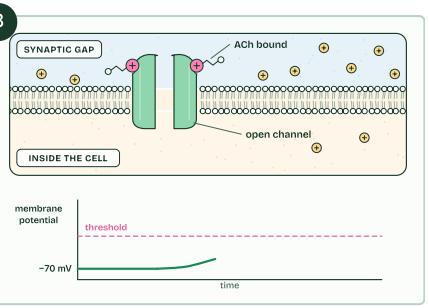
At rest the channel is **closed** and the inside is about **−70 mV**.

2



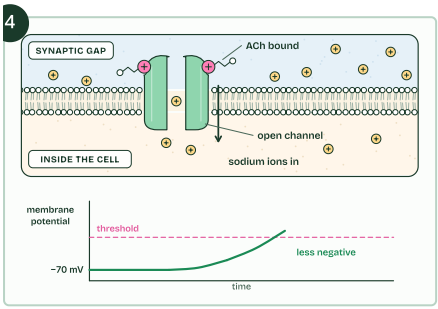
Acetylcholine from the presynaptic neuron binds the receptor.

3



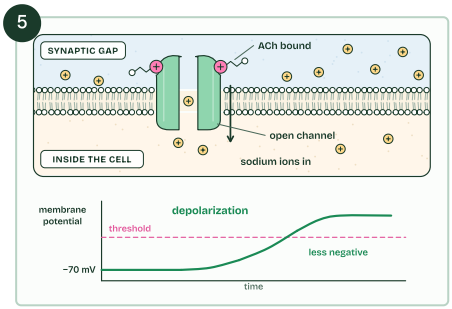
The receptor changes shape and the **channel opens**.

4



Positive ions diffuse in, down their gradient. The potential climbs.

5



The inside is **less negative**: the membrane has **depolarized**, and may reach the threshold.

PREDICT

Acetylcholine binds a receptor and positively charged ions flow into the cell. What happens to the membrane potential?

(A) It becomes more negative, because ions have moved into the cell

(B) It does not change, because ions in and ions out balance

(C) It becomes less negative, because positive charge is added inside

(D) It becomes more negative, because the receptor pumps out sodium ions

Decide before you look. Answer on page 36.

08 A receptor that *wakes a second protein*

C2.1.9 HL TRANSMEMBRANE RECEPTORS THAT ACTIVATE G PROTEINS

A great many receptors do not open a channel. Instead they pass the signal to a **G protein** on the inside of the membrane. The human genome has hundreds of these **G protein-coupled receptors**, and they respond to hormones, neurotransmitters, light and smells.

The G protein sits next to the receptor holding a molecule of **GDP**, and it is off. When a ligand binds the receptor, the receptor changes shape and switches the G protein on: it lets go of GDP and takes up **GTP**. The active G protein moves along the membrane and switches on an **enzyme**, which makes a small molecule that spreads through the cell. That molecule is a **second messenger**: the ligand is the first messenger, and this is the second.

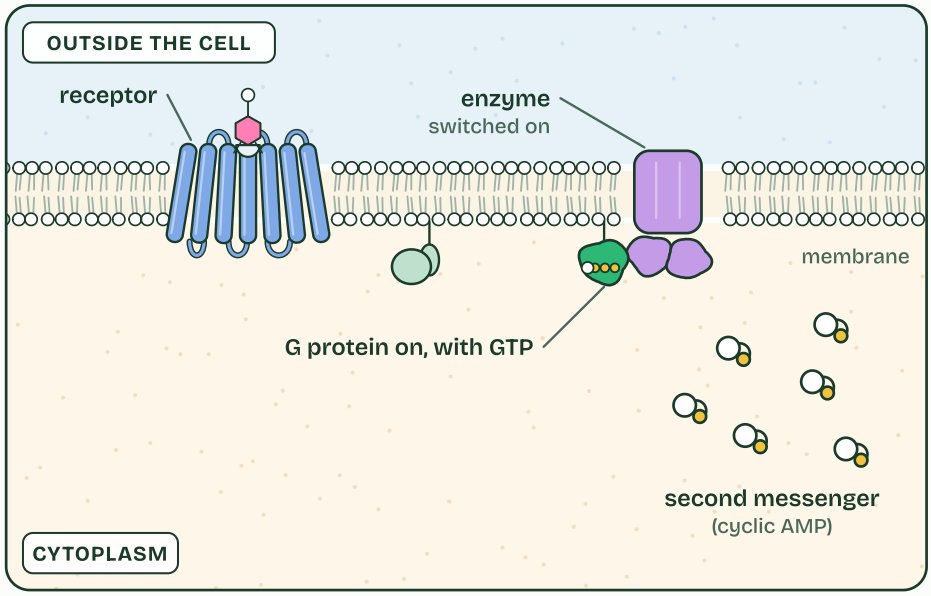
KEY POINTS

- A **G protein** is off with **GDP** and on with **GTP**.
- The ligand switches on the **receptor**; the receptor switches on the **G protein**.
- The G protein switches on an **enzyme** that makes a **second messenger**.

KEY TERMS

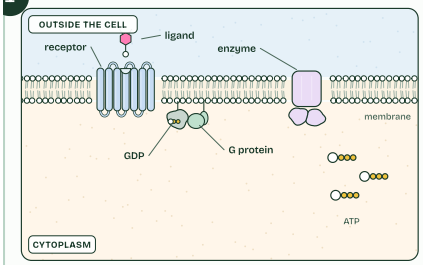
G protein
A protein inside the cell, attached to the inside of the membrane, that is switched on when GDP is swapped for GTP, and then switches on an enzyme or a channel.

second messenger
A small molecule made inside a cell in response to a signal at the receptor. It spreads fast and switches on proteins inside the cell. The first messenger is the signal outside.



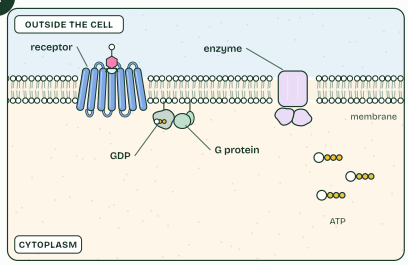
STEP BY STEP 4 STEPS

1



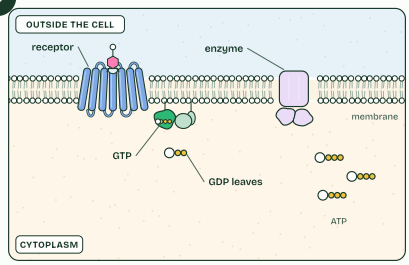
A **ligand** approaches the receptor. The **G protein** beside it holds **GDP** and is off.

2



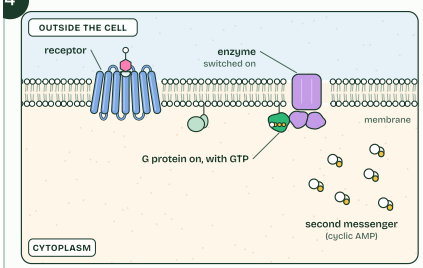
The ligand binds. The receptor changes shape and is **on**.

3



The G protein **swaps GDP for GTP**. It is now **on**.

4



It switches on an **enzyme**, which makes a **second messenger**.

PREDICT

What switches a G protein on?

(A) The binding of GDP to the G protein

(B) The receptor, after a ligand has bound it, makes the G protein swap GDP for GTP

(C) The ligand itself entering the cell and binding the G protein

(D) The breakdown of ATP by the plasma membrane

Decide before you look. Answer on page 36.

09

C2.1.10 HL MECHANISM OF ACTION OF EPINEPHRINE (ADRENALINE) RECEPTORS

Adrenaline: from *receptor to glucose*

When you are frightened, the adrenal glands release **adrenaline** (epinephrine) into the blood. In a liver cell, it works through a G protein and a second messenger. Follow the steps:

Adrenaline binds a **receptor** in the plasma membrane of the liver cell.
The receptor activates a **G protein** (GDP is swapped for GTP).
The G protein activates the enzyme **adenylyl cyclase**.
Adenylyl cyclase makes **cyclic AMP (cAMP)** from ATP. cAMP is the **second messenger**.
cAMP activates a **protein kinase**, and a chain of kinases follows.
The last enzyme breaks down **glycogen** to glucose, which leaves the cell and **raises the glucose in the blood**.

Because every step is an enzyme making many products, a tiny amount of adrenaline has a huge effect, in seconds. Now watch the film below. Slide **Adrenaline**, and see what a **beta blocker**, which fits the receptor and does not switch it on, does.

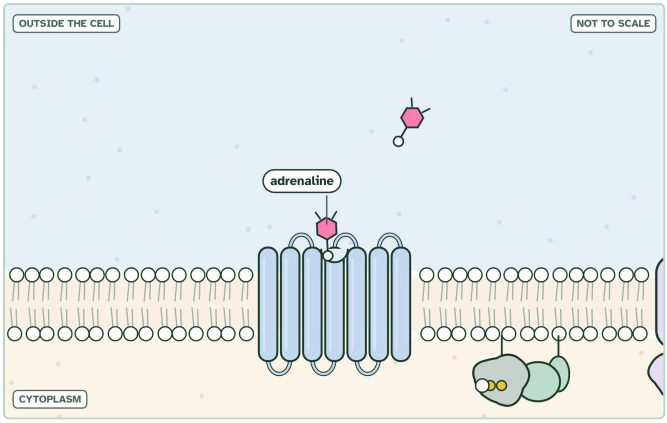
KEY POINTS

- Adrenaline → **receptor** → **G protein** → **adenylyl cyclase** → **cAMP** → **kinases** → glucose.
- **cAMP** is the **second messenger**.
- The pathway **amplifies**, so the response is fast and large.

KEY TERMS

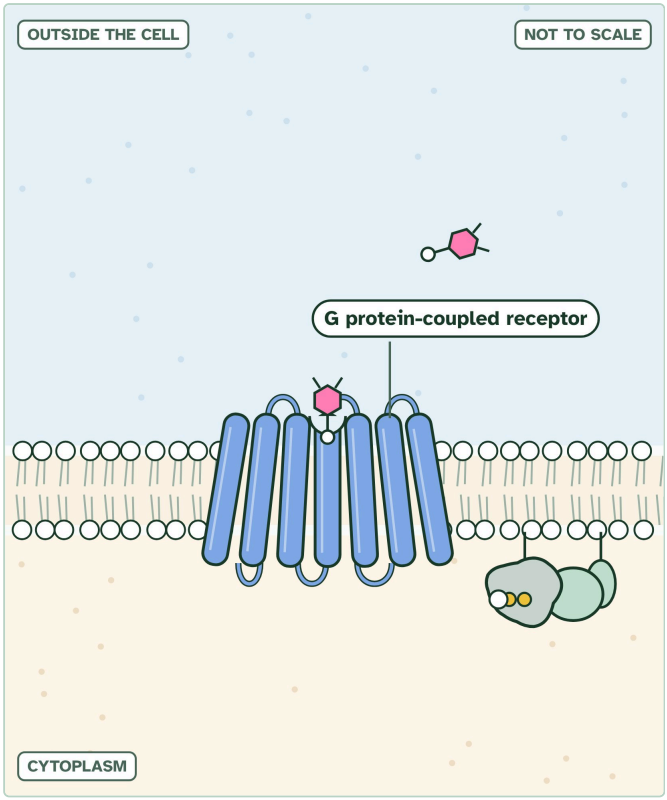
adrenaline
The hormone, an amine, released by the adrenal glands in danger or stress. Epinephrine is the same molecule. It prepares the body for action.

1 RECEPTION



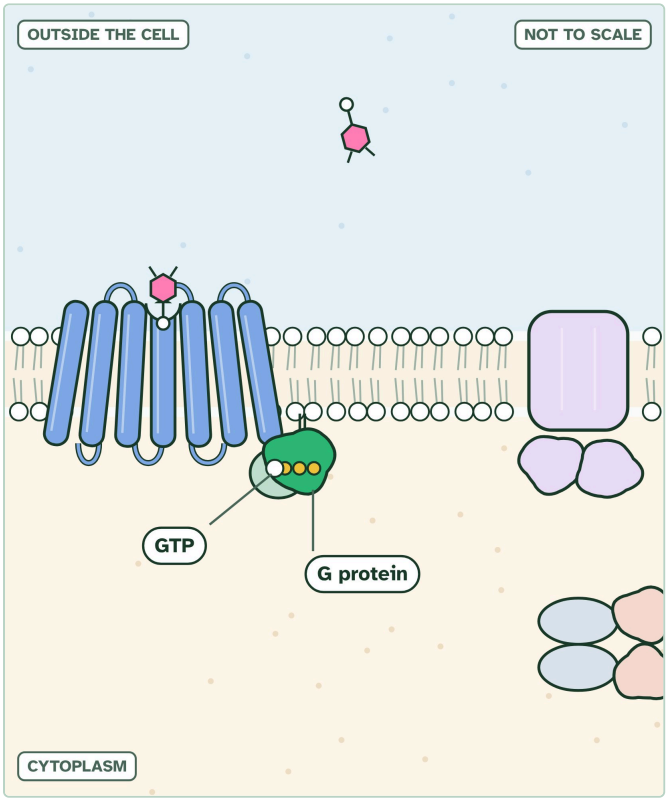
Adrenaline reaches a liver cell. It is a polar ligand and cannot cross the membrane, so it binds a **receptor** on the surface: a **G protein-coupled receptor**.

2 RECEPTION



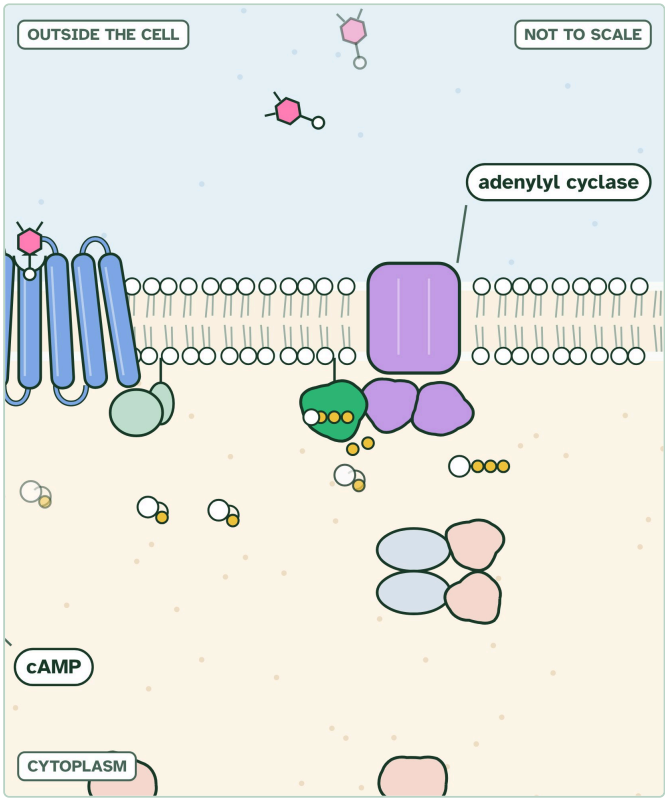
Binding changes the receptor's shape on the inside of the membrane. This is **reception**: the message is now inside the cell, although adrenaline is not.

3 TRANSDUCTION



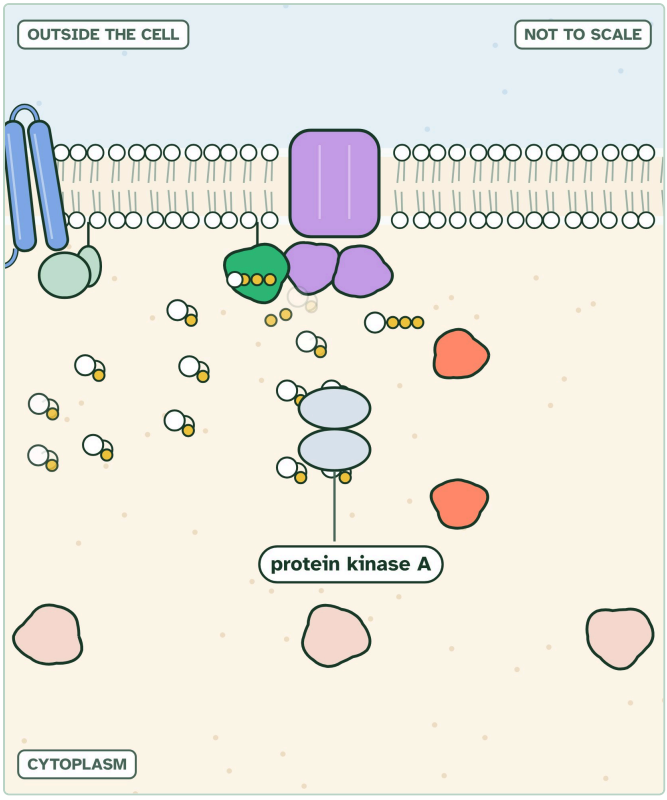
The changed receptor switches on a **G protein**. It swaps **GDP** for **GTP**, and its active part breaks away along the membrane.

4 CAMP 11 · GLUCOSE 0



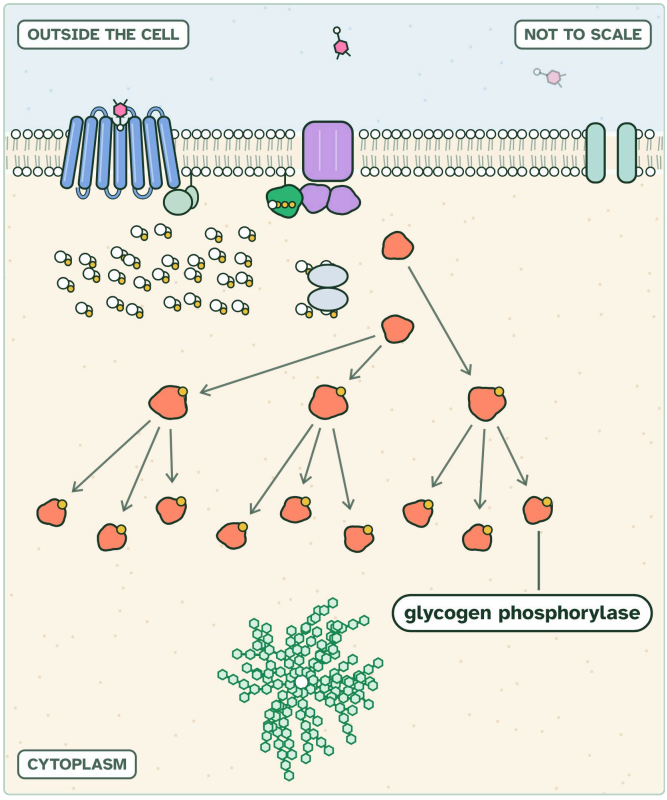
The G protein switches on **adenylyl cyclase**, which turns ATP into **cyclic AMP** (cAMP) again and again. cAMP is the **second messenger**.

5 CAMP 25 · GLUCOSE 0



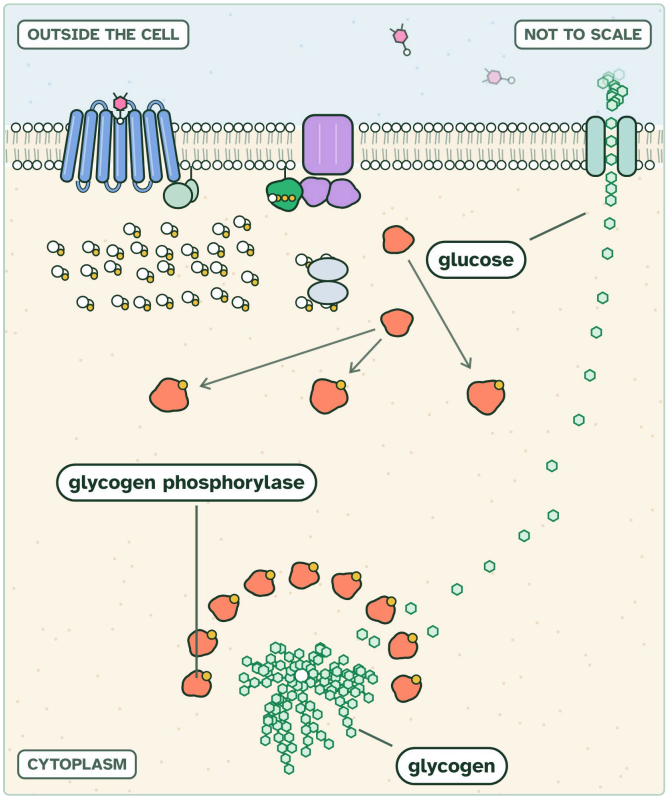
cAMP binds **protein kinase A** and sets its active parts free. **Transduction** has begun.

6 CAMP 31 · GLUCOSE 0



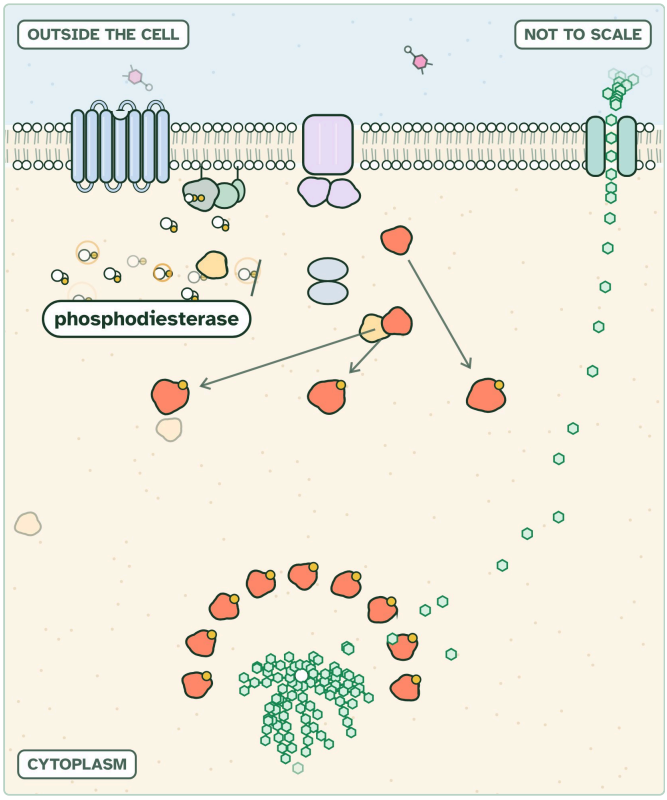
A **phosphorylation cascade**: each kinase adds a phosphate (yellow) from ATP to many molecules of the next, switching each one on. The signal is **amplified** at every step.

7 CAMP 31 · GLUCOSE 44



The last enzyme, **glycogen phosphorylase**, breaks **glycogen** down, and glucose leaves the cell for the blood. This is the **response**: fuel for fight or flight.

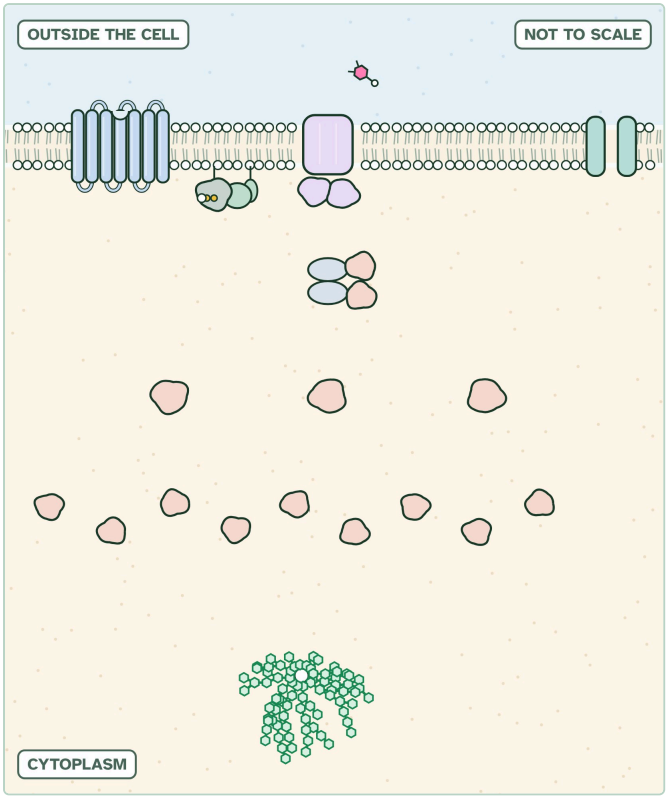
8 CAMP 5 · GLUCOSE 112



Switching off. Adrenaline leaves the receptor, the G protein turns its GTP back to GDP, **phosphodiesterase** breaks cAMP down and **phosphatases** take the phosphates off.

9

CAMP 0 · GLUCOSE 130



Back at rest, ready for the next signal. The response lasts only as long as the signal.

Watch it move, and change it as it runs: biologybybradford.com/guides/ib-biology-c2-1-chemical-signalling#adrenaline

REMEMBER IT

R G A C K: rack up the glucose

R	G	A	C	K
R	G	A	C	K
Receptor	**G** protein	**A**denylyl cyclase	**c**AMP	**K**inases
adrenaline binds	GDP out, GTP in	switched on	second messenger	glycogen to glucose

PREDICT

A drug binds the adrenaline receptor but does not change its shape. What will happen when adrenaline is also present?

(A) More cAMP is made, because there are now more ligands

(B) Less cAMP is made, because the drug blocks adrenaline from the binding site

(C) The same cAMP is made, because the drug has no effect on the pathway

(D) The drug is turned into cAMP by the receptor

Decide before you look. Answer on page 36.

IN THE EXAM

Outline the action of adrenaline (4 marks): binds to a **receptor** in the plasma membrane; activates a **G protein**; which activates **adenylyl cyclase**; making **cAMP**, the second messenger; which activates **kinases**; glycogen is broken down to glucose.

NATURE OF SCIENCE

Two names, one molecule. *Adrenaline* and *epinephrine* were both coined around 1900 by researchers who isolated the hormone from the adrenal glands, and both names mean "on the kidney". Each is still used: epinephrine mostly in the USA, adrenaline in much of the rest of the world. Agreeing on names, and knowing both, lets scientists and doctors everywhere share what they find.

10 Insulin: *move the transporters*

C2.1.11 HL TRANSMEMBRANE RECEPTORS WITH TYROSINE KINASE ACTIVITY

Insulin is a protein hormone, so it cannot cross the plasma membrane and binds a receptor on the surface of a muscle or fat cell. The insulin receptor is a **tyrosine kinase receptor**: the part inside the cell is an enzyme.

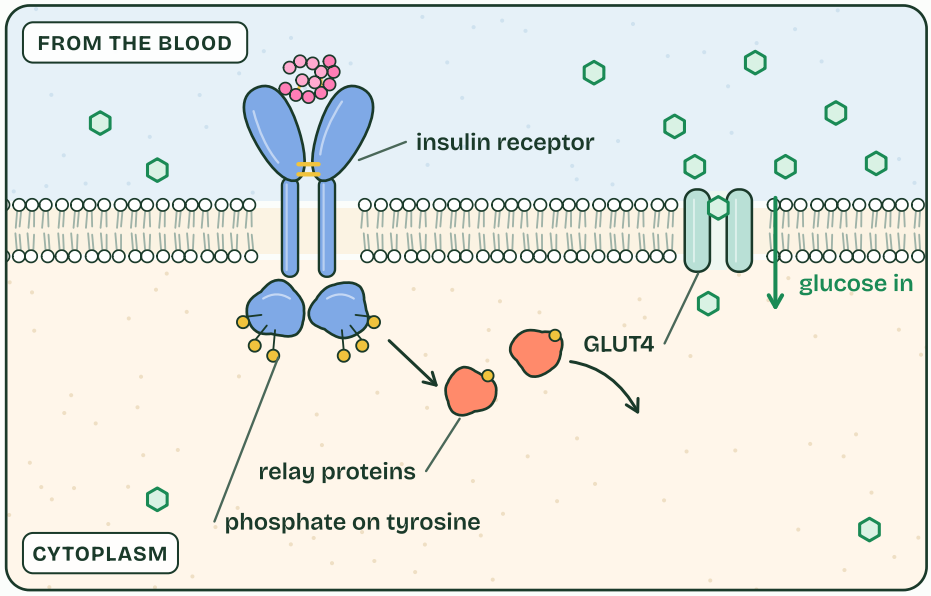
When insulin binds, the receptor changes shape, and the enzyme part adds phosphate groups to **tyrosine** amino acids on the receptor (**phosphorylation**). The phosphorylated tyrosines are docking sites that switch on relay proteins, and a sequence of reactions follows. It ends with **vesicles** that carry **glucose transporter proteins** (GLUT4) moving to the plasma membrane and fusing with it. The membrane now has many more transporters, so glucose enters the cell faster by facilitated diffusion, and the blood glucose falls.

KEY POINTS

- Insulin binds a **tyrosine kinase** receptor; the receptor **phosphorylates tyrosine** inside the cell.
- A sequence of reactions moves **vesicles with glucose transporters** to the plasma membrane.
- More transporters: **more glucose in**, less in the blood.

KEY TERMS

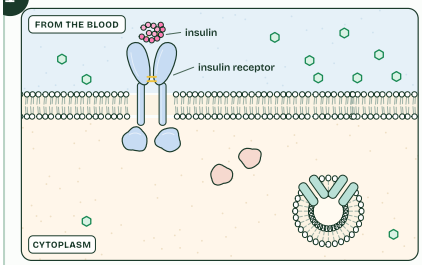
tyrosine kinase receptor
A transmembrane receptor whose inside part is an enzyme (a kinase). When a ligand binds, it adds phosphate groups to tyrosine amino acids.



STEP BY STEP

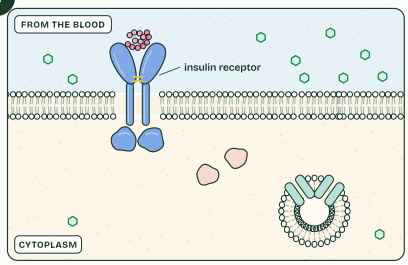
6 STEPS

1



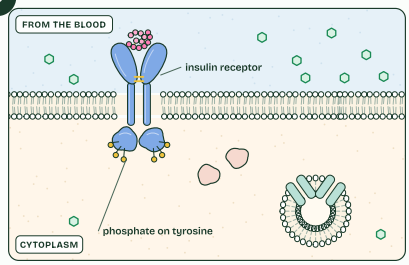
Insulin from the blood reaches its receptor.

2



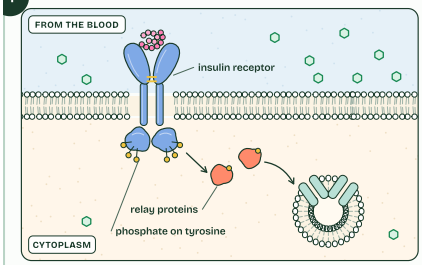
It binds, and the receptor changes shape.

3



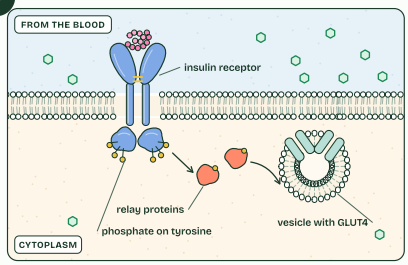
The enzyme part of the receptor adds **phosphate to tyrosine**.

4



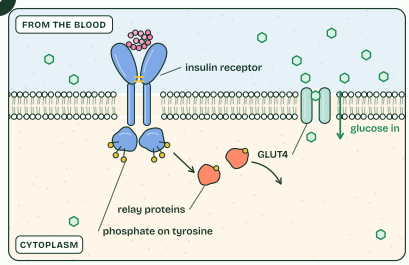
The phosphorylated receptor switches on **relay proteins**.

5



Vesicles carrying **glucose transporters** move toward the membrane.

6



They fuse with it. **Glucose** now enters the cell faster.

PREDICT

A muscle cell is given insulin. What is the direct effect on the plasma membrane?

(A) Glucose transporter proteins are added to it by vesicles that fuse with it

(B) Glucose is made in the membrane from the fatty acids of the bilayer

(C) The membrane becomes impermeable to glucose

(D) Insulin itself carries glucose across the membrane

Decide before you look. Answer on page 37.

11 A hormone that *switches on a gene*

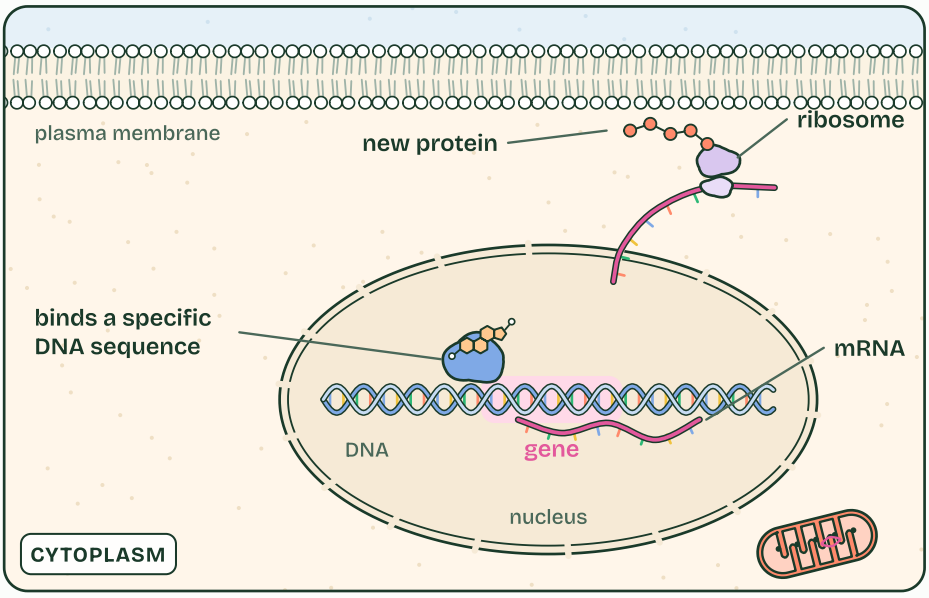
C2.1.12 HL INTRACELLULAR RECEPTORS THAT AFFECT GENE EXPRESSION

Steroid hormones, such as **oestradiol**, **progesterone** and **testosterone**, are lipids made from cholesterol. They pass straight through the phospholipid bilayer and bind a receptor **inside the cell**, so they need no pathway of relay molecules at the membrane.

The ligand binds a site on the receptor and **activates** it. The activated receptor moves into the nucleus (some start there), where it binds to **specific DNA sequences** next to a gene and **promotes transcription** of that gene. The mRNA is translated on ribosomes and the cell makes more of a protein. Because the cell has to make mRNA and then protein, the response is **slow** (hours) but it **lasts**, compared with the seconds of a G protein pathway. The receptor is the transcription factor: a hormone receptor and a switch for a gene in one.

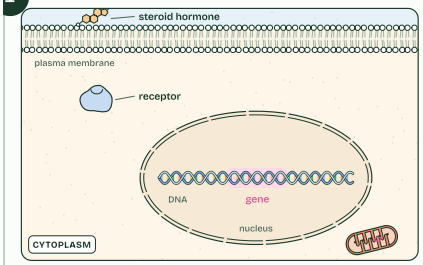
KEY POINTS

- A steroid is **hydrophobic**, so it crosses the membrane and binds an **intracellular receptor**.
- The active receptor binds **specific DNA** and **promotes transcription**.
- It changes **which proteins** a cell makes: slower, longer-lasting.



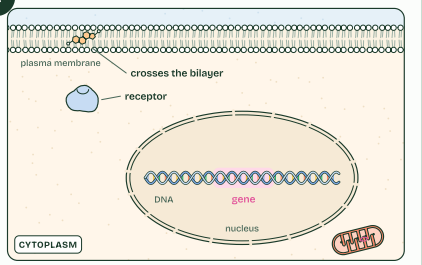
STEP BY STEP 6 STEPS

1



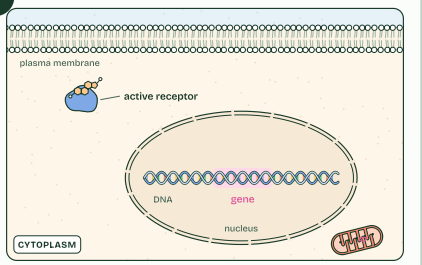
A **steroid hormone** is lipid-soluble.

2



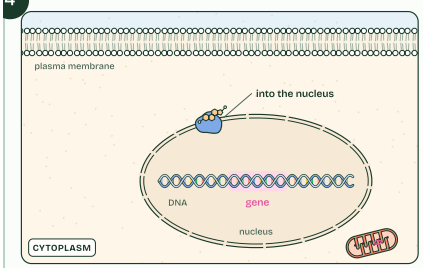
It **diffuses through** the phospholipid bilayer into the cell.

3



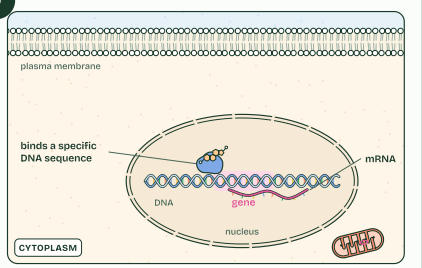
It binds an **intracellular receptor**, which becomes active.

4



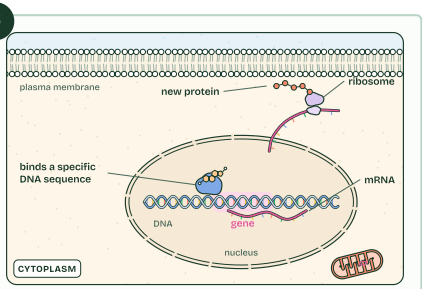
The complex moves into the **nucleus**.

5



It binds a **specific DNA sequence** and **promotes transcription** of the gene.

6



The mRNA leaves the nucleus and is **translated** into a new protein.

PREDICT

Why does a steroid hormone take longer to act on a cell than adrenaline does?

(A) It has to travel further in the blood before it reaches the cell

(B) It changes gene expression, so mRNA and then protein must be made

(C) It cannot cross the cell membrane, so it needs to be moved by vesicles

(D) It is broken down by enzymes before it reaches the cell

Decide before you look. Answer on page 37.

IN THE EXAM

Explain how steroid hormones affect target cells (3 marks): they are lipid-soluble and **diffuse through the plasma membrane**; they bind an **intracellular receptor**, which becomes active; the complex binds **specific DNA sequences** and **promotes transcription** of a gene.

12 Two *steroids*, two targets

C2.1.13 HL EFFECTS OF THE HORMONES OESTRADIOL AND PROGESTERONE ON TARGET CELLS

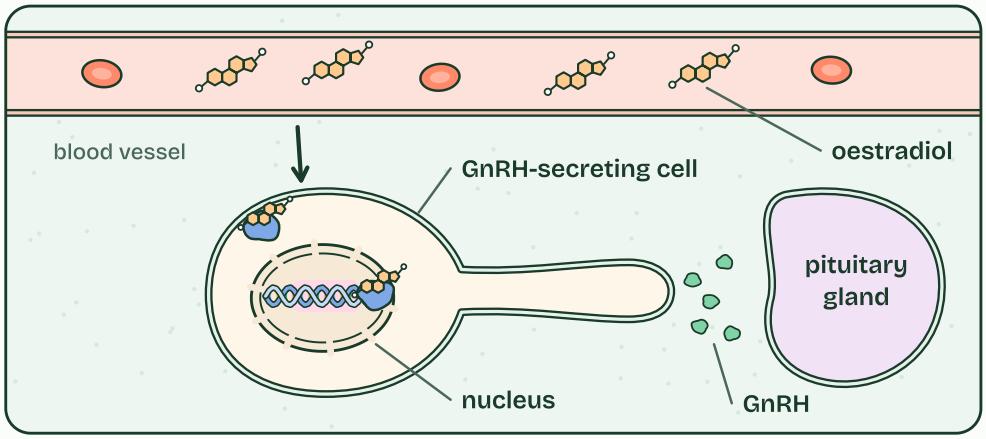
Oestradiol and progesterone are made by the ovary and both act through intracellular receptors. Each has many targets. The course asks for one target for each.

Oestradiol, made by the growing follicle, acts on **cells in the hypothalamus that secrete gonadotropin-releasing hormone (GnRH)**. It enters them and its receptor changes how much of the gene for GnRH is transcribed. In the early part of the cycle small amounts of oestradiol reduce the release of GnRH. When oestradiol is high for long enough, it increases it instead, which triggers a surge in LH from the pituitary gland and so ovulation. (The whole cycle is in D1.3.)

Progesterone, made by the corpus luteum after ovulation, acts on the cells of the **endometrium**, the lining of the uterus. Its receptors switch on genes that make the lining thicker, with more glands that secrete nutrients and more blood vessels, so that an embryo can implant. If there is no pregnancy, progesterone falls and the lining is shed.

KEY POINTS

- **Oestradiol:** acts on **GnRH-secreting cells** in the hypothalamus.
- **Progesterone:** acts on the **endometrium**, to prepare it for implantation.
- Both are **steroids**: they enter cells and change **gene expression**.

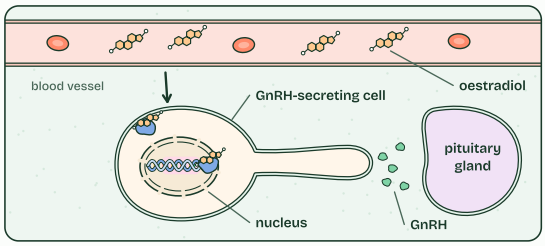


Oestradiol enters and acts on the GnRH gene.
Low levels reduce GnRH; high levels raise it (LH surge).

SWITCH IT

2 SETTINGS

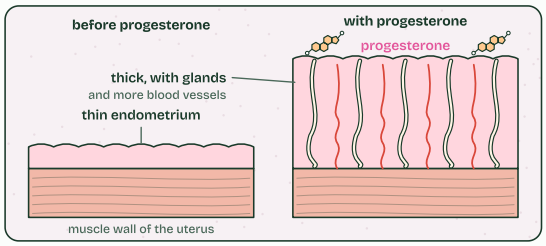
1



Oestradiol enters and acts on the GnRH gene.
Low levels reduce GnRH; high levels raise it (LH surge).

Oestradiol

2



It changes gene expression in endometrium cells.
The lining thickens and secretes, ready for implantation.

Progesterone

PREDICT

A target cell has no receptor for progesterone. What is its response to a high concentration of progesterone?

(A) None: it has no receptor to bind the hormone and activate

(B) A weak response, because progesterone diffuses into every cell

(C) A strong response, because progesterone enters the nucleus anyway

(D) It makes more oestradiol

Decide before you look. Answer on page 37.

13 Switching a signal *off, or up*

C2.1.14 HL REGULATION OF CELL SIGNALLING PATHWAYS BY POSITIVE AND NEGATIVE FEEDBACK

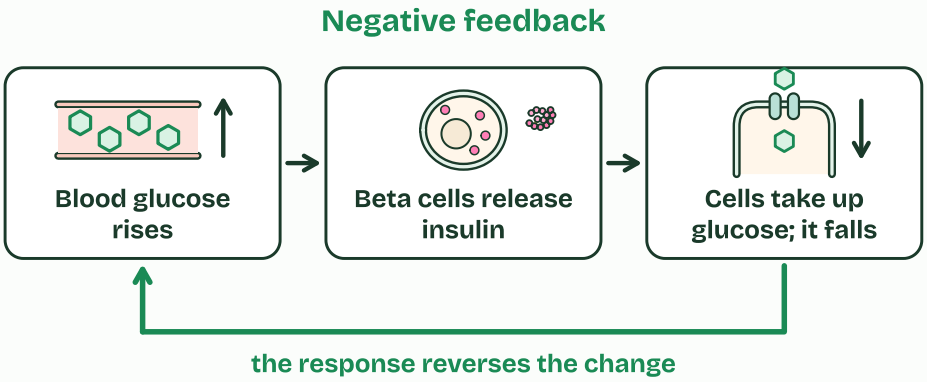
A signalling pathway has to be controlled, or a cell would keep on responding. The usual control is feedback: the result of the pathway affects the pathway.

In **negative feedback** the result **opposes** the change that started it. Insulin lowers blood glucose, and as glucose falls, beta cells release less insulin (D3.3). Negative feedback keeps a variable steady and is the most common form of regulation in the body.

In **positive feedback** the result **amplifies** the change. In labour, the baby's head presses on the cervix, which sends a signal to the hypothalamus, so the pituitary gland releases **oxytocin**. Oxytocin makes the uterus contract harder, which presses the baby harder on the cervix, and so on, with stronger contractions until the baby is born, when the pressure stops. The lit *Vibrio fischeri* cells that make more autoinducer are a positive feedback in bacteria. Positive feedback is not a steady state: it speeds a process until something outside ends it.

KEY POINTS

- **Negative:** the result **reverses** the change. Stable. Example: insulin and glucose.
- **Positive:** the result **amplifies** the change. Example: oxytocin in labour.
- Positive feedback needs an **end**: the birth, or the supply running out.



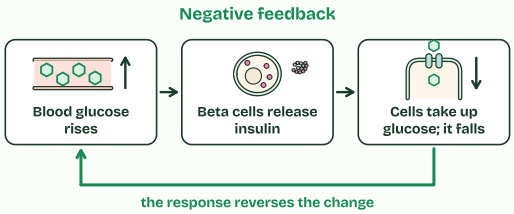
Negative: the output of the pathway switches the pathway off.

Stable. Most signals in the body are controlled this way.

SWITCH IT

2 SETTINGS

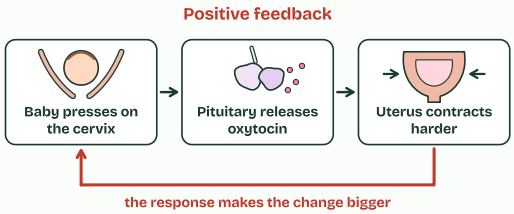
1



Negative: the output of the pathway switches the pathway off.
Stable. Most signals in the body are controlled this way.

Negative feedback

2



Positive: the output makes the pathway work harder.
Fast, runs away from the start, and needs something to end it.

Positive feedback

PREDICT

Which is an example of positive feedback?

(A) Insulin lowers blood glucose, so less insulin is released

(B) Oxytocin makes the uterus contract, which causes more oxytocin to be released

(C) Sweating cools the body, so sweating stops

(D) ADH retains water, so the blood becomes more dilute and ADH falls

Decide before you look. Answer on page 37.

IN THE EXAM

Distinguish between positive and negative feedback (2 marks): in **negative** feedback the response **reduces or reverses** the change, keeping the variable near a set point; in **positive** feedback the response **increases** the change, driving the process to completion.

Key terms

Every term this guide defines, A to Z, with the chapter it is in. Cover the right-hand side and test yourself.

adrenaline 09
The hormone, an amine, released by the adrenal glands in danger or stress. Epinephrine is the same molecule. It prepares the body for action.

binding site 01
A region on a protein with a shape and chemistry that fit one particular molecule.

depolarizes 07
Becomes less negative inside, so the voltage across the membrane moves toward zero.

G protein 08
A protein inside the cell, attached to the inside of the membrane, that is switched on when GDP is swapped for GTP, and then switches on an enzyme or a channel.

ligand 01
A signalling chemical that binds to a receptor.

quorum sensing 02
The way bacteria detect their population density by the concentration of a signalling molecule they release, and switch genes on or off together when it passes a threshold.

receptors 01
Proteins with a binding site for a specific signalling chemical. Binding makes the receptor change shape, which starts a response in the cell.

second messenger 08
A small molecule made inside a cell in response to a signal at the receptor. It spreads fast and switches on proteins inside the cell. The first messenger is the signal outside.

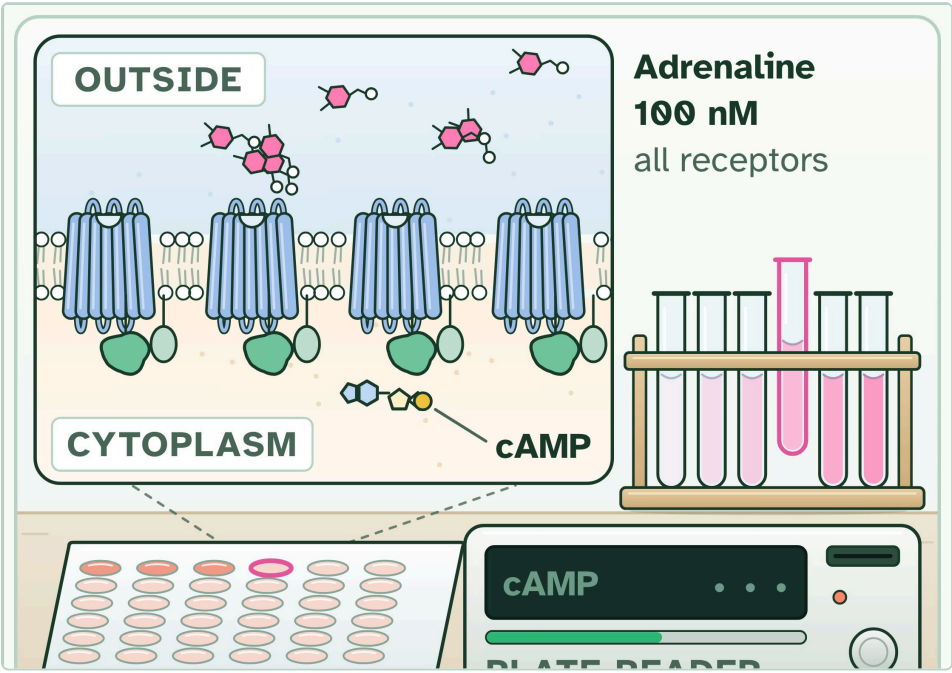
signal transduction pathway 06
A sequence of molecular events inside a cell that passes a signal from a receptor to the cell's response.

target cells 01
The cells that have receptors for a particular signalling chemical and so respond to it.

tyrosine kinase receptor 10
A transmembrane receptor whose inside part is an enzyme (a kinase). When a ligand binds, it adds phosphate groups to tyrosine amino acids.

Dry lab: *Dose and response*

A cell makes a response in proportion to the receptors that a ligand occupies. Test adrenaline, a look-alike and a beta blocker over six concentrations, with a full or half set of receptors, and see how the curve moves.



Run it online: change the variables, run the trials, and the table and graph fill in as you go. `biologybybradford.com/guides/ib-biology-c2-1-chemical-signalling#lab`

Your question

How does the response of a cell depend on the concentration of a ligand, and how do a look-alike ligand, a blocker or fewer receptors change it?

What you can change

The ligand (adrenaline, a look-alike or adrenaline with a beta blocker) and the number of receptors (normal or half). The six concentrations are fixed, from 0.1 to 10 000 nM, so that curves can be compared.

What to record

For each test, the response at each concentration, the half-way concentration and the maximum response. Repeat a test to see the measurement wobble. Download the CSV to plot your own log-scale graph.

Find out

- **How does the response depend on concentration?** Run adrenaline at all six concentrations, from 0.1 to 10 000 nM. Where does the curve rise fastest, and where does it flatten?
- **What does the half-way point tell you?** Read off the concentration that gives half the maximum response. A lower value means the ligand binds more tightly.
- **What does a look-alike do?** Run the look-alike ligand and then adrenaline with the beta blocker. Both bind the receptor. Which curve moves right, and what does that say about how much is needed?
- **What if there are fewer receptors?** Switch to half the receptors and repeat adrenaline. Does the half-way point change, or the maximum, or both?

Record

- For each test: the ligand, the receptor number, and the six readings in the table.
- The concentration that gives half the maximum response, and the largest response, for each test.
- A repeat of one test, to see how much of the difference between two curves could be measurement error.
- Download the CSV to plot your own graph. The concentration axis is a log scale: why?

Your question How does the response of a cell depend on the concentration of a ligand, and how do a look-alike ligand, a blocker or fewer receptors change it?**What you can change**The ligand (adrenaline, a look-alike or adrenaline with a beta blocker) and the number of receptors (normal or half). The six concentrations are fixed, from 0.1 to 10 000 nM, so that curves can be compared.**What to record**For each test, the response at each concentration, the half-way concentration and the maximum response. Repeat a test to see the measurement wobble. Download the CSV to plot your own log-scale graph.

Back to receptors

A cell carries a fixed number of adrenaline receptors. Use your curves to explain why its response levels off, and why a beta blocker moves the curve right without lowering its top.

QUESTIONS ON THE LAB

QUESTION 1

You raise the concentration of adrenaline from 1000 nM to 10 000 nM. What happens to the response?

(A) It rises another tenfold, because ten times more ligand binds

(B) It hardly changes, because nearly all the receptors are already occupied

(C) It falls, because the extra ligand blocks the receptor

Answer on page 37.

QUESTION 2

A beta blocker is added alongside adrenaline. What does the dose-response curve do?

(A) It moves to the left, because the drug helps adrenaline bind

(B) It moves to the right, because the drug occupies receptors and more adrenaline is needed for the same response

(C) It does not move, because the drug is not adrenaline

Answer on page 37.

Check yourself

The check for this guide is online: a fresh paper of past-paper style questions from the exam bank on C2.1 each time, marked as you go, and saved to your Exam practice progress when you are signed in. Scan the code, or type the link.

biologybybradford.com/exam-maker/sit?topics=C2.1&level=HL&paper=quiz&marks=15&src=ep

Answers

PREDICTIONS IN THE CHAPTERS

01 Three ligands, a circle, a square and a triangle, are added to a receptor with a triangular binding site. Which one will switch the receptor on?

B **The triangle, because its shape fits the binding site**

Binding depends on the shape and chemistry of the binding site, which are fixed by the protein's tertiary structure. Only the ligand that fits binds, so a receptor is specific. The two shapes that do not fit leave it off.

02 A single Vibrio fischeri cell in a large volume of seawater is given the genes for light. Will it glow?

B **No, because the autoinducer it makes spreads out and never reaches the threshold**

Quorum sensing depends on the concentration of the signal. One cell in a large volume makes too little autoinducer, and it disperses, so the genes for light stay off. The same cell glows when it is among many others.

03 Which signalling chemical would be the best choice for a message that has to reach every muscle in the body, and last for several minutes?

B **A hormone, because it travels in the blood to all target cells and lasts**

The blood carries a hormone everywhere, and its effect lasts as long as it remains in the blood. A neurotransmitter works only across one synapse and is removed in milliseconds.

05 Which sentence correctly describes the part of a transmembrane receptor that lies in the lipid bilayer?

B **It is made mostly of hydrophobic amino acids, which are at home in the lipid core**

The membrane-spanning region has hydrophobic amino acids on the outside of the protein, in contact with the fatty acid tails. The hydrophilic regions are the parts that face the water on either side.

06 A single molecule of a hormone binds to a single receptor, yet the cell makes millions of glucose molecules. What best explains this?

B **Each step of the pathway switches on many molecules of the next step, so the signal is amplified**

In a transduction pathway one active molecule activates many of the next, so a very small signal produces a very large response. The hormone is not used up, does not enter the cell and does not become the product.

07 Acetylcholine binds a receptor and positively charged ions flow into the cell. What happens to the membrane potential?

C **It becomes less negative, because positive charge is added inside**

Positive ions entering make the inside less negative, so the potential moves toward zero. Nothing is pumped: the ions move down their gradient through the open channel, which needs no ATP.

08 What switches a G protein on?

B **The receptor, after a ligand has bound it, makes the G protein swap GDP for GTP**

The ligand binds the receptor on the outside. The shape change in the receptor makes the G protein release GDP and take up GTP, and that switches it on. The ligand never touches the G protein.

09 A drug binds the adrenaline receptor but does not change its shape. What will happen when adrenaline is also present?

B **Less cAMP is made, because the drug blocks adrenaline from the binding site**

The drug occupies the binding site, so fewer receptors bind adrenaline and fewer G proteins are switched on. Beta blockers work this way, which is why they slow the heart.

10 A muscle cell is given insulin. What is the direct effect on the plasma membrane?

A Glucose transporter proteins are added to it by vesicles that fuse with it

Insulin triggers a pathway that moves vesicles carrying GLUT4 to the membrane. Facilitated diffusion then moves glucose in down its gradient. Without insulin, most of the transporters are in vesicles inside the cell. In type 1 diabetes there is no insulin; in type 2 the cells respond poorly.

11 Why does a steroid hormone take longer to act on a cell than adrenaline does?

B It changes gene expression, so mRNA and then protein must be made

Adrenaline starts an enzyme cascade in seconds, using proteins already in the cell. A steroid works through transcription and translation, which take much longer, although the new protein may last for hours or days.

12 A target cell has no receptor for progesterone. What is its response to a high concentration of progesterone?

A None: it has no receptor to bind the hormone and activate

A hormone only affects cells that have its receptor, the target cells. Progesterone passes through every cell's membrane, but a cell with no receptor cannot respond.

13 Which is an example of positive feedback?

B Oxytocin makes the uterus contract, which causes more oxytocin to be released

In positive feedback the response drives more of the same signal. The other three are negative feedback, in which the response removes the stimulus.

QUESTIONS ON THE DRY LAB

Q1 You raise the concentration of adrenaline from 1000 nM to 10 000 nM. What happens to the response?

B It hardly changes, because nearly all the receptors are already occupied

The curve flattens at the top, because the response can be no greater than when every receptor is occupied. Extra ligand has no free receptors left to find.

Q2 A beta blocker is added alongside adrenaline. What does the dose-response curve do?

B It moves to the right, because the drug occupies receptors and more adrenaline is needed for the same response

The blocker competes for the binding site, so at a given concentration fewer receptors hold adrenaline. A high enough concentration of adrenaline can still win most of the sites, which is why the maximum is reached late rather than lost.

How this was made. The course structure, the activities and the teaching choices come from my own classroom, my presentations and my years of teaching IB and AP Biology. I use Claude, an AI, to help write and build the interactive guides, lesson plans, slides and practice questions, and to draw the diagrams and code the interactives. I direct the work and review it against the IB and AP specifications before it goes live.

Written and drawn for Biology by Bradford, biologybybradford.com. Free to print and share with a class.