Cell Biology

Unit 5 · Lesson 1 · How cells talk

The notes for Lesson 1 of Unit 5: chapters 5.1 to 5.3 of the unit book, with their figures, worked examples, exam traps and quizzes, in one file. The full unit book, with every chapter, the exam question bank and the glossary, is linked at the end.

Lesson 1 of 3 | 3 chapters | Chapters 5.1 to 5.3

About these notes

These are the notes for **Lesson 1 · How cells talk** of the University free n easy video lessons on Cell Biology Unit 5, Cell Signaling and Cell Communication. They are chapters 5.1 to 5.3 of the unit book, unchanged, so a page here is the same page in the full book.

5.1 Cell communication: autocrine, paracrine and endocrine signals

A cell in your body is never alone. It receives chemical messages from other cells telling it to grow, divide, secrete, move or die. Biologists sort these messages by one simple question: how far does the signal travel from the cell that makes it to the cell that answers? A signal that acts back on its own maker is autocrine; one that acts on close neighbours is paracrine; one that travels through the blood to distant organs is endocrine. Add contact-dependent signalling, where the signal never leaves the membrane, and synaptic signalling by nerve cells, and you have the full map that every later chapter builds on.

The parts of any signalling event

Every signal has the same four parts. The **signalling cell** makes and releases a **signal molecule** (also called a ligand, from the Latin for "to bind"). The **target cell** carries a **receptor**, a protein that binds that ligand specifically. Binding changes the receptor's shape, and the target cell turns that change into a **response**: an enzyme switched on, a gene turned on, a channel opened.

The same ligand can give different responses in different cells. Acetylcholine slows the heart muscle cell but makes skeletal muscle contract, because the two cells carry different receptors

for it. So the response depends on the receptor and the machinery behind it, not only on the signal.

Five modes, sorted by distance

1. **Endocrine.** Endocrine cells release **hormones** into the blood, which carries them throughout the body. Insulin from the pancreas, adrenaline from the adrenal medulla and thyroxine from the thyroid are examples. Because blood dilutes them, hormones act at very low concentrations, typically below 10^{-8} M, so their receptors must bind tightly. Endocrine signals are slow to arrive (seconds to minutes) but reach every tissue.
2. **Paracrine.** The signal diffuses through the fluid between cells and acts on cells nearby, usually within a short distance. It must not spread far, so the target cells take it up quickly, enzymes destroy it, or the extracellular matrix traps it. Growth factors during wound healing, histamine from mast cells in an allergy, and nitric oxide (NO) from blood-vessel lining are paracrine. NO lasts only about 5–10 seconds outside cells, which keeps it local.
3. **Autocrine.** The cell responds to the signal it released itself. A T cell activated by an antigen secretes the growth factor interleukin-2 (IL-2) and also carries IL-2 receptors, so it drives its own division. Autocrine loops also appear in groups of identical cells that must decide together, and in cancer cells that make their own growth factors and stop needing outside permission to divide.
4. **Synaptic.** A nerve cell sends an electrical impulse along its axon and releases a **neurotransmitter** at a synapse, a gap of tens of nanometres to one target cell. This is a very local, very fast form of paracrine signalling. The neurotransmitter reaches a high concentration at the synapse (acetylcholine reaches about 5×10^{-4} M) and so its receptors can bind it with low affinity and let go quickly.
5. **Contact-dependent (juxtacrine).** The signal stays attached to the signalling cell's surface and acts only on a cell that touches it. The membrane protein Delta on one cell binding the receptor Notch on its neighbour is the classic case: it tells the neighbour not to become the same cell type, which spaces out nerve cells in a developing embryo.

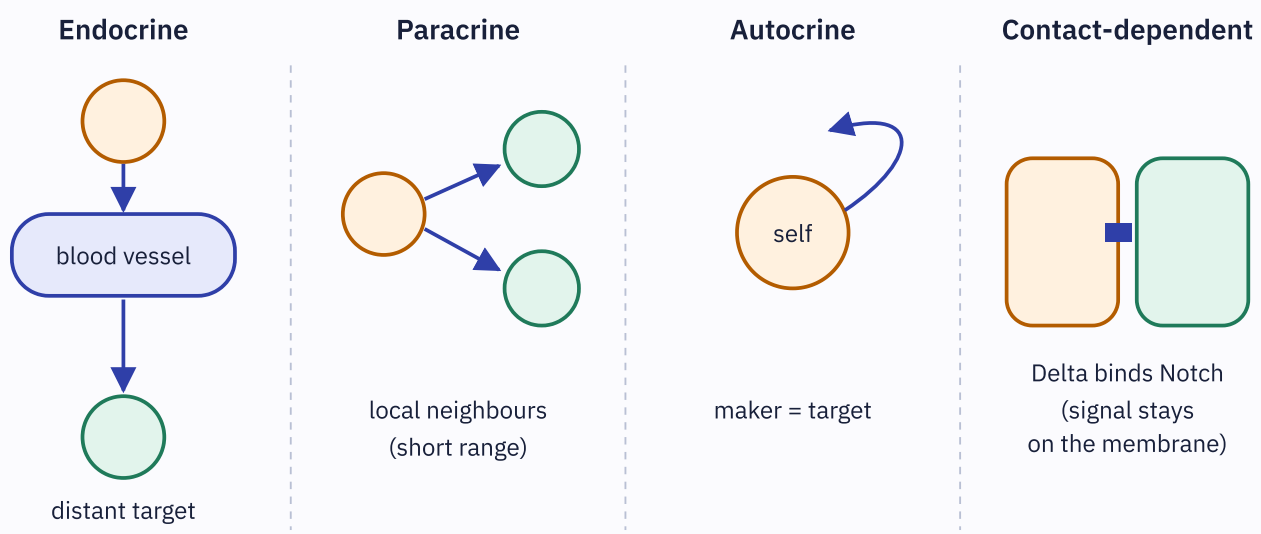


Figure 5.1.1 Four ways a signal reaches its target. Orange cells send, green cells receive. Notice that only the endocrine signal enters the blood, and only the contact-dependent signal never leaves the sender's membrane.

Why distance decides the design

Distance controls three things at once. First, **concentration**: a hormone diluted in about five litres of blood needs a high-affinity receptor, while a neurotransmitter released into a tiny synaptic gap can use a low-affinity one. Second, **speed**: synaptic signals act in milliseconds, endocrine ones in seconds to hours. Third, **reach**: one endocrine gland can coordinate the whole body, while a paracrine signal shapes one patch of tissue. The same molecule can work in more than one mode. Adrenaline is a hormone when the adrenal gland secretes it and a neurotransmitter when certain neurons release it.

A signal must also be switched off. Hormones are removed by the liver and kidneys; neurotransmitters are broken down (acetylcholinesterase destroys acetylcholine) or pumped back into the nerve ending; paracrine factors are degraded or trapped locally. A signal that cannot be removed keeps the target switched on, which is often how a disease or a toxin works.

WORKED EXAMPLE

Question (6 marks). Classify each signal as endocrine, paracrine, autocrine, synaptic or contact-dependent, and give one reason for each. (a) Insulin from pancreatic β cells lowers blood glucose by acting on muscle and fat. (b) Platelets at a cut release platelet-derived growth factor, which makes nearby fibroblasts divide. (c) An activated T cell releases IL-2 and divides in response. (d) A motor neuron releases acetylcholine onto one muscle fibre. (e) In a fly embryo, a cell with Delta on its surface stops the cell it touches from becoming a nerve cell. (f) Endothelial cells release NO, which relaxes the smooth muscle around the same vessel.

1. (a) **Endocrine**: insulin enters the blood and acts on distant tissues.
2. (b) **Paracrine**: the growth factor diffuses only to nearby fibroblasts at the wound.
3. (c) **Autocrine**: the same cell makes the IL-2 and carries the IL-2 receptor.
4. (d) **Synaptic**: the neurotransmitter is released at a synapse onto one specific target.
5. (e) **Contact-dependent**: Delta stays bound to the sender's membrane, so only a touching cell responds.
6. (f) **Paracrine**: NO is a gas that diffuses a short distance and lasts only seconds, so it acts on the neighbouring muscle layer.

Award one mark per correct label with a reason. The reason, not the label, is what earns the mark in most university schemes.

EXAM TRAPS

- "Paracrine" and "autocrine" are not decided by the molecule but by who responds. IL-2 acting on the same T cell is autocrine; acting on a neighbouring T cell it is paracrine.
- Synaptic signalling is chemical, not purely electrical. The electrical impulse travels along the axon; the synapse itself uses a neurotransmitter.
- Do not write that hormones are always proteins. Steroids (cortisol, estrogen) and amines (adrenaline, thyroxine) are hormones too.
- The examiner's favourite question: "With neat diagrams, explain the different modes of cell signalling." Draw all modes, label sender, signal, receptor and target, and add one example each.

CHECK YOURSELF

– REMEMBER **Name the four parts of any signalling event.** 2 marks

Signalling cell, signal molecule (ligand), receptor on the target cell, and the response of the target cell.

– REMEMBER **Give one example each of an endocrine and a paracrine signal.** 2 marks

Endocrine: insulin, adrenaline or thyroxine. Paracrine: nitric oxide, histamine, or a growth factor at a wound.

– UNDERSTAND **Why do hormone receptors need higher affinity than neurotransmitter receptors?** 3 marks

Hormones are diluted in the blood to very low concentrations (typically below 10^{-8} M), so only a tight-binding receptor is occupied. At a synapse the neurotransmitter is concentrated (about 5×10^{-4} M), so a low-affinity receptor fills quickly and also releases the ligand fast, allowing rapid on-off signalling.

– UNDERSTAND **How is a paracrine signal kept local?** 3 marks

It is taken up quickly by target cells, destroyed by extracellular enzymes, trapped by the extracellular matrix, or is chemically short-lived (NO lasts about 5–10 seconds).

– APPLY **Acetylcholine slows the heart but contracts skeletal muscle. What does this tell you about signalling?** 3 marks

The response is set by the target cell, not by the signal. Heart muscle and skeletal muscle carry different acetylcholine receptors (a muscarinic GPCR in the heart, a nicotinic ion channel in skeletal muscle) linked to different machinery.

– APPLY **A tumour cell secretes a growth factor and carries its receptor. Which mode is this, and why is it dangerous?** 3 marks

Autocrine. The cell stimulates its own division and no longer depends on signals from other cells, so normal tissue control is lost.

– ANALYZE **Adrenaline acts both as a hormone and as a neurotransmitter. How can one molecule fit two modes?** 4 marks

The mode is defined by the route and range, not the chemistry. Released into the blood by the adrenal medulla it reaches all tissues (endocrine). Released at a nerve ending onto one target it acts locally and quickly (synaptic). The receptors are the same family; the delivery differs.

BEYOND THE SYLLABUS

Bacteria also signal: in quorum sensing, each cell releases small autoinducer molecules, and when enough cells are present the concentration crosses a threshold and the whole population switches on genes together, for example for light production or biofilm formation. Cells also send exosomes, small membrane vesicles carrying proteins and RNA, which some researchers treat as a sixth mode of communication. Synthetic biologists now build artificial receptors (such as synthetic Notch, or synNotch) to programme engineered cells. None of this is needed for the exam; search "quorum sensing" and "extracellular vesicles signalling" to read further.

5.2 Cell-surface and intracellular receptors

A receptor is the protein that recognises a signal and starts the response. Where the receptor sits depends on the signal: a large or water-loving molecule such as insulin or adrenaline cannot cross the lipid bilayer, so its receptor must sit in the plasma membrane with a binding site facing outside. A small fat-soluble molecule such as cortisol or estrogen slips through the membrane, so its receptor waits inside the cell, in the cytosol or the nucleus. This split into cell-surface and intracellular receptors is the first classification every examiner asks for.

You need: the lipid bilayer and membrane proteins from Unit 2, *Plasma membrane structure: fluid mosaic model* and *Membrane proteins and lipids*.

Cell-surface receptors: three classes

All cell-surface receptors are transmembrane proteins. The ligand binds outside, and the receptor passes the message across the membrane by changing shape. They fall into three classes by what the inside part does.

1. **Ion-channel-coupled receptors** (ligand-gated channels). Binding opens a channel, ions flow, and the membrane voltage changes within milliseconds. The nicotinic acetylcholine receptor at the nerve–muscle junction lets Na^+ in and makes the muscle contract. Unit 2, *Ion channels: ligand-gated and voltage-gated*, covers how the channels work.
2. **G-protein coupled receptors** (GPCRs). The receptor activates a G protein inside the cell, which then switches an enzyme or channel on or off. This is the largest family; Chapter 5.3 is devoted to it.

3. **Enzyme-coupled receptors**. The inside part is an enzyme, or binds one directly. The main group is the **receptor tyrosine kinases** (RTKs), receptors for insulin, epidermal growth factor (EGF) and platelet-derived growth factor (PDGF). Cytokine receptors, which borrow a separate kinase called JAK, belong here too (Chapter 5.5).

How a receptor tyrosine kinase works

An RTK has one membrane-spanning helix. The steps are:

1. The ligand binds and brings two receptor chains together (dimerisation). The insulin receptor is already a linked dimer, and ligand binding changes its shape instead.
2. Each kinase domain phosphorylates tyrosine residues on its partner: **autophosphorylation** (more exactly, cross-phosphorylation).
3. The phosphotyrosines become docking sites for signalling proteins that carry an **SH2 domain**, a module that binds a phosphorylated tyrosine.
4. One docked adaptor, Grb2, brings Sos, which activates the small G protein **Ras**. Ras starts the MAP kinase chain Raf → MEK → ERK, and ERK enters the nucleus to switch on genes for cell division. Unit 4, *Cancer and oncogenes such as Ras and Raf*, shows what happens when Ras is stuck on.

Intracellular receptors

Steroid hormones (cortisol, aldosterone, estrogen, progesterone, testosterone), thyroid hormone, retinoic acid and vitamin D are small and hydrophobic. They cross the membrane and bind receptors of the **nuclear receptor superfamily**. These receptors are transcription factors: each has a ligand-binding domain, a DNA-binding domain and a region that activates transcription.

Some wait in the cytosol. The glucocorticoid receptor, which binds cortisol, sits in the cytosol held inactive by chaperone proteins such as Hsp90. Cortisol binding releases the chaperones, the receptor moves into the nucleus, binds a short DNA sequence called a hormone response element, and turns genes on. Others, such as the thyroid hormone receptor, are already in the nucleus bound to DNA. Because they act by changing gene expression, their responses take tens of minutes to hours, unlike the seconds of most surface receptors.

Nitric oxide is a special case. It crosses membranes as a gas and binds an intracellular enzyme, soluble guanylyl cyclase, which makes the second messenger cGMP (Chapter 5.4). So "intracellular receptor" does not always mean a nuclear receptor.

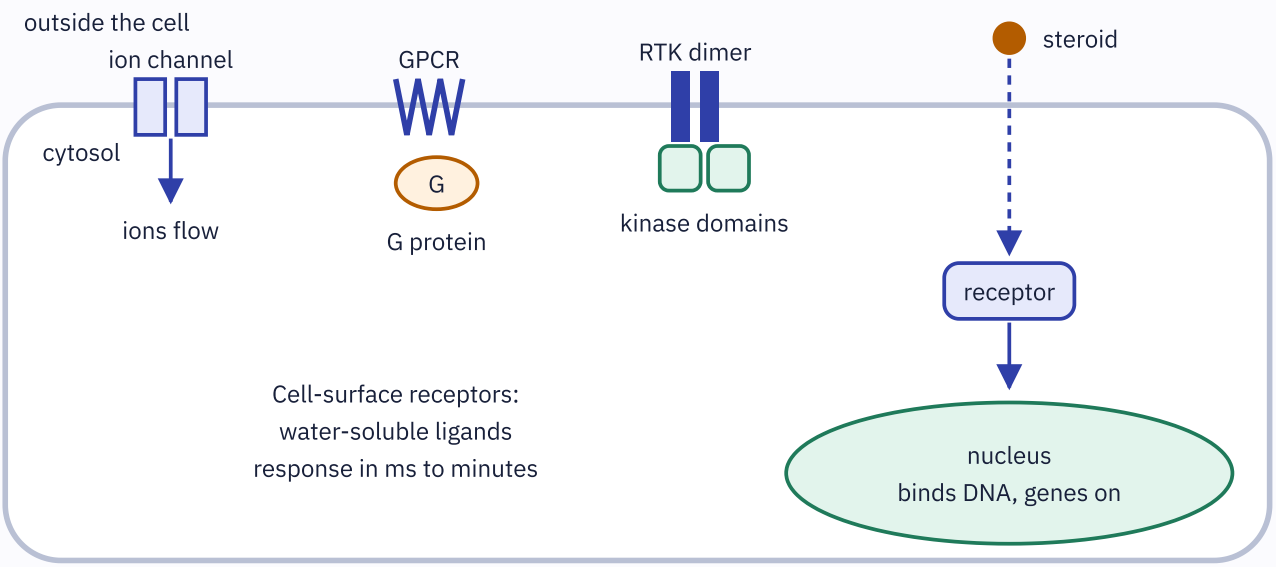


Figure 5.2.1 The three classes of cell-surface receptor sit in the membrane; a steroid crosses the membrane and binds an intracellular receptor, which carries it into the nucleus. Notice that only the intracellular route acts directly on DNA.

How tightly a receptor binds: occupancy

Binding is reversible: L + R ⇌ LR, where L is the ligand, R the free receptor and LR the bound complex. The **dissociation constant** K_d = [L][R]/[LR] has units of concentration. A small K_d means tight binding. The fraction of receptors occupied, θ (theta), follows from it:

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θ = [L] / ([L] + Kd)
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Here [L] is the free ligand concentration. When [L] = K_d, θ = 0.5, so K_d is the ligand concentration that fills half the receptors.

WORKED EXAMPLE

Question (5 marks). A hormone receptor has K_d = 2 nM. Find the fraction of receptors occupied when the hormone is at (a) 0.2 nM, (b) 2 nM, (c) 18 nM. What concentration gives 90% occupancy?

1. (a) $\theta = 0.2 / (0.2 + 2) = 0.2 / 2.2 = 0.091$, about 9%.
2. (b) $\theta = 2 / (2 + 2) = 0.50$, exactly half.
3. (c) $\theta = 18 / (18 + 2) = 18 / 20 = 0.90$, 90%.
4. For $\theta = 0.9$: $0.9([L] + 2) = [L]$, so $0.1[L] = 1.8$ and $[L] = 18$ nM. Going from 10% to 90% occupancy needs about an 81-fold rise in ligand.

The units cancel in θ, so any concentration unit works as long as [L] and K_d use the same one.

EXAM TRAPS

- Do not write that steroid receptors sit in the membrane. Classical steroid receptors are intracellular; they bind DNA.
- Small K_d means high affinity, not low. Students often reverse this.
- The insulin receptor is an RTK, not a GPCR, even though it is a "hormone receptor".
- Examiners often ask "classify receptors with examples". Give both levels: surface (three classes) and intracellular (cytosolic and nuclear), with one ligand each.

CHECK YOURSELF

– REMEMBER **Name the three classes of cell-surface receptor.** 3 marks

Ion-channel-coupled receptors, G-protein coupled receptors, enzyme-coupled receptors (mainly receptor tyrosine kinases).

– REMEMBER **What is an SH2 domain?** 1 mark

A protein module that binds a phosphorylated tyrosine, letting signalling proteins dock on an activated RTK.

– UNDERSTAND **Why can cortisol have an intracellular receptor but adrenaline cannot?** 3 marks

Cortisol is a small hydrophobic steroid that diffuses across the lipid bilayer. Adrenaline is charged and water-soluble, so it cannot cross; it must bind a receptor on the surface (a GPCR).

– UNDERSTAND **Describe how the glucocorticoid receptor reaches DNA.** 4 marks

Held in the cytosol by Hsp90 and other chaperones; cortisol binds; chaperones leave; receptor enters the nucleus; binds the hormone response element; activates transcription of target genes.

– APPLY **A receptor has K_d = 5 nM. What fraction is bound at 15 nM ligand?** 2 marks

θ = 15 / (15 + 5) = 0.75, so 75% of receptors are occupied.

– APPLY **An RTK has its tyrosines mutated to phenylalanine. What happens to signalling?** 3 marks

Phenylalanine cannot be phosphorylated, so no phosphotyrosine docking sites form, SH2 proteins such as Grb2 cannot bind, and Ras and the downstream pathway are not activated, even though the ligand still binds.

– ANALYZE **Why are responses through nuclear receptors slower than through ion channels?** 4 marks

An ion channel changes membrane voltage the moment it opens (milliseconds). A nuclear receptor must move to the nucleus, start transcription, and the mRNA must be processed and translated before new protein changes the cell, which takes minutes to hours.

BEYOND THE SYLLABUS

Many cancer drugs block RTKs. Imatinib inhibits the BCR-ABL kinase in chronic myeloid leukaemia, and gefitinib and erlotinib inhibit the EGF receptor in some lung cancers. Antibodies such as trastuzumab bind the HER2 receptor on the cell surface. Steroids also have fast "non-genomic" effects through membrane receptors, an active research area. This is not for the exam; search "tyrosine kinase inhibitors" and "nuclear receptor superfamily" to read on.

5.3 G-protein coupled receptors

G-protein coupled receptors (GPCRs) are the largest family of cell-surface receptors in animals. They detect adrenaline, histamine, serotonin, many neurotransmitters, light in the eye, smells and some tastes. About a third of approved drugs act on them. Every GPCR works the same way: the ligand changes the receptor's shape, the receptor switches on a G

protein inside the cell, and the G protein switches on an enzyme or ion channel. Learning one GPCR well teaches you all of them.

> You need: the three classes of surface receptor from Chapter 5.2.

Structure of the receptor

A GPCR is a single polypeptide chain that crosses the plasma membrane seven times as α-helices, so it is also called a **seven-transmembrane** (7TM) or serpentine receptor. The N-terminus is outside the cell and the C-terminus inside. The ligand binds in a pocket formed by the helices, or on the outer loops and N-terminus for large ligands. The inner loops and C-terminal tail face the cytosol and contact the G protein.

The G protein is a switch

The G protein that GPCRs use is **heterotrimeric**: three different subunits, α, β and γ. The α subunit binds a guanine nucleotide. With GDP bound, it is off. With GTP bound, it is on. β and γ stay tightly joined as one βγ unit. The α and γ subunits carry lipid tails that keep the G protein on the inner face of the membrane.

1. **Rest.** The G protein sits as αβγ with GDP on α. The receptor is empty.
2. **Activation.** The ligand binds; the receptor changes shape and binds the G protein. It acts as a **guanine nucleotide exchange factor** (GEF): it makes α release GDP. GTP, more plentiful in the cytosol, binds in its place.
3. **Splitting.** GTP-bound α changes shape and separates from βγ. Both α-GTP and βγ can now act on target proteins called **effectors**. One active receptor can switch on many G proteins one after another, the first step of amplification.
4. **Switching off.** The α subunit is itself a slow GTPase. It hydrolyses GTP to GDP within seconds to minutes, lets go of the effector, and rejoins βγ. **RGS proteins** (regulators of G-protein signalling) speed up this hydrolysis.

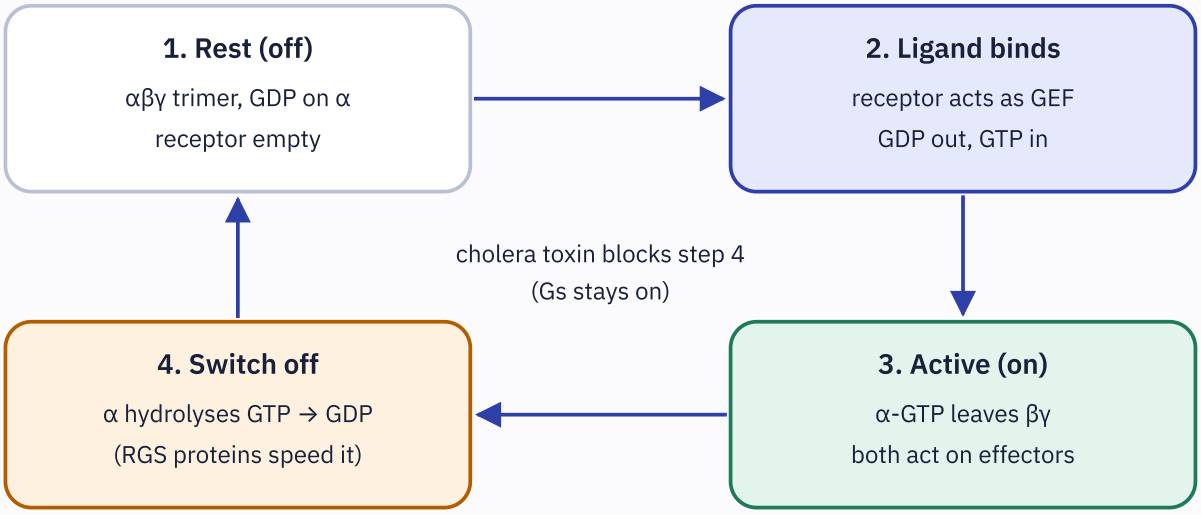


Figure 5.3.1 The G-protein cycle. The receptor only acts at step 2; the timer that ends the signal is the α subunit's own GTPase at step 4. Notice that anything that stops step 4 leaves the pathway on.

Main G proteins and their effectors

A TYPE	EFFECTOR	RESULT	EXAMPLE SIGNAL
Gs (stimulatory)	Adenylyl cyclase on	cAMP rises	Adrenaline at β-adrenergic receptors
Gi (inhibitory)	Adenylyl cyclase off; βγ opens K^+ channels	cAMP falls; heart slows	Acetylcholine at heart muscarinic receptors
Gq	Phospholipase C-β on	IP_3 and DAG; Ca^{2+} rises	Adrenaline at α_1 receptors; histamine H_1
Gt (transducin)	cGMP phosphodiesterase on	cGMP falls; channels close	Light at rhodopsin in rod cells

The second messengers in this table (cAMP, IP_3, DAG, Ca^{2+}) are the subject of Chapter 5.4. Notice that adrenaline uses different receptors in different tissues, which is how one hormone raises cAMP in the heart but Ca^{2+} in blood-vessel muscle.

Desensitisation: turning the receptor down

If adrenaline stays high, the cell stops responding as strongly. A **G-protein-coupled receptor kinase** (GRK) phosphorylates the active receptor's tail. **β-arrestin** then binds the phosphorylated tail, blocks the G protein from binding, and helps pull the receptor into the cell

by endocytosis. The receptor is later recycled or destroyed. This explains why some asthma inhalers that stimulate β_2 receptors lose effect with heavy use.

Toxins that jam the switch

Cholera toxin chemically modifies (ADP-ribosylates) the α subunit of Gs so it cannot hydrolyse GTP. Gs stays on, cAMP stays high in intestinal cells, chloride and water pour into the gut, and the patient loses litres of fluid as diarrhoea. **Pertussis toxin** (whooping cough) modifies Gi so the receptor can no longer activate it; Gi stays in the off state with GDP and is unable to inhibit adenylyl cyclase. Both toxins raise cAMP, but by opposite routes.

WORKED EXAMPLE

Question (6 marks). Liver cells are given adrenaline, and cAMP is measured. Predict the cAMP level, compared with untreated cells given adrenaline, in each case, and explain. (a) Cells pre-treated with cholera toxin. (b) Cells given GTPγS, a GTP analogue that α cannot hydrolyse. (c) Cells with a mutant receptor that binds adrenaline but cannot bind Gs. (d) Cells over-expressing an RGS protein that acts on Gs.

1. (a) **Higher and longer.** Gsα cannot hydrolyse GTP, so once activated it stays on and keeps adenylyl cyclase working.
2. (b) **Higher and longer**, for the same reason: α loads the analogue and cannot turn it to GDP. This is how researchers prove a response uses a G protein.
3. (c) **No rise.** Binding still happens, but the receptor cannot act as a GEF on Gs, so no GTP is loaded.
4. (d) **Lower and shorter.** Faster GTP hydrolysis shortens the time each Gsα spends on, so less cAMP is made.

The pattern to learn: anything that blocks GTP hydrolysis keeps the pathway on; anything that blocks GDP–GTP exchange keeps it off.

EXAM TRAPS

- The receptor does not bind GTP. The α subunit does; the receptor only makes α release GDP.
- Heterotrimeric G proteins (αβγ) are not the same as small G proteins such as Ras, which are single chains activated by Sos after an RTK (Chapter 5.2).
- βγ is not just a passive partner. It opens K^+ channels in the heart and recruits GRKs.
- Write "seven transmembrane α-helices", not "seven subunits". A GPCR is one chain.
- The favourite long question: "Explain the mechanism of GPCR signalling with a neat diagram, and how it is switched off."

CHECK YOURSELF

– REMEMBER **How many times does a GPCR cross the membrane?** 1 mark

Seven times, as α-helices; N-terminus outside, C-terminus inside.

– REMEMBER **Name the effector of Gs and of Gq.** 2 marks

Gs: adenylyl cyclase. Gq: phospholipase C-β.

– UNDERSTAND **Why is the α subunit called a timer?** 3 marks

It switches itself off by hydrolysing its bound GTP to GDP. The rate of this hydrolysis sets how long each activated α stays on, whatever the receptor does.

– UNDERSTAND **Explain desensitisation of a GPCR.** 4 marks

With prolonged ligand, GRK phosphorylates the active receptor; β-arrestin binds the phosphorylated receptor, blocks G-protein coupling, and promotes endocytosis, so fewer receptors respond.

– APPLY **Why does cholera cause watery diarrhoea?** 4 marks

Cholera toxin ADP-ribosylates Gsα in intestinal cells, blocking its GTPase. Gs stays active, adenylyl cyclase keeps making cAMP, and cAMP-driven chloride secretion draws water into the gut.

– APPLY **Pertussis toxin is added to heart cells, then acetylcholine. Does the heart slow?** 3 marks

No. The toxin stops the receptor activating Gi, so Gi is unable to inhibit adenylyl cyclase and its βγ does not open K^+ channels; the slowing effect is lost.

– ANALYZE **Adrenaline relaxes airway muscle but constricts some blood vessels. How can one ligand do both?** 4 marks

The tissues carry different adrenergic receptors. β_2 receptors couple to Gs and raise cAMP, which relaxes airway smooth muscle; α_1 receptors couple to Gq and raise Ca^{2+}, which contracts vascular smooth muscle. The receptor and G protein, not the ligand, set the response.

BEYOND THE SYLLABUS

The 2012 Nobel Prize in Chemistry went to Robert Lefkowitz and Brian Kobilka for work on GPCRs, including the crystal structure of a β_2 receptor bound to its G protein. Research now studies "biased agonists", drugs that steer a receptor towards G-protein or towards β-arrestin signalling, to keep a drug's benefit and lose its side effects. Cryo-electron microscopy has made new GPCR structures routine. This is not for the exam; search "biased agonism" and "GPCR cryo-EM" to read further.

Key terms of this lesson

TERM	MEANING OR FORMULA	CHAPTER
Endocrine / paracrine / autocrine	Signal via blood to distant cells / to nearby cells / back to the cell that made it	5.1
Contact-dependent signalling	Membrane-bound signal acts only on a touching cell (Delta–Notch)	5.1
K_d	$K_d = [L][R]/[LR]$; ligand concentration that fills half the receptors	5.2
Fractional occupancy	$\theta = [L] / ([L] + K_d)$	5.2
Receptor tyrosine kinase	Ligand → dimerisation → cross-phosphorylation → SH2 docking → Ras → MAP kinases	5.2
Nuclear receptor	Intracellular receptor for steroids and thyroid hormone; a ligand-activated transcription factor	5.2
GPCR	Seven-transmembrane receptor acting as GEF for a heterotrimeric G protein (αβγ)	5.3
Gs / Gi / Gq	Adenylyl cyclase on / adenylyl cyclase off / phospholipase C-β on	5.3

Glossary (terms used in this lesson)

Agonist A ligand that binds a receptor and activates it.

Autocrine Signalling in which a cell responds to a signal it released.

β-arrestin Protein that binds a phosphorylated GPCR, stops G-protein coupling and promotes endocytosis.

cAMP Cyclic AMP; second messenger made by adenylyl cyclase, activates PKA.

Endocrine Signalling by hormones carried in the blood to distant cells.

GEF Guanine nucleotide exchange factor; makes a G protein release GDP so GTP can bind.

IP_3 Inositol 1,4,5-trisphosphate; releases Ca^{2+} from the ER.

K_d	Dissociation constant; ligand concentration at which half the receptors are bound.
Paracrine	Signalling to nearby cells through the extracellular fluid.
Second messenger	Small intracellular molecule that relays a signal from a receptor (cAMP, cGMP, IP_3, DAG, Ca^{2+}).

The full unit book

Every chapter of Unit 5, the unit summary, the exam question bank with model answers and the full glossary: Cell Biology · Unit 5 · Cell Signaling and Cell Communication (one file, works offline).

Sources and further reading

- Alberts B. et al., *Molecular Biology of the Cell*, Garland Science / W. W. Norton: the chapters on cell signalling and on cell junctions and the extracellular matrix (from memory; check the edition you are prescribed).
- Lodish H. et al., *Molecular Cell Biology*, W. H. Freeman: the chapters on signal transduction and on integrating cells into tissues (from memory; check).
- Karp G., *Cell and Molecular Biology: Concepts and Experiments*, Wiley: the chapters on cell signalling and on interactions between cells and their environment (from memory; check).
- Cooper G. M., *The Cell: A Molecular Approach*, Sinauer / Oxford University Press: the chapter on cell signalling (from memory; check).
- Alberts B. et al., *Molecular Biology of the Cell*, 4th edition (2002), "General Principles of Cell Communication", free on NCBI Bookshelf: ncbi.nlm.nih.gov/books/NBK26813 (source of the hormone and acetylcholine concentrations and the nitric oxide half-life used in Chapter 5.1).
- Wikipedia, "Gap junction": en.wikipedia.org/wiki/Gap_junction (consulted for the connexon structure and the range of size limits quoted in Chapter 5.7).

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