CORE IDEA 3: ENERGY AND EQUILIBRIUM
TOPIC 3.3: COMMUNICATION AND EQUILIBRIUM IN ORGANISMS (CELL SIGNALLING)

Learning Outcomes:

Candidates should be able to:

Core Idea 3B: Communication and Equilibrium in Organisms

(m) outline the main stages of cell signaling:

- **(i)** ligand-receptor interaction
- **(ii)** signal transduction (phosphorylation cascade and signal amplification)
- **(iii)** cellular response (change in gene expression)

(Knowledge of intracellular receptors is not required)

(n) explain the roles and nature of second messengers (including cyclic AMP)

(o) explain the role of kinases and phosphatases in signal amplification

(p) outline how insulin and glucagon regulate the concentration of blood glucose through the respective tyrosine kinase receptor and G-protein linked receptor.

(The outline should be limited to describing how the ligand induces a conformational change in a membrane-bound receptor to trigger downstream signaling pathways that elicit physiological changes in blood glucose concentration. Details of different second messengers and specific kinases activated in the pathway are not required.)

Use the knowledge gained in this section in <u>new situations</u> or to <u>solve related problems</u>.

References:

Reece, J. B. et al. (2018). Campbell Biology (11th Ed). Chapter 9: Cellular Signalling, pp. 214 – 231.

LECTURE OUTLINE:

1. Introduction
2. Types of Extracellular Signals
3. Stages of Cell Signalling
    - **3.1.** Stage 1: Ligand-Receptor Interaction (Reception of signal)
    - **3.2.** Stage 2: Signal Transduction
        - **3.2.1** Second Messengers
        - **3.2.2** Phosphorylation Cascade
        - **3.2.3** Signal Amplification
    - **3.3.** Stage 3: Cellular Response
4. G-protein Linked Receptors (GPLRs)
    - **4.1.** Structure of GPLR
    - **4.2.** Regulation of Blood Glucose Concentration by Glucagon via GPLR
5. Receptor Tyrosine Kinase (RTK)
    - **5.1.** Structure of RTK
    - **5.2.** Regulation of Blood Glucose Concentration by Insulin via RTK
6. Advantages of Cell Signalling Pathways in Multicellular Organisms

1. Introduction

- Large multicellular organisms contain many different organs and tissue types. For all of these organs and tissues to work together as a unified whole, cell-to-cell communication is essential.

- Cells need to be able to receive and respond to extracellular signals. For e.g., communication between neurone and muscle cell for muscular contraction, communication between cells of the endocrine gland and target cell for homeostatic control etc.

2. Types of Extracellular Signals

- Extracellular signals molecules fall into two classes.

1. The **larger class of signals** consists of molecules that are **too large or too hydrophilic (i.e. polar OR charged)** to pass through the cell surface membrane of the target cell (Relate this to the property of the phospholipid bilayer). This class of molecules relay their signals through the receptors embedded in the cell surface membrane of the target cells. For example, **peptide hormones** (e.g. glucagon, insulin) bind to receptors on the surface of their target cells to relay their signals.

2. The **smaller class of signals** consists of molecules that are **small or hydrophobic (i.e. non-polar)** to diffuse across the cell surface membrane into the target cells. These signal molecules either activate intracellular enzymes or bind to intracellular receptors proteins that regulate gene expression. For example, **steroid hormones** (e.g., cortisol, testosterone, and oestrogen) diffuse directly across the cell surface membrane of target cells, bind to an intracellular receptor before exerting its effect on gene expression.

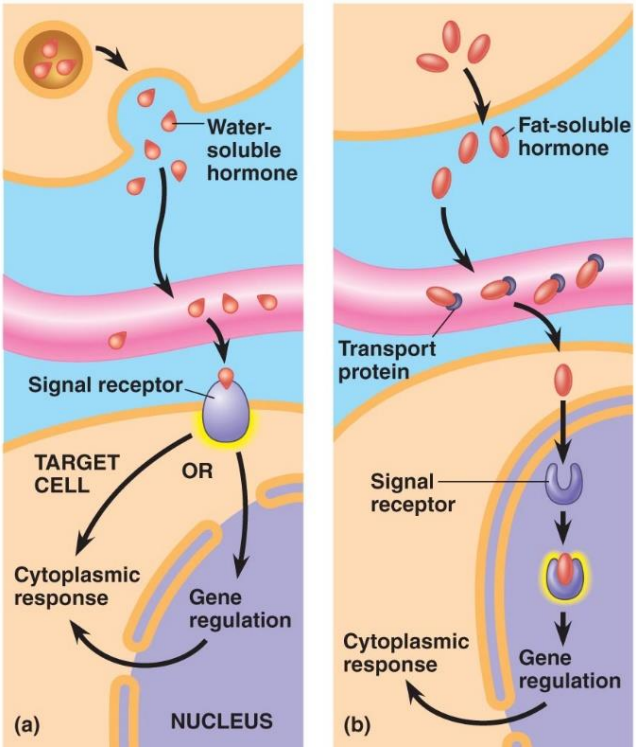


Fig. 2.1: (a) Hydrophilic signal molecule binds to membrane receptor to relay signal; (b) Hydrophobic signal molecule enters cell directly to bind to intracellular receptor.

- In this topic, we will focus on the larger class of signalling molecules, namely the **peptide hormones glucagon and insulin**.

Learning Outcomes:

(m) Outline the main stages of cell signalling:

i. ligand-receptor interaction

ii. signal transduction (phosphorylation cascade and signal amplification)

iii. cellular response (change in gene expression)

(n) Explain the roles and nature of second messengers (including cyclic AMP)

(o) Explain the role of kinases and phosphatases in signal amplification

3. Stages of Cell Signalling

- **Cell signalling** refers to the processes in which cells are stimulated or inhibited by extracellular signals.
- These extracellular signals are called **ligands** (first messengers**)**, since the initiate the cell signalling pathway.
- Cell signalling comprises of 3 stages shown in Fig. 3:

    1. Stage 1: Ligand-receptor Interaction (Reception of signal)
    2. Stage 2: Signal Transduction
    3. Stage 3: Cellular Response

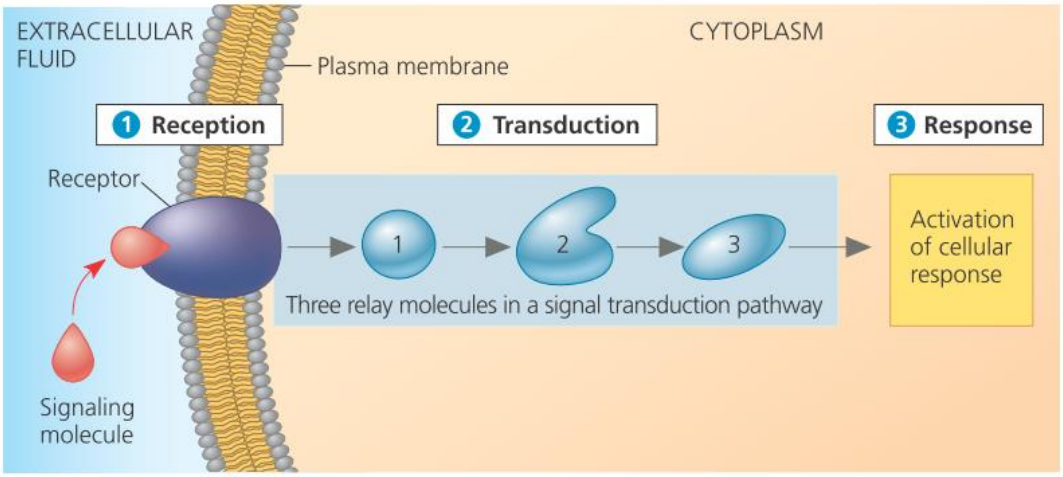


Fig. 3. The three main stages of cell signalling

3.1 Stage 1: Ligand-Receptor Interaction

- **Cell surface receptors** generally consist of three discrete domains:

  1. an **extracellular domain** facing the extracellular fluid, which contains the **ligand-binding site**,
  2. a **transmembrane (membrane-spanning) domain** that spans the cell surface membrane, and
  3. the **intracellular / cytoplasmic domain** segment facing the cytosol, which interacts with molecules within the cell.

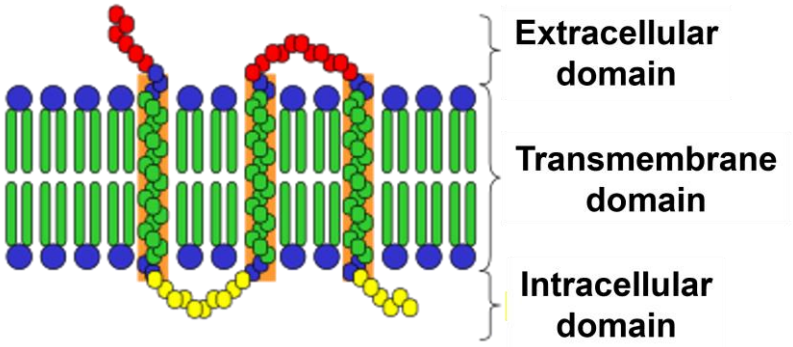


Fig. 3.1. Three domains of a cell surface receptor

- When a ligand arrives at the cell surface, it binds to the ligand-binding site of the receptor's extracellular domain because **the ligand has a 3D configuration that is complementary to the ligand-binding site**.
- This explains why ligand-receptor interactions are **specific**. For example, the growth hormone receptor binds to growth hormone but not to other hormones.
- Ligand binding **induces a conformational change** in the receptor. This conformational change is transmitted through the transmembrane domain to the cytoplasmic domain. This results in **activation** of the receptor.
- Most cell surface receptors proteins belong to one of the three large families:

  1. G-protein linked receptors (GPLR);
  2. Enzyme-linked receptors (e.g., Receptor Tyrosine Kinase (RTK)); and
  3. Ion channel-linked receptors (ICLR).

  The difference among these three classes is the type of ligands they bind to, as well as the intracellular signals generated upon receptor activation.

- In this topic, we will focus on **G-protein linked receptors** and **enzyme-linked receptor (Receptor Tyrosine Kinase)**.

3.2 Stage 2: Signal Transduction

- **Signal transduction** refers to the conversion of an extracellular signal from one physical or chemical form to another (e.g., conversion of light to a chemical signal, or of an extracellular signal to an intracellular signal), that can bring about a specific cellular response.

- Signal transduction occurs after activation of receptor. It requires a sequence of changes in a series of different molecules in a multi-step pathway. These molecules are called relay molecules, which are usually proteins.

- In a signal transduction pathway, the ligand is not passed along the pathway.

- The information (triggered by the conformational change in the receptor protein) is passed on via two mechanisms:

  1. **Production of second messengers**; and

  2. **Phosphorylation cascades** involving kinases and phosphotases**.**

3.2.1 Second Messengers

- Second messengers are substances released into the cytoplasm after the first messenger (ligand) binds to its receptor, hence **relaying a signal to the interior of the cell**.

- Second messengers are **small**, **non-protein**, ***usually*** **water-soluble molecules,** or **ions**. They do not have enzymatic activity, but rather they **act as cofactors or allosteric regulators of target enzymes**.

- Second messengers affect many processes in the cell, thus allowing a **cell to respond to a single event at the cell surface membrane with many events inside the cell**.

- Second messengers **amplify the signal** because a small number of them could result in the activation of a large number of downstream molecules.

Example of second messenger: Cyclic Adenosine Monophosphate (cAMP)

- Cyclic Adenosine Monophosphate (cAMP) is generated from Adenosine Triphosphate (ATP) in a reaction catalysed by the membrane-bound enzyme known as **adenylyl (*or* adenylate) cyclase**.

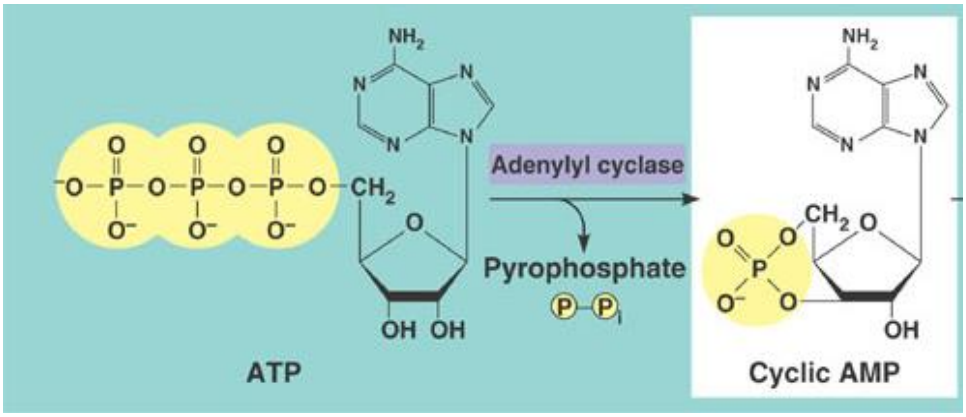


Fig. 3.2.1.1. The formation of cAMP

- cAMP acts as a **second messenger** the G-protein linked receptor (GPLR) signalling pathway.
- cAMP binds to the allosteric site of protein kinase A (PKA), causing a **3D conformational change** that **activates** PKA. Activated PKA then proceeds to activate other downstream enzymes.

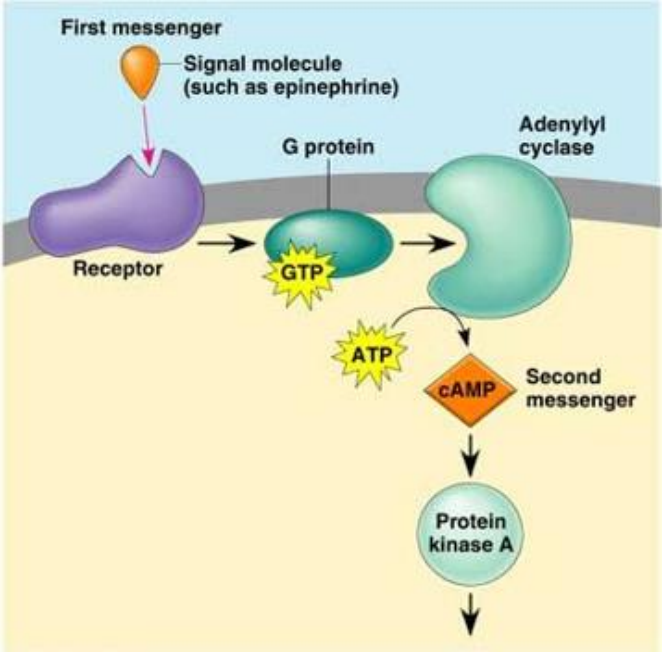


Fig. 3.2.1.2. cAMP as a second messenger in GPLR signalling pathway

- cAMP levels do not remain high in the cell for a long period. An enzyme, **cAMP phosphodiesterase** converts cAMP into AMP, thus leading to the cessation of signal transduction.

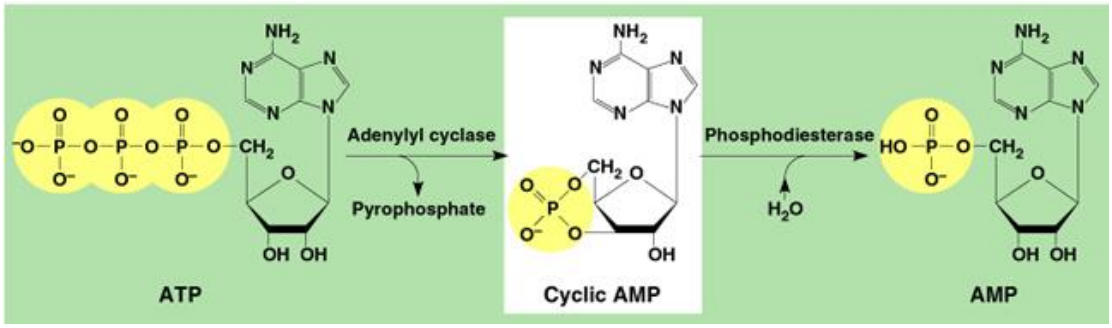


Fig. 3.2.1.3. Synthesis and Hydrolysis of cAMP

3.2.2 Phosphorylation Cascade

- Proteins may be phosphorylated or dephosphorylated, which is a form of post-translational chemical modification. The phosphorylation status of proteins can determine whether they are active or inactive. Phosphorylation is **reversible**.

	Protein phosphorylation	Protein dephosphorylation
Definition	**Adding of phosphate groups** to specific amino acid residues of proteins	**Removal of phosphate groups** from specific amino acid results of proteins
Enzyme responsible	Protein **kinases**, which **transfer phosphate groups from ATP** to proteins	Protein **phosphatases**, which remove phosphate groups from proteins by **hydrolysis**
Result	Change in R group interactions within the protein causes it to **change in 3D configuration**	
Protein activity status	Usually causes protein to be **activated**	Usually causes protein to be **inactivated**

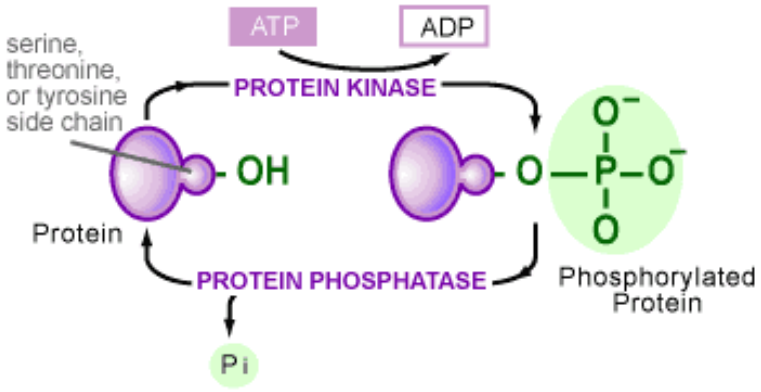


Fig. 3.2.2.1. Phosphorylation and dephosphorylation of proteins

- A **phosphorylation cascade** is a sequence of events whereby one protein kinase phosphorylates another, causing a series of reactions leading to the phosphorylation of thousands of cellular proteins. This eventually leads to a cellular response.

- Phosphorylated proteins may be inactivated via the removal of phosphate groups by phosphatases. Thus, the activity of a protein regulated by phosphorylation depends on the balance between active kinase molecules and active phosphatase molecules in the cell.

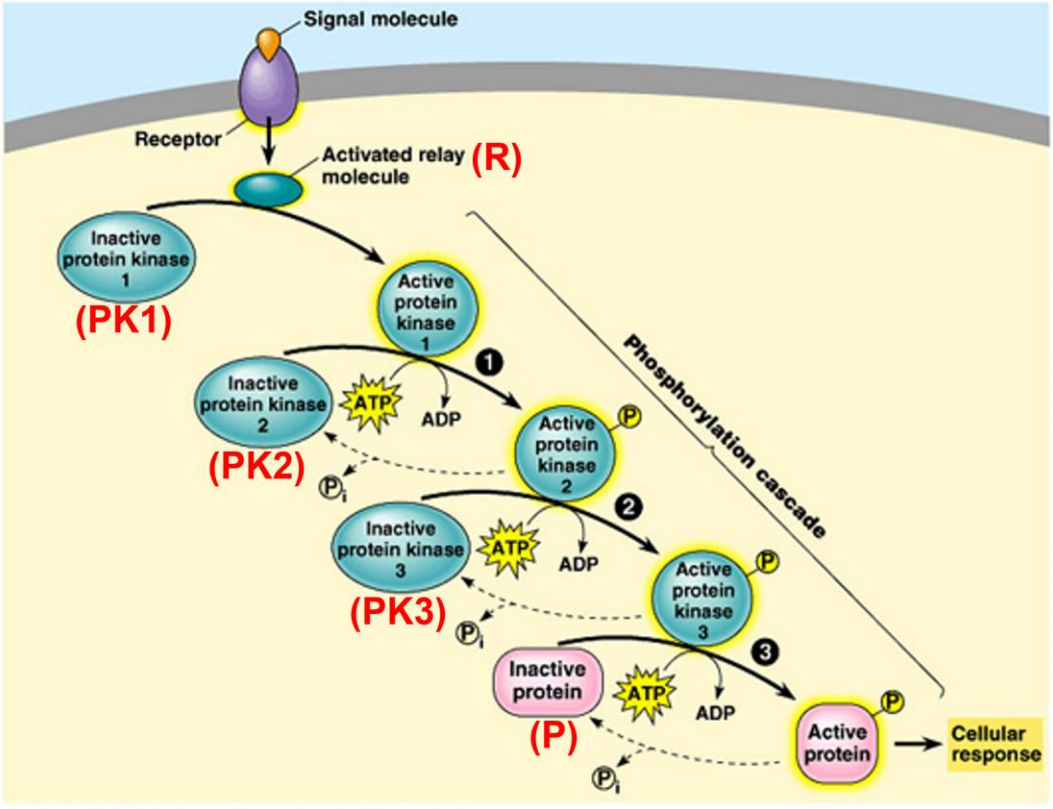


Fig. 3.2.2.2. A Phosphorylation Cascade
(bold arrows denote phosphorylation while dotted arrows denote dephosphorylation)

3.2.3 Signal Amplification

- **Signal amplification** refers to the process of **enhancing signal strength** as a signal is relayed through a signal transduction pathway.

- This occurs when each component in the pathway activates **multiple copies of the next component**, allowing a **small quantity of the signal molecules** to result in **a large number of activated molecules** at the end of the pathway, hence **eliciting a large cellular response** in the target cell.

- In Fig. 3.2.1.2 above, signal amplification can be achieved when a single activated relay molecule (R) activates more than 1 molecule of protein kinase 1 (PK1), and each PK1 activates more than 1 molecule of PK2, and each molecule of PK2 activates more than 1 molecule of PK3. This results in an **exponential increase in the number of activated molecules**, eventually leading to a large number of inactive protein (P) becoming activated, which then triggers the cellular response.

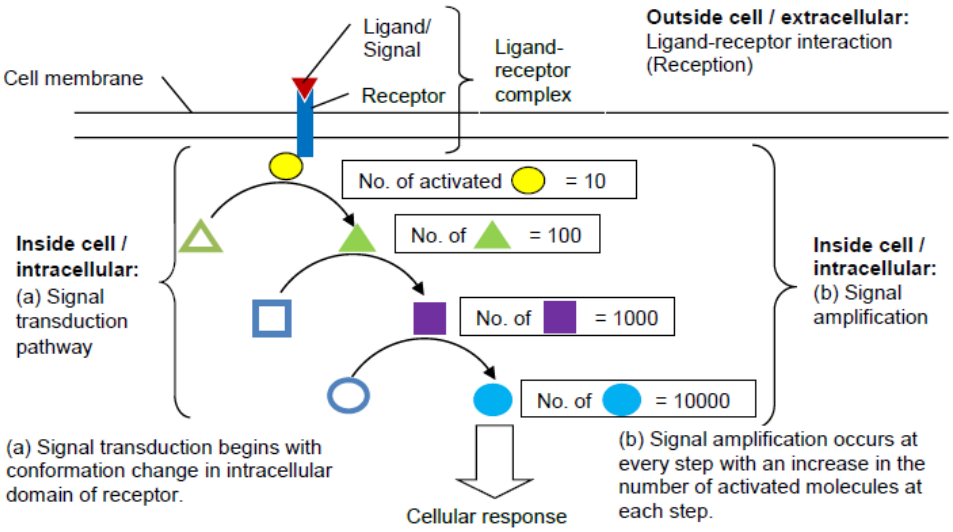


Fig. 3.2.3. Signal amplification results in exponential increase in number of activated molecules

3.3 Stage 3: Cellular Response

- A transduced signal triggers a specific cellular response. Examples of such responses include:

  1. Regulation of Protein Synthesis

  Signal transduction may result in activated proteins which act as **transcription factors**. This would lead to a **change in gene expression** by **upregulating or downregulating the transcription of specific genes** or **turning genes on or off**.

  2. Regulation of Metabolic Pathways

  Signal transduction may result in the **activation or inactivation of key metabolic enzymes or proteins**, causing immediate change in the metabolism of the cell e.g. activating glycogen synthase results in the synthesis of glycogen from glucose.

  3. Alteration of Cell Characteristics e.g., via Changes in Cytoskeleton

  Signal transduction may result in **changes to the cytoskeleton, resulting in vesicular movement** e.g. vesicles containing protein transporters may move towards the cell surface membrane and fuse, introducing these protein transporters to the cell surface.

- Not all signals give rise to the same cellular responses in different cell types. This is **the specificity of cell signalling.**

  (a) Different cell types can have different responses to the same signal

  For e.g. in liver cells, insulin will stimulate conversion of glucose to glycogen. In adipose cells, insulin will inhibit breakdown of triglycerides.

  (b) Same cells can have the same response to different signals

  For e.g. both glucagon and adrenaline stimulate liver cells to mobilise glucose. These different signals act by the same transduction pathway to stimulate the breakdown and inhibit the synthesis of glycogen.

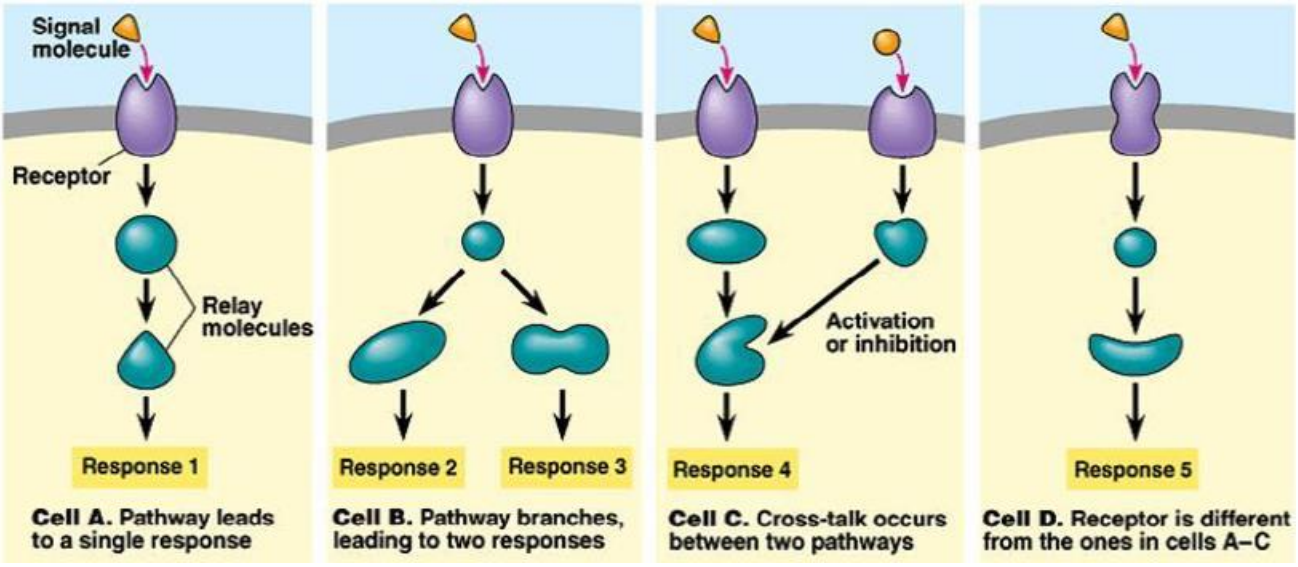


Fig. 3.3. Specificity of cell signalling

CHECKPOINT (1)

Fill in the blanks to summarise your understanding on the three stages of cell signalling.

The signal molecule acts as a first _____, binding to the ligand-binding site on a specific receptor.

The _____ interaction causes the receptor to undergo a _____ _____ and become _____.

The activated receptor triggers the synthesis of many molecules of _____ _____ (e.g. cAMP), which will activate downstream _____ _____ (e.g protein kinases).

These enzymes go on to activate other enzymes and/or proteins via a series of phosphorylation reactions known as _____ _____. During this process, the signal is _____ as a single signal molecule results in the activation of many downstream relay proteins.

Signal transduction allows the initial signal to be transduced into a form that can bring about a specific _____ _____, which could include changes in the gene expression profile of the cell or the activation/ deactivation of cellular proteins/ enzymes.

Learning Outcome 3(p)[modified]:

Outline how glucagon regulates the concentration of blood glucose through the G-protein linked receptor.

4. G-protein linked receptors (GPLRs)

(We have taught the structure and function of GPLR in CI1.2 Biomolecules: Proteins.)

4.1 Structure of GPLR

- G-protein linked receptors (GPLRs) or G-protein couple receptors (GPCRs) are **protein receptors** embedded in the cell surface membrane.
- GPLR is has a **tertiary protein structure** and is folded into a **globular** conformation.
- GPLR has three distinct domains:
    - **Extracellular domain**: faces the extracellular fluid and contains the ligand-binding site.
    - **Transmembrane domain**: comprises seven α-helices which span the width of the cell surface membrane, connecting the extracellular and intracellular domains.
    - **Intracellular domain**: faces the cytosol and contains the G-protein binding site.

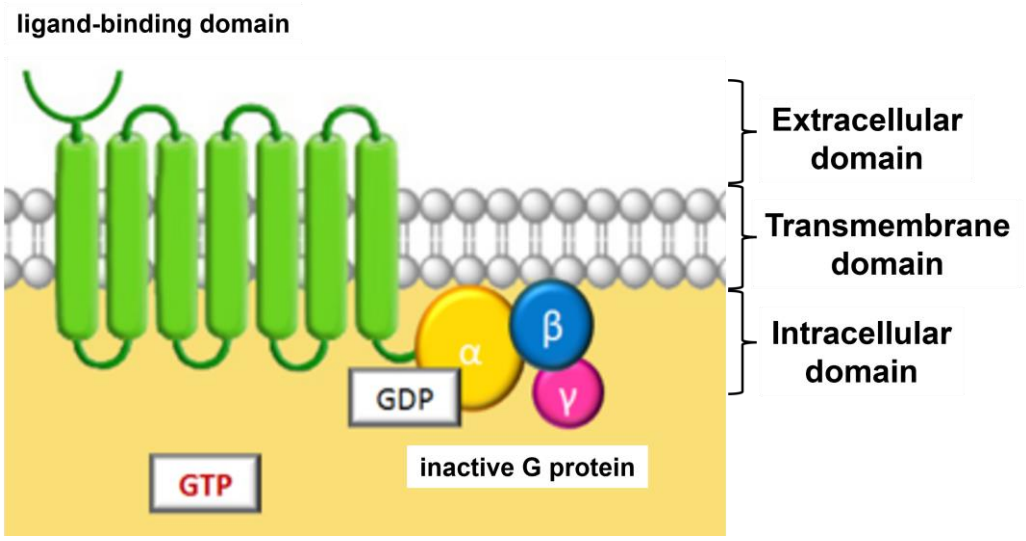


Fig. 4.1.1 Structure of the GPLR

- The G-protein comprises three subunits – Gα, Gβ and Gγ.
    - When the Gα subunit is bound to **Guanosine Diphosphate (GDP)**, the G protein has an **inactive** conformation.
    - When the Gα subunit is bound to **Guanosine Triphosphate (GTP)**, the G protein has an **active** conformation, which can proceed to activate a downstream protein/ enzyme, leading to the production of a second messenger.
- This GDP-to-GTP exchange in the Gα subunit is triggered by a **conformational change in the GPLR**, which results from **ligand binding** at the extracellular domain of the receptor.

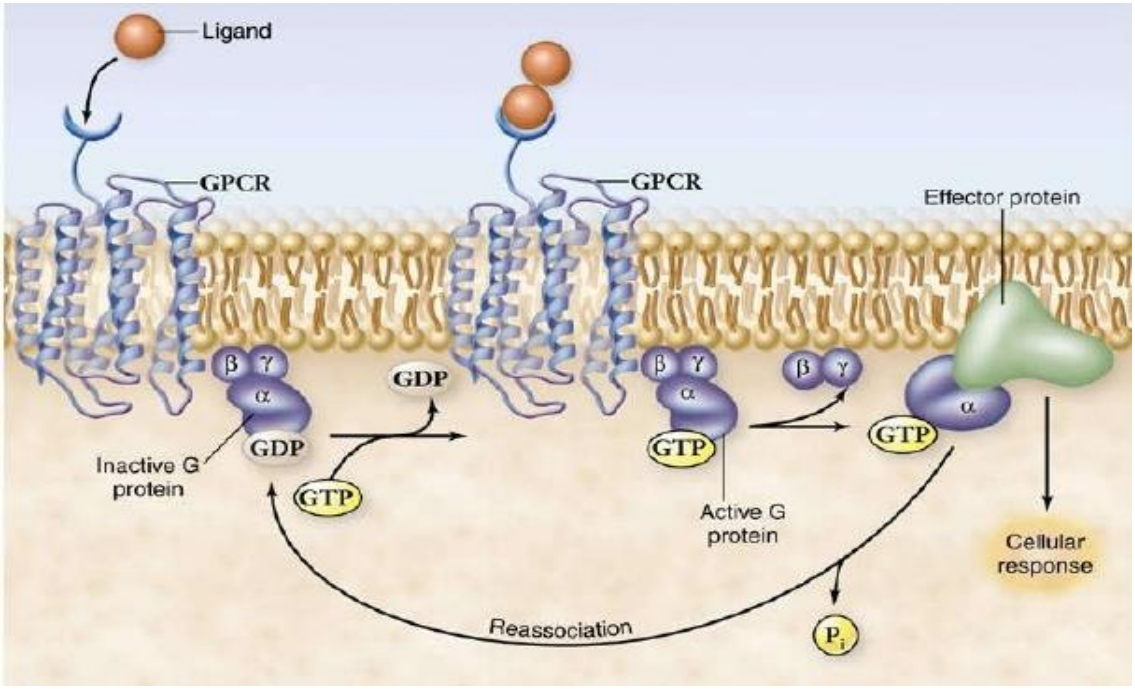
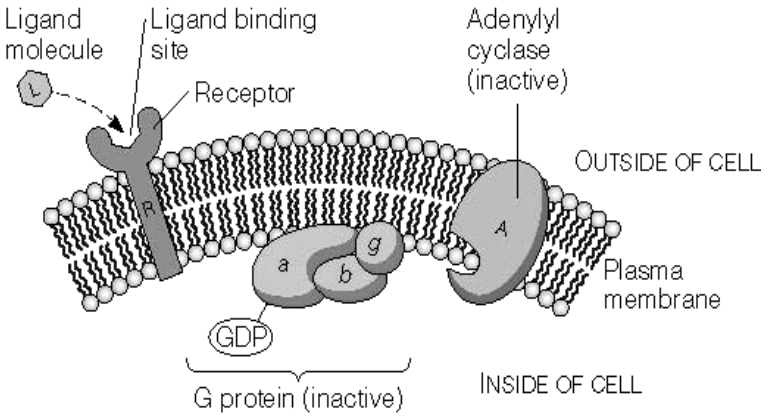
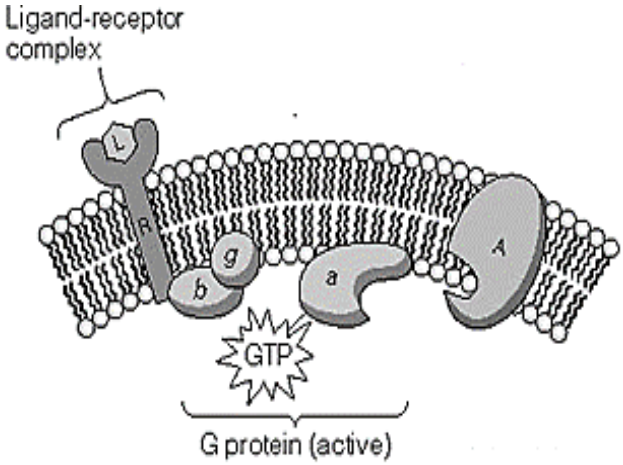
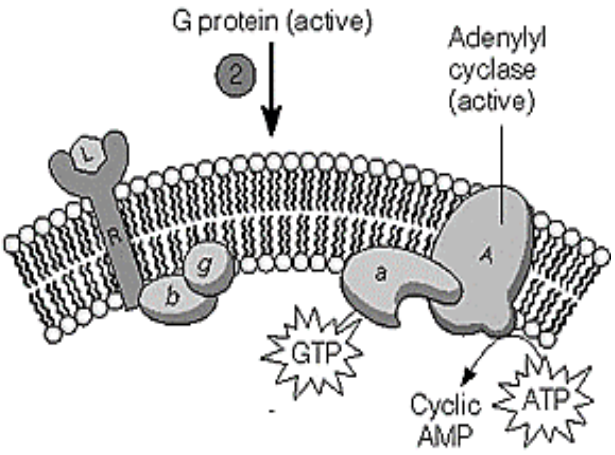
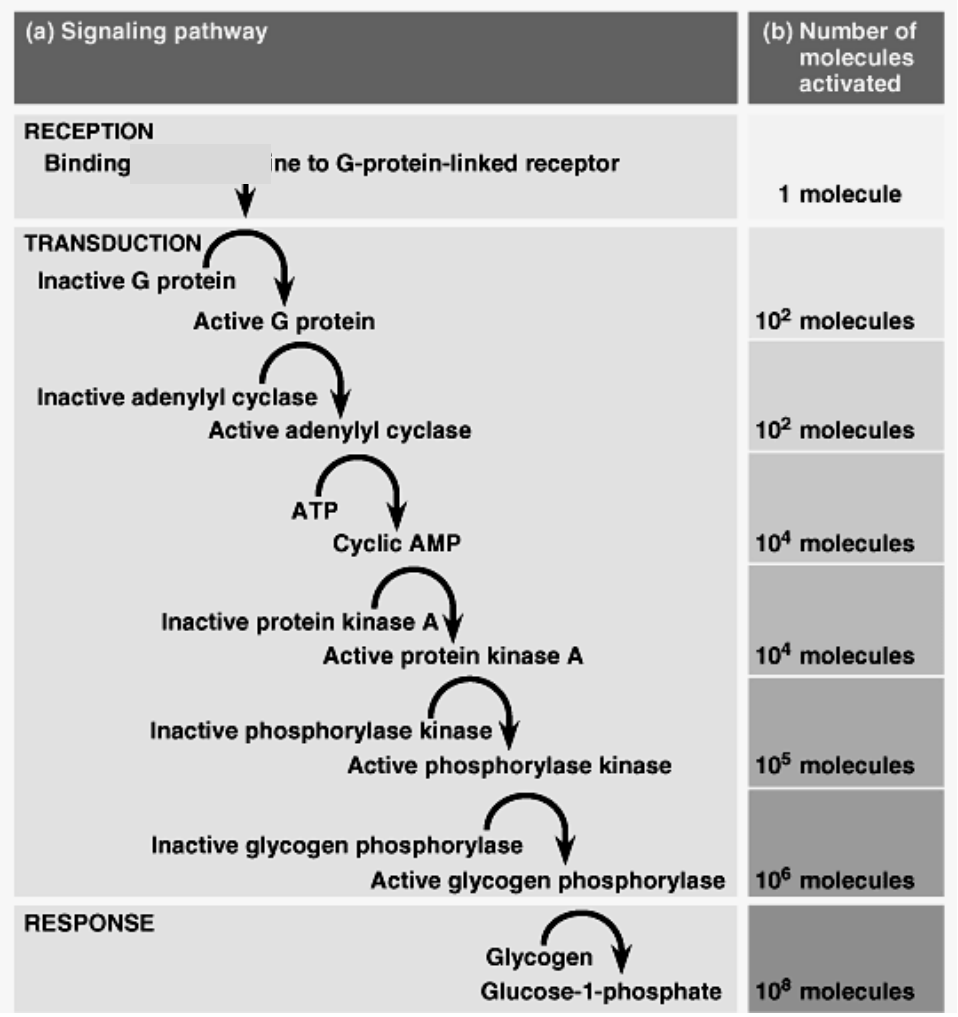


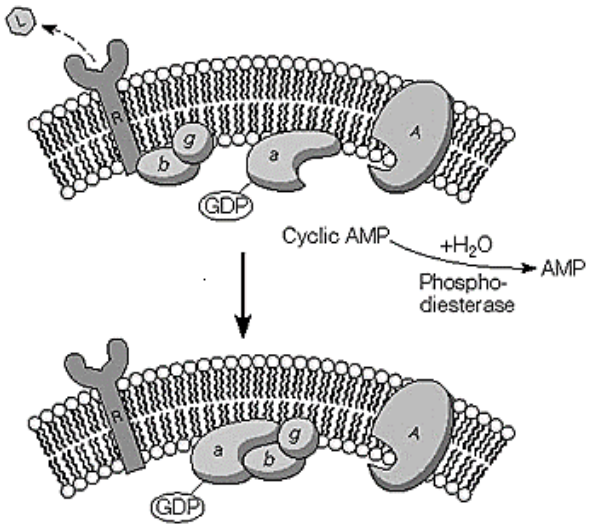
Fig. 4.1.2. Activation of G protein resulting from GDP-GTP exchange in the Gα subunit

4.2 Regulation of Blood Glucose Concentration by Glucagon via GPLR

Stage	Details
Stimulus	▪ Decrease in blood glucose concentration (hypoglycaemia) results in the release of the hormone **glucagon** from **α-cells** in the **Islets of Langerhans in the pancreas**. ▪ Glucagon is carried by circulatory system to its target cells (in the liver).
Ligand-Receptor Interaction	▪ Glucagon, being a **large** and **polar** peptide hormone, is **unable to enter the cell**. It binds to the extracellular ligand-binding site of GPLR on the surface of liver cells. ▪ **Ligand-receptor interaction** triggers a **conformational change** in the cytoplasmic domain of the GPLR, activating it. 

Signal Transduction	▪ The activated receptor interacts with an inactive **G-protein** at its intracellular domain, causing the G protein to become activated. ▪ In the Gα subunit, **GDP detaches** and is replaced by **GTP.**  ▪ The GTP-bound Gα subunit **dissociates** from the Gβγ subunits, which then **translocates along the cell surface membrane** and binds to the enzyme **adenylyl cyclase**. ▪ **Adenylyl cyclase is activated** and catalyses the conversion of **ATP to cAMP**. ▪ Each adenylyl cyclase converts many ATP to cAMP, hence **amplifying the signal**.  ▪ **cAMP acts as a second messenger** and binds to the allosteric site of protein kinase A, activating it. ▪ Each activated **protein kinase A (PKA)** phosphorylates hence: o **activates phosphorylase kinase** o **deactivates glycogen synthase**

	▪ The signal is thus transduced via a **phosphorylation cascade.** At each phosphorylation step, each activated kinase can activate many downstream relay molecules, hence the signal is further amplified. 
Cellular Response	1. **<u>Increased glycogenolysis</u>**. Phosphorylase kinase phosphorylates and activates **glycogen phosphorylase** which catalyses the breakdown of glycogen to glucose molecules, resulting in increased in blood glucose concentration. 2. **<u>Decreased glycogenesis</u>**. PKA phosphorylates and deactivates **glycogen synthase**, resulting in a decreased rate of glycogen synthesis. 3. **<u>Gluconeogenesis</u>**. The production of glucose from non-carbohydrate sources like amino acids or fatty acids is stimulated. 4. **<u>Reduction of glucose uptake into cells</u>**. Cell surface membrane with embedded glucose transporters invaginate inwards to form vesicles to **reduce the number of glucose transporters at the cell surface membrane**, hence reducing uptake of glucose into cells. All of the above metabolic reactions cause **blood glucose level to increase back to normal**.

Termination of Response	▪ The **GTPase** portion of the Gα subunit hydrolyses GTP into GDP, causing G protein to return to its inactive state. ▪ The effect of cAMP ceases when cAMP is hydrolysed to AMP by **phosphodiesterase** (see section 3.2.1).  ▪ This results in the cessation of signal transduction.

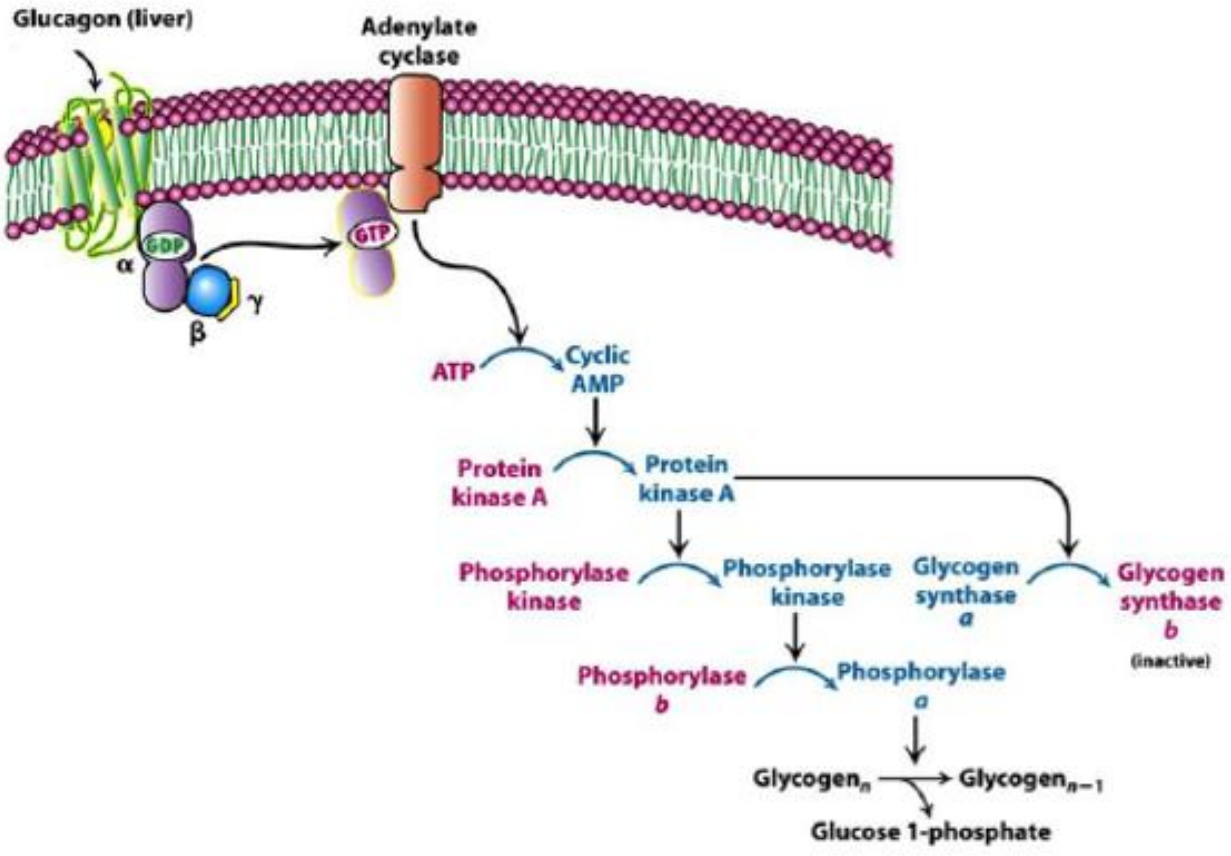
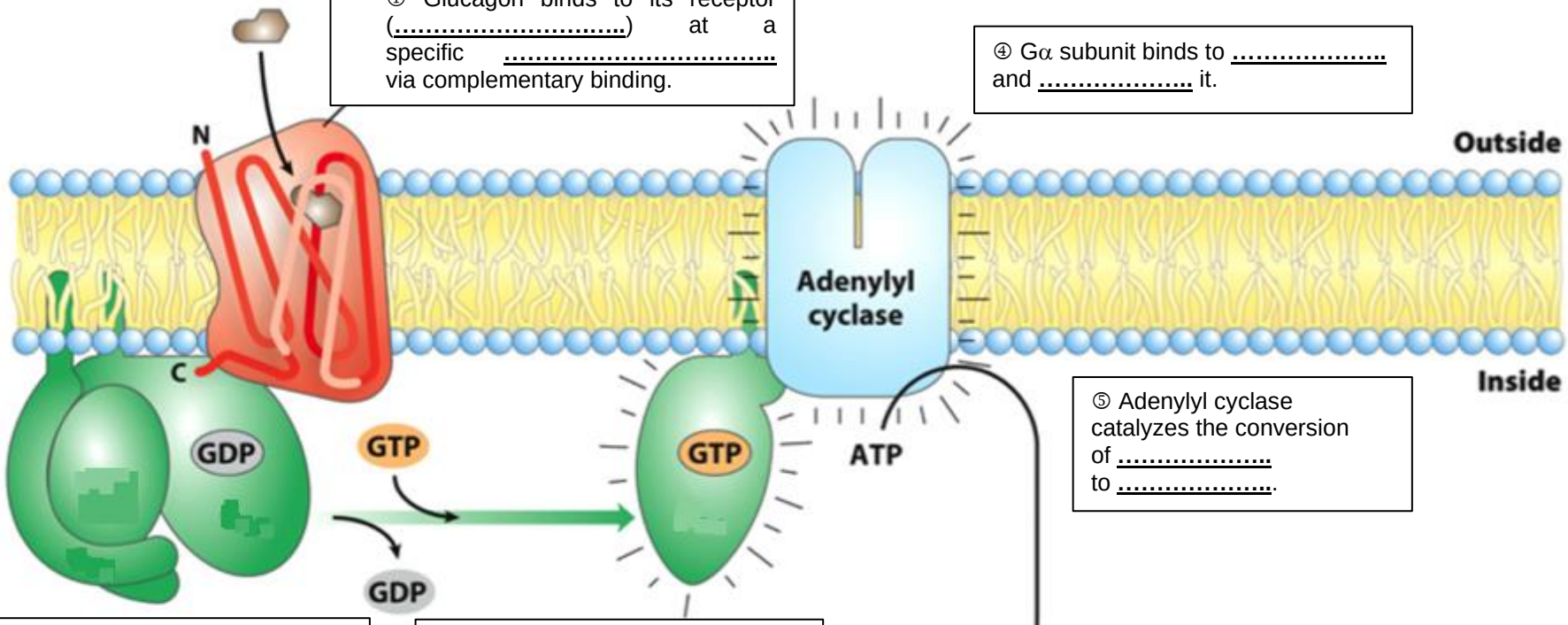


Fig. 4.2. The glucagon signalling pathway

CHECKPOINT (2)

Fill in the blanks below to describe the sequence of events which occur after Glucagon binds to its receptor.



① Glucagon binds to its receptor (……..) at a specific …….. via complementary binding.

② Ligand-receptor interaction causes the receptor to undergo a ……..……., leading to the activation of the G-protein associated to it.

③ …….. on Gα subunit is displaced by ……. This leads to the dissociation of …….. subunit from the …….. dimer (Gβγ).

④ Gα subunit binds to …….. and …….. it.

⑤ Adenylyl cyclase catalyzes the conversion of …….. to ……..

⑥ cAMP, acting as a ……., activates PKA.

⑦ PKA phosphorylates other cellular proteins and enzymes via a ……..……, resulting in cellular response.

⑧ cAMP is cleaved to …….. by …….. thus terminating the signal transduction.

Learning Outcome (p)[modified]:

Outline how insulin regulates the concentration of blood glucose through the tyrosine kinase receptor.

5. Receptor Tyrosine Kinase (RTK)

5.1 Structure of RTK

- Receptor Tyrosine Kinases (RTKs) belong to a major class of **protein receptors** embedded in the cell surface membrane. They are characterised by having **enzymatic activity**.
- Like the GPLR, RTK has three distinct domains:
  - **Extracellular domain**: faces the extracellular fluid and contains the ligand-binding site.
  - **Transmembrane domain**: comprises a single transmembrane α-helix which spans the width of the cell surface membrane, connecting the extracellular and intracellular domains.
  - **Intracellular domain**: faces the cytosol and contains a number of tyrosine amino acid residues. This domain functions as **tyrosine kinase**, which is an enzyme that **catalyses the transfer of phosphate groups from ATP to tyrosine** residues on a substrate protein, activating it.

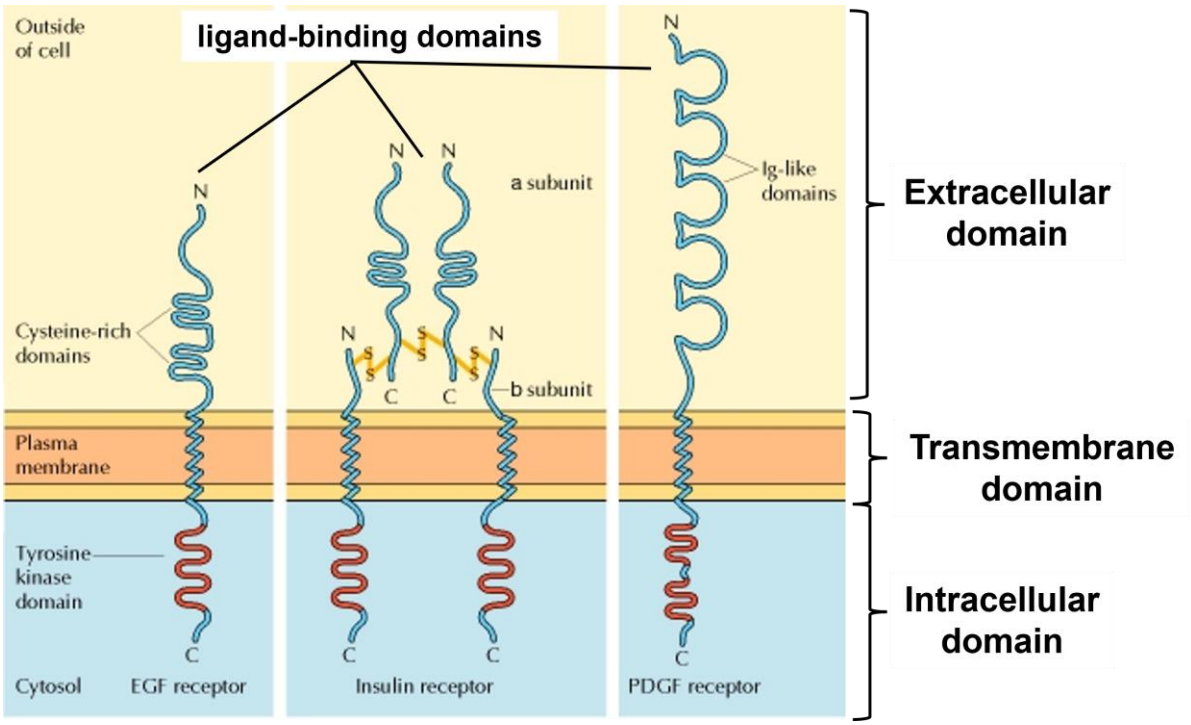
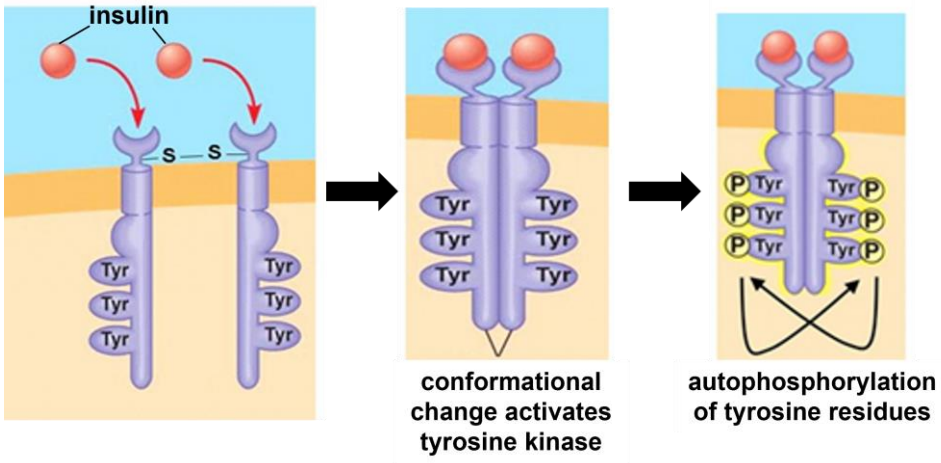
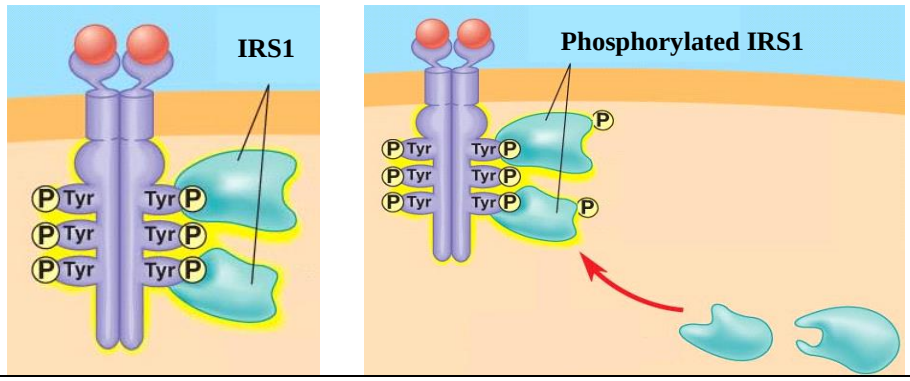


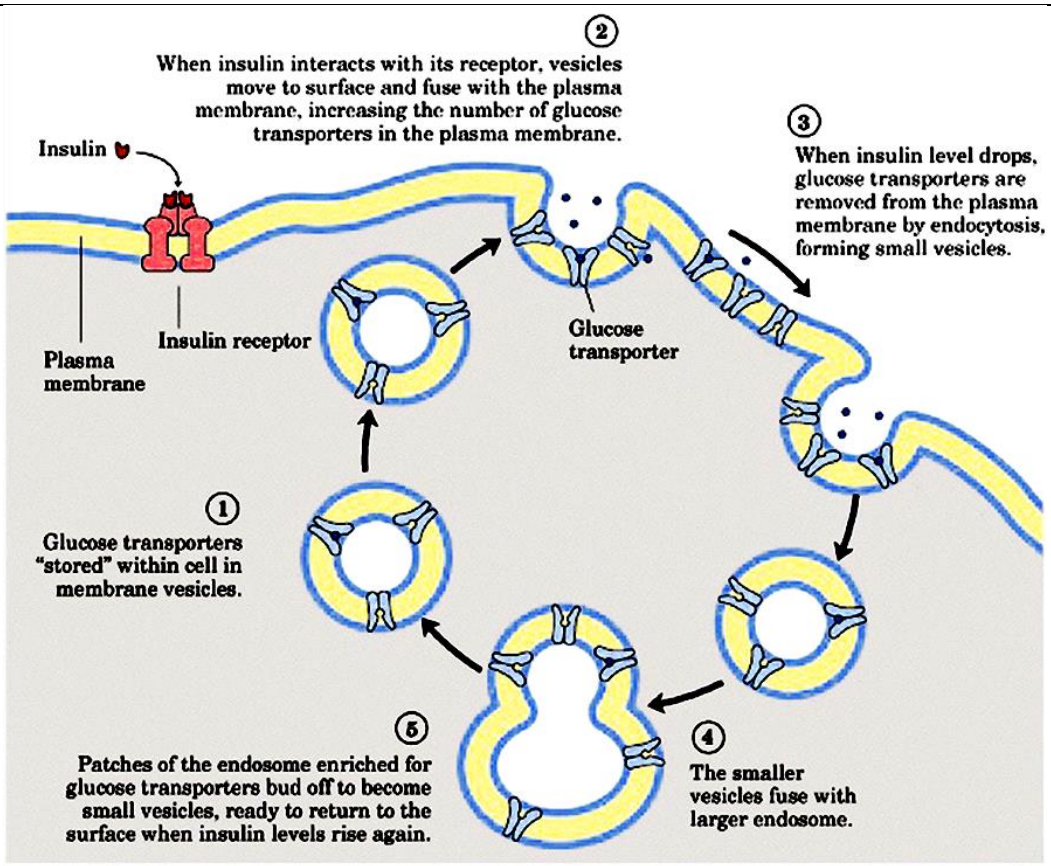
Fig. 5.1: Structure of the RTK

- Most classes of RTKs are single subunit receptors while others exist as multimeric complexes.

5.2 Regulation of Blood Glucose Concentration by Insulin via RTK

Stage	Details
Stimulus	▪ Increase in blood glucose concentration (hyperglycaemia) results in the release of the hormone **insulin** from **β-cells** in the **Islets of Langerhans in the pancreas**. ▪ Insulin is carried by circulatory system to its target cells (in the liver, skeletal muscles and adipose tissues).
Ligand-Receptor Interaction	▪ Insulin, being a **large** and **polar** peptide hormone, is unable to enter the cell. It binds to the extracellular ligand-binding site of RTK on the surface of target cells. ▪ Ligand-receptor interaction triggers a **conformational change** (receptor dimerization) in RTK. The **tyrosine kinase** in the cytoplasmic domain of RTK is activated. ▪ The activated tyrosine kinase of each receptor **phosphorylates the tyrosine residues** (at the cytoplasmic tails) of the other receptor in a process known as **autophosphorylation** or **cross-phosphorylation.** 
Signal Transduction	▪ The phosphorylated tyrosine residues (phosphotyrosines) then serve as **docking ports** for **insulin receptor substrate 1 (IRS1)**. IRS1 undergoes phosphorylation and becomes activated.

	▪ Activated IRS1 goes on to **phosphorylate** other relay proteins leading to **phosphorylation cascade** which **amplifies** the signal. 
Cellular Response	1. **<u>Increased glycogenesis</u>**. Activation of glycogen synthase results in increased conversion of excess glucose into glycogen. 2. **<u>Decrease glycogenolysis</u>**. Inactivation of glycogen phosphorylase results in decreased hydrolysis of glycogen to glucose. 3. **<u>Decreased gluconeogenesis</u>**. Reduction in the rate of glucose synthesis from non-carbohydrate sources e.g. amino acids and fatty acids. 4. **<u>Increased glucose uptake into cells</u>**. Increase in number of glucose transporters on cell surface membrane due to: a. **Increased expression of genes coding for glucose transporters** (e.g. GLUT4), which facilitate uptake of glucose into cells via facilitated diffusion. b. **Increased translocation of vesicles containing glucose transporters towards cell surface membrane**. When these vesicles fuse with the cell surface membrane, glucose transporters are embedded on the membrane and facilitate uptake of glucose into the cell.



All of the above metabolic reactions cause **blood glucose level to decrease back to normal**.

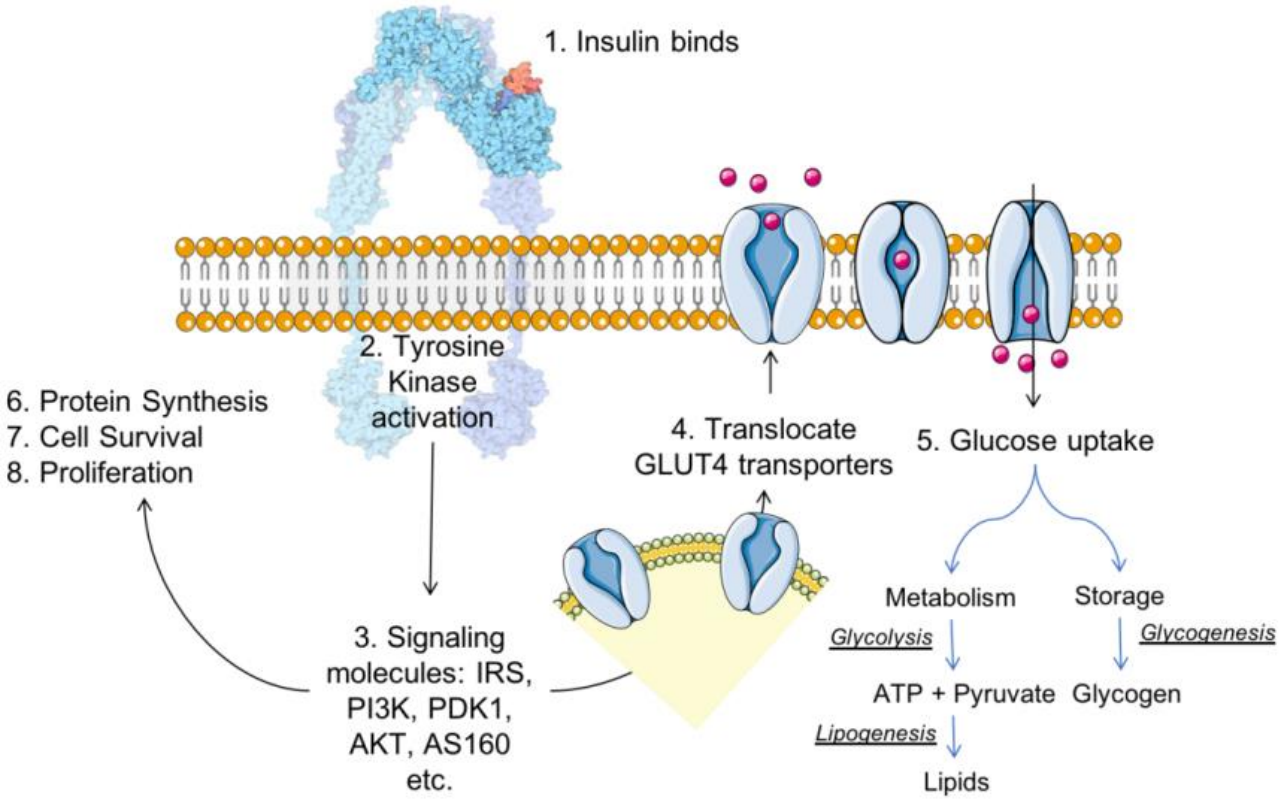
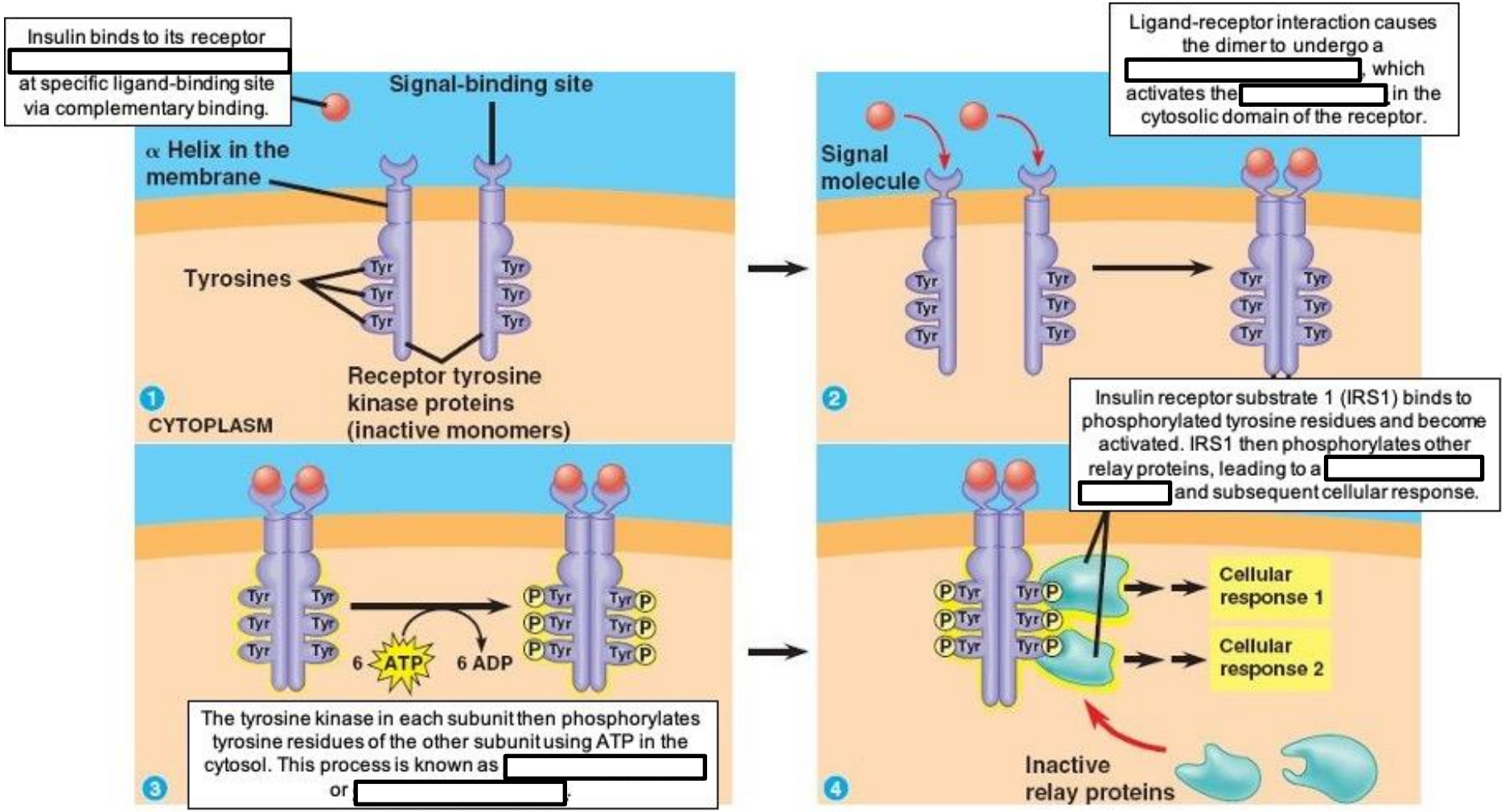


Fig. 5.2. The insulin signalling pathway

CHECKPOINT (3)

Fill in the blanks below to describe the sequence of events which occur after Insulin binds to its receptor.



6. Advantages of Cell Signalling pathways in multicellular organisms

1. Signal Amplification

- Use of cell signalling pathway allows amplified cellular responses to single signal molecule.
- Binding of **one** signal molecule (first messenger) can lead to production of **multiple second messengers** to activate **multiple protein kinases** involved in triggering cellular responses.

2. Target specificity

- Hormones only bind to specific receptors with **complementary ligand-binding sites**. This allows for specific target cells to respond to signal molecules secreted into the bloodstream.
- E.g., insulin binds liver cells but not to brain cells.

3. Simultaneous activation of multiple cells

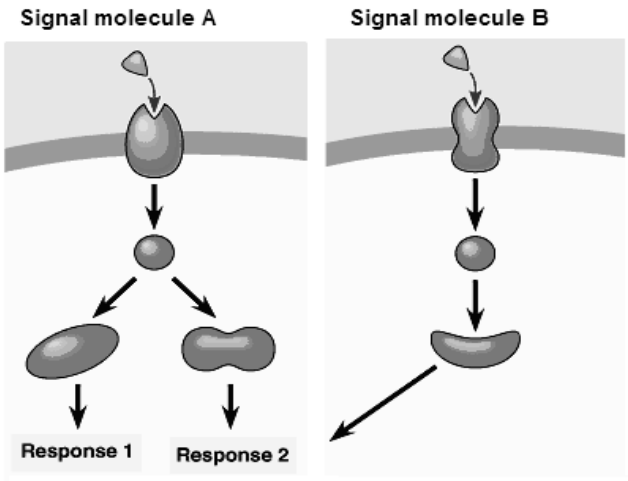
- Certain physiological processes **require multiple organs / cells to respond in a coordinated manner** to restore homeostatic conditions. A single type of signal molecule can bind to multiple cell types with the same receptors and activate them at the same time.
- E.g., insulin binds both liver and muscle cells to effect a decrease in blood glucose concentration back to normal.

4. Trigger numerous cellular responses in a single cell

- Binding of one signal molecule to receptor can trigger different chemical reactions (cellular responses) in the cell.
- E.g., insulin triggers increased glucose uptake, increased glycogenesis and decreased glycogenolysis.

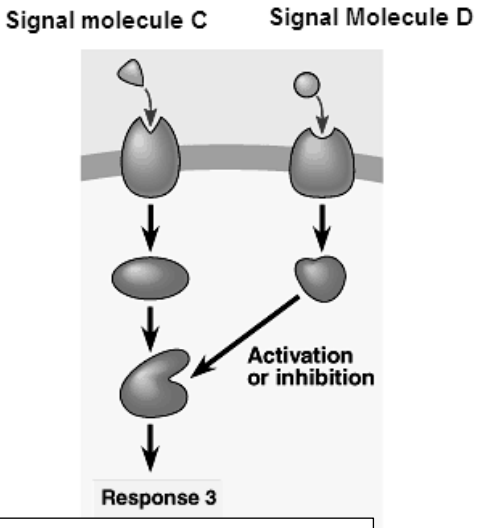
5. Regulation of cellular response

- Multistep pathways afford greater opportunity for coordination and regulation allowing for fine-tuning of cellular response.



Branching – e.g. binding of glucagon stimulates gluconeogenesis and glycogenolysis.

Interaction – e.g. binding of epinephrine also stimulates glycogenolysis.



Interaction – e.g. binding of insulin stimulates glycogenesis but binding of epinephrine inhibits it.

CHECKPOINT (4)

Fill in the table below to summarise the effects of the hormones Glucagon and Insulin.

Name of Hormone	Name of Receptor	Cellular Response	Effect on blood glucose level
Glucagon		1) Glycogen _____ is activated, hence glycogen is _____. 2) Glycogen _____ is inactivated, hence glycogen is _____.	
Insulin		1) Glycogen _____ is activated, hence glycogen is _____. 2) Glycogen _____ is inactivated, hence glycogen is _____. 3) Increase in translocation of _____ (GLUT) to cell surface membrane, which results in increased uptake of _____ into the cell.	

CHECKPOINT (5)

*State if each of the following statement is true (**T**) or false (**F**).*

(a)	Binding of ligand to the receptor causes change in the receptor conformation.	T / F
(b)	Testosterone-receptor complex can enter the nucleus to alter the rate of transcription of genes.	T / F
(c)	Kinases are a group of enzymes which phosphorylate other molecules.	T / F
(d)	Activation of G-protein activates adenylyl cyclase to convert cAMP to ATP	T / F
(e)	Insulin binds to receptor tyrosine kinase.	T / F
(f)	Glycogen binds to G-protein linked receptor.	T / F
(g)	ATP is a second messenger.	T / F
(h)	IRS-1 is a second messenger.	T / F
(i)	Oestrogen hormone is a first messenger.	T / F

Glossary of Terms

Cell signalling

The processes in which cells are stimulated or inhibited by extracellular signals, usually chemical signals produced by other cells.

Signal transduction pathway

A mechanism linking a mechanical or chemical stimulus to a specific cellular response.

Signal transduction

Conversion of a signal from one physical or chemical form to another (e.g., conversion of light to a chemical signal, or of an extracellular signal to an intracellular signal).

Signal amplification

Process of enhancing signal strength as a signal is relayed through a signal transduction pathway, with each component in the pathway activating multiple copies of the next component; allowing for a small quantity of the signal molecules to elicit a large cellular response from the target cell.

Protein kinase

An enzyme that catalyses the transfer of phosphate groups from ATP (or GTP) to a protein e.g., protein kinase A

Protein phosphatase

An enzyme that removes phosphate groups from proteins (dephosphorylation), often functioning to reverse the action of protein kinase.

Second messenger

A small non-protein, water-soluble molecule, or ion, such as calcium ion (Ca^{2+}) or cyclic AMP, which relays a signal to a cell's interior in response to a signalling molecule bound by a signal receptor protein.

Cyclic AMP (cAMP)

A form of adenosine monophosphate in which the phosphate is part of a ring-shaped structure. It functions as an intracellular second messenger in eukaryotic cells, mediating the effects of various signalling molecules by activating protein kinase A. It is also a regulator of some bacterial operons (e.g., the *lac* operon).

Adenylyl cyclase (or adenylate cyclase)

An enzyme located on the cytosolic face of the plasma membrane that catalyses the synthesis of cAMP from ATP. It is activated by specific ligand-receptor interactions on the extracellular face of the plasma membrane that results in active G proteins.

Protein kinase A

A serine or threonine kinase, activated by the second messenger cAMP, that catalyses the phosphorylation of serine or threonine residues in target proteins.

G-protein coupled receptor (GPCR) / G-protein linked receptor (GPLR)

A cell surface receptor that upon binding of the signal molecule, undergoes a conformation change that causes it to bind and activate a specific G-protein.

Receptor tyrosine kinase (RTK)

A cell surface receptor with enzyme (tyrosine kinase) activity. Upon binding of a signal molecule, undergoes dimerization which activates its kinase activity to catalyse the transfer of phosphate groups from ATP to tyrosine residues on itself or, other cytoplasmic substrates. The phosphorylated tyrosine then activates other signal transduction proteins inside the cell.

RTK that binds insulin, however, already exists as a dimer prior to insulin binding.