

## Communication & Signalling

Multicellular organisms

Cells in multicellular organism communicate using extracellular signalling molecules

Signal Molecule Examples

1. Steroid Hormones (testosterone & oestrogen)
2. Peptide Hormones (insulin)
3. Neurotransmitters

General Mechanism

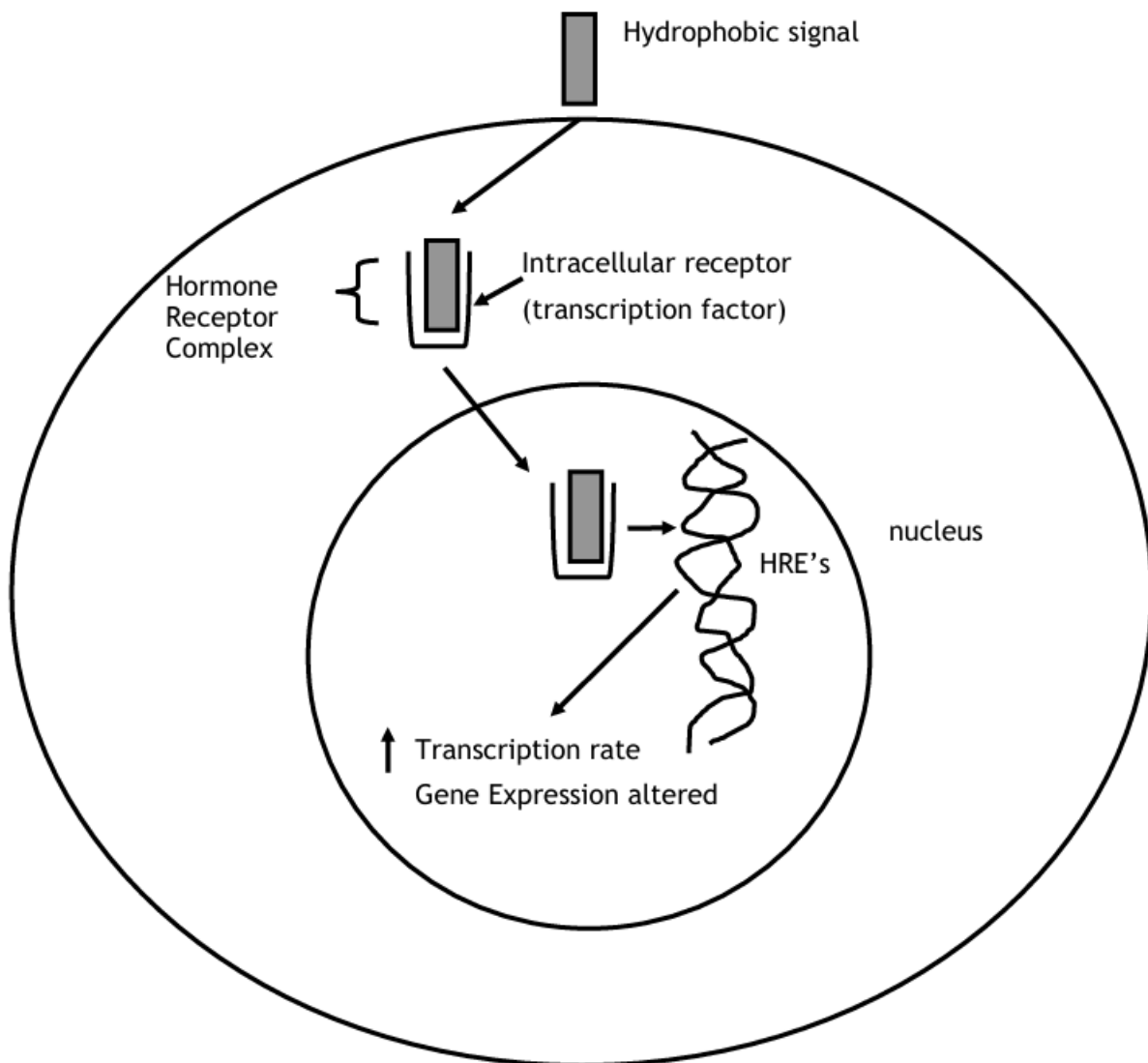
1. Receptor molecules are proteins found on the surface of the plasma membrane or within the cytosol/nucleus of the target cell.
2. These receptors have a binding site for a specific extracellular signal molecule
3. The binding of the signal molecule (ligand) changes the conformation of the receptor
4. This initiates an intracellular response within the cell.

| Type of Signalling Molecule | Molecule can pass through membrane | Location of receptor | Examples of extracellular signal                 |
|-----------------------------|------------------------------------|----------------------|--------------------------------------------------|
| Hydrophilic                 | no                                 | Plasma membrane      | Peptide hormones (insulin)<br>Neurotransmitters  |
| Hydrophobic                 | yes                                | Cytosol or nucleus   | Steroid Hormones<br>(testosterone and oestrogen) |

## Hydrophobic Signalling

Extracellular hydrophobic signals (steroid hormones oestrogen/ testosterone)

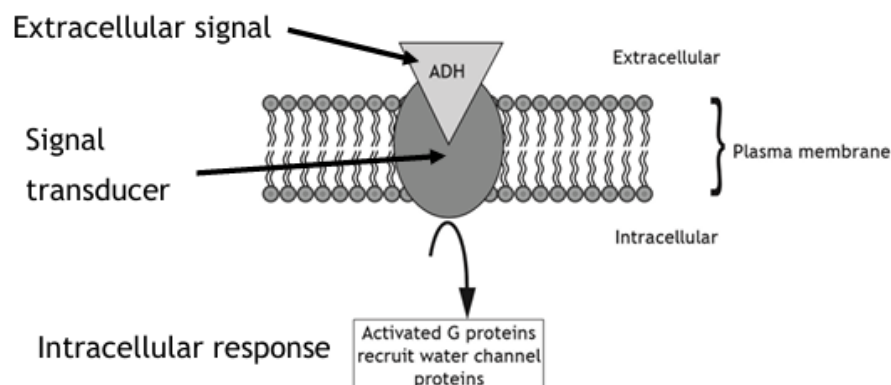
1. Hydrophobic signalling molecules can diffuse directly through the phospholipid bilayers of membrane
2. They bind to specific intracellular receptors (transcription factors) found in the cytosol/nucleus forming the hormone receptor complex.
3. The hormone-receptor complex moves to the nucleus where it binds to specific sites on DNA called hormone response elements (HREs).
4. This influences the rate of transcription affecting the gene expression of many different genes.



## Hydrophilic Signalling

Extracellular hydrophilic signals (peptide hormones/neurotransmitters)

1. These signal molecules (ligands) cannot enter the cytosol but instead bind to the extracellular face of transmembrane surface receptors, changing their conformation.
2. The activated transmembrane receptors then act as a signal transducers by converting the extracellular ligand-binding event into intracellular signals i.e. transducing the signal;
3. These intracellular signals involve G proteins or cascades of phosphorylation by kinases
  - (a) G protein intracellular Mechanism  
G-proteins relay signals from activated receptors to target proteins (enzymes/ ion channels)



### (b) Phosphorylation cascade Intracellular Mechanism

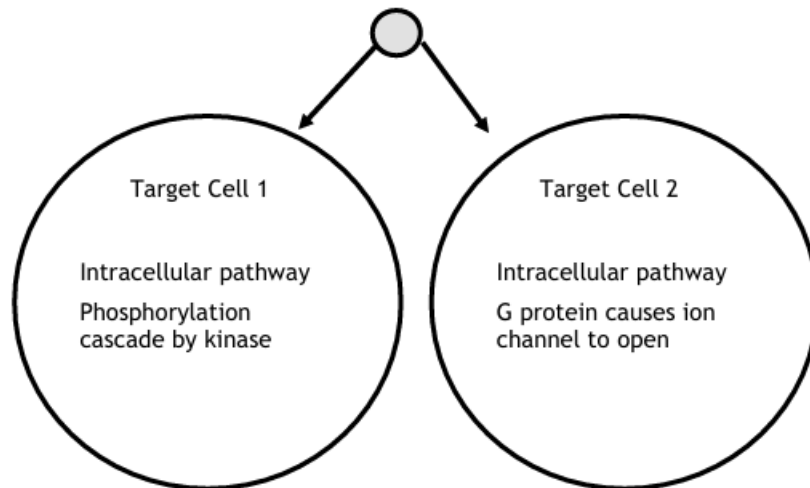
One kinase activates the next in the sequence through phosphorylation. These cascade result in

- (i) Phosphorylation of many proteins as a result of the original signalling event.
- (ii) Activation of more than one intracellular signalling pathway

## Communication & Signalling

### Tissue Specific Response

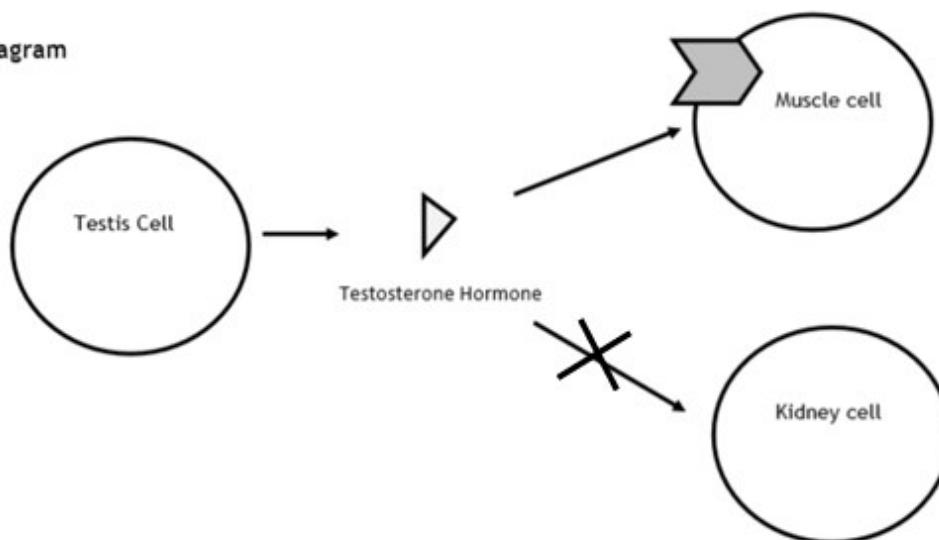
The same signal may have different effects on different target cell types due to differences in the intracellular signalling molecules/pathways.



### Target vs Non Target Cells

Different cells produce specific signals that can only be detected and responded to by cells with the specific receptor

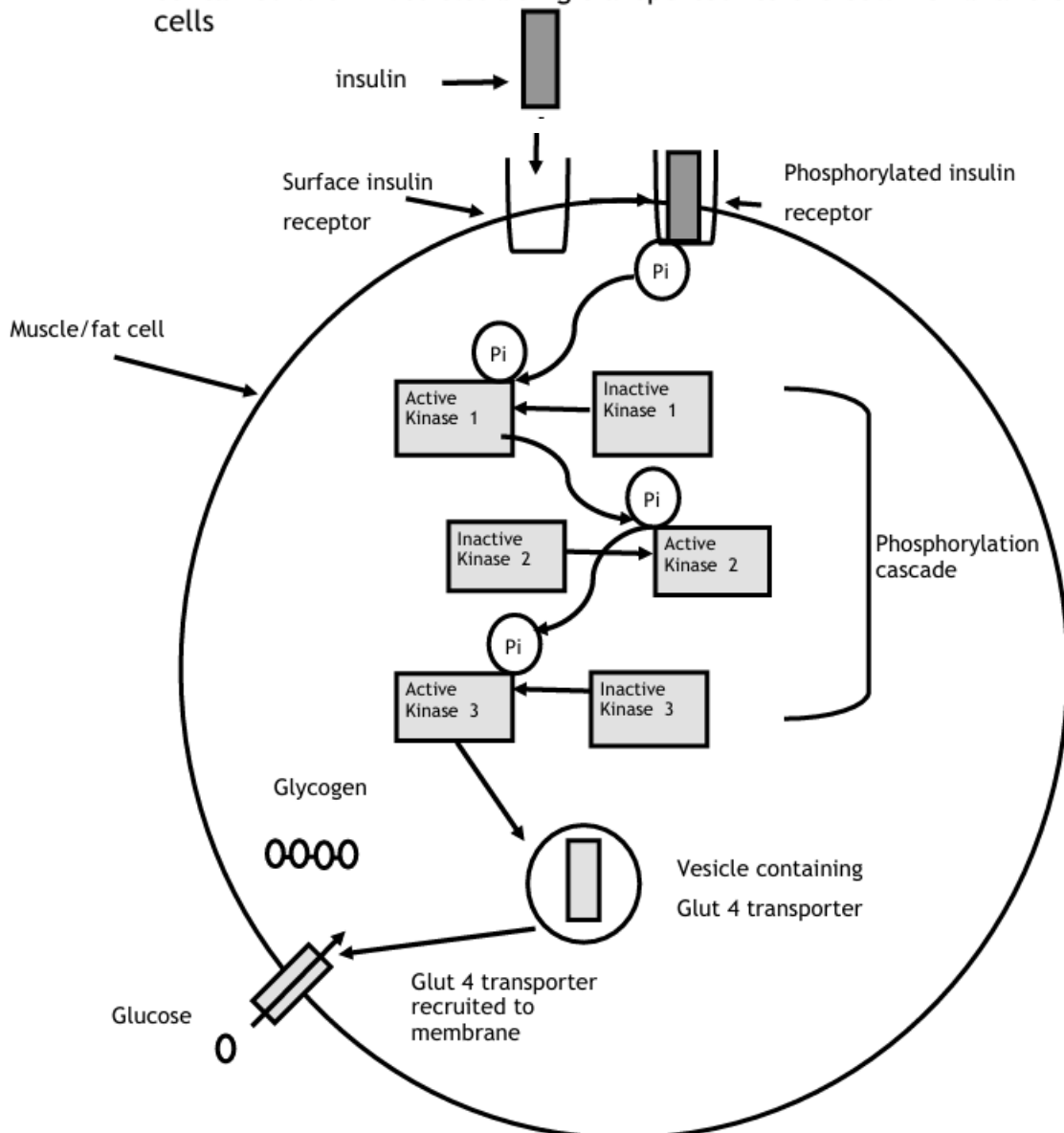
Diagram



## Hydrophilic Signalling: Insulin and Diabetes Mellitus

### Insulin Signalling Mechanism

1. Insulin cannot enter the cytosol but instead binds to the extracellular face of its transmembrane surface insulin receptor on muscle/fat cells.
2. This causes a conformational change in the insulin receptor that triggers a phosphorylation cascade as the intracellular response.
3. The insulin receptor is phosphorylated and acts as a kinase by phosphorylating the next kinase in the series of reactions.
4. This phosphorylation cascade eventually causes GLUT4 glucose transporter proteins contained within vesicles being transported to the cell membrane of fat and muscle cells



## Hydrophilic Signalling: Insulin and Diabetes Mellitus

Diabetes mellitus

Type 1

Failure to produce insulin

Type 2

Loss of receptor function

Generally associated with obesity

Solution

Exercise triggers recruitment of GLUT4 improving glucose uptake in fat/ muscle cells

