MEGA LECTURE

IB DP BIOLOGY

Theme C: Interaction and Interdependence

C2.1 Chemical Signalling

Revision Notes · Higher Level only

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Original notes prepared for the IB Diploma Programme Biology course (first assessment 2025)

What the syllabus requires

Every understanding in C2.1 is **Higher Level only** — the entire topic is assessed only in the HL papers. Use this checklist as a final sweep before the exam; each row is unpacked in the sections that follow.

Understanding (all HL)	You should be able to...
Cell-to-cell communication	Explain why multicellular organisms depend on chemical signals and outline the universal signal → receptor → response sequence.
Types of signalling	Distinguish endocrine, paracrine, autocrine, synaptic and juxtacrine signalling, and pheromones between organisms, by distance and target.
Receptors	Compare cell-surface (membrane) receptors with intracellular receptors, and explain ligand specificity in terms of complementary shape.
Hydrophilic signals	Explain why hydrophilic ligands bind surface receptors and trigger transduction and second messengers such as cAMP, with amplification.
Hydrophobic signals	Explain why lipophilic signals cross the membrane, bind intracellular receptors and alter gene expression as transcription factors.
Transduction pathways	Sequence receptor activation, transduction and cellular response, referring to G-protein-coupled receptors.
Regulation	Describe signal termination, receptor down-regulation and feedback control.

> **Exam note:** Because C2.1 is HL only, questions are frequently multi-step and ask you to *predict* where a receptor sits or *compare* peptide with steroid action. Learn the reasoning, not just the labels.

1. Why cells must talk to one another [HL]

A single-celled organism responds to its environment as one unit. A human, built from tens of trillions of cells, cannot: for the whole body to behave as a coordinated organism, cells that may be metres apart must influence one another. **Chemical signalling** is the language that makes this coordination possible — it lets cells regulate growth, division, metabolism, movement and death in step with the needs of the organism.

The universal three-step logic

Almost every signalling event, however different in detail, follows the same sequence. Learn it as a spine onto which every example hangs.

- **Signal (ligand):** a signalling cell releases a chemical messenger, or displays one on its surface.
- **Reception:** the messenger binds a specific **receptor** protein on or in a target cell. Only cells with the matching receptor can respond.
- **Response:** binding changes the receptor, which triggers events inside the target cell — an enzyme switched on, a channel opened, or a gene transcribed.

So the flow is always **signal → receptor → response**. The specificity of the whole system rests on one fact: a cell responds to a signal *only if* it possesses the complementary receptor. This is why a single hormone circulating to every tissue affects only a few of them.

> **Key idea:** The signal carries no instructions of its own. Identical adrenaline molecules cause the heart to beat faster and the liver to release glucose — the different outcomes are set by the *receptors and machinery* of each target cell, not by the signal.

2. Types of signalling: distance and target [HL]

Chemical signalling is classified by *how far* the signal travels and *which* cells it reaches. The same molecule can sometimes act in more than one of these modes, so classify by behaviour in the situation described, not by the molecule's name.

Type	How the signal travels / target	Example
Endocrine	Hormone secreted into the blood; carried long distances to any cell with the receptor.	Insulin from the pancreas acting on liver and muscle.
Paracrine	Diffuses a short distance through tissue fluid to nearby cells.	Histamine released in an inflamed tissue acting on local blood vessels.
Autocrine	Acts back on the same cell that released it.	A cancer cell secreting a growth factor that stimulates its own division.
Synaptic	Neurotransmitter released across a narrow synaptic cleft to one target cell.	Acetylcholine at a neuromuscular junction.
Juxtacrine (direct contact)	Signal molecule stays membrane-bound; requires cells to touch.	Antigen presentation between immune cells; Notch signalling in development.
Pheromones	Chemical released to the environment; signals *between* organisms of the same species.	Sex-attractant pheromones in moths; alarm pheromones in ants.

Reading the differences

Endocrine signalling is **slow to start but body-wide and sustained**, because the blood carries hormones everywhere and they persist. Synaptic signalling is **fast, brief and precisely targeted** — one neuron to one cell across a gap of roughly 20 nm. Paracrine and autocrine signalling are **local**: the messengers are broken down or taken up quickly so they do not spread. Juxtacrine signalling needs physical contact, and pheromones are unique in crossing *between* individuals rather than within one body.

> **Classify by asking two questions:** (1) How far does the signal go — same cell, neighbour, across a synapse, whole body, or between organisms? (2) Is it carried in blood, tissue fluid, a synaptic cleft, or by direct contact? The two answers pin down the type.

A closer look at synaptic signalling

Synaptic signalling is a specialised, extremely local form of paracrine signalling. When a nerve impulse reaches the end of a neuron, it triggers the release of **neurotransmitter** molecules (for example acetylcholine or noradrenaline) into the tiny **synaptic cleft**. These diffuse across the gap and bind

receptors on the target cell, changing its behaviour — for instance opening ion channels to pass the signal on. Because the gap is minute and the neurotransmitter is quickly broken down or reabsorbed, the signal is **fast and short-lived** and reaches only the one cell on the far side of the synapse. This precise targeting is the opposite of the broadcast nature of endocrine signalling.

Nervous versus endocrine signalling

These two coordinating systems illustrate the trade-off between speed and reach.

Feature	Nervous (synaptic)	Endocrine (hormonal)
Signal	Neurotransmitter across a synapse	Hormone in the blood
Speed of onset	Very fast (milliseconds)	Slower (seconds to minutes)
Duration	Brief	Longer-lasting
Target	One specific cell	Any cell in the body with the receptor
Distance	Very short (across a synapse)	Long (whole body)

3. Receptors: where the signal is read [HL]

A **receptor** is a protein that binds a specific signalling molecule (its **ligand**) and, as a result, changes shape or activity. Receptors fall into two great classes defined by their location, and that location is decided by one property of the signal: whether it can cross the plasma membrane.

Feature	Cell-surface (membrane) receptor	Intracellular receptor
Location	Spans the plasma membrane; ligand-binding site faces outside.	In the cytoplasm or nucleus.
Binds signals that are	Hydrophilic (water-soluble), which cannot cross the membrane.	Hydrophobic / lipophilic, which diffuse through the membrane.
What binding does	Triggers signal transduction inside the cell (relayed message).	Forms a receptor–ligand complex that acts on DNA.
Typical speed	Fast (seconds); response often short-lived.	Slow (hours); response longer-lasting.

Ligand specificity and complementarity

Binding is specific because the ligand and the receptor's binding site have **complementary shapes and chemistry** — the same lock-and-key / induced-fit logic seen in enzymes and antibodies. Only a molecule whose shape and charge distribution fit the site will bind and activate the receptor. This explains why cells ignore the flood of other molecules around them and respond to just their own signals, and why drugs can be designed to block a receptor by mimicking its ligand's shape.

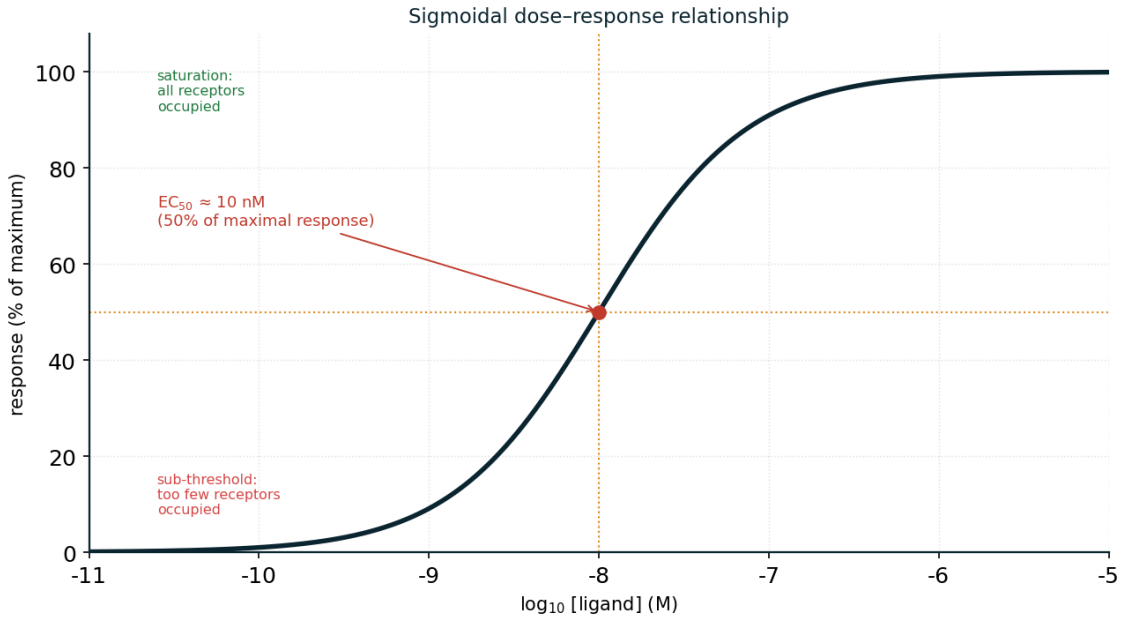

Figure 1. Sigmoidal dose–response curve: as ligand concentration rises, more receptors are occupied and the response rises steeply through the EC_{50} (here ≈ 10 nM, modelled) before saturating once receptors are fully bound — the basis of hormone sensitivity at very low blood concentrations.

> **Exam link:** Receptor specificity is the same molecular principle as enzyme specificity (C1.1) and antibody–antigen binding (C3). Examiners like answers that connect these — complementary shape underlies all three.

4. Hydrophilic signals and second messengers [HL]

Peptide hormones (such as insulin and glucagon), adrenaline and most neurotransmitters are **hydrophilic**. Because the interior of the phospholipid bilayer is hydrophobic, these molecules **cannot cross the membrane**. They must therefore act from outside, binding a **cell-surface receptor**.

Signal transduction

When the ligand binds the extracellular part of the receptor, the receptor changes shape and passes the message to the inside of the cell. This relay is **signal transduction**: the external signal is converted into an internal one. Often the activated receptor switches on the production of a **second messenger** — a small intracellular molecule (the first messenger being the ligand itself) that spreads the signal through the cytoplasm.

A classic second messenger is **cyclic AMP (cAMP)**, made from ATP by the membrane enzyme **adenylyl cyclase**. cAMP then activates enzymes (such as protein kinases) that alter the cell's behaviour.

The amplification cascade

A crucial advantage of transduction is **amplification**. Each step can activate many molecules in the next step, so a tiny number of signal molecules produces a large response:

- one bound receptor activates many molecules of adenylyl cyclase,
- each adenylyl cyclase makes many molecules of cAMP,
- each cAMP activates a kinase, and each kinase phosphorylates many target molecules.

The result is a branching cascade in which a handful of hormone molecules can release millions of glucose molecules from a liver cell. This is why hormones are effective at extremely low blood concentrations.

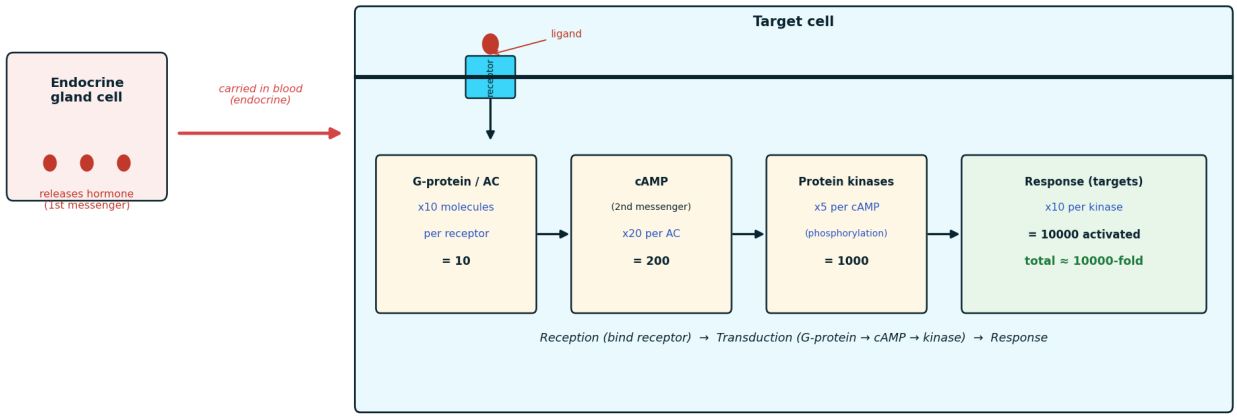

Figure 2. Endocrine signalling and the amplification cascade: a hormone released into the blood binds a cell-surface receptor, activating a G-protein → adenylyl cyclase (AC) → cAMP → kinase cascade. With the illustrative stage multipliers shown, 1 hormone molecule activates ≈ 10000 target molecules (audited).

> **Why this design?** Amplification gives sensitivity (a faint signal produces a strong response) and speed (enzymes act far faster than making new proteins). The trade-off is that the response is short-lived and needs active termination — see Section 7.

5. Hydrophobic signals and gene expression [HL]

Steroid hormones (oestrogen, testosterone, cortisol) and thyroxine are **hydrophobic / lipophilic**. Being lipid-soluble, they **diffuse directly through the plasma membrane** and so do not need a surface receptor. Instead they bind **intracellular receptors** in the cytoplasm or nucleus.

Acting as transcription factors

The hormone–receptor complex that forms is a **transcription factor**: it enters the nucleus (if not already there), binds to specific regulatory sequences of DNA, and switches particular genes on or off. This changes which proteins the cell makes, and therefore its long-term behaviour — for example the growth of reproductive tissues under sex hormones.

Slower but longer-lasting

Because the response requires transcription and translation of new mRNA and protein, it is **slow to appear** (typically hours). But the newly made proteins persist, so the effect is **sustained**, matching the roles these hormones play in growth, development and long-term metabolic adjustment. Contrast this with the fast, transient action of hydrophilic signals in Section 4.

> **Contrast to remember:** Hydrophilic → surface receptor → second messenger → fast, brief. Hydrophobic → intracellular receptor → altered gene expression → slow, lasting. Solubility decides everything downstream.

Side-by-side comparison

This single table captures the most heavily examined contrast in the whole topic. Learn it thoroughly — many C2.1 marks come straight from these rows.

Feature	Hydrophilic signal	Hydrophobic (lipophilic) signal
Examples	Peptide hormones (insulin, glucagon), adrenaline, most neurotransmitters	Steroid hormones (oestrogen, testosterone, cortisol), thyroxine
Crosses membrane?	No — repelled by the hydrophobic bilayer core	Yes — dissolves in and diffuses through the bilayer
Receptor location	Cell-surface (membrane) receptor	Intracellular (cytoplasm or nucleus) receptor
Mechanism	Signal transduction; second messengers (e.g. cAMP); enzyme cascade	Hormone–receptor complex acts as a transcription factor on DNA
Main effect	Alters activity of existing proteins	Alters gene expression (which proteins are made)
Speed	Fast (seconds)	Slow (hours)
Duration	Short-lived	Long-lasting

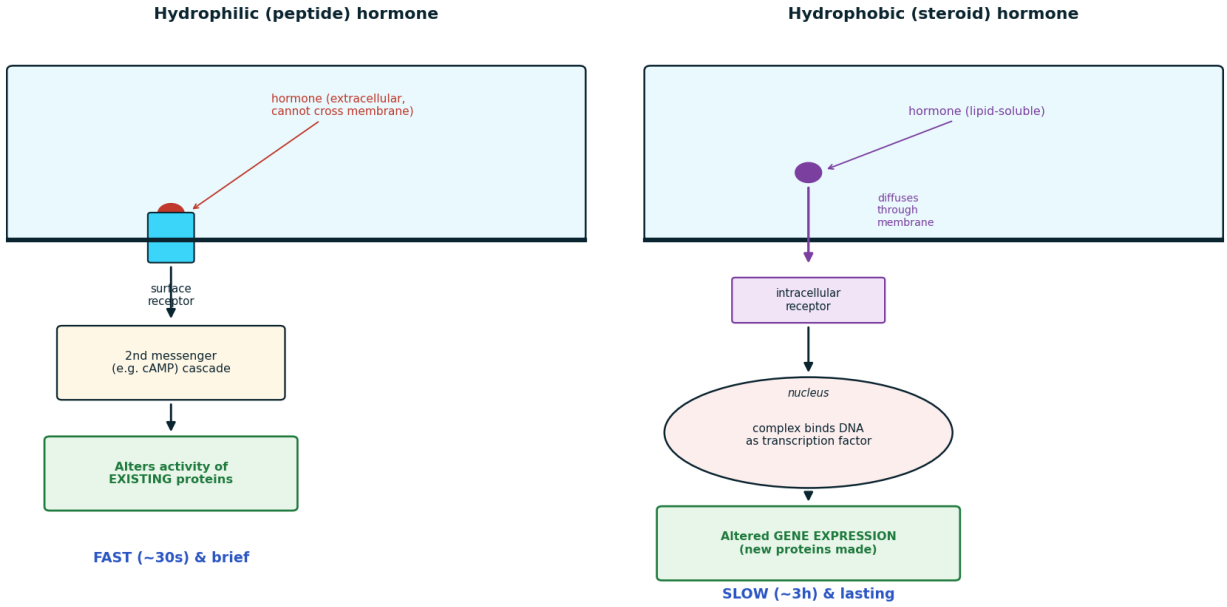

Figure 3. Peptide (hydrophilic) hormones bind surface receptors and act through a second-messenger cascade — fast (modelled ≈ 30 s) but brief. Steroid (hydrophobic) hormones diffuse through the membrane, bind intracellular receptors and act as transcription factors — slow (modelled ≈ 3 h, 360× slower to take effect) but long-lasting.

6. Signal transduction pathways in detail [HL]

For hydrophilic signals, the journey from outside the cell to the final response passes through three conceptual stages. Being able to lay them out in order is a common HL exam skill.

Stage	What happens
1. Reception	The ligand binds the extracellular site of a cell-surface receptor; the receptor changes conformation.

Stage	What happens
2. Transduction	The activated receptor relays and amplifies the signal through the cell, typically via second messengers and cascades of protein activation (e.g. phosphorylation).
3. Response	The final effectors alter cell behaviour — activating an enzyme, opening a channel, changing the cytoskeleton, or switching a gene.

G-protein-coupled receptors (GPCRs)

A very large and important family of cell-surface receptors are the **G-protein-coupled receptors**. Conceptually they work like this:

- the ligand binds the receptor on the outside;
- the receptor activates an associated **G-protein** on the inner membrane surface;
- the active G-protein switches on an effector enzyme — for example adenylyl cyclase, which makes cAMP;
- the second messenger then drives the cellular response through a kinase cascade.

The adrenaline pathway (Section 8) is a textbook GPCR example. You are not required to memorise every protein name, but you should be able to describe the **reception → transduction/amplification → response** logic and say where a G-protein and a second messenger fit in.

7. Regulation: switching signals off [HL]

A signal that could not be turned off would be useless — the cell must return to rest so it can respond again. Regulation of signalling is as important as the signal itself.

- **Signal termination:** the ligand is removed (broken down by enzymes, reabsorbed, or it simply diffuses away), and second messengers are destroyed — for example cAMP is broken down to AMP by the enzyme phosphodiesterase. This ends the response promptly once the signal falls.
- **Receptor down-regulation:** after prolonged stimulation a cell reduces the number of receptors on its surface (by internalising them), so it becomes less sensitive. This desensitisation prevents overstimulation; up-regulation does the reverse when signal is scarce.
- **Feedback control:** the response often feeds back to switch off the original signal. **Negative feedback** keeps outputs stable — for example rising thyroxine inhibits the glands that stimulate its own release, holding blood levels within a narrow range.

> **Exam link:** Signal termination and negative feedback are the reason hormone levels and blood glucose stay within homeostatic limits (C3.1). Amplification makes the response strong; termination makes it controllable.

8. Worked examples of real pathways [HL]

Adrenaline — fight or flight via cAMP

Adrenaline is hydrophilic, so it acts on a **cell-surface GPCR**. In a liver cell: adrenaline binds → the G-protein activates adenylyl cyclase → cAMP is produced as a **second messenger** → cAMP activates protein kinases → a cascade activates the enzymes that break down glycogen, releasing glucose into the blood. Amplification means a low concentration of adrenaline mobilises a large amount of glucose within

seconds — ideal for a rapid stress response.

Steroid hormones — oestrogen and testosterone

These are hydrophobic, so they **diffuse through the membrane** and bind **intracellular receptors**. The hormone–receptor complex acts as a **transcription factor**, binding DNA and switching on genes for the development and maintenance of reproductive tissues and secondary sexual characteristics. The effect is slow to appear but long-lasting — the signature of gene-level action.

Insulin and glucagon — opposing endocrine signals

Both are peptide (hydrophilic) hormones acting on **surface receptors**. Insulin (released when blood glucose is high) triggers uptake and storage of glucose; glucagon (released when glucose is low) triggers its release. Their opposing endocrine actions, coordinated by negative feedback, hold blood glucose steady — a clear link between chemical signalling and homeostasis.

Quorum sensing — signalling in bacteria

Even single-celled bacteria signal chemically. In **quorum sensing** each cell releases small signalling molecules; as the population grows, the concentration of these molecules rises. Above a threshold (a 'quorum'), the molecules switch on genes across the whole population — coordinating behaviours such as biofilm formation or bioluminescence. It shows that the signal → receptor → response logic and threshold-based gene control extend even to prokaryotes.

9. Skills and worked examples [HL]

Worked example 1 — classify a signalling type

A damaged mast cell releases histamine, which diffuses a short distance and makes the walls of nearby capillaries more leaky. Name the type of signalling and justify it.

Reasoning: the signal is not carried in blood to distant organs (not endocrine), does not act on the releasing cell (not autocrine), and crosses no synapse. It travels a *short distance through tissue fluid to neighbouring cells*.

Answer: paracrine signalling.

Worked example 2 — predict receptor location from solubility

Hormone X is a small lipid-soluble steroid. Hormone Y is a water-soluble peptide. Predict where each binds its receptor and why.

X (lipophilic): diffuses through the phospholipid bilayer, so it binds an **intracellular receptor** and acts on gene expression — slow, lasting.

Y (hydrophilic): cannot cross the hydrophobic membrane interior, so it binds a **cell-surface receptor** and works through signal transduction — fast, brief.

Rule: solubility predicts receptor location. Lipid-soluble → inside; water-soluble → surface.

Worked example 3 — sequence a transduction pathway

Put these adrenaline-response events in order: (i) cAMP activates protein kinase; (ii) adrenaline binds receptor; (iii) glucose released; (iv) adenylyl cyclase makes cAMP; (v) G-protein activated.

Correct order: (ii) → (v) → (iv) → (i) → (iii).

That is: reception (bind) → transduction (G-protein → cyclase → cAMP → kinase) → response (glucose released). Each arrow is a point of amplification.

Worked example 4 — compare peptide and steroid hormone action

State three differences between the way a peptide hormone and a steroid hormone act on a target cell.

- **Receptor location:** peptide binds a surface receptor; steroid binds an intracellular receptor.
- **Mechanism:** peptide triggers signal transduction and second messengers; steroid acts as a transcription factor altering gene expression.
- **Speed/duration:** peptide response is fast and short-lived; steroid response is slow to start but long-lasting.

Worked example 5 — interpret a receptor-blocker experiment

A drug that fits a cell's adrenaline receptor but does not activate it (a 'blocker') is added to liver cells. When adrenaline is then applied, no glucose is released. Explain the result and predict the effect of the same drug on a steroid hormone.

Explanation: the drug occupies the receptor's binding site by complementary shape, so adrenaline cannot bind. With no reception there is no transduction, no cAMP and no cascade, so no glucose is released — the pathway is blocked at step one.

Prediction: a steroid hormone acts on an *intracellular* receptor after crossing the membrane, so a drug blocking a **surface** receptor would **not** affect it. This is exactly how you would experimentally distinguish the two mechanisms.

Common pitfalls

- Saying steroid hormones use surface receptors — they use **intracellular** receptors because they cross the membrane.
- Thinking a second messenger *carries* the signal into the cell — it is made *inside* the cell and **amplifies and spreads** the message.
- Claiming a hydrophilic hormone diffuses into the cell — it cannot cross the hydrophobic bilayer, which is exactly why it needs a surface receptor.
- Confusing the hormone (first messenger) with the second messenger (e.g. cAMP): the hormone stays outside, cAMP works inside.

• Forgetting that a signal must be **terminated** — amplification without an off-switch would be uncontrollable.

10. Quick reference [HL]

Idea	Statement
Universal logic	signal (ligand) → receptor → response; a cell responds only if it has the matching receptor.
Signalling types	endocrine (blood, body-wide) · paracrine (local) · autocrine (self) · synaptic (neurotransmitter) · juxtacrine (contact) · pheromone (between organisms).
Hydrophilic signal	cannot cross membrane → surface receptor → transduction + second messenger (cAMP) → fast, brief.
Hydrophobic signal	crosses membrane → intracellular receptor → transcription factor → altered gene expression → slow, lasting.
Amplification	each step activates many of the next, so few ligands → large response; hormones act at very low concentration.
GPCR pathway	ligand → receptor → G-protein → adenylyl cyclase → cAMP → kinase cascade → response.
Regulation	termination (ligand removed, cAMP broken down), receptor down-regulation, negative feedback.

11. Test yourself [HL]

Attempt these without notes; full answers follow.

1. Explain why a multicellular organism needs chemical signalling that a single-celled organism does not.

2. Distinguish between autocrine and paracrine signalling.

3. A hormone is described as lipid-soluble. Predict its receptor location and the general nature of its effect on the cell.

4. Explain what is meant by a second messenger and give one example.

5. Describe how amplification allows a hormone to be effective at very low concentration.

6. State two differences between the action of adrenaline and the action of oestrogen on their target cells.

7. Explain why signalling must be terminated, naming one way this is achieved.

8. Outline how quorum sensing shows the signal-receptor-response logic in bacteria.

Answers

1. A single-celled organism responds as one unit, but a multicellular organism must coordinate trillions of cells that may be far apart. Chemical signals let cells influence one another so growth, metabolism and behaviour are regulated for the whole organism rather than each cell acting alone.

2. Both are local. In **autocrine** signalling the cell responds to a signal it released itself; in **paracrine** signalling the signal diffuses a short distance to act on *nearby* cells.

3. Being lipid-soluble it crosses the plasma membrane, so it binds an **intracellular receptor**. The complex acts as a transcription factor altering gene expression — a slow but long-lasting effect.

4. A second messenger is a small molecule made *inside* the cell in response to a signal binding a surface receptor; it relays and amplifies the signal through the cytoplasm. Example: **cyclic AMP (cAMP)**, made from ATP by adenylyl cyclase.

5. Transduction is a cascade in which each activated molecule activates many molecules of the next step: one receptor → many enzymes → much cAMP → many kinases → a very large response. So a few hormone molecules trigger a large effect, and the hormone works at low blood concentration.

6. (i) Adrenaline binds a **surface** receptor and works via a second messenger; oestrogen binds an **intracellular** receptor and alters gene expression. (ii) Adrenaline's effect is fast and brief; oestrogen's is slow and long-lasting.

7. Without termination the response would continue uncontrollably and the cell could not respond to new signals. It is achieved by removing the ligand or breaking down the second messenger — for example phosphodiesterase converts cAMP to AMP — and by negative feedback and receptor down-regulation.

8. Each bacterium releases a signalling molecule; as the population grows the molecule's concentration rises. Above a threshold it binds receptors and switches on genes across the population (the **response**), coordinating group behaviour — the same signal → receptor → response logic seen in animal cells.