REVISION GUIDE

How cells *pass a message on*

Cell communication and signal transduction

A hormone in your blood never enters the liver cell it changes. A T cell is switched on by touch, and bacteria in a squid light up only when there are enough of them. Follow a signal from the cell that sends it, through the receptor and the relay inside, to what the cell does, and see what happens when one link breaks.

11 chapters · a dry lab

The interactive guide, with every animation:

biologybybradford.com/guides/ap-biology-unit-4-cell-communication

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By the end you can

- [ ] Describe how cells communicate by direct contact: gap junctions, plasmodesmata and immune cells that touch 4.1.A
- [ ] Explain how local regulators and hormones reach target cells over short and long distances 4.1.B
- [ ] Explain how bacteria use quorum sensing to switch genes on together once their population is dense enough 4.1.A 4.3.A
- [ ] Describe how a ligand binds the ligand-binding domain of its receptor one to one, and where receptors sit for hydrophilic and hydrophobic ligands 4.2.B
- [ ] Describe the parts of a signal transduction pathway, and how kinases and phosphatases switch relay proteins on and off 4.2.A
- [ ] Explain how a G protein-coupled receptor, a second messenger and a ligand-gated channel relay and amplify a signal 4.2.B
- [ ] Describe how signals from the environment change gene expression, cell function and phenotype, or trigger apoptosis 4.3.A
- [ ] Predict how a mutation or a chemical that changes one part of a pathway changes the cell's response 4.3.B

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

01

4.1.A CELL COMMUNICATION BY DIRECT CONTACT

Cells that *touch* to talk

Every cell in your body is listening for messages, and nearly all of them arrive as chemicals. The first thing that sorts them is how far the chemical has to travel. The shortest trip is no trip at all: cells that touch can pass a message straight across.

Animal cells side by side can be joined by **gap junctions**: a ring of proteins in each membrane, the two rings lined up to make a tunnel from one cytoplasm into the next. Ions and small molecules such as sugars pass through; proteins are too big. Heart muscle cells are joined this way, so the electrical signal to contract runs from cell to cell and the heart beats as one.

Plant cells are boxed in by walls, but the walls are crossed by **plasmodesmata**: narrow channels lined with plasma membrane, so the cytoplasm of one cell runs on into the next. Water, ions, sugars and signaling molecules move along them from cell to cell.

The third kind of contact needs no tunnel. A molecule held on the surface of one cell binds a receptor on the other. In your immune system an **antigen-presenting cell** (APC) shows a fragment of a pathogen on its surface. A **helper T cell** whose receptor fits that fragment binds it and is switched on; one whose receptor does not fit passes by. Killer T cells recognize infected cells by touch in the same way.

KEY POINTS

- Gap junctions: protein tunnels between animal cells.
- Plasmodesmata: channels through plant cell walls.
- Surface contact: a molecule on one cell binds a receptor on the other (an APC and a T cell).

KEY TERMS

gap junctions
Channels made of protein rings in the membranes of two neighboring animal cells, lined up to join their cytoplasm. Ions and small molecules pass through.

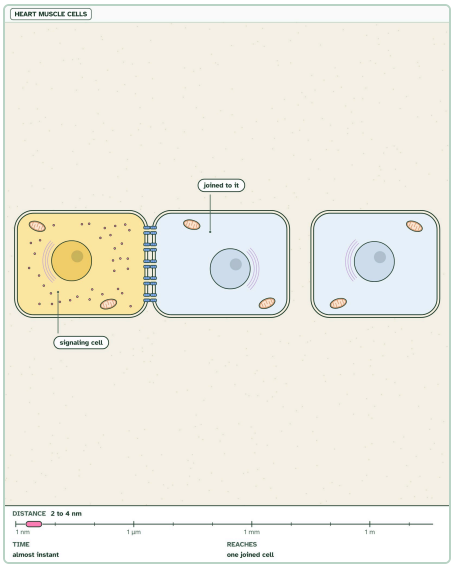
plasmodesmata
Narrow channels through the walls of neighboring plant cells, lined with plasma membrane, so the cytoplasm of one cell is continuous with the next.

antigen-presenting cell
A cell, such as a macrophage, that takes in a pathogen and displays fragments of it on its surface for T cells to recognize.

helper T cell
A white blood cell that, once switched on by an antigen-presenting cell, releases signals that start and direct an immune response.

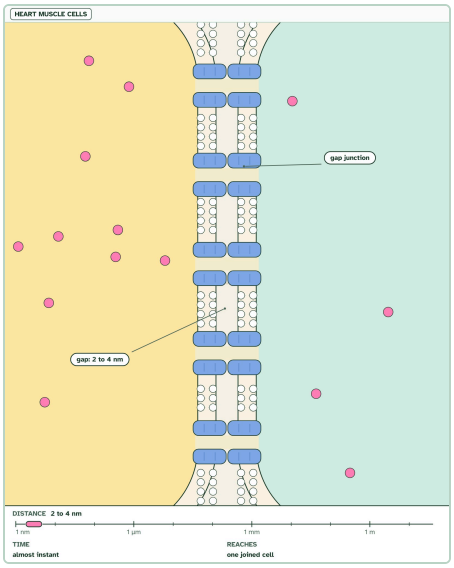
ANIMATION · SIGNALING BY CONTACT
7 MOMENTS

1 DIRECT CONTACT



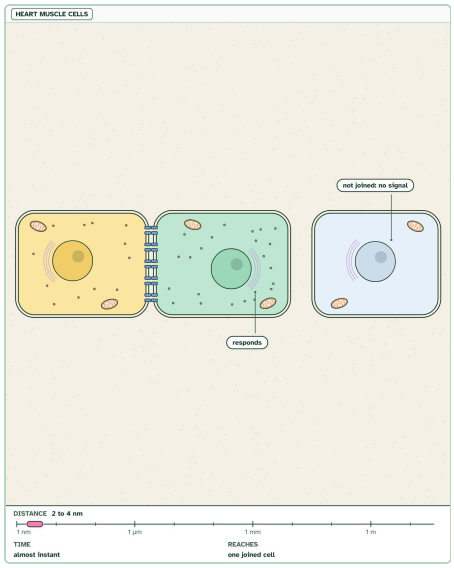
The shortest reach: **direct contact.** In animal tissues such as heart muscle, neighboring cells are joined by **gap junctions**, channels that link their cytoplasm.

2 DIRECT CONTACT



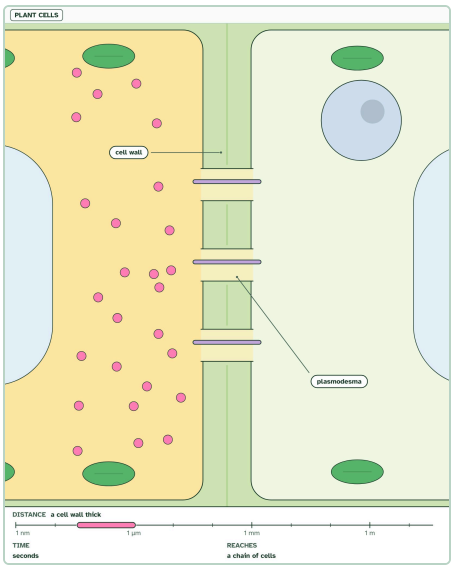
Ions and small signal molecules pass straight from one cell into the next, with no receptor on the way. The message arrives almost at once, but only in a cell that is joined.

3 DIRECT CONTACT



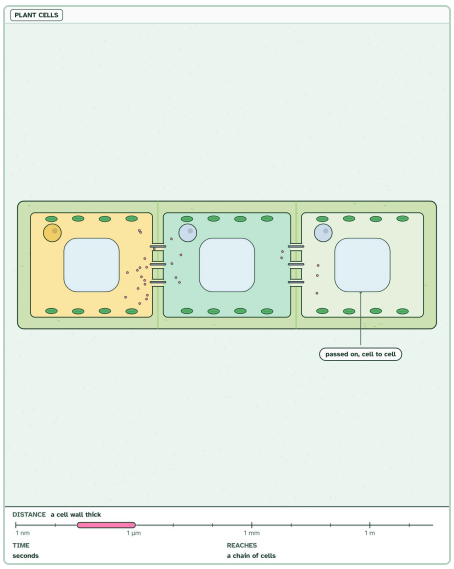
Ions and small signal molecules pass straight from one cell into the next, with no receptor on the way. The message arrives almost at once, but only in a cell that is joined.

4 DIRECT CONTACT



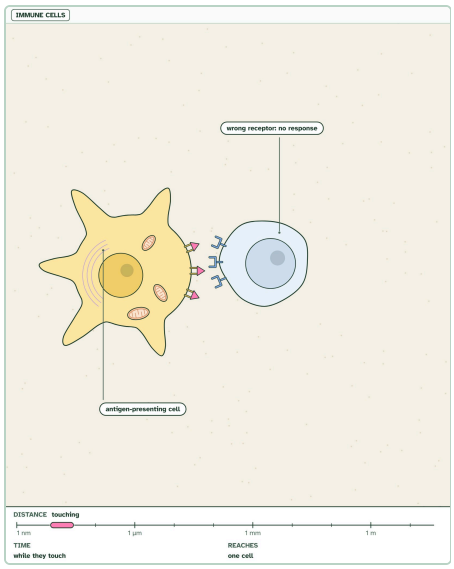
Signal molecules move along them from cytoplasm to cytoplasm, and on from cell to cell.

5 DIRECT CONTACT



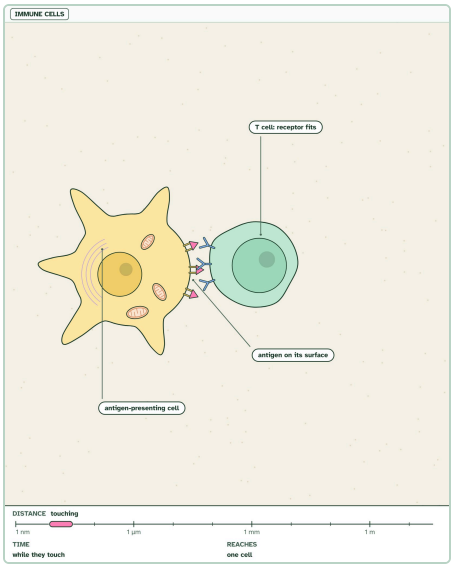
Signal molecules move along them from cytoplasm to cytoplasm, and on from cell to cell.

6 DIRECT CONTACT



Cell-surface contact. An antigen-presenting cell holds a piece of antigen on its surface. A T cell whose receptor does not fit touches it and moves on.

7 DIRECT CONTACT



A T cell whose **receptor fits** binds, and it is activated. The signal never left the surface of the sending cell: its reach is one cell.

Watch it move, and change it as it runs: biologybybradford.com/guides/ap-biology-unit-4-cell-communication#contact

PREDICT

A drug blocks the gap junctions of one heart muscle cell. The signal to contract reaches its neighbors as usual. What does the blocked cell do?

(A) It contracts first, because the signal is trapped inside it

(B) It keeps in time, because the signal reaches it in the blood

(C) It misses the beat, because the ions cannot pass into it

(D) It contracts twice, once for each neighbor that it touches

Decide before you look. Answer on page 45.

WATCH OUT

Direct contact still uses chemicals: ions through a gap junction, a fragment of pathogen on an APC. What makes it direct is that nothing has to cross the fluid between the cells.

02 Near *or far*

4.1.B SIGNALING OVER SHORT AND LONG DISTANCES

Most signals do cross the fluid between cells, and how far they go sorts them into two kinds. A **local regulator** acts on cells near the one that released it, over a fraction of a millimeter, and is then broken down or taken up.

In **paracrine signaling** a cell releases molecules that diffuse to its neighbors: a growth factor from one cell makes the cells around it divide. In **synaptic signaling** a neuron releases a **neurotransmitter** into a cleft about 20 nm wide, and it reaches receptors on the next cell in well under a millisecond.

A **hormone** goes much further. In **endocrine signaling** a gland releases it into the blood, which carries it round the body in about a minute. It reaches almost every cell, but only its **target cells**, the ones with a receptor for it, respond. Plants signal over long distances too, their hormones carried in the xylem and phloem: the second film.

Five hormones the AP course names

Hormone	Made in	Main targets
Insulin	beta cells of the pancreas	liver, muscle and fat cells: take up glucose
Human growth hormone	pituitary gland	liver, bone and muscle: growth
Thyroid hormones	thyroid gland	nearly every cell: a faster metabolism
Testosterone	testes	muscle, bone, reproductive organs
Estrogen	ovaries	uterus, breasts, bone

KEY POINTS

- Local regulators: paracrine (diffuse to neighbors) and synaptic (across a 20 nm cleft).
- Hormones: endocrine, in the blood, to target cells anywhere.
- A cell is a target only if it has the receptor.

KEY TERMS

local regulator
A signaling molecule that acts on cells close to the cell that released it, before it is broken down or taken up.

paracrine signaling
Signaling by a local regulator that diffuses through the fluid between cells to targets nearby.

synaptic signaling
Signaling across a synapse: a neuron releases a neurotransmitter, which crosses the narrow cleft to receptors on the next cell.

neurotransmitter
A chemical released by a neuron at a synapse that binds receptors on the next cell.

hormone
A signaling molecule released into the blood by a gland, which carries it to target cells all over the body.

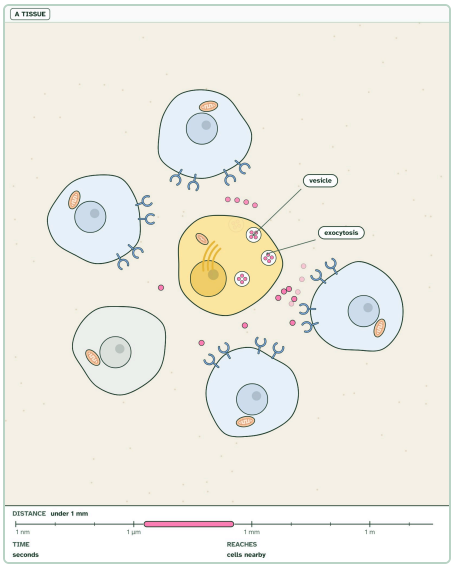
endocrine signaling
Long-distance signaling: a gland releases a hormone into the blood, which carries it to target cells anywhere in the body.

target cells
The cells that carry a receptor for a particular signal, and so respond to it.

ANIMATION · LOCAL REGULATORS

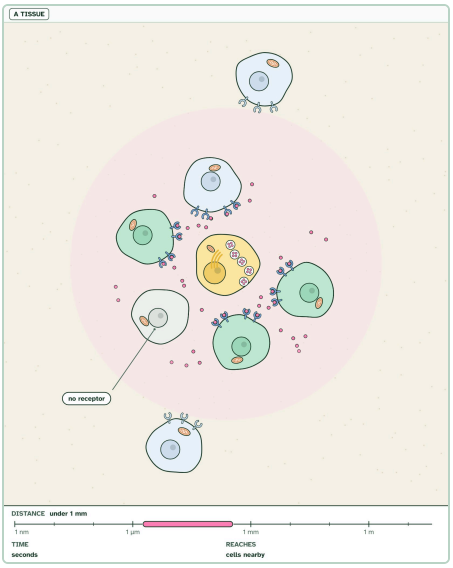
6 MOMENTS

1 LOCAL REGULATORS



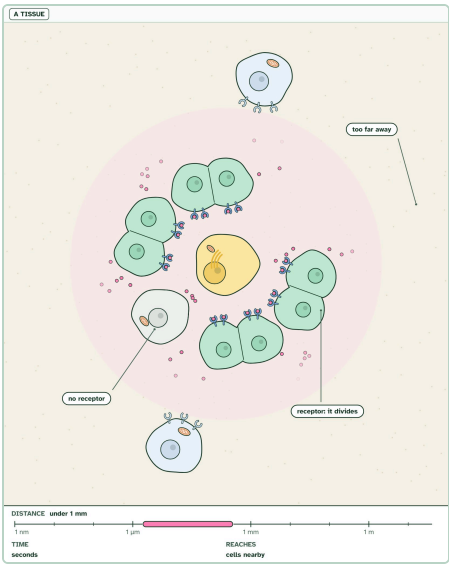
A **local regulator**. This cell releases a growth factor by **exocytosis**: vesicles fuse with its membrane and empty to the outside.

2 LOCAL REGULATORS



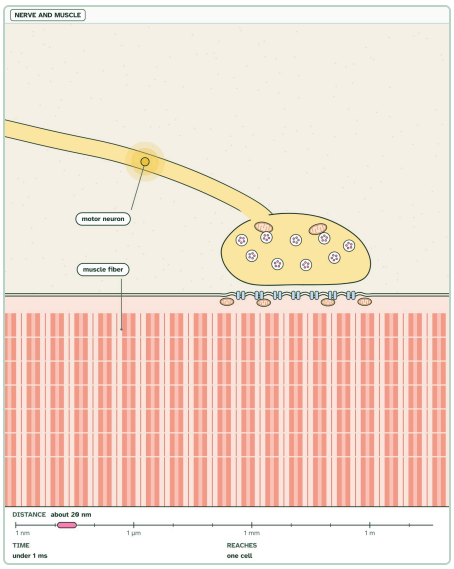
The molecules **diffuse** through the fluid between the cells. This is **paracrine** signaling: they reach cells a short way off within seconds.

3 LOCAL REGULATORS



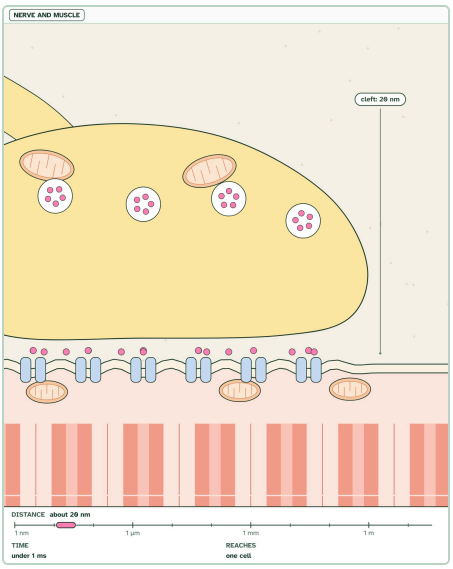
Only nearby cells **with the receptor** respond, here by dividing. A neighbor without the receptor does not, and further away the signal is too dilute and is broken down.

4 LOCAL REGULATORS



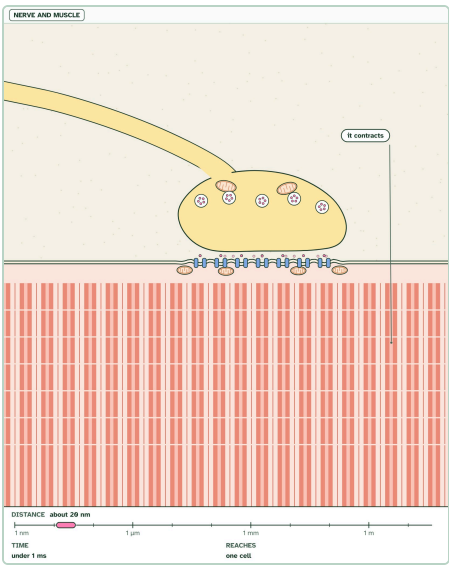
Synaptic signaling is more local still. A nerve impulse reaches the end of a motor neuron, beside a muscle fiber.

5 LOCAL REGULATORS



Vesicles release a **neurotransmitter**. It diffuses across the synaptic cleft, only about 20 nm, in under a millisecond.

6 LOCAL REGULATORS

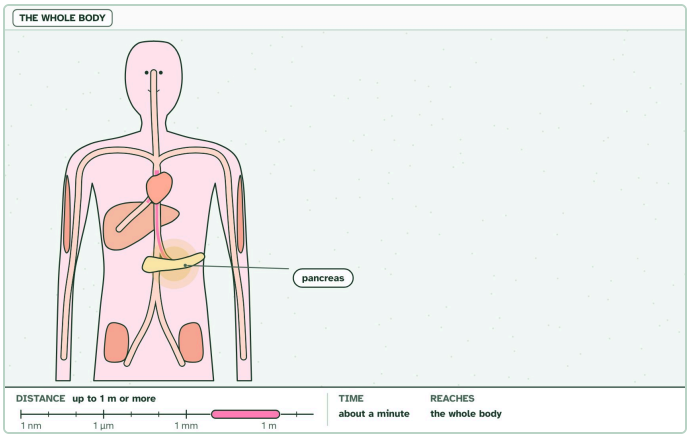


It binds to receptors on the muscle cell, ion channels open and the fiber **contracts**. An enzyme then breaks the neurotransmitter down: a brief signal, to one cell.

Watch it move, and change it as it runs: biologybybradford.com/guides/ap-biology-unit-4-cell-communication#distance

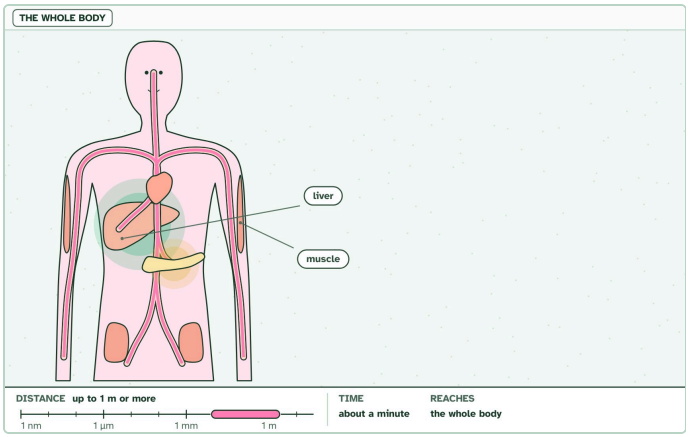
ANIMATION · NEAR OR FAR: COMPARE THEM 6 MOMENTS

1 LONG DISTANCE



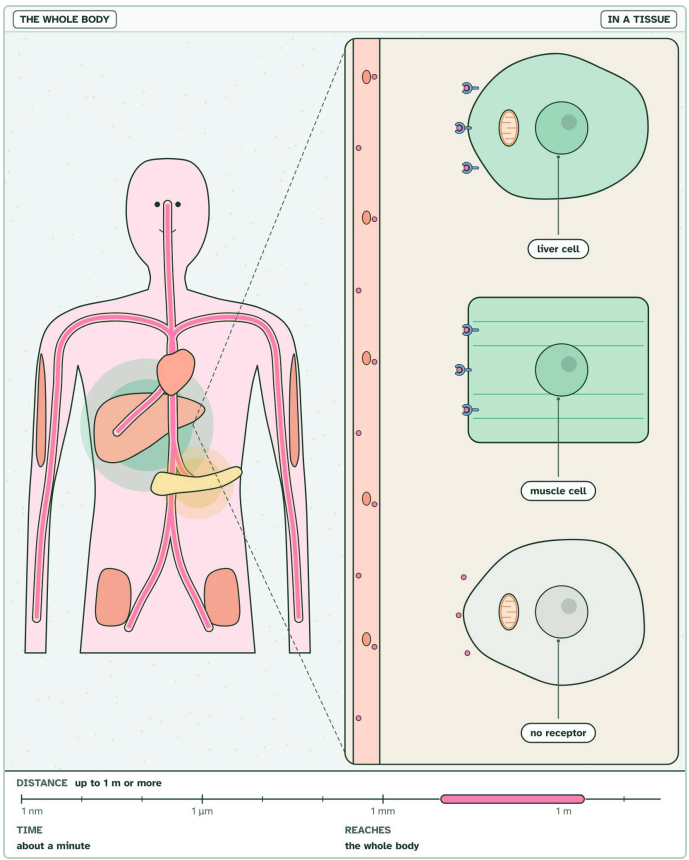
The longest reach: **endocrine** signaling. Beta cells in the pancreas release the hormone **insulin** into the blood.

2 LONG DISTANCE



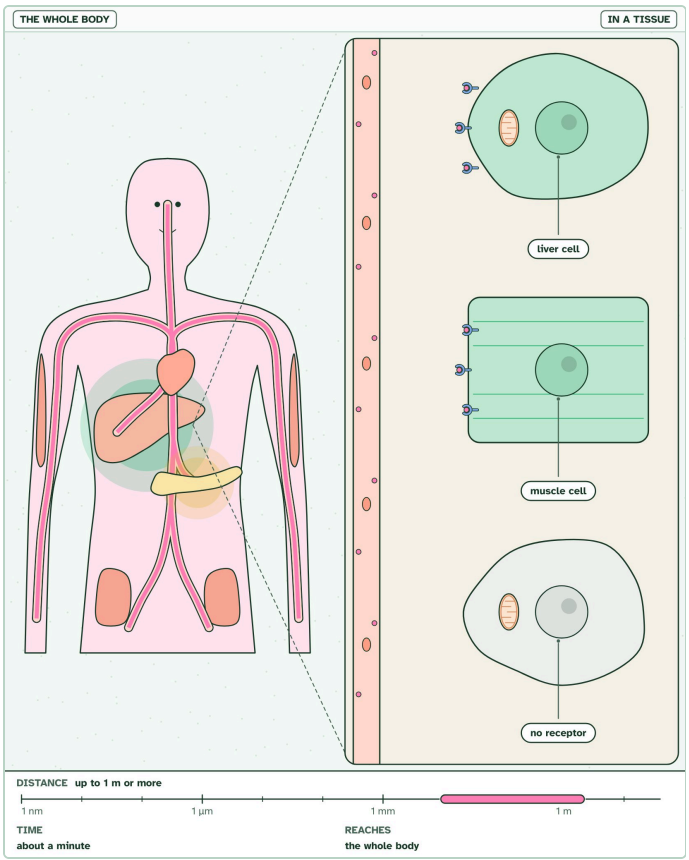
The blood carries it to every part of the body, a meter or more away, in about a minute.

3 LONG DISTANCE



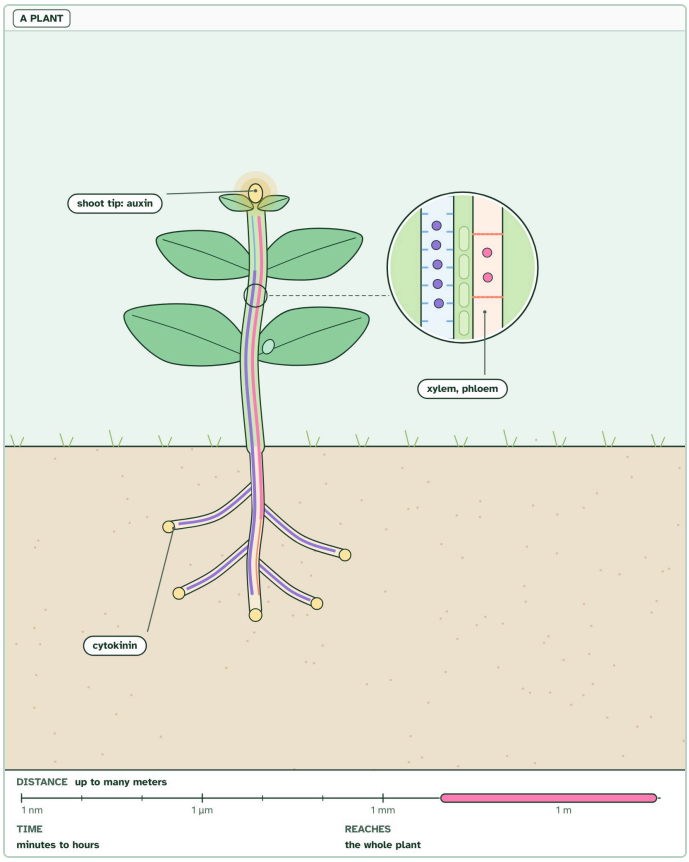
It passes almost every cell, but only cells **with the insulin receptor**, such as liver and muscle cells, respond. A cell without the receptor does nothing.

4 LONG DISTANCE



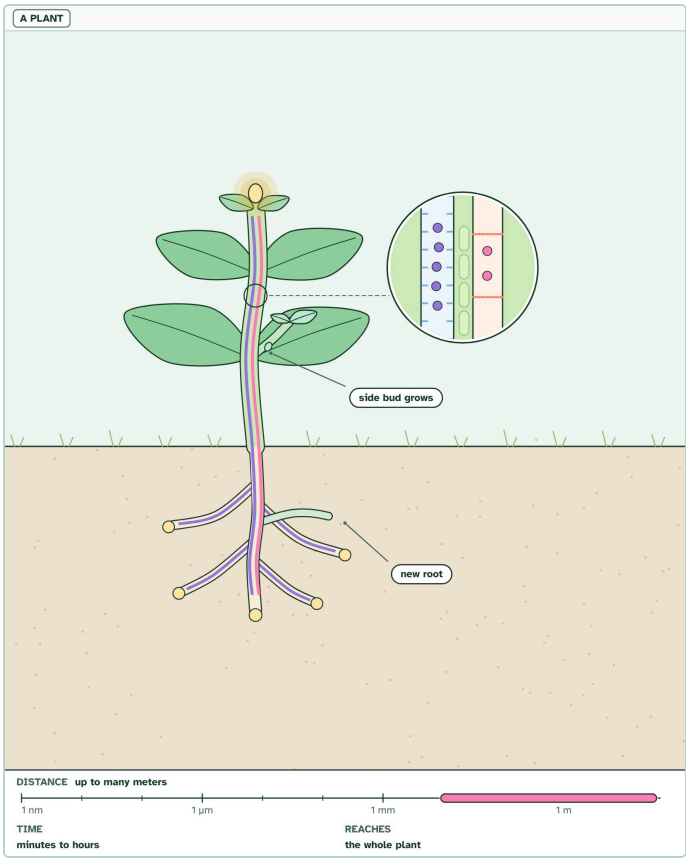
A hormone arrives more slowly than a nerve impulse, but it reaches the whole body and its effect lasts longer.

5 LONG DISTANCE



Plants signal over long distances too, through their vascular tissue. **Cytokinin** made in the root tips travels up in the xylem, and **auxin** made in the shoot tip moves down towards the roots.

6 LONG DISTANCE



Again only cells with the right receptor respond: a side bud grows out, and a new root branches. Longer reach, slower signal, wider spread.

Watch it move, and change it as it runs: biologybybradford.com/guides/ap-biology-unit-4-cell-communication#distance

PREDICT

A neuron releases a neurotransmitter and the pancreas releases insulin at the same moment. Which reaches its target cells first, and why?

(A) Insulin, because it is a larger molecule that is made in bigger amounts

(B) The neurotransmitter, because it has a gap of only 20 nm to cross

(C) Both at once, because every signaling molecule diffuses at one speed

(D) Insulin, because the blood carries it faster than anything can diffuse

Decide before you look. Answer on page 45.

WATCH OUT

A hormone in the blood reaches nearly every cell in the body, not only its targets. What makes a cell a target is its receptor, not where it is.

03

4.1.A 4.3.A QUORUM SENSING

Bacteria that *count heads*

One bacterium making light, or a toxin, or a slimy biofilm, wastes its effort: these only pay off when thousands do them together. So many bacteria wait until they are crowded, and they find out how crowded by chemistry. Each cell releases a small signaling molecule, an **autoinducer**, and carries receptors for it. This is **quorum sensing**: signaling that measures population density.

The ocean bacterium *Vibrio fischeri* lives in the light organ of the Hawaiian bobtail squid. Spread thin in seawater, its autoinducer drifts away and stays dilute, and the cells stay dark. Packed into the squid, the molecules build up. Above a threshold they bind receptors inside the bacteria (the autoinducer is small enough to cross the membrane), and the bound receptors switch on the genes for light. Glowing cells make more autoinducer, so the whole population lights up together. The squid hunts at night and uses the glow to hide its shadow from fish below.

The response is a change in gene expression, set off by the cells' environment: how many neighbors they have. *Vibrio cholerae* and *Pseudomonas aeruginosa* use quorum sensing to time their biofilms and toxins, which is why drugs that jam the signal are being tested.

KEY POINTS

- Every cell releases an autoinducer; more cells, higher concentration.
- Above a threshold it binds receptors and switches genes on in every cell.
- A population acts together only when it is big enough for it to matter.

KEY TERMS

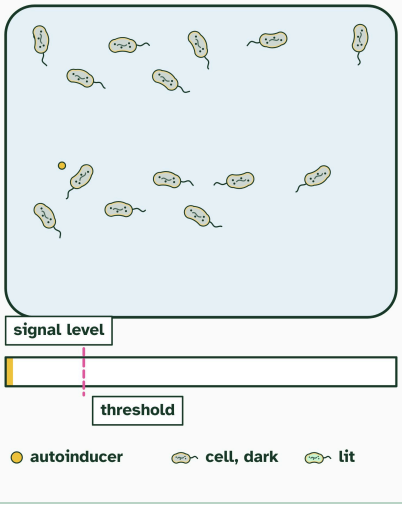
autoinducer
A small signaling molecule that bacteria release and also detect. Its concentration rises with the number of cells.

quorum sensing
Signaling that lets bacteria detect their population density from the concentration of a molecule they all release, and switch genes on together once it passes a threshold.

ANIMATION · BACTERIA COUNTING EACH OTHER

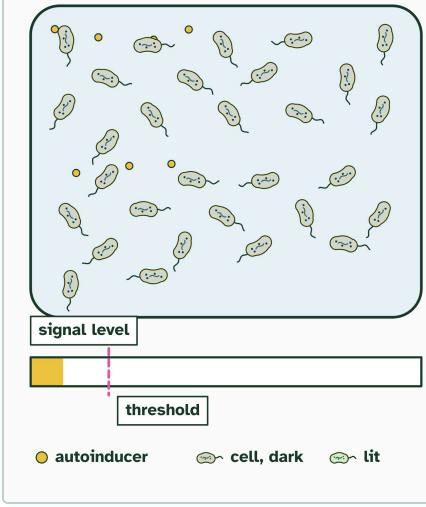
5 MOMENTS

1 14 CELLS, DARK



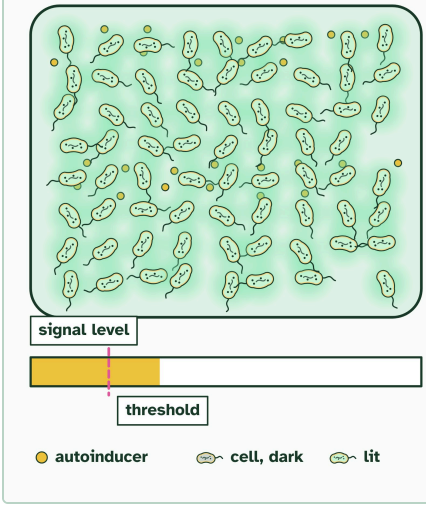
A few **Vibrio fischeri** cells in seawater. Each releases a little of a signaling molecule, an **autoinducer**, but it drifts away. The cells stay dark.

2 30 CELLS, DARK



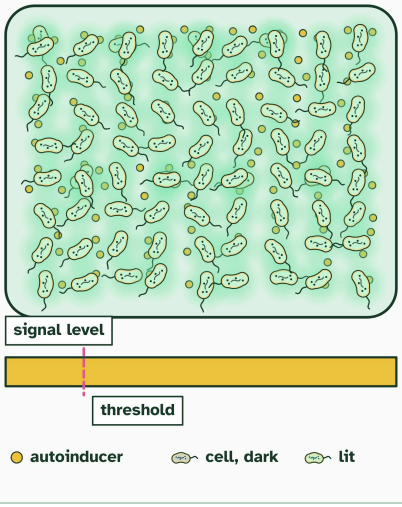
The cells divide, and more of them are making the autoinducer.

3 70 CELLS, LIGHT ON



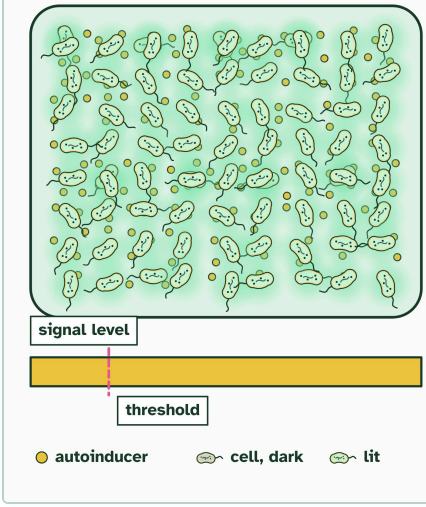
The molecules now arrive faster than they drift away, so the **concentration builds up**. Each cell is measuring how many cells are around it.

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/ap-biology-unit-4-cell-communication#quorum

PREDICT

A flask of *Vibrio fischeri* has just begun to glow. You dilute it tenfold with fresh seawater. What happens to the light?

(A) It fades, as the autoinducer is now below the threshold

(B) It grows brighter, as each cell now has more room and food

(C) It stays the same, as the light genes cannot switch off again

(D) It flickers, as the cells take turns making the autoinducer

Decide before you look. Answer on page 45.

04

4.2.B LIGANDS AND RECEPTORS

A receptor *fits one* messenger

A signaling molecule is a **ligand**, and the protein it binds is its **receptor**. Part of the receptor, the **ligand-binding domain**, has a shape and a pattern of charges that fit one ligand, the way an active site fits its substrate. The fit is one to one: the insulin receptor binds insulin and nothing else in your blood. The ligand can be a protein such as insulin, a short peptide, or a small molecule such as epinephrine or a steroid.

Binding is weak and reversible: ligands come and go, so the more ligand there is, the more receptors are filled at any moment (the dry lab measures this). A cell with no receptor for a ligand cannot respond to it, however much is around.

Where the receptor sits depends on the ligand. The core of the membrane is hydrophobic. Hydrophilic and large ligands (proteins, peptides, epinephrine) cannot cross it, so their receptors span the membrane. Hydrophobic ligands, such as the steroids testosterone and estrogen, slip through the bilayer, and their receptors wait in the cytoplasm or the nucleus.

KEY POINTS

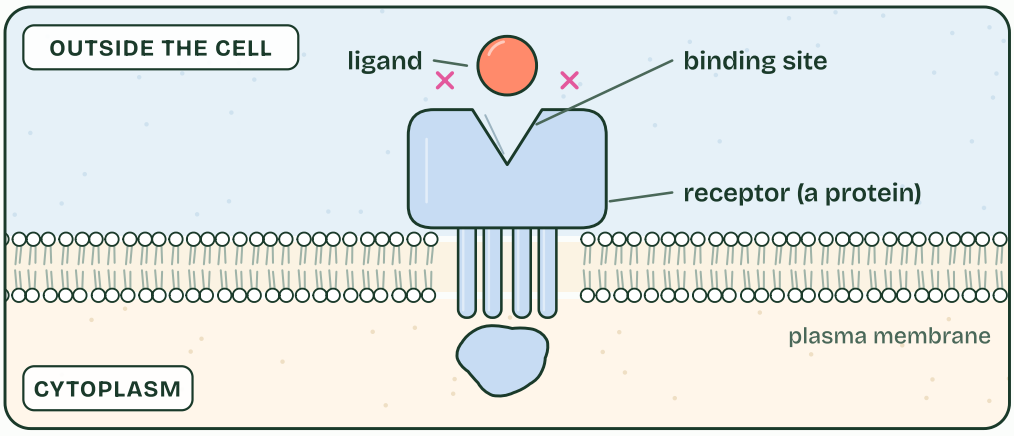
- The ligand-binding domain fits one ligand: one to one.
- Hydrophilic or large ligand: a receptor in the membrane.
- Hydrophobic ligand (a steroid): a receptor inside the cell.

KEY TERMS

ligand
A molecule that binds specifically to a receptor. In signaling, the chemical messenger itself.

receptor
A protein, in the plasma membrane or inside the cell, with a binding site for one particular ligand. Binding changes its shape.

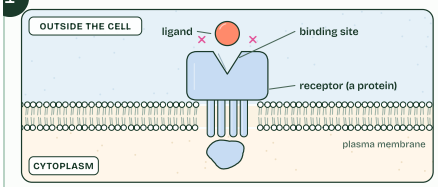
ligand-binding domain
The part of a receptor protein whose shape and charges fit its ligand.



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

SWITCH IT 3 SETTINGS

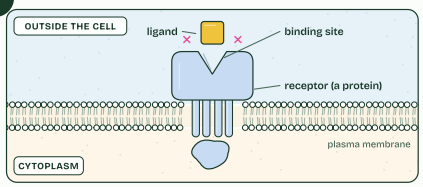
1



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

Circle

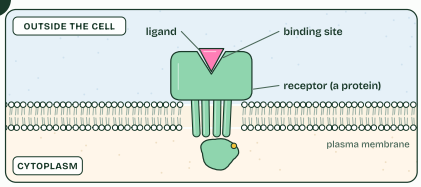
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Square: the shape does not fit the binding site, so it does not bind and the receptor stays off.

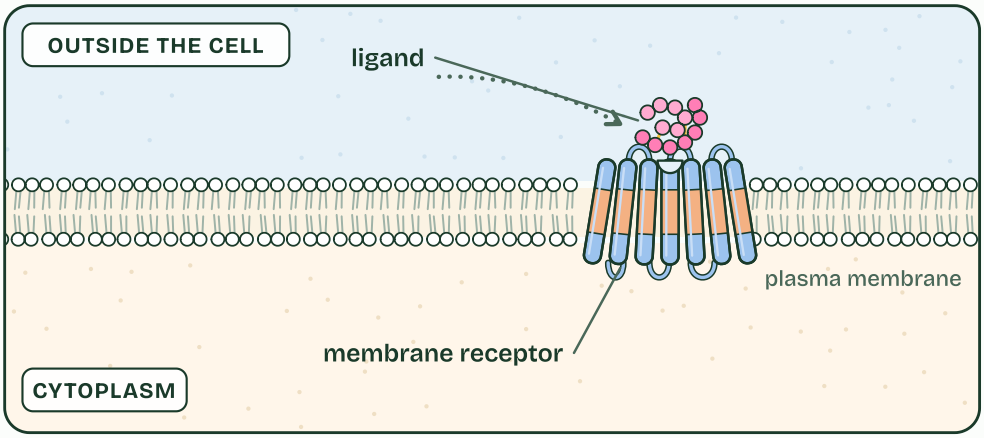
Square

3



Triangle: the shape fits the binding site, so it binds and the receptor changes shape and switches on.

Triangle



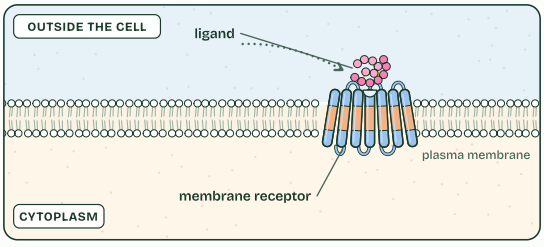
Water-soluble ligand: cannot cross the bilayer.

It binds the outside of a transmembrane receptor.

hydrophilic amino acids hydrophobic amino acids

SWITCH IT 2 SETTINGS

1



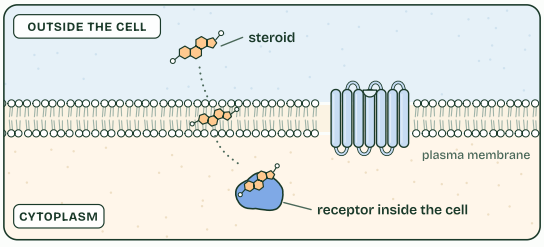
Water-soluble ligand: cannot cross the bilayer.

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

A new drug is a short chain of amino acids, a peptide, and it must act on liver cells. Where do you expect to find its receptor?

(A) In the nucleus, because the drug must change which genes are read

(B) In the cytoplasm, because every ligand diffuses straight into cells

(C) Anywhere in the cell, since a receptor binds whatever reaches it

(D) In the plasma membrane, with its binding domain facing out

Decide before you look. Answer on page 45.

WATCH OUT

With a receptor in the membrane, the ligand never enters the cell. The receptor carries the message across by changing shape, and molecules inside relay it on.

05 Reception, *transduction*, response

4.2.A COMPONENTS OF A SIGNAL TRANSDUCTION PATHWAY

Every pathway in this guide runs in three stages. In **reception** the ligand binds its receptor, and the receptor changes shape. In **transduction** that change is passed along a chain of molecules inside the cell, each switching on the next. In the **response** the last molecules do something: an enzyme starts work, a channel opens, a gene is read. The whole chain is a **signal transduction pathway**, and it links what the receptor senses to what the cell does.

Most relay molecules are proteins, and the commonest way to switch one on or off is to change it slightly: **protein modification**. The usual change is a phosphate group. A **protein kinase** takes the end phosphate from ATP and adds it to an amino acid of its target. The new negative charges change how the target folds, and so what it does. Often the target is itself a kinase, so kinase switches on kinase in a **phosphorylation cascade**, each one acting on many of the next.

Switching off matters as much. A **protein phosphatase** takes the phosphate off again, so each relay goes back to rest once the signal stops. The cell responds while the ligand is there, and stops when it goes.

KEY POINTS

- Reception, transduction, response.
- Kinases add phosphate from ATP; phosphatases take it off.
- A cascade: each kinase switches on many of the next.

KEY TERMS

reception
The first stage of cell signaling: the ligand binds its receptor and the receptor changes shape.

transduction
The middle stage of cell signaling: the change in the receptor is relayed through a series of molecules inside the cell, each switching on the next.

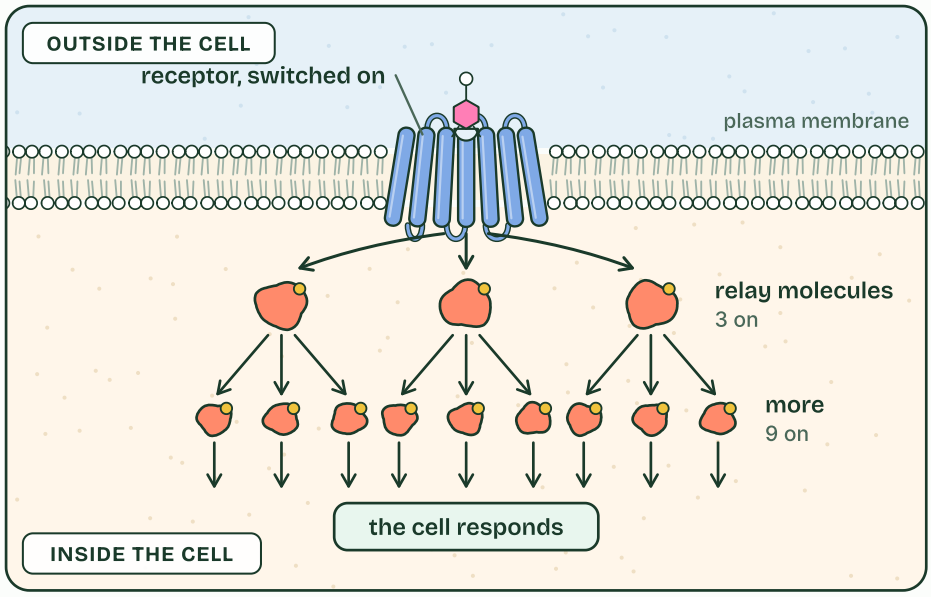
response
The last stage of cell signaling: what the cell does, such as switching on an enzyme, opening a channel or reading a gene.

signal transduction pathway
The series of molecular steps that links a signal at a receptor to the cell's response.

protein kinase
An enzyme that takes the end phosphate from ATP and adds it to a particular amino acid of another protein.

phosphorylation cascade
A chain of kinases in which each phosphorylates, and so activates, many molecules of the next.

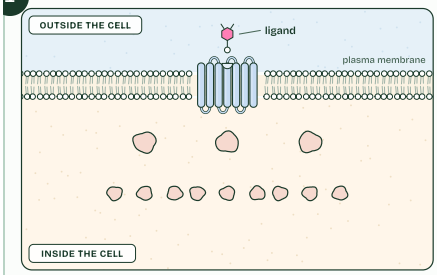
protein phosphatase
An enzyme that removes a phosphate group from a protein, undoing the work of a kinase.



STEP BY STEP

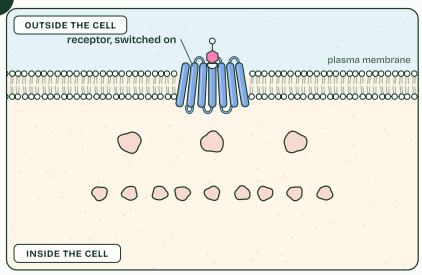
5 STEPS

1



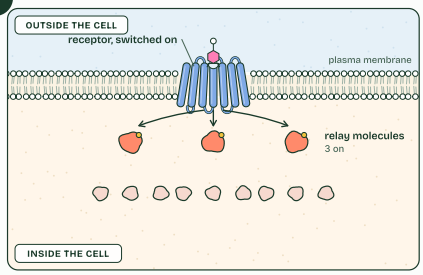
The **ligand** arrives at its receptor in the plasma membrane.

2



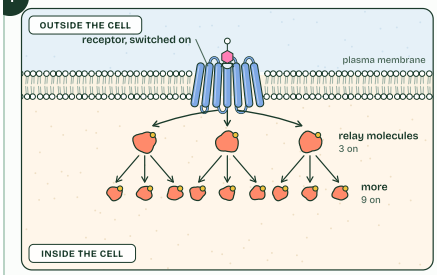
It binds, and the receptor changes shape: it is **switched on**.

3



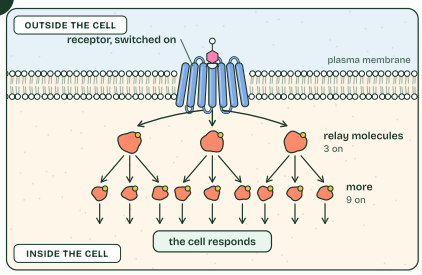
The receptor activates several **relay molecules** inside the cell.

4



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

5



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

PREDICT

What does a protein kinase do to the protein it acts on?

(A) It takes a phosphate off and returns it to ADP

(B) It adds a phosphate group taken from ATP

(C) It cuts the protein at one particular bond

(D) It copies the protein so the cell has two

Decide before you look. Answer on page 45.

REMEMBER IT

The three stages: ring, tell, run

R Ring	T Tell	R Run
Reception the ligand rings the doorbell	**Transduction** the message is passed inside	**Response** the cell acts on it

WATCH OUT

The phosphate a kinase adds is a switch, not fuel. It changes the shape of the protein it is put on; the cell is not storing energy there.

06

4.2.B G PROTEIN-COUPLED RECEPTORS

A receptor that *wakes a G protein*

The biggest family of receptors in eukaryotes is the **G protein-coupled receptor** (GPCR). It is one protein chain that weaves through the membrane seven times, its ligand-binding domain outside. On the inside it meets a **G protein**, made of three parts (alpha, beta and gamma) held to the inner face of the membrane. About 800 human genes code for GPCRs, among them the receptors for epinephrine, many neurotransmitters, smells and light.

At rest the G protein holds a molecule of **GDP** and is off. When a ligand binds, the receptor's intracellular domain changes shape, and the changed receptor makes the G protein let go of its GDP and pick up a **GTP** in its place. With GTP bound, the alpha part leaves beta and gamma, slides along the membrane to an enzyme, often **adenylyl cyclase**, and switches it on.

The G protein is a timer. Its alpha part slowly breaks its own GTP down to GDP, and when it does, it lets go of the enzyme and rejoins beta and gamma, off again. While the ligand is still bound, the receptor switches it straight back on.

KEY POINTS

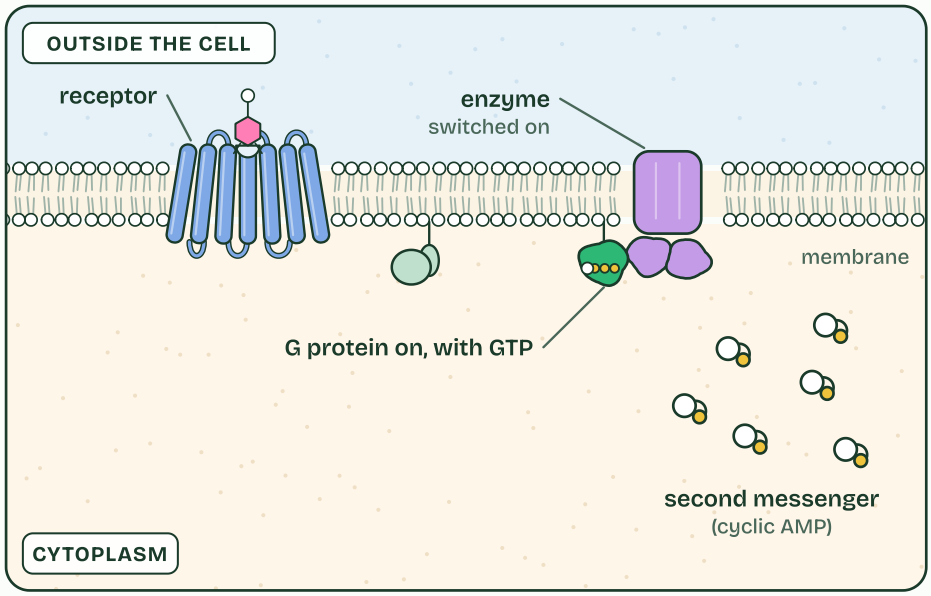
- A GPCR crosses the membrane seven times.
- G protein: off with GDP, on with GTP; the receptor makes it swap.
- The active G protein switches on adenylyl cyclase.

KEY TERMS

G protein-coupled receptor
A receptor that crosses the membrane seven times and, when its ligand binds, switches on a G protein on the inside of the membrane.

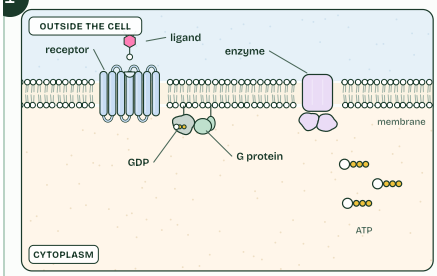
G protein
A protein of three parts on the inner face of the membrane that is off holding GDP and on holding GTP. Switched on by a receptor, it switches on an enzyme or a channel.

adenylyl cyclase
The enzyme in the plasma membrane that makes cyclic AMP from ATP when a G protein switches it on.



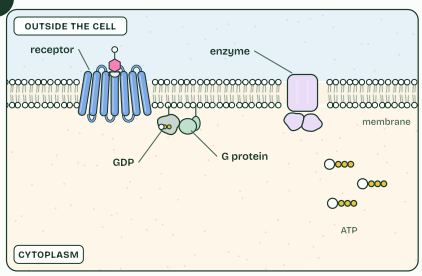
STEP BY STEP 4 STEPS

1



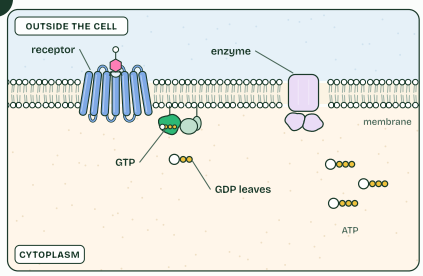
A **ligand** approaches the receptor. The **G protein** beside it holds **GDP** and is off.

2



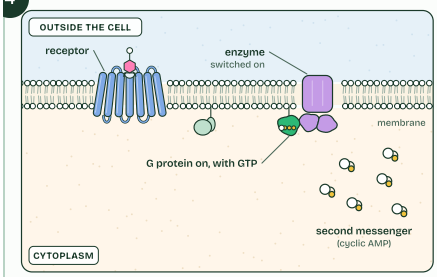
The ligand binds. The receptor changes shape and is **on**.

3



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

4



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

PREDICT

Epinephrine binds its receptor. Which event switches the G protein on?

(A) The ligand enters the cell and binds the G protein itself

(B) The G protein turns its GDP into GTP by adding phosphate

(C) The G protein splits a GTP into GDP to release its energy

(D) The changed receptor makes it swap its GDP for a GTP

Decide before you look. Answer on page 45.

WATCH OUT

GDP does not become GTP. The G protein gives up a GDP and takes a new GTP. Only when it switches off does it break that GTP back down to GDP.

07

4.2.A 4.2.B EPINEPHRINE, CAMP AND THE CASCADE

One hormone, *millions* of glucose

Here is one pathway from start to finish, the example the AP course names: **epinephrine** telling a liver cell to break down glycogen. A fright makes the adrenal glands release epinephrine into the blood, and within seconds it reaches the liver.

Epinephrine binds a GPCR on a liver cell. That is reception.
The receptor changes shape inside, and the G protein swaps GDP for GTP.
The G protein switches on adenylyl cyclase, which turns ATP into **cyclic AMP** (cAMP), again and again.
cAMP binds **protein kinase A** and sets its active parts free.
Protein kinase A phosphorylates phosphorylase kinase, which phosphorylates glycogen phosphorylase: the cascade.
Glycogen phosphorylase breaks glycogen down, and glucose leaves the cell for the blood. That is the response.

cAMP is a **second messenger**: a small molecule the cell makes once the receptor is active, which spreads through the cytoplasm and carries the message on. Epinephrine is the first messenger, and it never enters the cell.

Each enzyme in the chain acts on many molecules, not one. One adenylyl cyclase makes many cAMP; each kinase phosphorylates many of the next. The signal is **amplified** at every step, so a few molecules of epinephrine outside release millions of glucose molecules inside, in seconds. Then it stops: when epinephrine leaves, the G protein breaks its GTP down, **phosphodiesterase** turns cAMP into AMP, and phosphatases take the phosphates off. The end of the film shows it.

KEY POINTS

- cAMP is the second messenger; epinephrine is the first and stays outside.
- Each step multiplies the signal: amplification.
- Phosphodiesterase and phosphatases switch the pathway off.

KEY TERMS

epinephrine
The hormone, also called adrenaline, released by the adrenal glands in stress or danger. In the liver it starts the breakdown of glycogen.

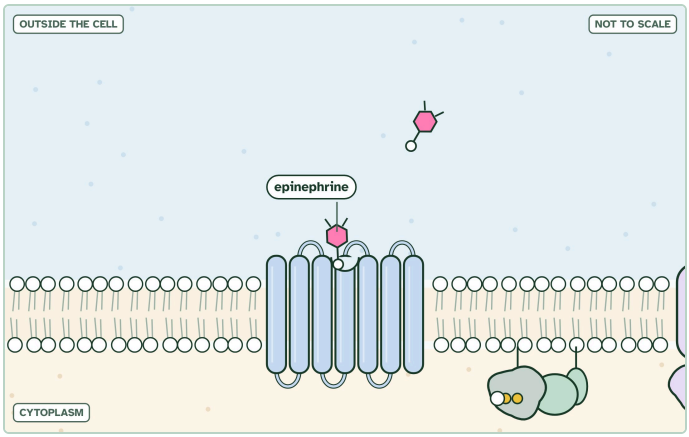
second messenger
A small molecule made inside a cell when a receptor is activated, which spreads through the cytoplasm and relays the signal on. Cyclic AMP is one.

amplified
Made larger at each step, because each active enzyme acts on many molecules of the next.

phosphodiesterase
The enzyme that breaks cyclic AMP down to AMP, ending its signal.

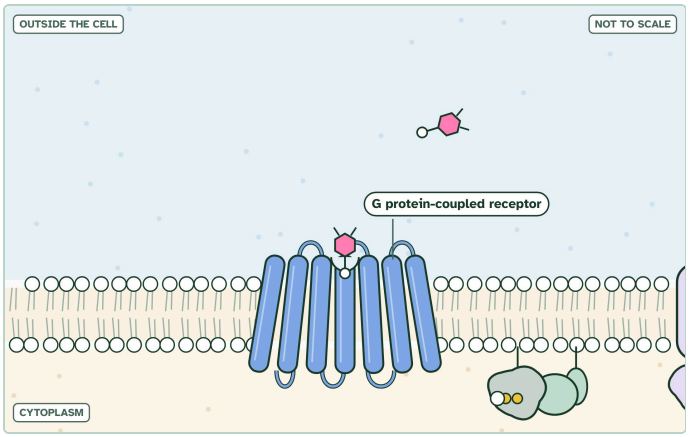
ANIMATION · EPINEPHRINE, RECEPTOR TO RESPONSE 9 MOMENTS

1 RECEPTION



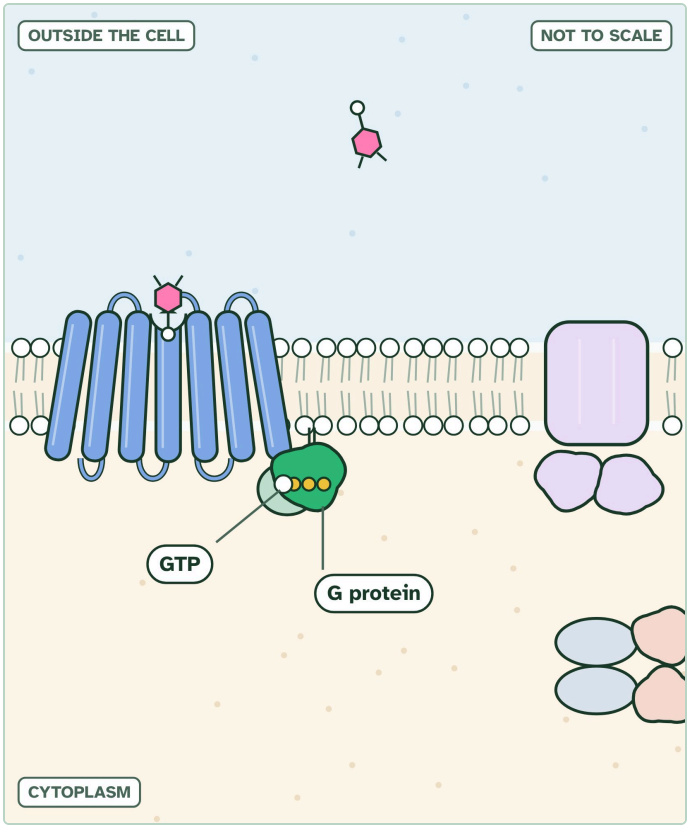
Epinephrine reaches a liver cell. It is a polar ligand and cannot cross the membrane, so it binds a **receptor** on the surface: a **G protein-coupled receptor**.

2 RECEPTION



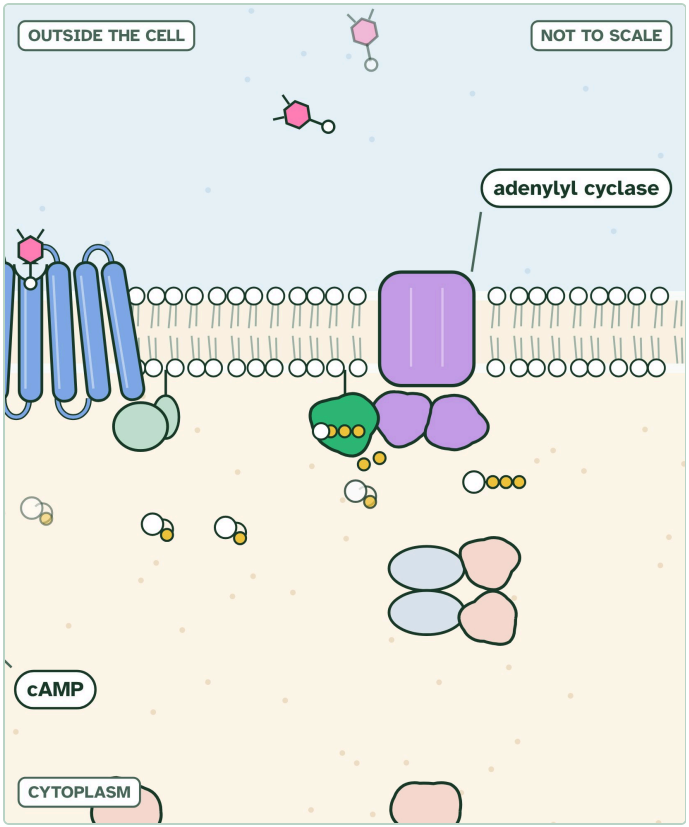
Binding changes the receptor's shape on the inside of the membrane. This is **reception**: the message is now inside the cell, although epinephrine is not.

3 TRANSDUCTION



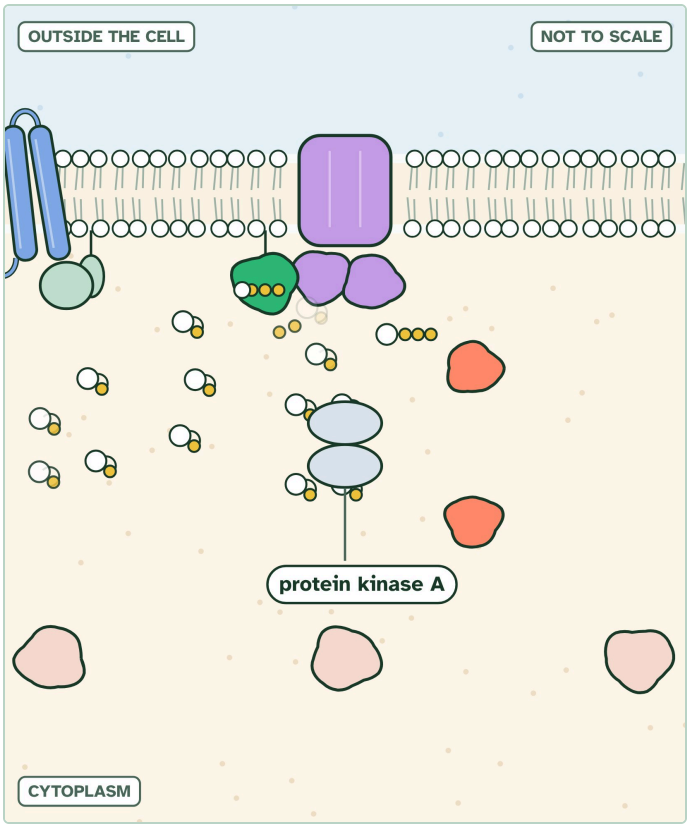
The changed receptor switches on a **G protein**. It swaps **GDP** for **GTP**, and its active part breaks away along the membrane.

4 CAMP 11 · GLUCOSE 0



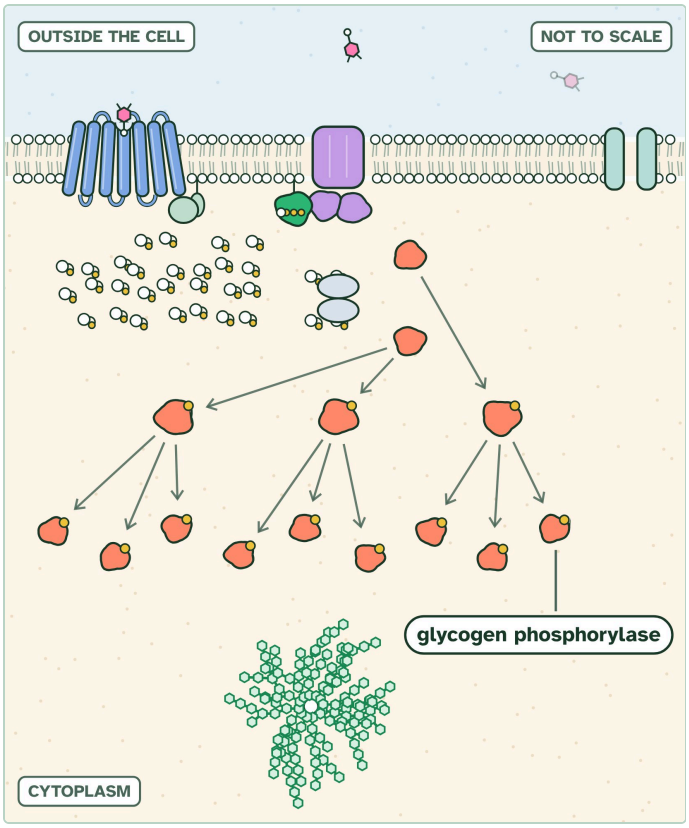
The G protein switches on **adenylyl cyclase**, which turns ATP into **cyclic AMP** (cAMP) again and again. cAMP is the **second messenger**.

5 CAMP 25 · GLUCOSE 0



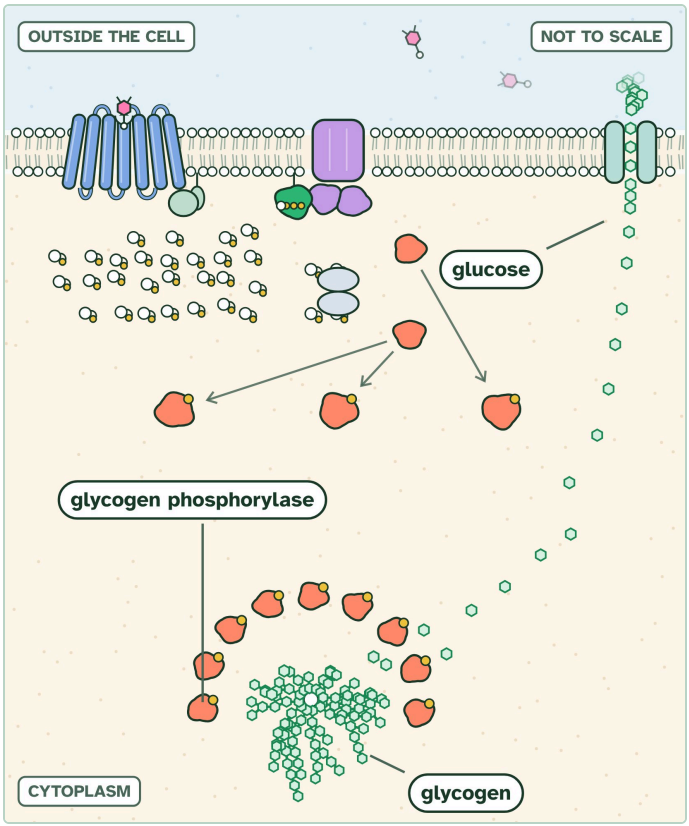
cAMP binds **protein kinase A** and sets its active parts free. **Transduction** has begun.

6 CAMP 31 · GLUCOSE 0



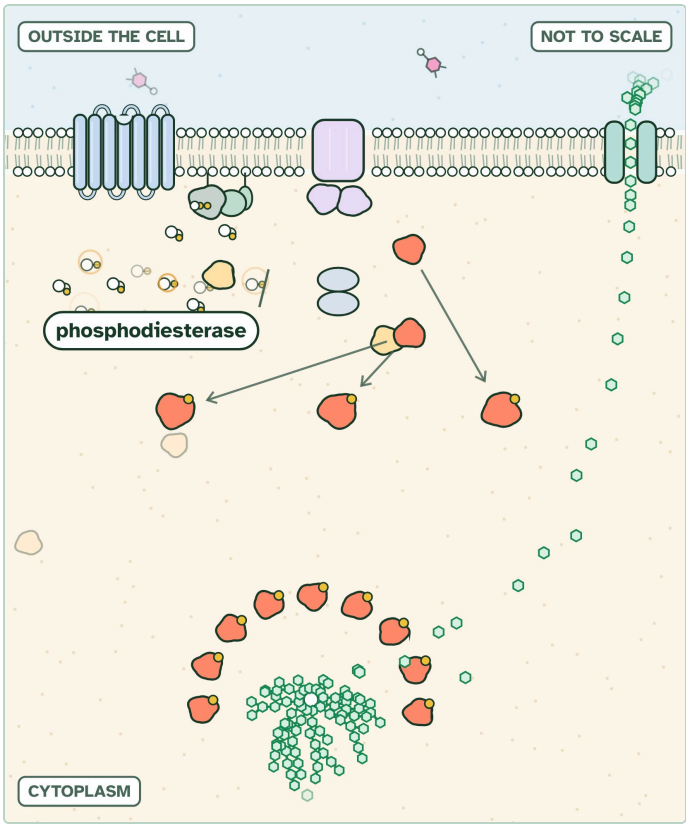
A **phosphorylation cascade**: each kinase adds a phosphate (yellow) from ATP to many molecules of the next, switching each one on. The signal is **amplified** at every step.

7 CAMP 31 · GLUCOSE 44



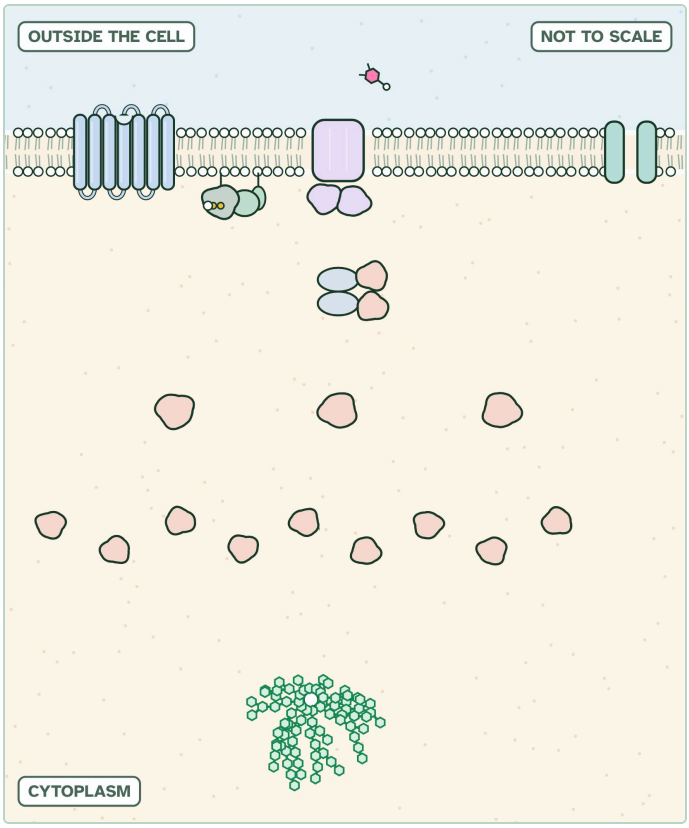
The last enzyme, **glycogen phosphorylase**, breaks **glycogen** down, and glucose leaves the cell for the blood. This is the **response**: fuel for fight or flight.

8 CAMP 5 · GLUCOSE 112



Switching off. Epinephrine 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/ap-biology-unit-4-cell-communication#cascade

PREDICT

Epinephrine switches on 10 receptors on a liver cell. If every active molecule in the pathway then switches on 10 of the next, about how many molecules are active three steps on?

(A) About 40, since 10 more are added at every step

(B) About 10, the same number as the receptors

(C) About 10 000, ten times more at every step

(D) About 30, since each step adds its own ten

Decide before you look. Answer on page 45.

REMEMBER IT

The epinephrine pathway in order: Real Gamers Always Collect Keys

R Real	G Gamers	A Always	C Collect	K Keys
Receptor epinephrine binds outside	**G protein** swaps GDP for GTP	**Adenylyl cyclase** turns ATP into cAMP	**cAMP** the second messenger	**Kinases** the cascade, then glycogen to glucose

WATCH OUT

cAMP is not the hormone, nor a piece of it. The cell makes cAMP from its own ATP after the hormone binds outside.

ON THE EXAM

A free-response question often gives a pathway as a diagram, with unfamiliar names. Find the receptor, the second messenger and the last enzyme, and say which arrow is amplification. The names change; the pattern does not.

08

4.2.B LIGAND-GATED ION CHANNELS

A receptor that is *a gate*

The fastest pathway is hardly a pathway at all. A **ligand-gated ion channel** is a receptor and a channel in one protein. When its ligand binds, the protein changes shape and the channel opens or closes, letting ions through or stopping them.

Where a motor neuron meets a muscle fiber, the neuron releases **acetylcholine**. It crosses the cleft and binds acetylcholine receptors in the fiber's membrane. Each receptor's channel opens, and positive ions, mostly Na^+, rush in down their gradient. The inside of the fiber, about −70 mV at rest, becomes less negative: it **depolarizes**. A big enough change starts an impulse along the fiber, and it contracts. An enzyme in the cleft breaks the acetylcholine down within milliseconds, so the channels close until the next signal.

No second messenger, no cascade: the response is a change in voltage, within a millisecond. Not every ligand-gated channel opens on binding. In the rod cells of your eye, channels stay open while cGMP is bound to them and close when light makes the cell break its cGMP down.

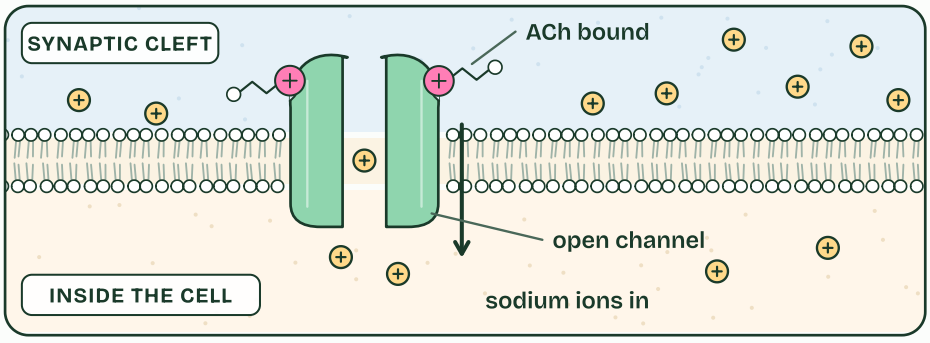
KEY POINTS

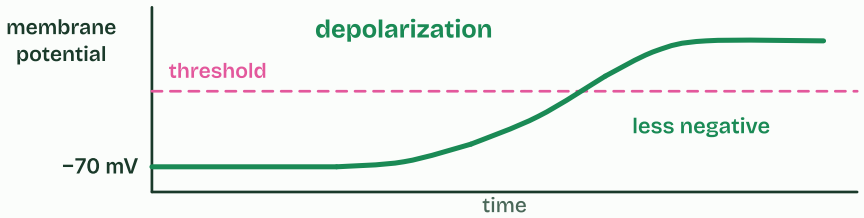
- Receptor and channel in one protein: binding opens or closes it.
- Acetylcholine opens channels; Na^+ in; the membrane depolarizes.
- The fastest response of all, with no second messenger.

KEY TERMS

ligand-gated ion channel
A membrane protein that is both a receptor and an ion channel: binding of its ligand opens or closes the channel.

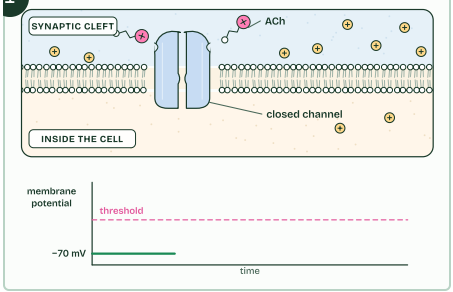
depolarizes
Becomes less negative inside, so the voltage across the membrane moves toward zero.





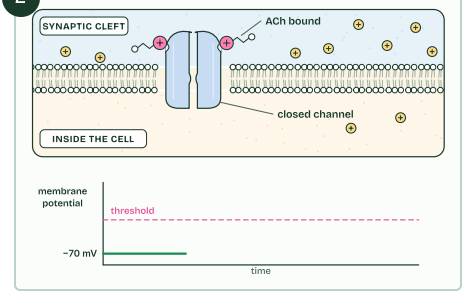
STEP BY STEP 5 STEPS

1



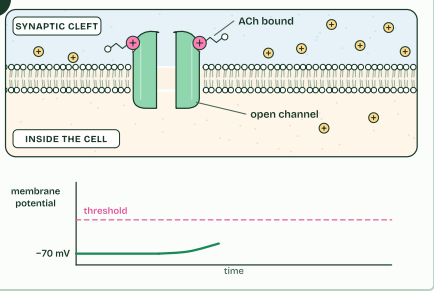
At rest the channel is **closed** and the inside is about **−70 mV**.

2



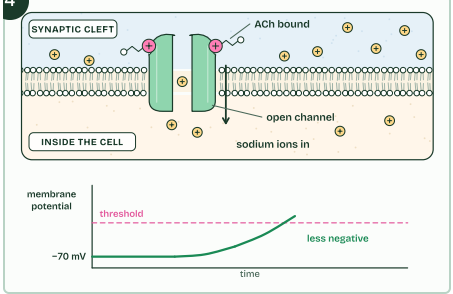
Acetylcholine from the presynaptic neuron binds the receptor.

3



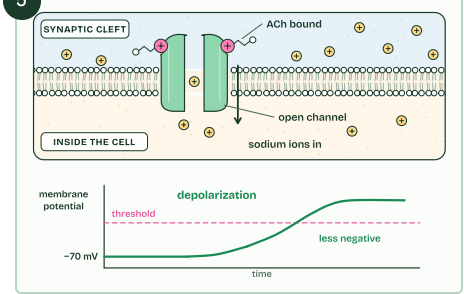
The receptor changes shape and the **channel opens**.

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 opens the channels and positive ions flow into the muscle fiber. What happens to the voltage across its membrane?

(A) It becomes more negative, as charge is carried in

(B) It stays at −70 mV, as a pump sends ions out

(C) It rises toward zero, as positive charge comes in

(D) It falls, as ATP is spent to open each channel

Decide before you look. Answer on page 46.

EXAMPLE

Nicotine fits the acetylcholine receptor too (the receptor is called nicotinic for that reason) and opens it in the brain, which is part of why nicotine is addictive. The cancers smoking causes come from other chemicals in the smoke, the carcinogens in its tar, not from nicotine.

09 Kinase receptors, and receptors *inside*

4.2.B 4.3.A RECEPTOR TYROSINE KINASES AND INTRACELLULAR RECEPTORS

Two more kinds of receptor cover most of the rest. A **receptor tyrosine kinase** spans the membrane and its intracellular domain is a kinase. Insulin is the example. Released by the beta cells of the pancreas when blood glucose rises, it binds receptors on liver, muscle and fat cells. Binding changes the receptor's shape, and its kinase domains add phosphates to tyrosines on the receptor itself. Relay proteins bind the phosphorylated tyrosines and start a cascade. In muscle and fat cells it ends with vesicles carrying glucose transporters (GLUT4) fusing with the plasma membrane, so glucose floods in and blood glucose falls.

Steroid hormones need no relay at the membrane. Testosterone and estrogen are lipids made from cholesterol: they diffuse through the bilayer and bind an **intracellular receptor** in the cytoplasm or nucleus. Hormone and receptor together bind specific DNA sequences beside their target genes and change how much those genes are transcribed. The cell makes more of some proteins and less of others. Thyroid hormones also act through receptors in the nucleus.

Compare the timing. Epinephrine and insulin change proteins that are already there, in seconds to minutes. A steroid has the cell make new ones, which takes hours, but the change lasts.

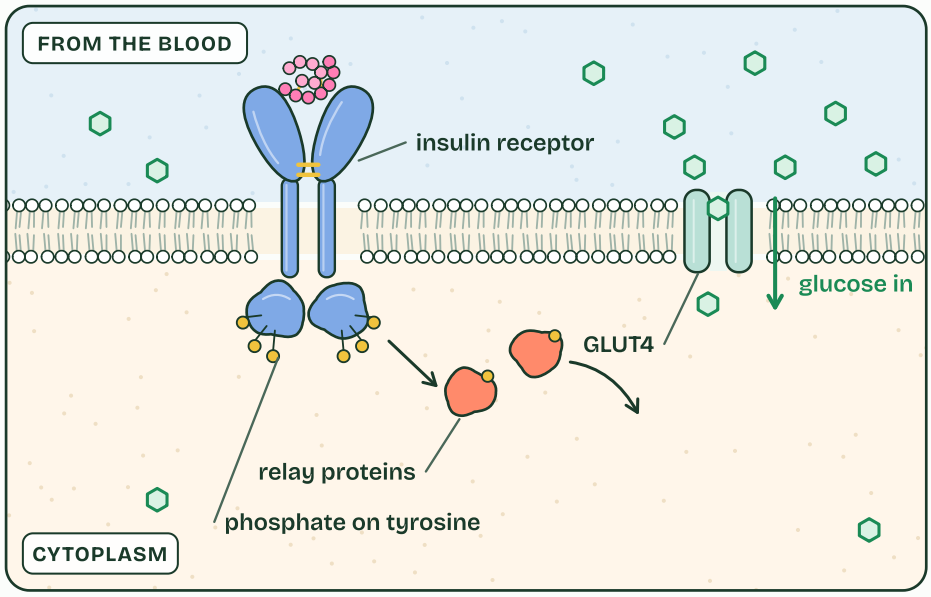
KEY POINTS

- Insulin: a receptor tyrosine kinase; ends with GLUT4 moved to the membrane.
- Steroids cross the membrane and bind intracellular receptors.
- The hormone and receptor change gene expression: slow, but lasting.

KEY TERMS

receptor tyrosine kinase
A receptor that spans the membrane and whose intracellular domain is a kinase. When its ligand binds, it adds phosphates to tyrosines on itself.

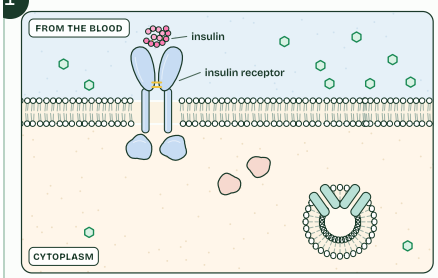
intracellular receptor
A receptor in the cytoplasm or nucleus for a hydrophobic ligand, such as a steroid hormone. Once the ligand binds, it acts as a transcription factor.



STEP BY STEP

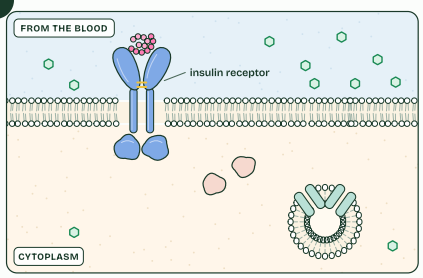
6 STEPS

1



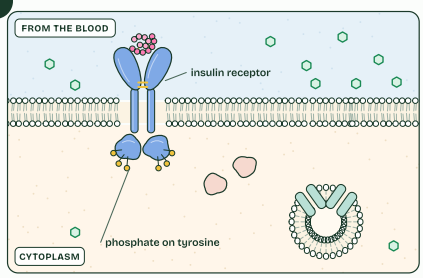
Insulin from the blood reaches its receptor.

2



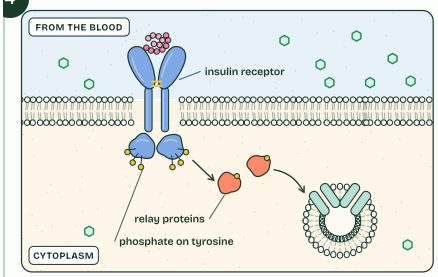
It binds, and the receptor changes shape.

3



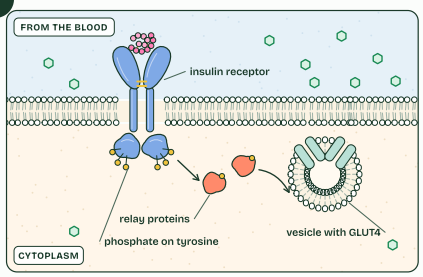
The enzyme part of the receptor adds **phosphate to tyrosine**.

4



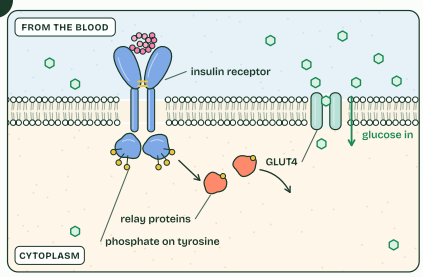
The phosphorylated receptor switches on **relay proteins**.

5

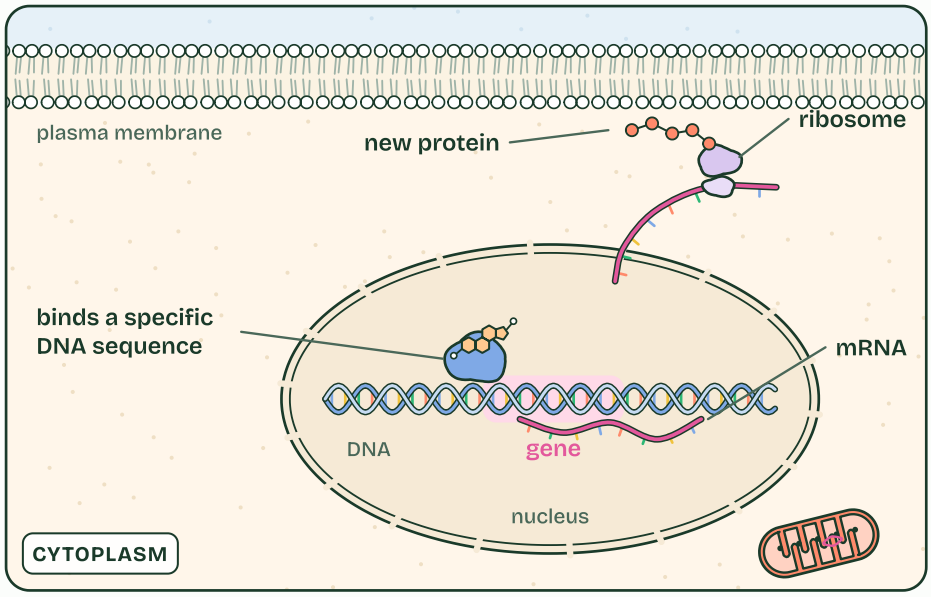


Vesicles carrying **glucose transporters** move toward the membrane.

6

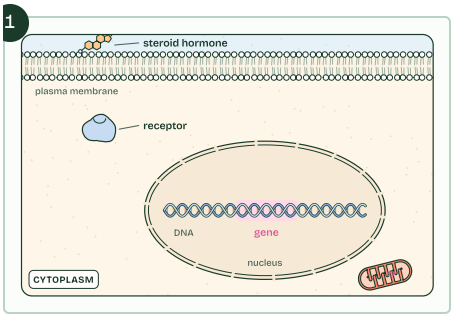


They fuse with it. **Glucose** now enters the cell faster.

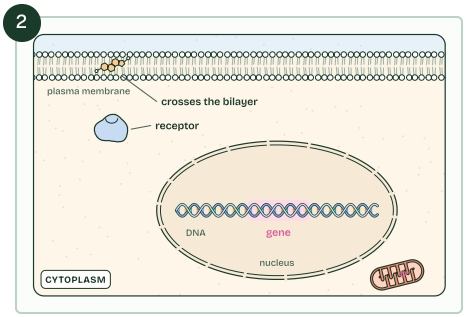


STEP BY STEP

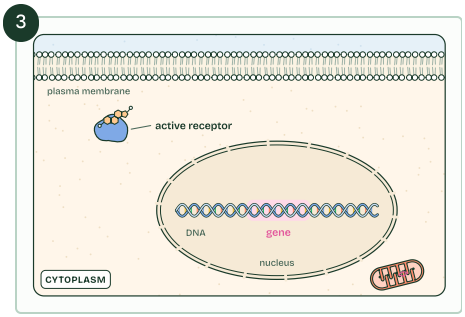
6 STEPS



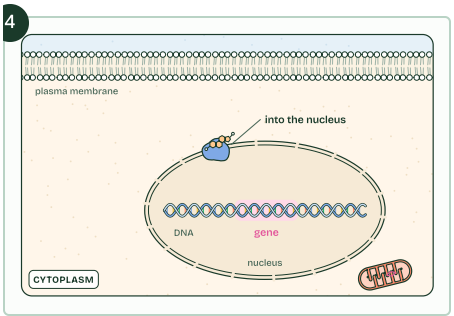
A **steroid hormone** is lipid-soluble.



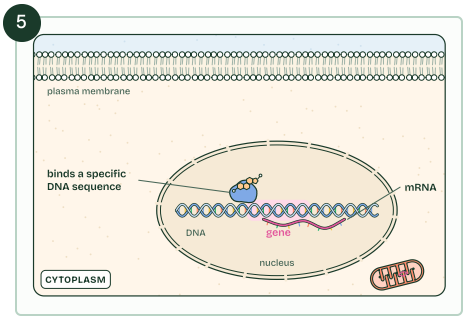
It **diffuses through** the phospholipid bilayer into the cell.



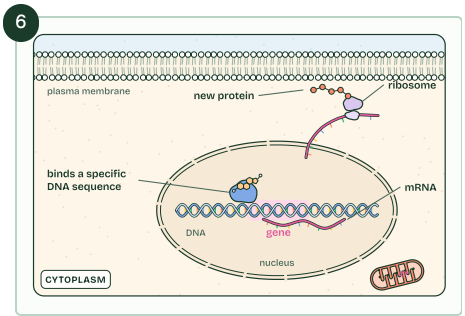
It binds an **intracellular receptor**, which becomes active.



The complex moves into the **nucleus**.



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



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

PREDICT

A cell is treated with a drug that stops transcription. Which of its responses is lost?

(A) Glucose release after epinephrine binds its receptor

(B) The opening of acetylcholine channels in its membrane

(C) The response to estrogen, which works through genes

(D) The faster glucose uptake after insulin binds its receptor

Decide before you look. Answer on page 46.

WATCH OUT

A question will tell you whether a ligand is hydrophobic or hydrophilic. Use it: hydrophobic crosses the membrane to a receptor inside; hydrophilic or large stays out, with its receptor in the membrane.

10

4.3.A RESPONSES TO SIGNALS

What a signal *makes a cell do*

Signal transduction is how a cell responds to its environment. The signal might come from the body around it (a hormone, a neighbor's surface), from other cells of its own kind (a mating factor, an autoinducer), or from outside the organism (a gas, light, the smell of food). Whatever starts it, the pathway ends in one of a few kinds of response.

Most change either **gene expression** or **cell function**. Some pathways end at transcription factors and change which genes are read, so the cell makes new proteins: slow, but it lasts. In ripening fruit the gas **ethylene** switches on the genes for enzymes that soften the cell walls and turn starch to sugar, and ripe fruit makes more ethylene, so one ripe banana in a bag ripens the rest. Other pathways change proteins the cell already has, so an enzyme starts or a channel opens: fast, and over when the signal stops.

Across many cells, either kind can change the **phenotype**: the fruit softens, an embryo grows testes. A signal can even end a cell's life by **apoptosis**, programmed cell death, which shapes a body as much as growth does. Tap each response in the figure for an example.

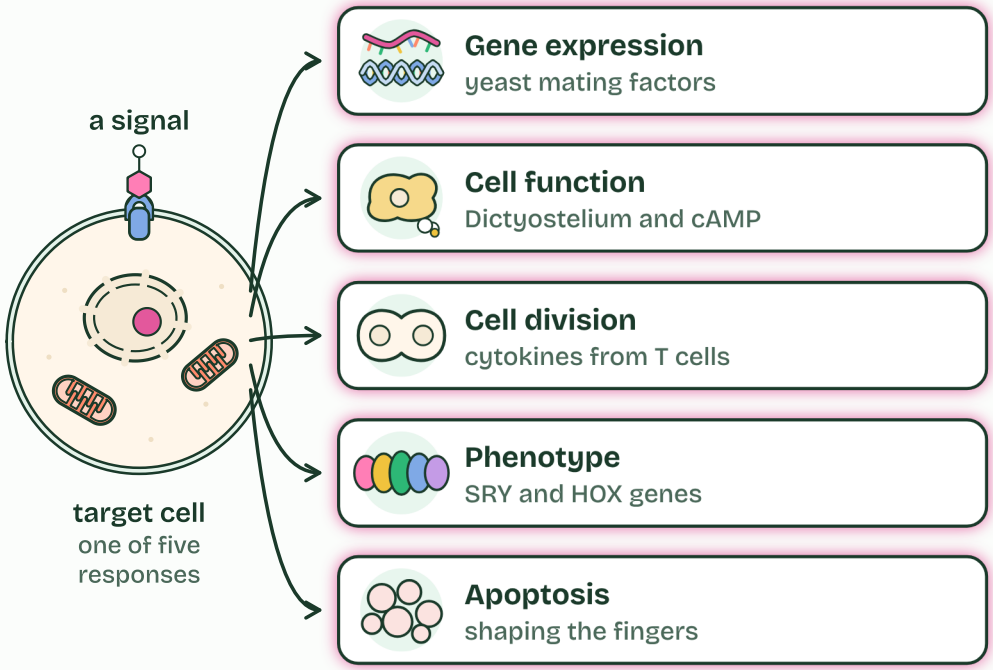
KEY POINTS

- The environment, inside the body or out, is what starts a pathway.
- Responses: gene expression, cell function (and division), phenotype, apoptosis.
- The same signal can do different things in different cells, depending on their receptors and pathways.

KEY TERMS

phenotype
The observable traits of an organism, from the shape of its body to the chemistry of its cells.

apoptosis
Programmed cell death: a cell dismantles itself in an orderly way in response to a signal.



Gene expression Yeast cells come in two mating types, a and α. Each releases a mating factor that binds a receptor on cells of the other type. The pathway switches on the genes for mating: the cell stops dividing and grows a bulge toward its partner.

Cell division Cytokines are small signaling proteins of the immune system. An activated helper T cell releases interleukin-2, which binds receptors on T cells and switches on the genes that drive the cell cycle: one cell becomes a clone of thousands.

Apoptosis A signal can tell a cell to die in an orderly way: it shrinks and breaks into small packages that other cells clear up. The webbing between the fingers of a human embryo is removed like this, and cytotoxic T cells signal infected cells to die.

Cell function A pathway can change what proteins already in the cell do. Starving amoebae of Dictyostelium release pulses of cAMP. Their neighbors crawl toward it and release cAMP of their own, until thousands gather into one slug that can move.

Phenotype In an embryo, signals decide what a tissue becomes. The SRY gene on the Y chromosome codes for a transcription factor that turns the gonads into testes, and their testosterone then builds a male body. HOX genes code for transcription factors that give each region along the head-to-tail axis its identity.

PREDICT

Gibberellin, a plant hormone, reaches cells in a germinating barley seed. Within hours they are making amylase, which they were not making before. What kind of response is this?

(A) Apoptosis, because the cells are using up their own food stores

(B) A change in gene expression, as a new protein is made

(C) Only a change in cell function, as an enzyme is unblocked

(D) A change of phenotype, as the whole seedling grows taller

Decide before you look. Answer on page 46.

11

4.3.B CHANGES IN SIGNAL TRANSDUCTION PATHWAYS

When a pathway *breaks*

Each step depends on the one before, so a change anywhere shows up in every step after it. A mutation in the ligand-binding domain can stop the ligand binding; one in the intracellular domain can stop the receptor passing the message on, or leave it switched on with no ligand at all. A change to any relay protein does the same further down. A chemical can do it too: some **activate** a part of the pathway, others **inhibit** it.

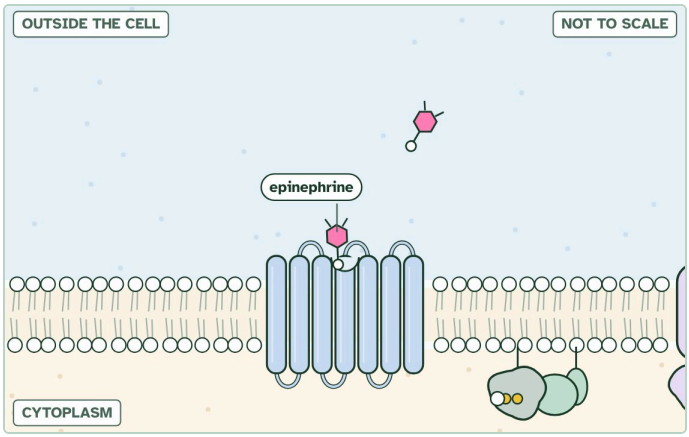
For every change, ask two questions. Is this part now stuck **off**, or stuck **on**? And what does every step after it do as a result? Make each prediction below, then set the film's **Fault** to that change and watch.

KEY POINTS

- A mutation in any domain of the receptor, or in any relay, changes every step after it.
- Chemicals can activate or inhibit a pathway: stuck on or stuck off.
- A cell with no working receptor does not respond, however much ligand there is.

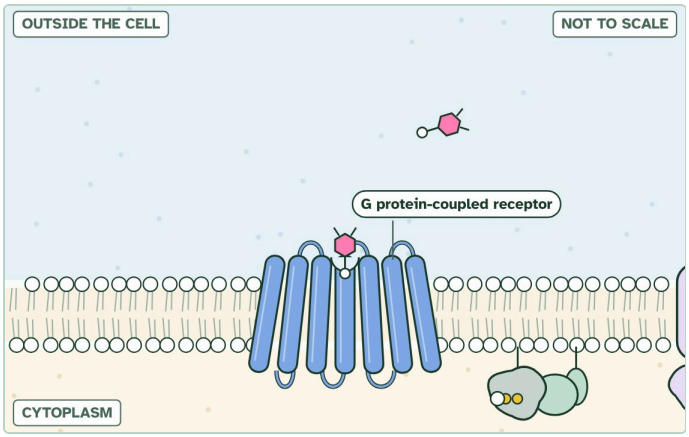
ANIMATION · BREAK THE PATHWAY
9 MOMENTS

1 RECEPTION



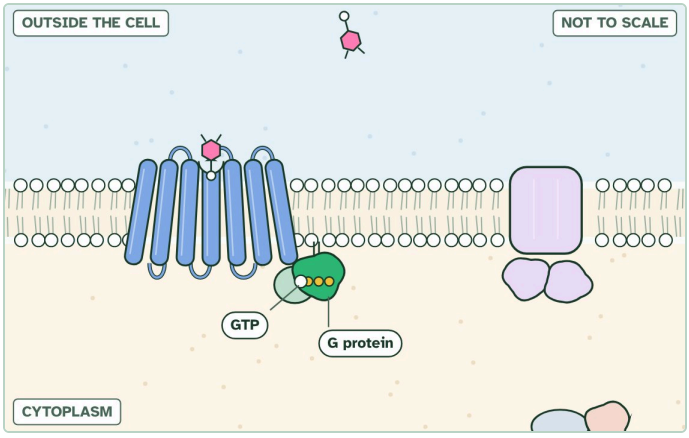
Epinephrine reaches a liver cell. It is a polar ligand and cannot cross the membrane, so it binds a **receptor** on the surface: a **G protein-coupled receptor**.

2 RECEPTION



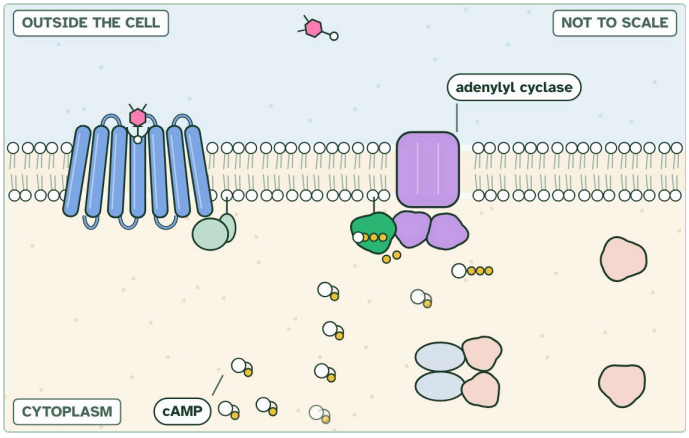
Binding changes the receptor's shape on the inside of the membrane. This is **reception**: the message is now inside the cell, although epinephrine is not.

3 TRANSDUCTION



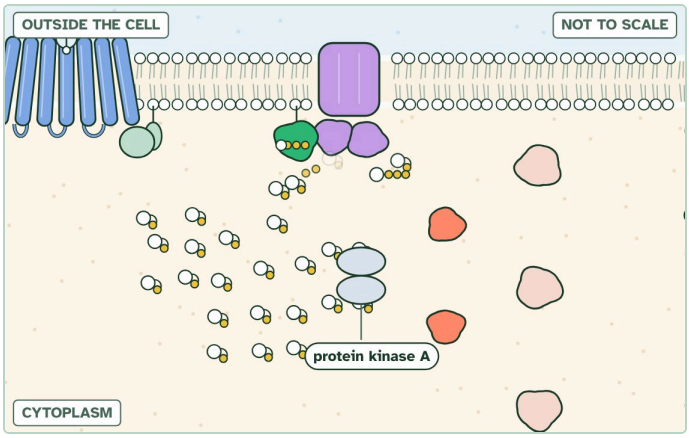
The changed receptor switches on a **G protein**. It swaps **GDP** for **GTP**, and its active part breaks away along the membrane.

4 CAMP 11 · KINASES ON 0 · GLUCOSE 0



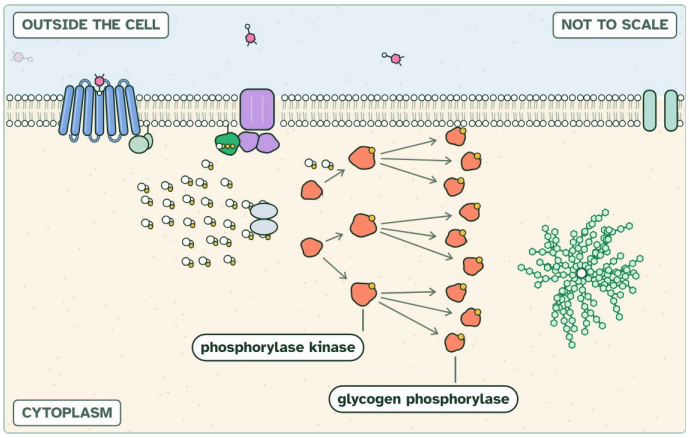
The G protein switches on **adenylyl cyclase**, which turns ATP into **cyclic AMP** (cAMP) again and again. cAMP is the **second messenger**.

5 CAMP 25 · KINASES ON 2 · GLUCOSE 0



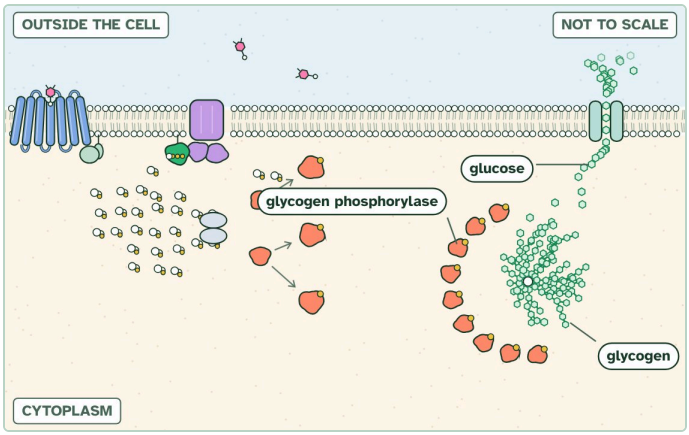
cAMP binds **protein kinase A** and sets its active parts free. **Transduction** has begun.

6 CAMP 28 · KINASES ON 14 · GLUCOSE 0



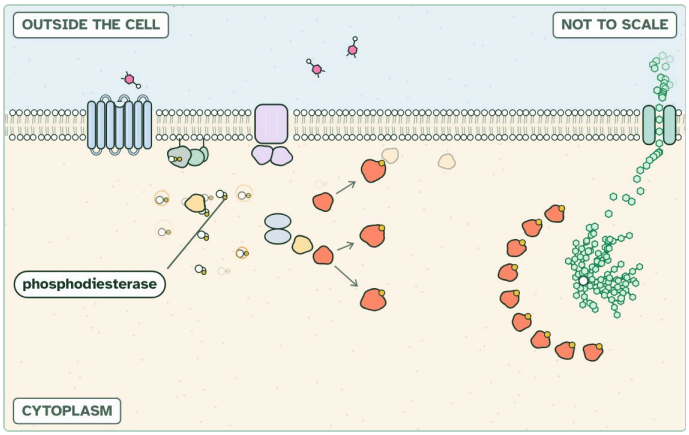
A **phosphorylation cascade**: each kinase adds a phosphate (yellow) from ATP to many molecules of the next, switching each one on. The signal is **amplified** at every step.

7 CAMP 28 · KINASES ON 14 · GLUCOSE 44



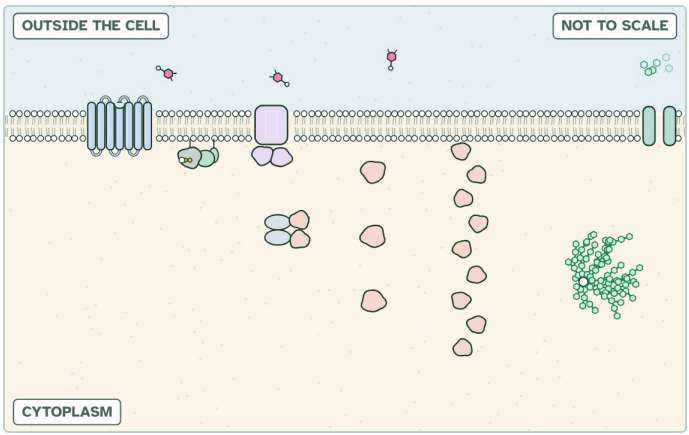
The last enzyme, **glycogen phosphorylase**, breaks **glycogen** down, and glucose leaves the cell for the blood. This is the **response**: fuel for fight or flight.

8 CAMP 4 · KINASES ON 14 · GLUCOSE 112



Switching off. Epinephrine 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 · KINASES ON 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/ap-biology-unit-4-cell-communication#changes

PREDICT

A beta blocker fits the binding site of the epinephrine receptor but does not change the receptor's shape. Epinephrine arrives. What happens to the cAMP in the cell?

(A) It rises higher, as there are now two ligands for each receptor

(B) It stays low, as epinephrine cannot reach the binding sites

(C) It rises as usual, as the blocker leaves the G protein alone

(D) It rises, then never falls again once epinephrine has gone

Decide before you look. Answer on page 46.

PREDICT

Cholera toxin changes the G protein so that it can no longer break down its GTP. What happens after the ligand leaves the receptor?

(A) The G protein switches off at once, as no ligand is bound

(B) cAMP falls, as the toxin also blocks adenylyl cyclase

(C) The receptor itself is destroyed, so the cell cannot respond

(D) Adenylyl cyclase stays on and keeps making cAMP

Decide before you look. Answer on page 46.

PREDICT

At high doses, caffeine inhibits phosphodiesterase. What does it do to a cell's response to epinephrine?

(A) It lasts longer, as cAMP is not broken down

(B) It stops at once, as cAMP can no longer be made

(C) It starts sooner, as the receptor binds faster

(D) Nothing at all, as caffeine acts outside cells

Decide before you look. Answer on page 46.

PREDICT

A mutation stops the phosphatase that takes the phosphate off glycogen phosphorylase. Epinephrine comes and then goes. What happens?

(A) Glycogen is never broken down, as the enzyme cannot be switched on

(B) Glucose release starts late, once enough phosphate has built up

(C) Glucose keeps leaving the cell after the signal has gone

(D) The G protein stays bound to GTP, so cAMP keeps being made

Decide before you look. Answer on page 46.

REMEMBER IT

The on and off switch: a Kinase Kicks the phosphate on, a Phosphatase Peels it off

K Kicks	P Peels
Kinase adds a phosphate from ATP	**Phosphatase** takes the phosphate off

ON THE EXAM

A question shows a pathway and changes one part: a mutated receptor, a drug, a toxin. Find that part, decide whether it is stuck on or stuck off, then follow every arrow after it to the response. Parts above the change carry on as normal.

Key terms

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

adenylyl cyclase 06
The enzyme in the plasma membrane that makes cyclic AMP from ATP when a G protein switches it on.

amplified 07
Made larger at each step, because each active enzyme acts on many molecules of the next.

antigen-presenting cell 01
A cell, such as a macrophage, that takes in a pathogen and displays fragments of it on its surface for T cells to recognize.

apoptosis 10
Programmed cell death: a cell dismantles itself in an orderly way in response to a signal.

autoinducer 03
A small signaling molecule that bacteria release and also detect. Its concentration rises with the number of cells.

depolarizes 08
Becomes less negative inside, so the voltage across the membrane moves toward zero.

endocrine signaling 02
Long-distance signaling: a gland releases a hormone into the blood, which carries it to target cells anywhere in the body.

epinephrine 07
The hormone, also called adrenaline, released by the adrenal glands in stress or danger. In the liver it starts the breakdown of glycogen.

G protein 06
A protein of three parts on the inner face of the membrane that is off holding GDP and on holding GTP. Switched on by a receptor, it switches on an enzyme or a channel.

G protein-coupled receptor 06
A receptor that crosses the membrane seven times and, when its ligand binds, switches on a G protein on the inside of the membrane.

gap junctions 01
Channels made of protein rings in the membranes of two neighboring animal cells, lined up to join their cytoplasm. Ions and small molecules pass through.

helper T cell 01
A white blood cell that, once switched on by an antigen-presenting cell, releases signals that start and direct an immune response.

hormone 02
A signaling molecule released into the blood by a gland, which carries it to target cells all over the body.

intracellular receptor 09
A receptor in the cytoplasm or nucleus for a hydrophobic ligand, such as a steroid hormone. Once the ligand binds, it acts as a transcription factor.

ligand 04
A molecule that binds specifically to a receptor. In signaling, the chemical messenger itself.

ligand-binding domain 04
The part of a receptor protein whose shape and charges fit its ligand.

ligand-gated ion channel 08
A membrane protein that is both a receptor and an ion channel: binding of its ligand opens or closes the channel.

local regulator 02
A signaling molecule that acts on cells close to the cell that released it, before it is broken down or taken up.

neurotransmitter 02
A chemical released by a neuron at a synapse that binds receptors on the next cell.

paracrine signaling 02
Signaling by a local regulator that diffuses through the fluid between cells to targets nearby.

phenotype 10
The observable traits of an organism, from the shape of its body to the chemistry of its cells.

phosphodiesterase 07
The enzyme that breaks cyclic AMP down to AMP, ending its signal.

phosphorylation cascade 05
A chain of kinases in which each phosphorylates, and so activates, many molecules of the next.

plasmodesmata 01
Narrow channels through the walls of neighboring plant cells, lined with plasma membrane, so the cytoplasm of one cell is continuous with the next.

protein kinase 05
An enzyme that takes the end phosphate from ATP and adds it to a particular amino acid of another protein.

protein phosphatase 05
An enzyme that removes a phosphate group from a protein, undoing the work of a kinase.

quorum sensing 03
Signaling that lets bacteria detect their population density from the concentration of a molecule they all release, and switch genes on together once it passes a threshold.

reception 05
The first stage of cell signaling: the ligand binds its receptor and the receptor changes shape.

receptor 04
A protein, in the plasma membrane or inside the cell, with a binding site for one particular ligand. Binding changes its shape.

receptor tyrosine kinase 09
A receptor that spans the membrane and whose intracellular domain is a kinase. When its ligand binds, it adds phosphates to tyrosines on itself.

response 05
The last stage of cell signaling: what the cell does, such as switching on an enzyme, opening a channel or reading a gene.

second messenger 07
A small molecule made inside a cell when a receptor is activated, which spreads through the cytoplasm and relays the signal on. Cyclic AMP is one.

signal transduction pathway 05
The series of molecular steps that links a signal at a receptor to the cell's response.

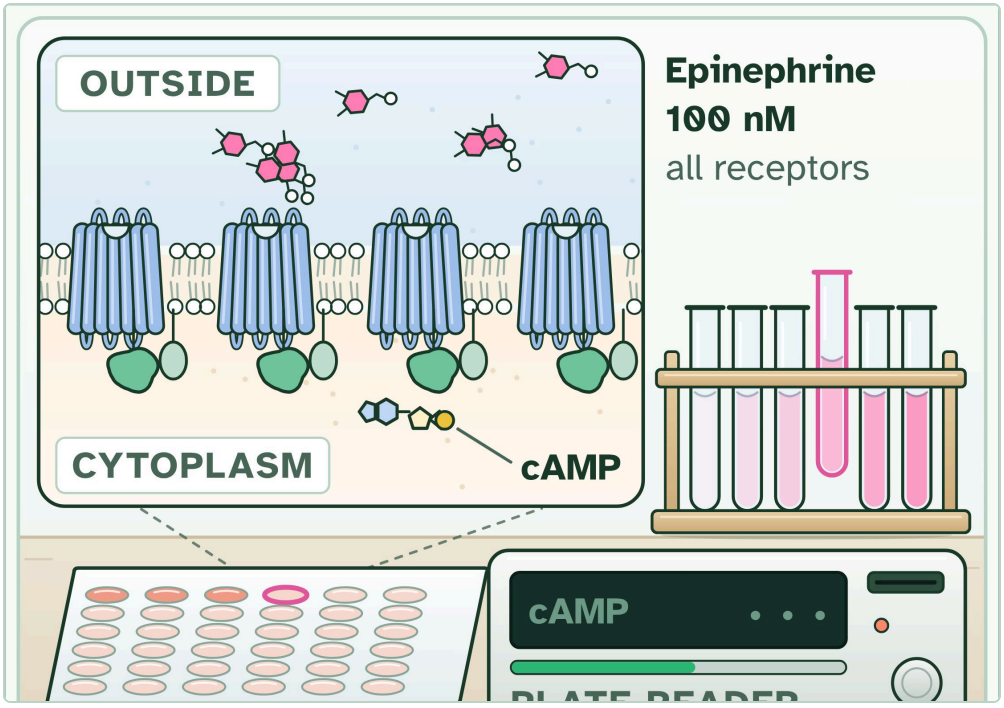
synaptic signaling 02
Signaling across a synapse: a neuron releases a neurotransmitter, which crosses the narrow cleft to receptors on the next cell.

target cells 02
The cells that carry a receptor for a particular signal, and so respond to it.

transduction 05
The middle stage of cell signaling: the change in the receptor is relayed through a series of molecules inside the cell, each switching on the next.

Dry lab: *Dose and response*

A liver cell's response grows with the share of its receptors that a ligand fills. Test epinephrine, a look-alike and a beta blocker over six concentrations, with a full or a 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/ap-biology-unit-4-cell-communication#lab`

Your question

How does a cell's response 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 (epinephrine, a look-alike, or epinephrine 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 concentration that gives half the maximum response, and the maximum. Repeat a test to see the measurement scatter. Download the CSV to plot your own graph on a log scale.

Find out

- **How does the response depend on concentration?** Run epinephrine at all six concentrations, from 0.1 to 10 000 nM. Where does the curve climb fastest, and where does it level off?
- **What does the half-way point tell you?** Read off the concentration that gives half the maximum response. The lower it is, the more tightly the ligand binds.
- **What does a look-alike do?** Run the look-alike ligand, then epinephrine with the beta blocker. Both fit the receptor. Which curve moves to the right, and what does that say about how much ligand is needed?
- **What if there are fewer receptors?** Switch to half the receptors and run epinephrine again. 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 judge how much of a difference between two curves could be measurement error.
- Download the CSV and plot your own graph. Why is the concentration axis a log scale?

Your question How does a cell's response 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 (epinephrine, a look-alike, or epinephrine 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 concentration that gives half the maximum response, and the maximum. Repeat a test to see the measurement scatter. Download the CSV to plot your own graph on a log scale.

Back to signaling

A liver cell has a fixed number of epinephrine receptors. Use your curves to explain why its response levels off, and what halving the receptors does to the curve.

QUESTIONS ON THE LAB

QUESTION 1

You raise epinephrine from 1000 nM to 10 000 nM. What happens to the response?

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

(B) It falls, as the extra ligand jams the receptors

(C) It barely changes: the receptors are nearly all full

(D) It doubles, as each receptor now binds two ligands

Answer on page 47.

QUESTION 2

Half the receptors are removed. Which part of the epinephrine curve changes?

(A) The maximum halves; the half-way point stays put

(B) The half-way point moves right; the maximum stays

(C) Nothing, because each receptor still binds the same

(D) Both double, as each receptor now does twice the work

Answer on page 47.

QUESTION 3

With the beta blocker present, the epinephrine curve moves right but still climbs high. Why?

(A) The blocker breaks down over time and stops working

(B) The blocker switches the receptors on a little itself

(C) The cells make new receptors once they are blocked

(D) Enough epinephrine outcompetes it for the sites

Answer on page 47.

Check yourself

The check for this guide is online: a fresh paper of past-paper style questions from the exam bank on 4.1 to 4.3 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?program=ap&units=U4&ced=4.1,4.2,4.3&paper=quiz&marks=15&src=ep

Answers

PREDICTIONS IN THE CHAPTERS

01 A drug blocks the gap junctions of one heart muscle cell. The signal to contract reaches its neighbors as usual. What does the blocked cell do?

C **It misses the beat, because the ions cannot pass into it**

The signal to contract is a flow of ions, and it reaches each cell through the gap junctions it shares with its neighbors. Blocked, the cell gets no ions and falls out of step. Changes to gap junction proteins are linked to irregular heartbeats in people.

02 A neuron releases a neurotransmitter and the pancreas releases insulin at the same moment. Which reaches its target cells first, and why?

B **The neurotransmitter, because it has a gap of only 20 nm to cross**

Diffusion is fast only over tiny distances, and a synaptic cleft is tiny. Insulin has to be carried round the body in the blood, which takes about a minute, and then leave the capillaries. Fast and local against slow and everywhere.

03 A flask of *Vibrio fischeri* has just begun to glow. You dilute it tenfold with fresh seawater. What happens to the light?

A **It fades, as the autoinducer is now below the threshold**

What the cells sense is the concentration of autoinducer, not the cells themselves. Dilute the flask and the concentration drops below the threshold, so the light genes switch off. As the cells divide again it builds back up, and the light returns.

04 A new drug is a short chain of amino acids, a peptide, and it must act on liver cells. Where do you expect to find its receptor?

D **In the plasma membrane, with its binding domain facing out**

A peptide is large and hydrophilic, so it cannot cross the hydrophobic core of the membrane. Its receptor must span the membrane, with the binding domain outside to catch it and another domain inside to pass the message on.

05 What does a protein kinase do to the protein it acts on?

B **It adds a phosphate group taken from ATP**

A kinase moves the end phosphate of ATP onto its target. Taking a phosphate off is the job of a phosphatase, the kinase's opposite. Neither cuts or copies the protein: they flip it between two shapes, on and off.

06 Epinephrine binds its receptor. Which event switches the G protein on?

D **The changed receptor makes it swap its GDP for a GTP**

The ligand stays outside and changes the receptor's shape. The receptor makes the G protein release its GDP, and a fresh GTP from the cytoplasm takes its place. Breaking GTP down to GDP comes later, and it switches the G protein off.

07 Epinephrine switches on 10 receptors on a liver cell. If every active molecule in the pathway then switches on 10 of the next, about how many molecules are active three steps on?

C **About 10 000, ten times more at every step**

The steps multiply, they do not add: 10, then 100, then 1000, then 10 000. A real cell has more steps and more molecules at each, which is how a hormone at a tiny concentration in the blood empties a liver cell's glycogen within seconds.

08 Acetylcholine opens the channels and positive ions flow into the muscle fiber. What happens to the voltage across its membrane?

C **It rises toward zero, as positive charge comes in**

Positive ions entering make the inside less negative, so the voltage moves toward zero: depolarization. Nothing is pumped and no ATP is spent; the ions run down their gradient through the open channel.

09 A cell is treated with a drug that stops transcription. Which of its responses is lost?

C **The response to estrogen, which works through genes**

Estrogen's receptor works by changing transcription, so without transcription it does nothing. The other three change proteins the cell already has: an enzyme switched on, a channel opened, transporters moved to the membrane. None needs a new gene to be read.

10 Gibberellin, a plant hormone, reaches cells in a germinating barley seed. Within hours they are making amylase, which they were not making before. What kind of response is this?

B **A change in gene expression, as a new protein is made**

The cells were not making amylase before, so a gene has been switched on: gibberellin's pathway changes gene expression. The amylase then digests the seed's starch to feed the seedling.

11 A beta blocker fits the binding site of the epinephrine receptor but does not change the receptor's shape. Epinephrine arrives. What happens to the cAMP in the cell?

B **It stays low, as epinephrine cannot reach the binding sites**

The blocker fills the receptors without switching them on, so no G protein is switched on, no cAMP is made and nothing downstream happens. Fault: **Receptor blocked**. Beta blockers slow a racing heart the same way.

11 Cholera toxin changes the G protein so that it can no longer break down its GTP. What happens after the ligand leaves the receptor?

D **Adenylyl cyclase stays on and keeps making cAMP**

The G protein switches off only by breaking down its GTP, so with that step blocked it stays on, and cAMP keeps being made with no signal at all. Fault: **G protein stuck**. In the cells lining the gut, the extra cAMP opens chloride channels; salt and water pour out, and the result is the severe diarrhea of cholera.

11 At high doses, caffeine inhibits phosphodiesterase. What does it do to a cell's response to epinephrine?

A **It lasts longer, as cAMP is not broken down**

Phosphodiesterase is one of the off switches. Block it and cAMP stays after epinephrine has gone, so protein kinase A and the cascade stay on. Fault: **cAMP kept**. At the amounts in a cup of coffee, caffeine's main effect is a different one: it blocks receptors for adenosine in the brain.

11 A mutation stops the phosphatase that takes the phosphate off glycogen phosphorylase. Epinephrine comes and then goes. What happens?

C **Glucose keeps leaving the cell after the signal has gone**

The kinases switch the enzyme on as usual, but nothing switches it off. Everything above it stops when epinephrine leaves; the enzyme does not, and glycogen keeps being broken down. Fault: **No phosphatase**. Off matters as much as on.

QUESTIONS ON THE DRY LAB

Q1 You raise epinephrine from 1000 nM to 10 000 nM. What happens to the response?

C **It barely changes: the receptors are nearly all full**

The response can be no bigger than when every receptor is filled, and by 1000 nM almost all of them are. Extra epinephrine finds few empty receptors, so the curve flattens at the top.

Q2 Half the receptors are removed. Which part of the epinephrine curve changes?

A **The maximum halves; the half-way point stays put**

Each receptor binds epinephrine just as tightly as before, so the share filled at any concentration is the same and the half-way point does not move. With half as many receptors to fill, the most the cell can do is halved. A cell with none would not respond at all.

Q3 With the beta blocker present, the epinephrine curve moves right but still climbs high. Why?

D **Enough epinephrine outcompetes it for the sites**

The blocker and epinephrine compete for the same binding site. At low epinephrine the blocker holds many receptors, so more epinephrine is needed for the same response. At high epinephrine it wins most sites back, so 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.