Chemical signalling

C2.1 · HL only

A circulating hormone does not make every cell respond

Delivery and recognition are different steps

Full C2.1 is HL only: receptors, quorum sensing, animal signals, receptor classes, pathways, steroid effects and feedback.

Use membrane proteins, ATP, diffusion and gene expression to explain each response.

All numerical data and pathway counts are invented teaching models.

A ligand needs compatible binding-site chemistry

Selective binding can initiate a conformational change

A receptor is a protein with a binding site compatible with a signalling ligand's shape and chemical properties.

Signal transduction connects reception to ion movement, enzyme activity, vesicle traffic or transcription.

Related ligands can sometimes bind one receptor. Specificity does not mean one molecule alone can ever occupy it.

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Reception, activation and response are different observations

Observation	**Interpretation and limit**
Ligand binds	Occupancy alone does not demonstrate activation
Agonist / antagonist	An agonist activates; an antagonist can reduce normal ligand activation
One cell responds	Compatible receptor plus downstream machinery permits the response
Another does not	Check signal availability, receptor/pathway expression and viability

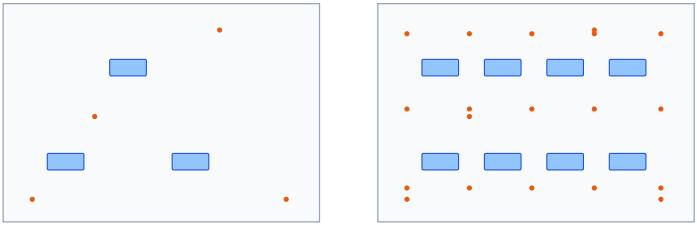
Name the denominator and baseline in a blocker comparison

1. **Invented readings.** Untreated 12; ligand 60; ligand plus proposed blocker 24 units.
2. **Raw comparison.** Final value fivefold; increase 400%. Raw value falls $(60 - 24)/60 = 60\%$ with blocker.
3. **Baseline correction.** Induced effects 48 and 12; suppression $(48 - 12)/48 = 75\%$. Calculations alone do not locate the blocker's action.

Local signal concentration changes gene regulation

Low local signal | **High local signal**

Bacteria (blue); autoinducer (orange)



Luminescence genes: low expression

Luminescence genes: activated

Autoinducer accumulation can activate luminescence genes.

A bacterial population does not need a counting organ

Production and loss determine local autoinducer concentration

Vibrio fischeri produces an autoinducer using LuxI. Sufficient local signal supports LuxR-mediated activation of luminescence genes.

The protein machinery produces light; autoinducer itself is not a packet of light. Regulation can reinforce signal production.

Cell density matters alongside fluid flow, diffusion, degradation and confinement; the network has additional controls.

Bulk light and light per cell can change by different ratios

1. **Invented bulk result.** Low-density light two units; high-density light 50 units: 25-fold.
2. **Normalize.** If cell number increased tenfold, light per cell increases $25/10 = 2.5$-fold.
3. **Test.** Compare fresh/conditioned cell-free medium under controlled nutrients, pH and growth; complementary receptor/synthesis evidence helps identify the mechanism.

Functional categories are not four chemical families

Signal category	Role and example
Hormone	Commonly blood-borne to distant targets, e.g. insulin
Neurotransmitter	Neuron-released signal; in a chemical synapse it crosses a short gap
Cytokine	Signalling protein, often coordinating immune-cell responses
Calcium ion	A cytosolic rise can activate calcium-binding proteins as an internal signal

Hormones and neurotransmitters are chemically diverse

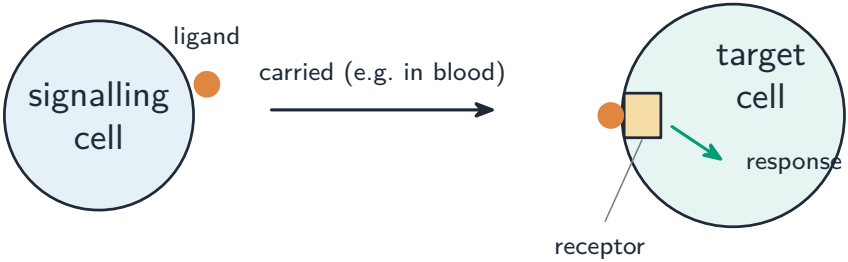
Different chemistry supports different delivery and receptor mechanisms

Hormones include amines such as epinephrine, proteins such as insulin, and steroids such as progesterone.

Neurotransmitters include amino acids, amines and peptides; acetylcholine has another structure. Nitric oxide is NO, not nitrous oxide N_2O.

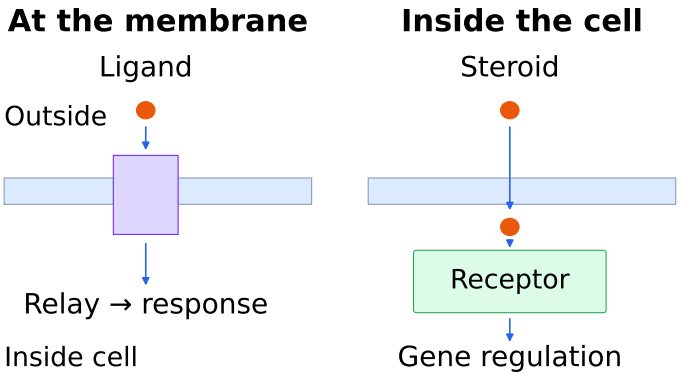
Peptides generally use membrane receptors; steroids can enter and use intracellular receptors. Thyroid hormones are an amino-acid-derived counterexample to "all amines use membrane receptors".

Cell signalling



The receptor triggers a response inside

Locate recognition relative to the plasma membrane



External binding can trigger an internal response.

Protein structure fits the membrane and aqueous surroundings

A receptor need not transport its ligand

A spanning receptor exposes hydrophobic side chains to membrane lipids, with aqueous-compatible regions outside and in cytosol.

An intracellular receptor is in cytoplasm or nucleus; a ligand must gain access before binding.

A soluble receptor can have a hydrophobic binding pocket inside an aqueous-compatible protein surface. Both routes need downstream machinery.

Explain nicotinic receptor depolarization without inventing an ATP pump

1. **Reception.** Acetylcholine increases opening probability of a ligand-gated cation channel.
2. **Current.** Near rest, sodium entry contributes to net inward positive current, depolarizing the membrane; potassium can also pass.
3. **Consequence.** Further electrical activity depends on threshold and other channels. Ion flow follows electrochemical gradients; opening does not guarantee an action potential.

One transmitter can act through different receptor classes

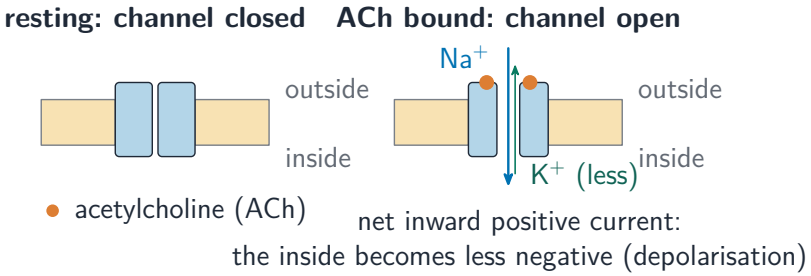
Do not turn every acetylcholine receptor into the same channel

Nicotinic receptors are ligand-gated channels; muscarinic acetylcholine receptors act through G proteins.

Removal of transmitter and channel closure help terminate the response. Transport processes maintain gradients over time.

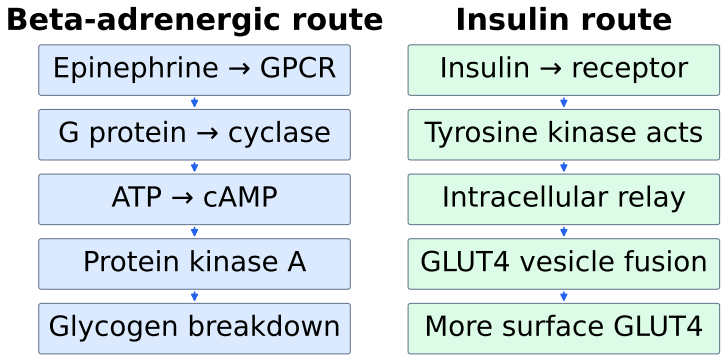
The ligand's name alone does not specify the intracellular mechanism or the target's response.

The nicotinic acetylcholine receptor



The receptor is itself the channel

Compare a second-messenger route with transporter insertion



Compare the cAMP route with GLUT4 insertion.

Trace the beta-adrenergic pathway across the membrane

1. **Reception.** Epinephrine binds a beta-adrenergic GPCR; a stimulatory G protein exchanges GDP for GTP.
2. **Second messenger.** The G protein activates adenylyl cyclase, converting ATP to cAMP inside the cell.
3. **Response.** cAMP helps activate protein kinase A; target phosphorylation can promote glycogen breakdown in a suitable cell. Epinephrine remains the extracellular first messenger.

Calculate amplification only from the supplied model

1. **Invented assumptions.** Two active receptors; four G proteins/cyclases per receptor; 50 cAMP molecules/second per cyclase for three seconds.
2. **Output.** $2 \times 4 \times 50 \times 3 = 1{,}200$ cAMP molecules.
3. **Limit.** This is not a fixed physiological ratio. ATP supplies material; amplification does not create matter or energy from nothing.

Signal termination makes a short pulse controllable

Activation needs appropriate switching-off processes

GTP hydrolysis helps inactivate G proteins; phosphodiesterases break down cAMP.

Phosphatases can remove protein phosphates, while receptor regulation also shapes responsiveness.

Other GPCRs can inhibit different effectors. Not every G protein increases cAMP.

Epinephrine and adrenaline refer to the same hormone

Naming conventions help researchers communicate internationally

The Greek and Latin roots of the two names refer to the adrenal glands near the kidneys.

Different names persist across naming traditions; they do not imply two different hormones or obligatory receptor pathways.

Use one name consistently in an explanation and identify the particular receptor route.

Connect insulin binding to surface glucose transporters

1. **Receptor.** Insulin binds outside to an existing multi-subunit receptor complex; activation promotes intracellular tyrosine phosphorylation.
2. **Relay.** Downstream signalling moves GLUT4-containing vesicles to the plasma membrane in responsive muscle/adipose cells.
3. **Response.** Vesicle fusion increases transporter number and facilitated-entry capacity when the glucose gradient supports uptake. The receptor receives insulin; GLUT4 transports glucose.

Redistribution can change the surface fraction without new synthesis

1. **Invented cell.** 100 GLUT4 molecules total: 20 then 50 at the surface.
2. **Comparisons.** 20% $\rightarrow$ 50%: 30 percentage points; 2.5-fold final surface number, a 150% increase.
3. **Limit.** Total number can stay unchanged. Uptake need not rise proportionally; do not extend GLUT4 insertion to every body cell or liver cell.

Link intracellular recognition to protein production

1. **Binding.** Oestradiol, progesterone or testosterone enters an appropriate cell and activates a compatible intracellular receptor.
2. **Expression.** The activated receptor interacts with specific DNA regulatory sequences and transcriptional machinery: altered mRNA and protein production.
3. **Specificity.** Receptor distribution, DNA regulation and partners shape tissue response. This does not change the genetic code or turn on every gene.

Compare mechanism and time without making an absolute rule

Transcription and translation take time

A transcription-mediated response often develops more slowly than direct ion-channel opening because RNA/protein production is involved.

Other steroid actions and membrane-receptor pathways exist; not every steroid effect is slow or every surface-receptor effect immediate.

Hormone identity and receptor expression must be interpreted with cell type and pathway context.

Oestradiol and progesterone have distinct target effects

Context	Effect and qualification
Oestradiol: much of cycle	Contributes to negative feedback on hypothalamic GnRH control
Sustained high pre-ovulatory oestradiol	Supports positive feedback in the hypothalamic–pituitary system and ovulatory surge
Neuronal route	Oestradiol-sensitive network inputs help control GnRH neurons
Progesterone: endometrium	Supports secretory maintenance after ovulation; does not simply duplicate oestradiol's proliferative effects

Negative feedback opposes the initiating change

1. **Disturbance.** Raised blood glucose stimulates insulin secretion.
2. **Effect.** Increased uptake/storage and reduced glucose output help lower glucose.
3. **Return.** Reduced glucose stimulation reduces further secretion. “Negative” describes regulatory direction, not a harmful effect.

Positive feedback reinforces the initiating change

1. **Disturbance.** Cervical stretch during labour stimulates oxytocin release.
2. **Effect.** Stronger uterine contractions can increase stretch and further stimulation.
3. **Termination / distinction.** Delivery interrupts the loop. Forward amplification alone is not feedback: an influence must return to an earlier stage.

Attempt all thirteen questions before checking

Compare the measured quantity with the proposed mechanism

Distinguish binding, activation, receptor location and downstream response.

Calculate raw/baseline-corrected changes, bulk/per-cell output, amplification and transporter fractions.

Explain four receptor mechanisms, steroid target effects and signed feedback; evaluate controls and specificity.

Check ratios and baselines independently

1. **Response data.** $10 \to 50$ units: fivefold final value and 400% increase. Blocker 20: 60% raw suppression; induced effects $40 \to 10$: 75% suppression.
2. **Quorum / cascade.** 30-fold bulk light with sixfold cells gives fivefold light/cell; $4 \times 3 \times 20 \times 2 = 480$ cAMP molecules.
3. **GLUT4.** $24/120 = 20\%$; $60/120 = 50\%$: 30 percentage points and 150% increase in surface number.

Keep the receptor mechanisms separate

Example	Mechanistic chain
Nicotinic acetylcholine	Ligand-gated channel → net inward positive current → depolarization near rest
Beta-adrenergic epinephrine	GPCR → G protein → cyclase → cAMP → kinase
Insulin	Receptor tyrosine phosphorylation → relay → GLUT4-vesicle insertion
Steroid	Intracellular receptor → DNA regulation → transcription/protein changes

Check yourself

Every mechanism needs a named link from reception to response

Binding need not activate a receptor; the same ligand can produce different effects through different receptor/pathway contexts.

An insulin receptor is not GLUT4. A G protein is not cAMP. NO is not N_2O. Fivefold final response is not a 500% increase.

A plateau or blocker result needs controls; amplification becomes feedback only when an effect returns to regulate an earlier step.