SEASON 2

# Understanding Cancer

## Lecture 3
## Types of cell signalling

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# RECAP:

## *What you hopefully should understand so far from Lecture 2*

- There are **8 hall marks of cancer developed by Hanahan and Weinberg: sustained proliferative signalling, evading growth suppressors, resisting apoptosis, enable replicative immortality, invasion and metastasis, angiogenesis, reprogramming energy metabolism and avoiding immune destruction**.
- There are **two contributing factors**: **genomic instability and tumour-promoting inflammation that underlies most of the hallmarks of cancer.**
- **The cell cycle** presents the phases in how **normal cells divide and grow. There are four phases: Gap 1 (G1), S phase, Gap 2 (G2) and Mitosis (M).**
- **There are two types of apoptotic pathways and depend on molecular scissors called caspases: intrinsic and extrinsic.**
- **Cancer cells interact with other cells in the EMT in order to invade and metastasise.**

# What will we learn today?

- What is cell signalling?
- Signalling type one: Paracrine signalling
- Signalling type two: Contact dependent signalling
- Signalling type three: Autocrine signalling
- Signalling type four: Endocrine signalling

# GENTLE REMINDER
# An ideal way of learning:

| Monday | Tuesday | Wednesday | Thursday | Friday | Saturday | Sunday |
|---|---|---|---|---|---|---|

5 Mini-lectures.

Approximate total time: 1 hour

**Divide over 7 days** at your **own pace**.

**Challenge yourself** with a quiz!

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# RECAP: How to support your learning?

- **Key facts with diagrams by HN designs presented in a simplified way.**
- **Glossary to help understand what key words mean.**
- **Summary doodle revision posters by HN designs.**
- **Quizzes to test your knowledge and reflect.**
- **Reference list for further reading.**

**Acknowledgements: Special thanks to my parents, family, friends and colleagues for their support and the respected teachers and health professions who taught me and installed the passion of cancer/oncology.**

# What is cell signalling?

# Key Facts: What is cell signalling?

**Cellular signalling** is **how cells communicate** and involves **three key steps:**

## RECEPTOR ACTIVATION

1

- A **internal or external stimuli** is activated when **bound to its specific receptor.**
- A stimuli is a **signal that can influence the properties of the cell.**

## SIGNAL TRANSDUCTION

2

- This step requires **cellular proteins and enzymes** that convert **the signal** to another signal forming a pathway.

## CELLULAR RESPONSE

3

**Target regulatory genes are transcribed in the nucleus** to make **changes to the protein levels made** to **start a response: growth, movement, differentiate to specialised cells, cell death and protein synthesis.**

**Dysregulation of cellular signal transduction pathways** underlies **most of hallmarks of cancer**.

Other **intracellular targets** are:

1) **Structural proteins** to **alter the shape of the cell.**

2) **Enzymes** that are involved in **chemical reactions of the cell.**

There are **different types of signalling pathways** and vary based on the **distance** travelled to reach the **target cells.**

# The Signalling Pathway

Step1 — Ligand(signal)

Step2 — Receptor

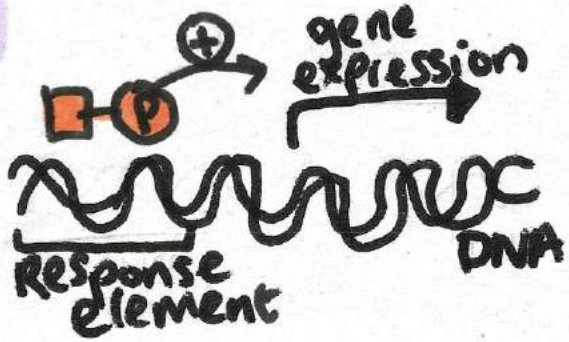
Step3 — Intracellular effector

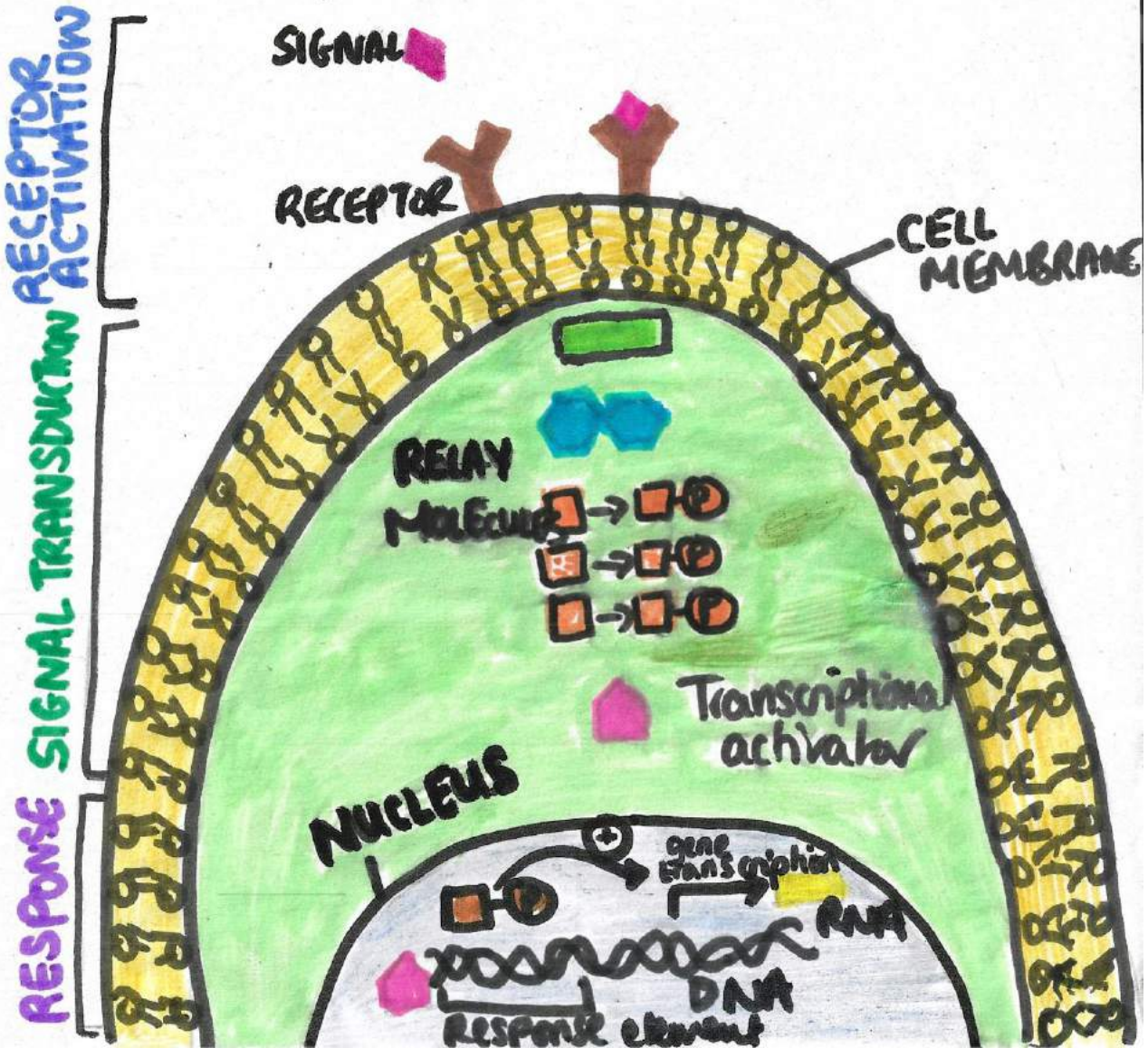
Step4 — Intracellular Transducers

Step5 — Secondary messengers cascade

Step6 — Transcription Factor

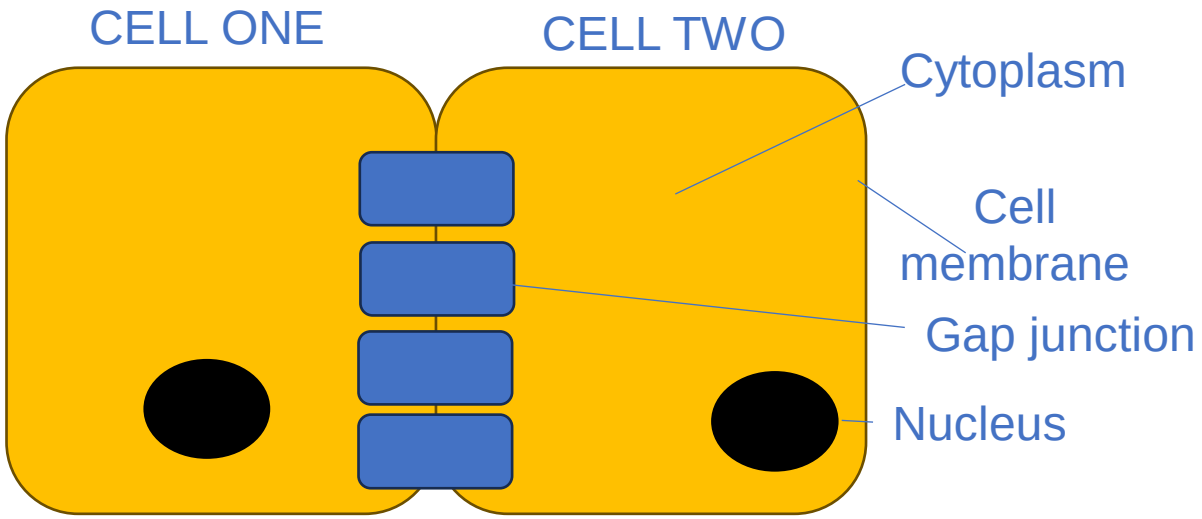
Step7



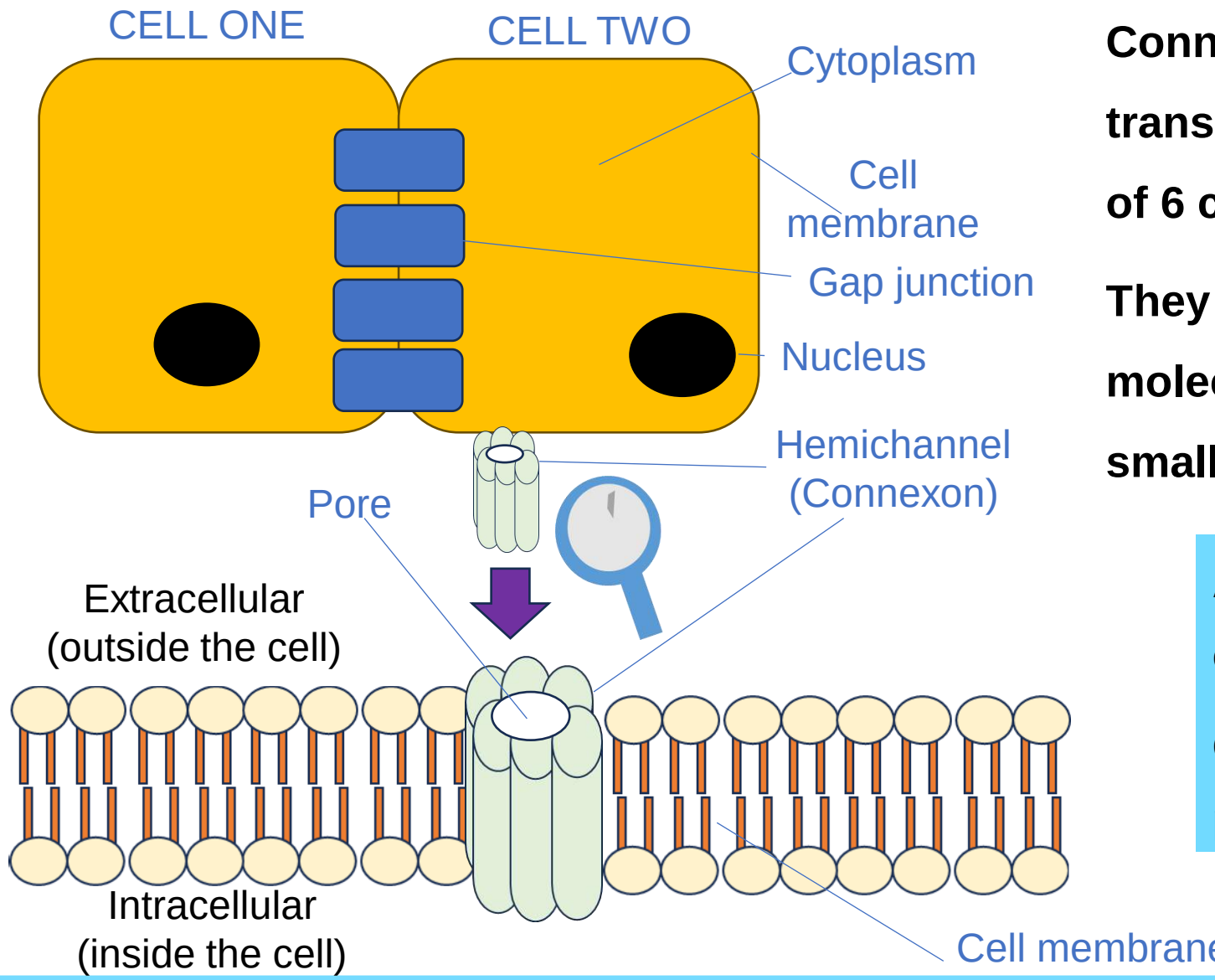
# Signalling type one: Paracrine signalling

# Key Facts: What is paracrine signalling?




A signal that is transmitted from **a cell connected by gap junctions to a nearby cells/adjacent cells.**

# Key Facts: Connexons



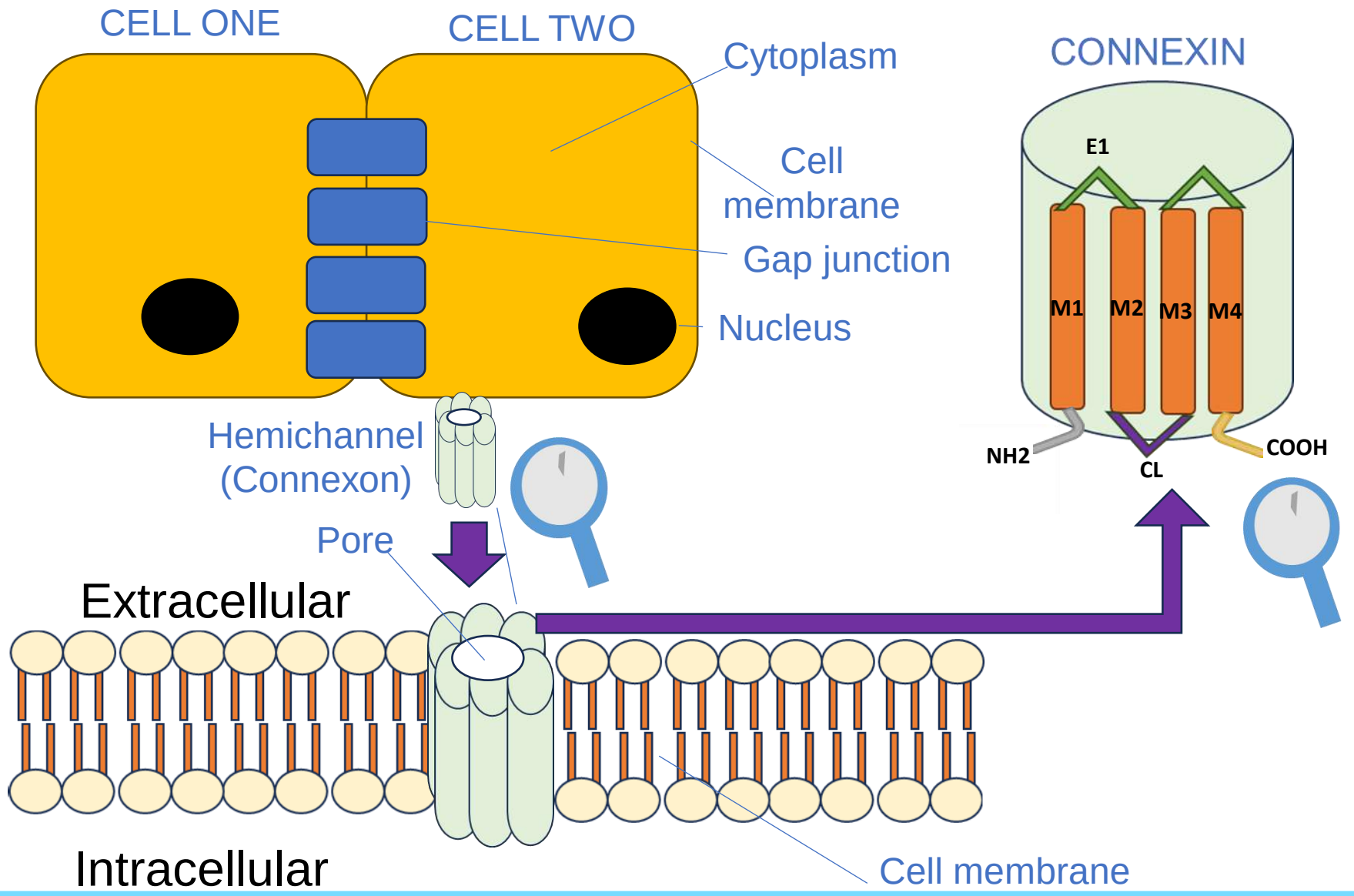

**Connexon hemichannels** are pore-forming **transmembrane protein channels made of 6 connexin proteins.**

**They help release signalling molecules/ligands e.g. ATP and uptake small molecules e.g. glucose.**

**ATP (adenosine triphosphate)** is the **energy source** used by **all cells.**

**Glucose** is a **sugar molecule** used to **produce energy.**

# Key Facts: Connexins




**Connexin** consist of:

- **Four membrane- spanning domains (M1, M2, M3, M4).**
- **Two extracellular loops (E1 and E2)**
- **One cytoplasmic loop (CL).**

# Key Facts: What are the features of a paracrine signalling pathway?

**Local signals**

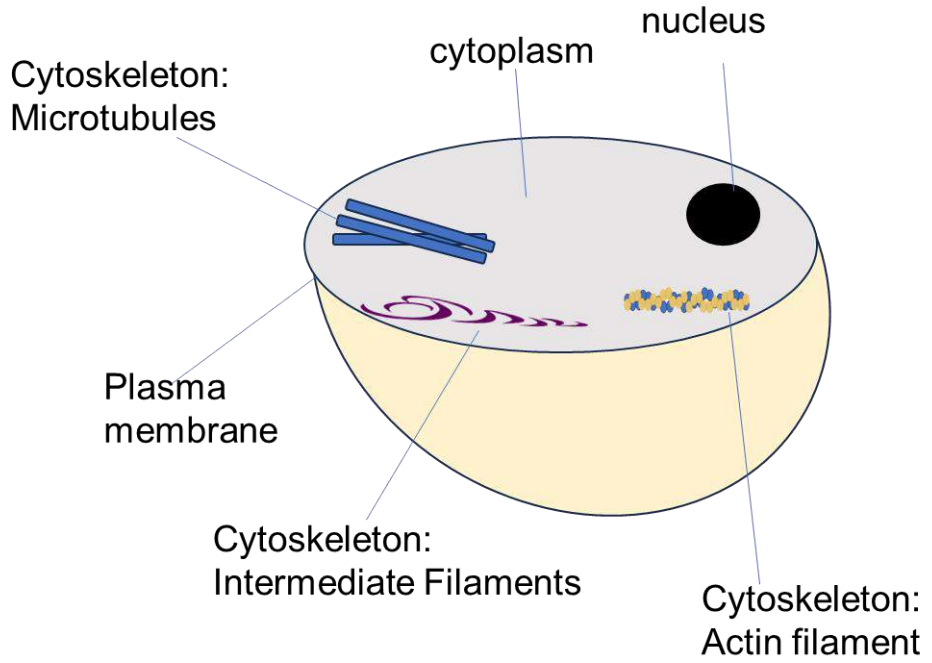
**Local levels or concentrations are high.**

**They can be degraded by enzymes or removed by neighbouring cells.**

**The signals move by a process called diffusion via the extracellular matrix (ECM) to allow quick responses.**

**The cell producing/secreting the signalling molecule/ligand affects target cells only, not itself.**

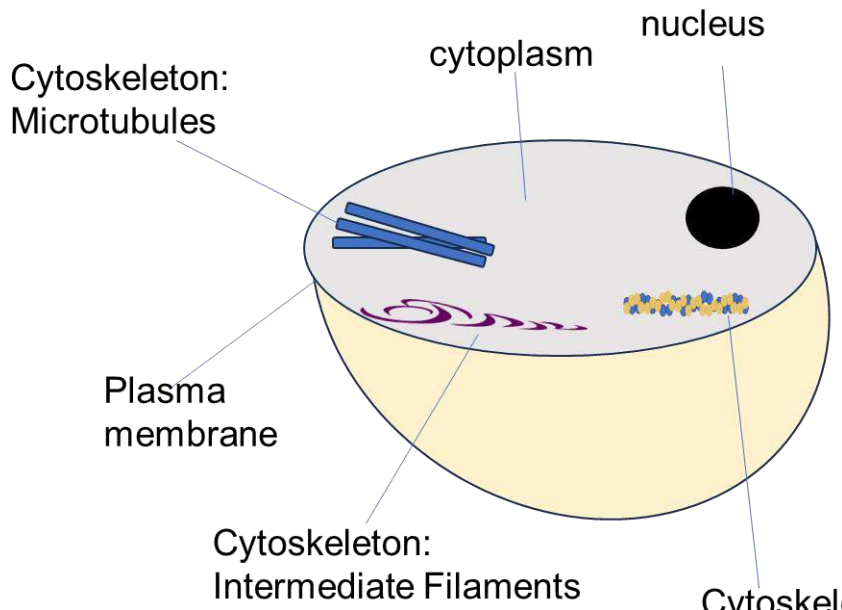
## ANIMAL CELL

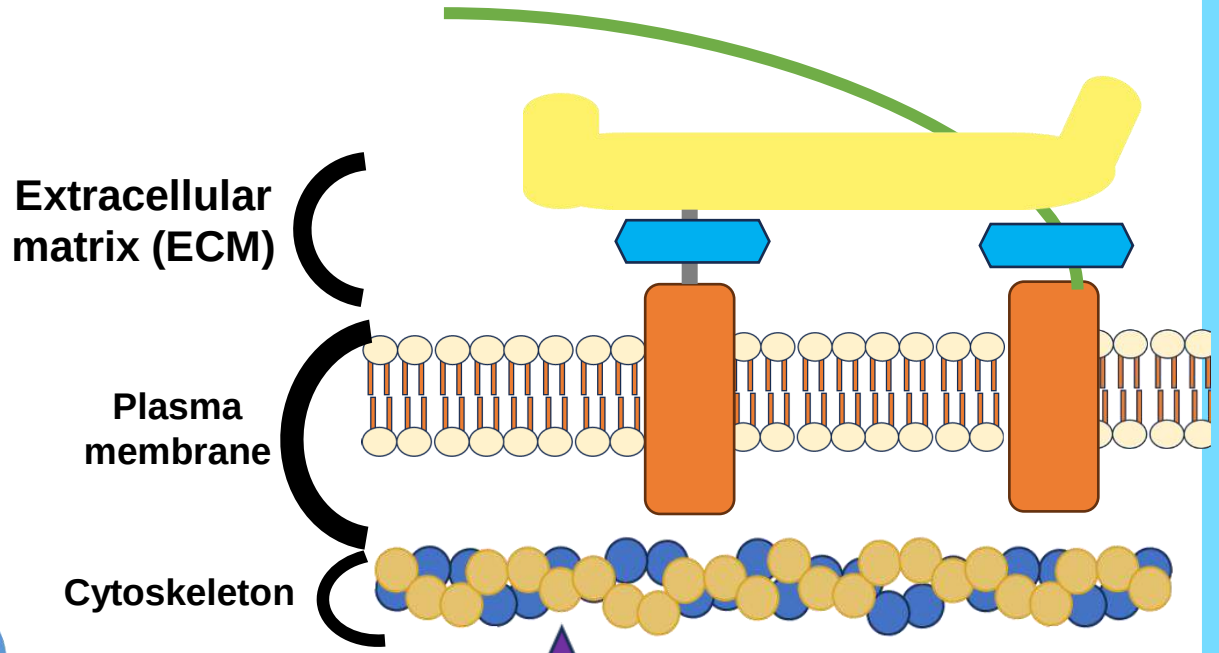


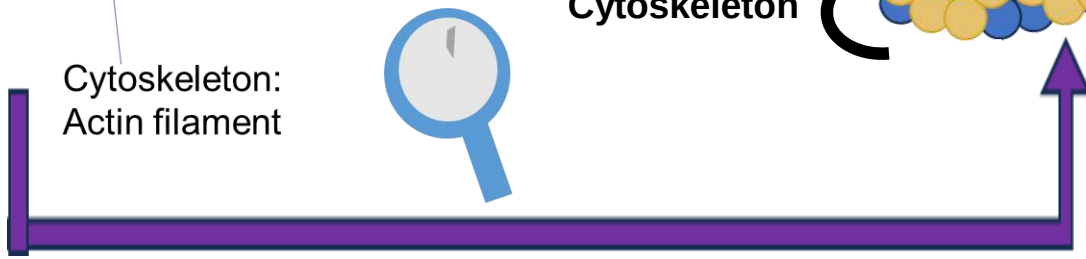

**Cytoskeleton:** It consists of **three types of proteins** that help the cell with **shape, movement and organisation.**

**ECM:** It forms a **meshwork of proteins secreted from cells.** This adds further adds **strength and support**.

# Key Facts: A closer look.




Glycoprotein

Integrin

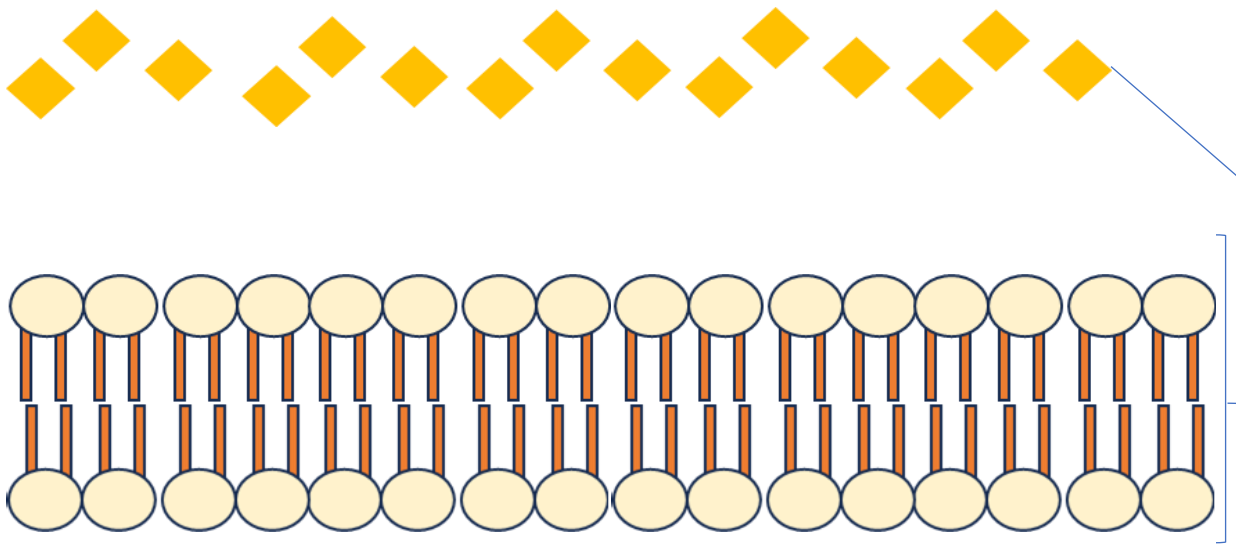
Actin filament

Collagen

Elastin

Fibronectin

# Key Facts: Diffusion.



**Extracellular**

(outside the cell)

Signaling Molecule (high concentration)

Cell membrane

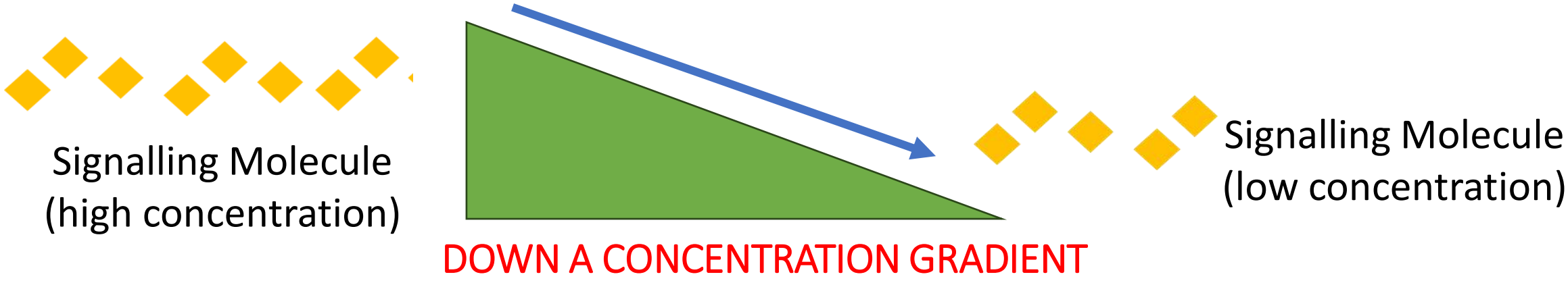
**Intracellular**

(inside the cell)

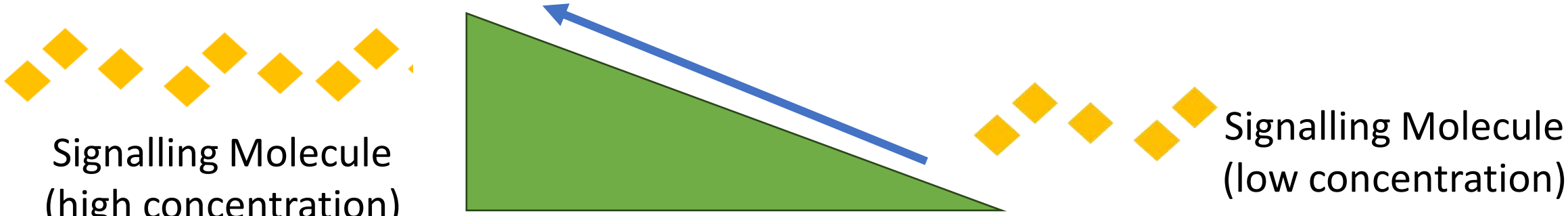
Signaling Molecule
(low concentration)

**Diffusion** is a **type of movement of particles moving from a high to a low concentration down a concentration gradient.**

# Key Facts: Concentration gradient




DOWN A CONCENTRATION GRADIENT




AGAINST THE CONCENTRATION GRADIENT (requires energy as ATP)

A **concentration gradient** is **the difference between two areas**.

# Key Facts: Example

## NEUROTRANSMITTERS

They are **chemical ligands** that transmits signals via **adjacent cells.**

# Key Facts: Example

- The **nervous system** is one of the organ systems found in the body.

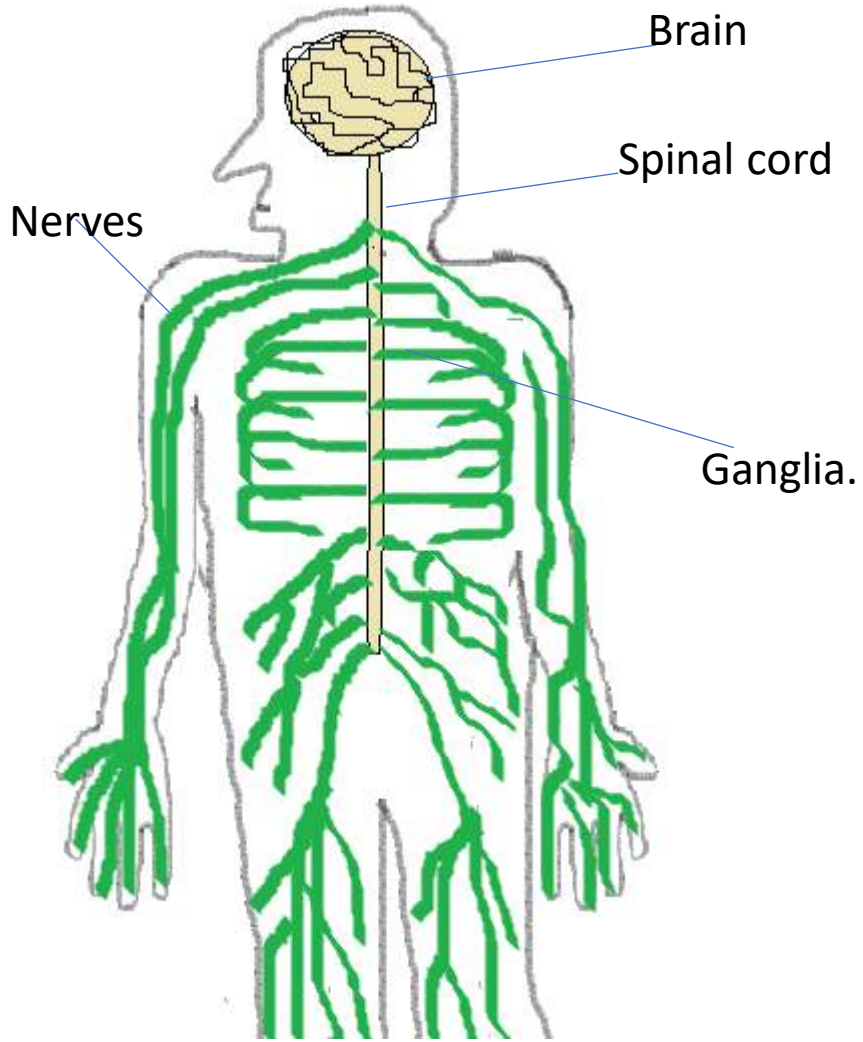
- It is divided into two types of systems:

**1) CENTRAL NERVOUS SYSTEM**

BRAIN AND SPINAL CORD

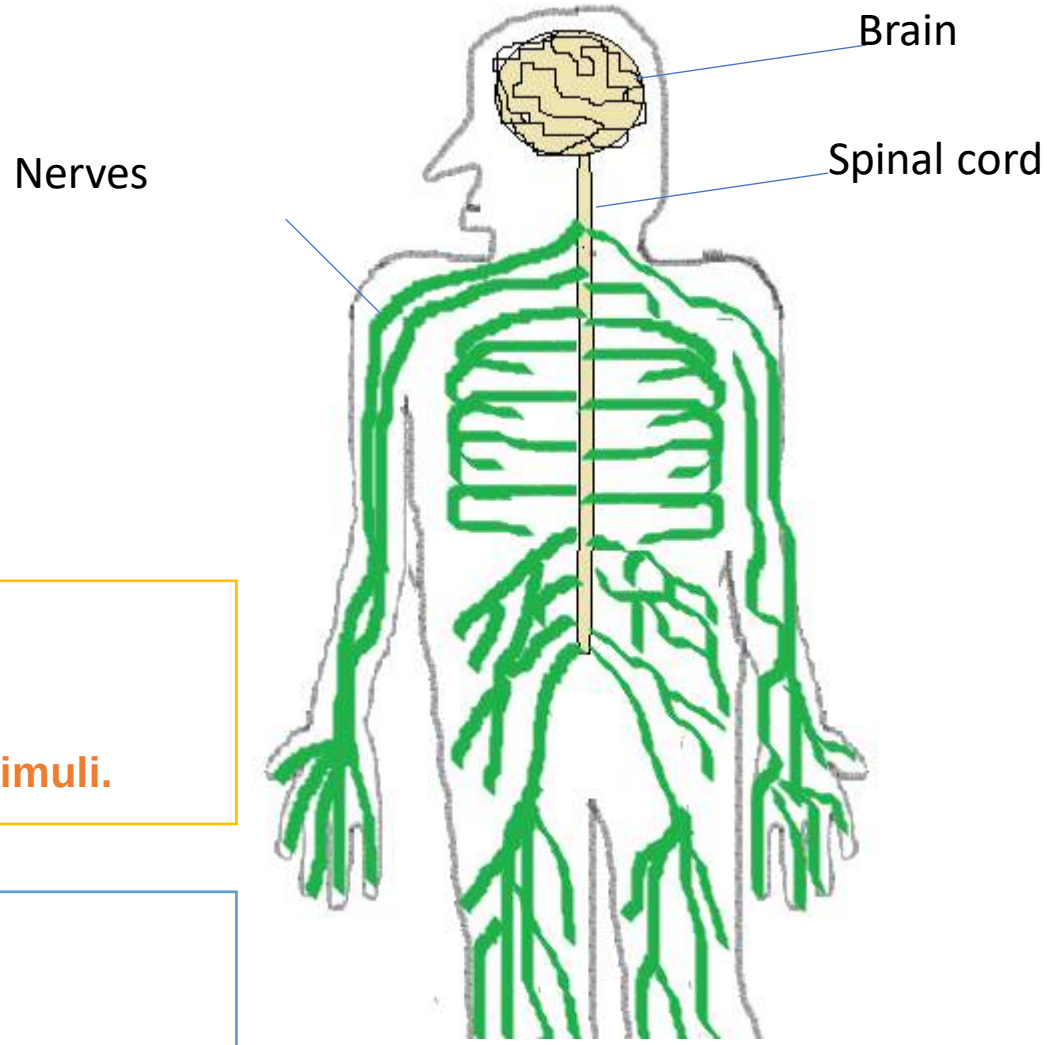
**2) PERIPHERAL NERVOUS SYSTEM.**

NERVES



# Key Facts: Example

The **role of the nervous system** is to **communicate via electrical messages (impulses)** to **coordinate a response to stimuli e.g. change to temperature, taste, protect from danger.**

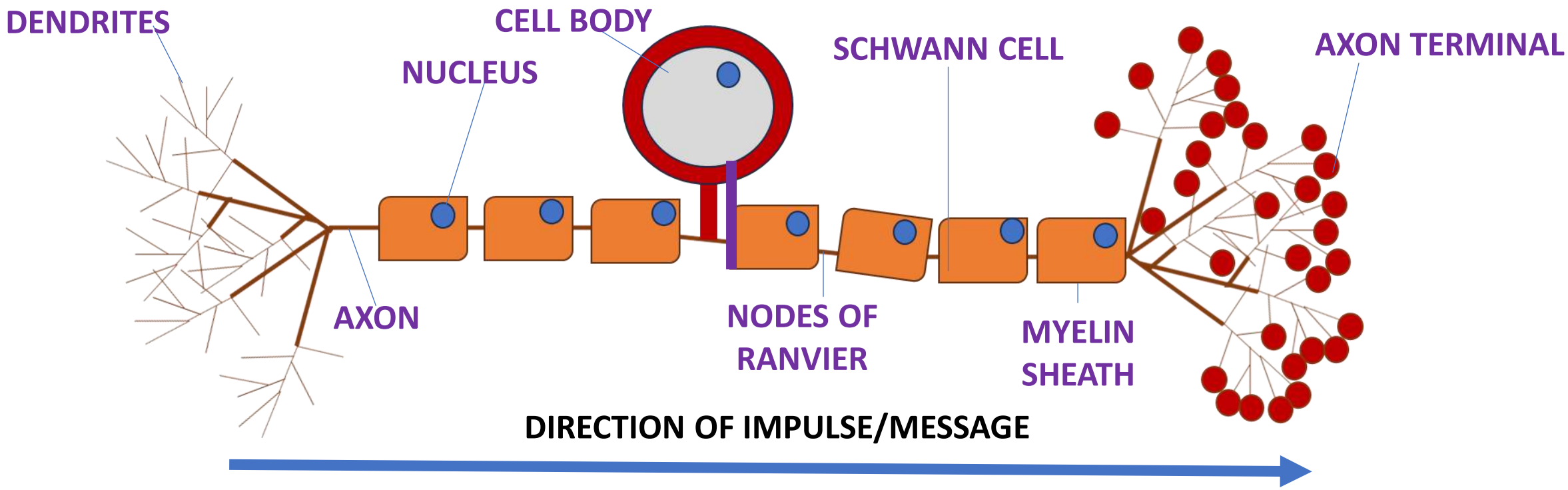



## Central Nervous System

- It consists of the **brain and spinal cord.**
- **It receives information and coordinates responses to stimuli.**

## Peripheral Nervous system

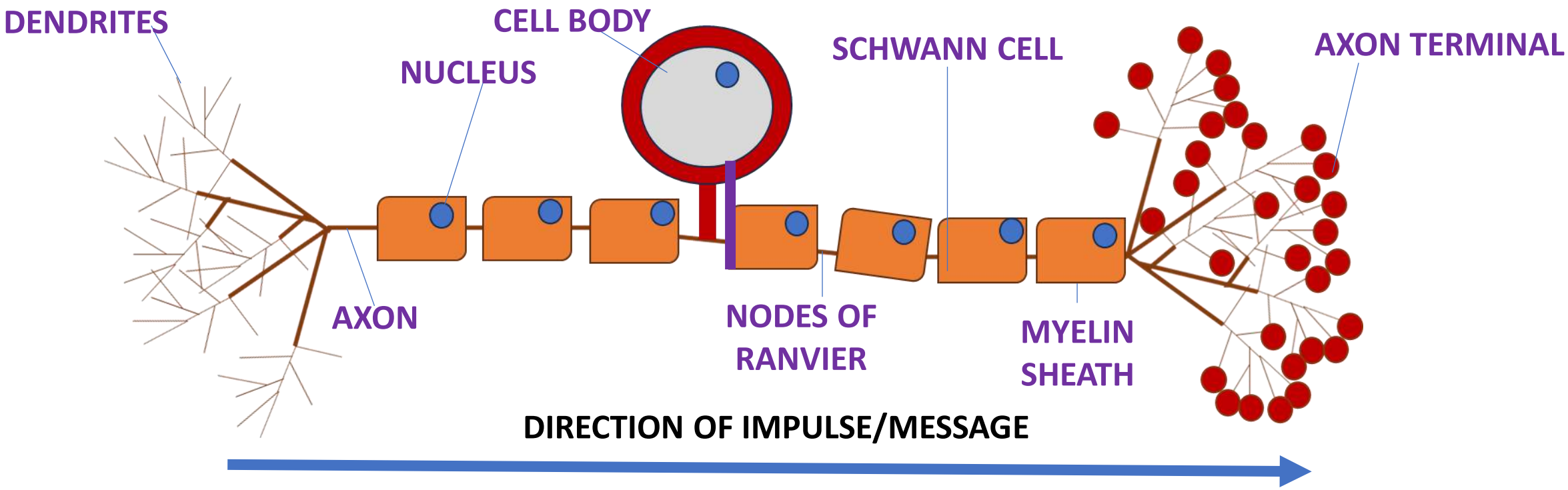
- It consists of **connective nerves.**
- **The nerves connected to the sense organs and to the effectors (muscle/glands) to conduct the response.**




**Nerve cells** otherwise known as **neurones** are **specialised cells** that **transmits the messages (impulses) electrically.**

**Dendrites receives the electrical messages.**

# Key Facts: Nerves

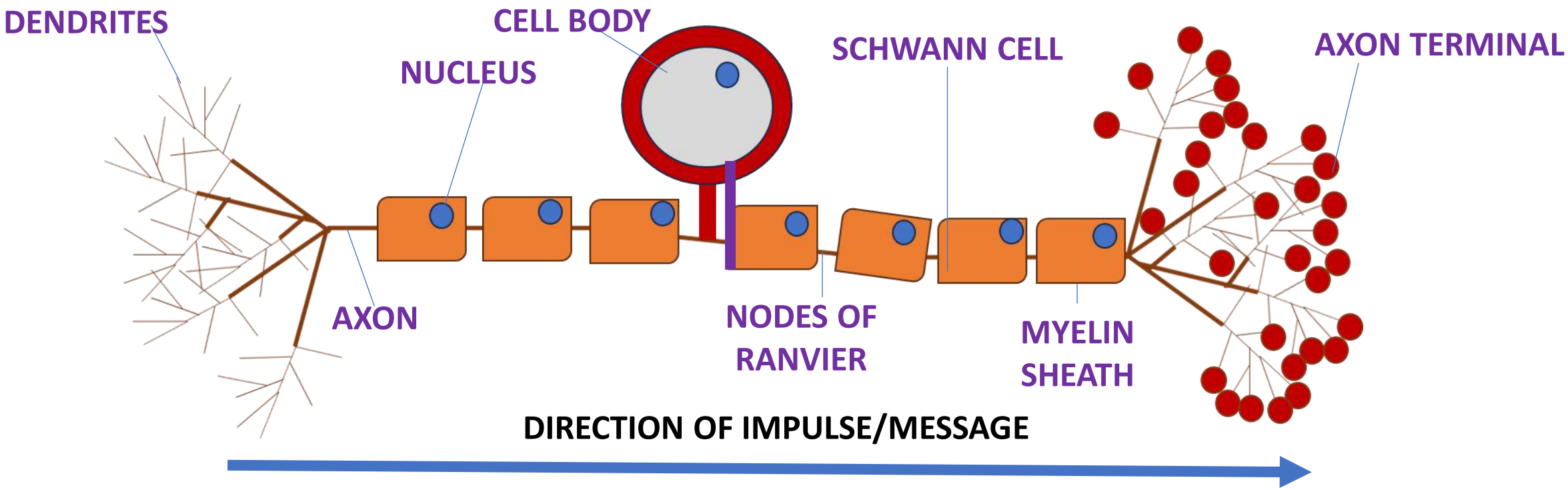



**Nerve cells** otherwise known as **neurones** are **specialised cells** that **transmits the messages (impulses) electrically.**

**Axon**

**A long tube** that **carries electrical impulses from one neuron to another.**

# Key Facts: Nerves



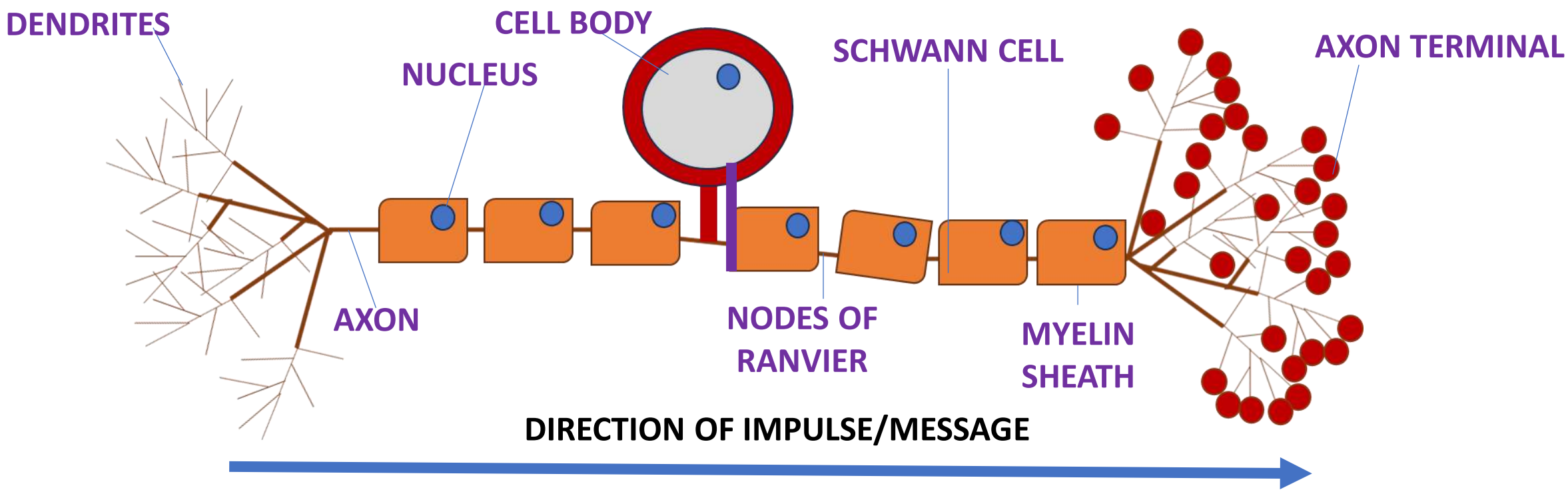

**Nerve cells** otherwise known as **neurones** are **specialised cells** that **transmits the messages (impulses) electrically.**

**Schwann cells.**

They contain a **fatty layer** called **myelin sheath to prevent electrical shock nor leaking impulses.**

**It provides insulation** and **helps speed up transmission of messages.**

# Key Facts: Nerves



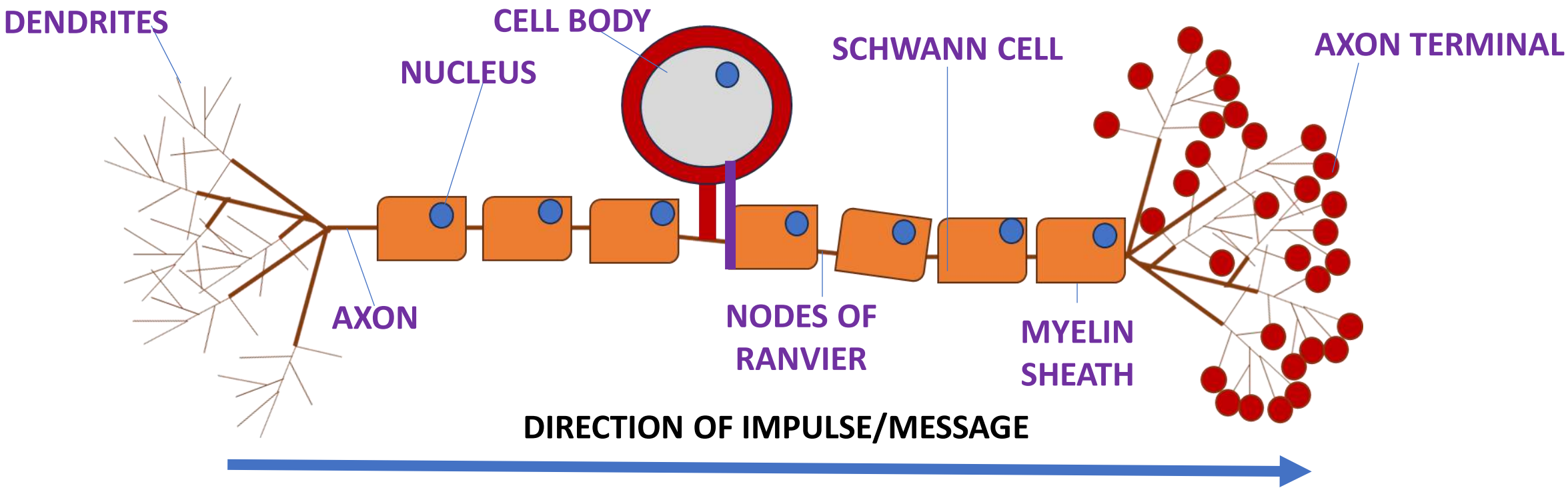

**Nerve cells** otherwise known as **neurones** are **specialised cells** that **transmits the messages (impulses) electrically.**

**The nodes of Ranvier.**

They are **small space between Schwann cells.**

They allow the **electrical impulse to jump to send message** at a **rapid rate along the axon.**

# Key Facts: Nerves

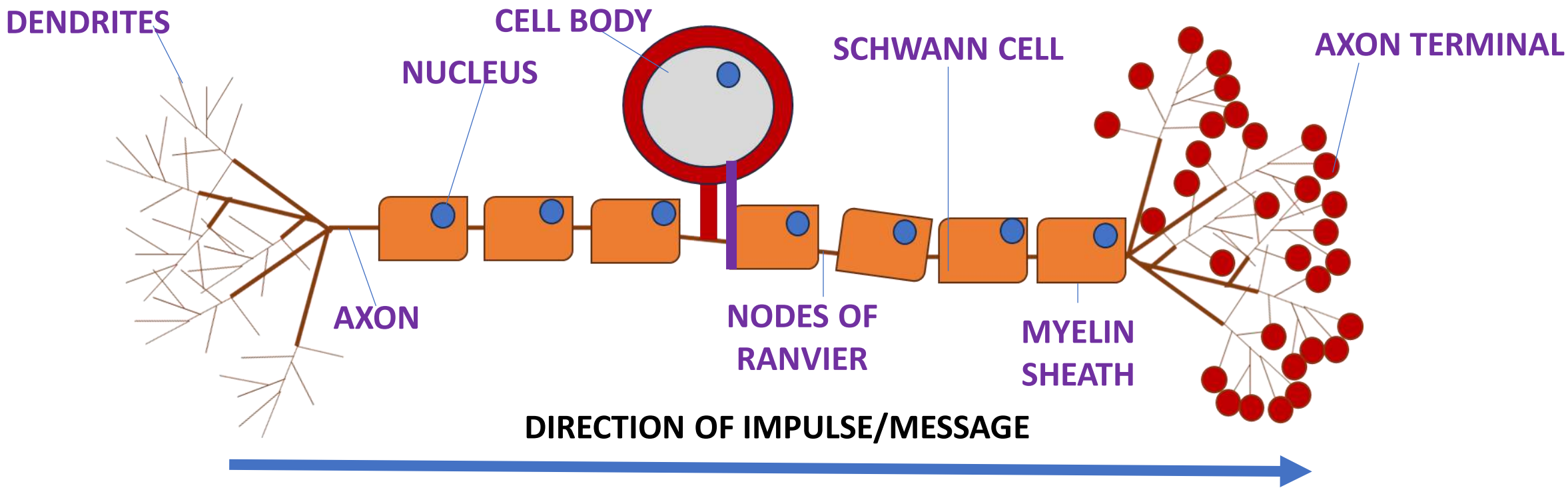



**Nerve cells** otherwise known as **neurones** are **specialised cells** that **transmits the messages (impulses) electrically.**

**Cell body.**

**The support centre with large surface area and nucleus.**

# Key Facts: Nerves

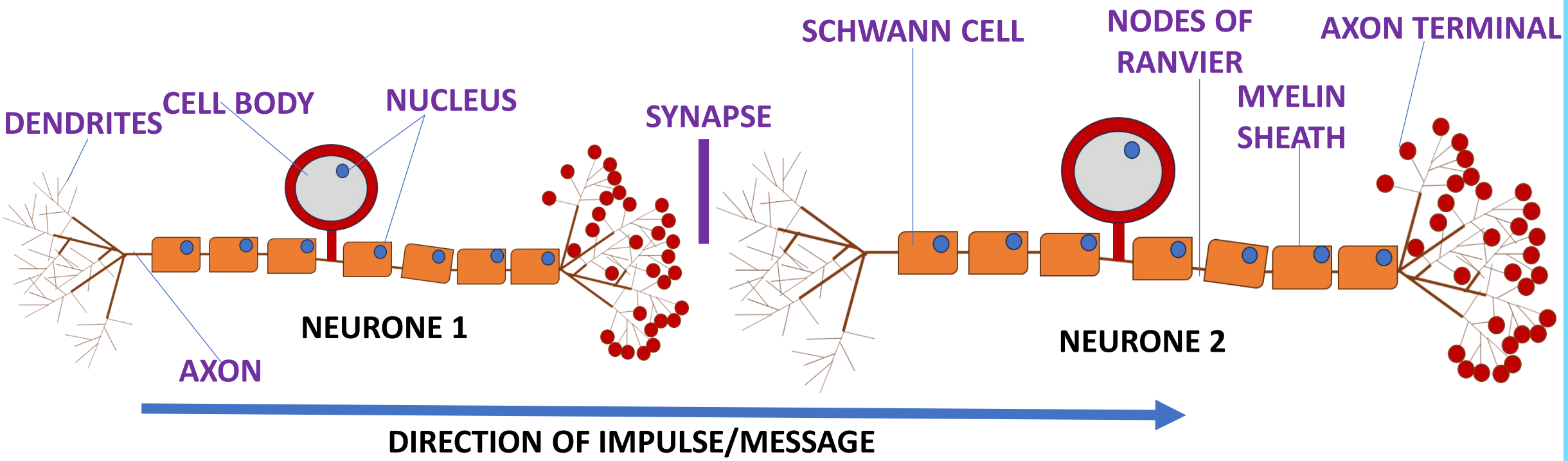



**Nerve cells** otherwise known as **neurones** are **specialised cells** that **transmits the messages (impulses) electrically.**

**Axon terminal**

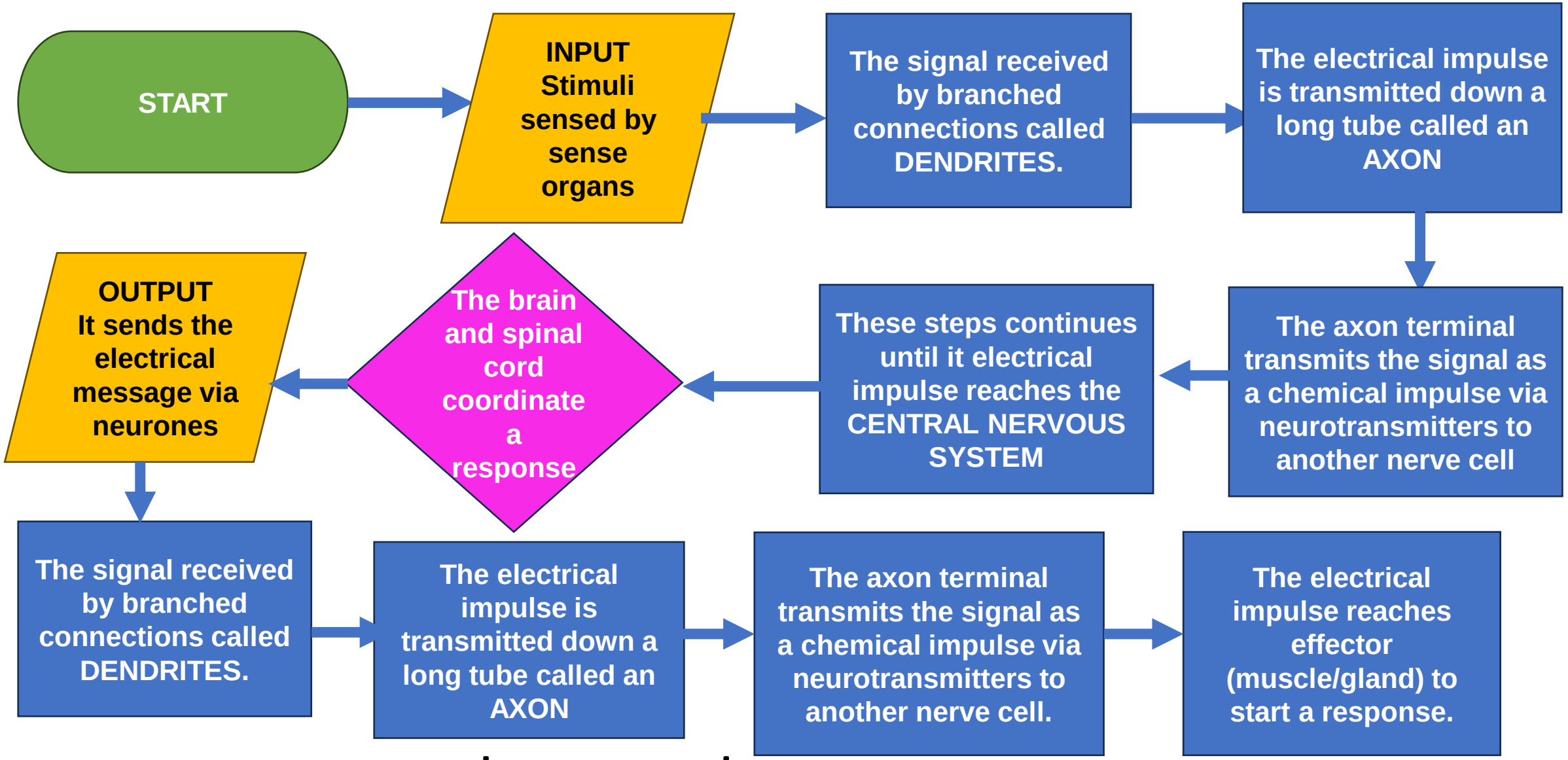
**It is finely branched to communicate with other nerve cells.**

# Key Facts: Nerves



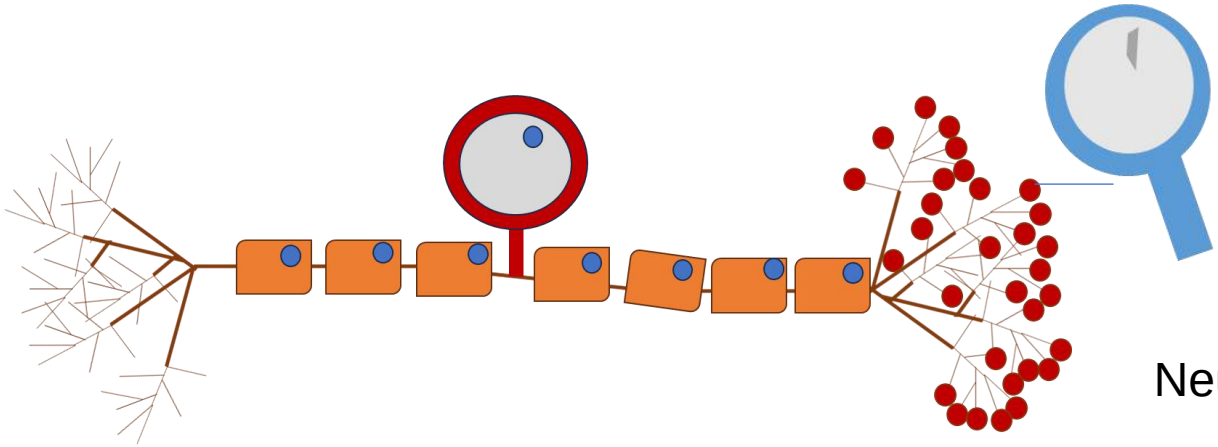

There is a **small gap** between the nerve cells called a **synapse** to allow signal **travel quickly** in **one direction** as a **chemical message** before **communicating electrically again.**

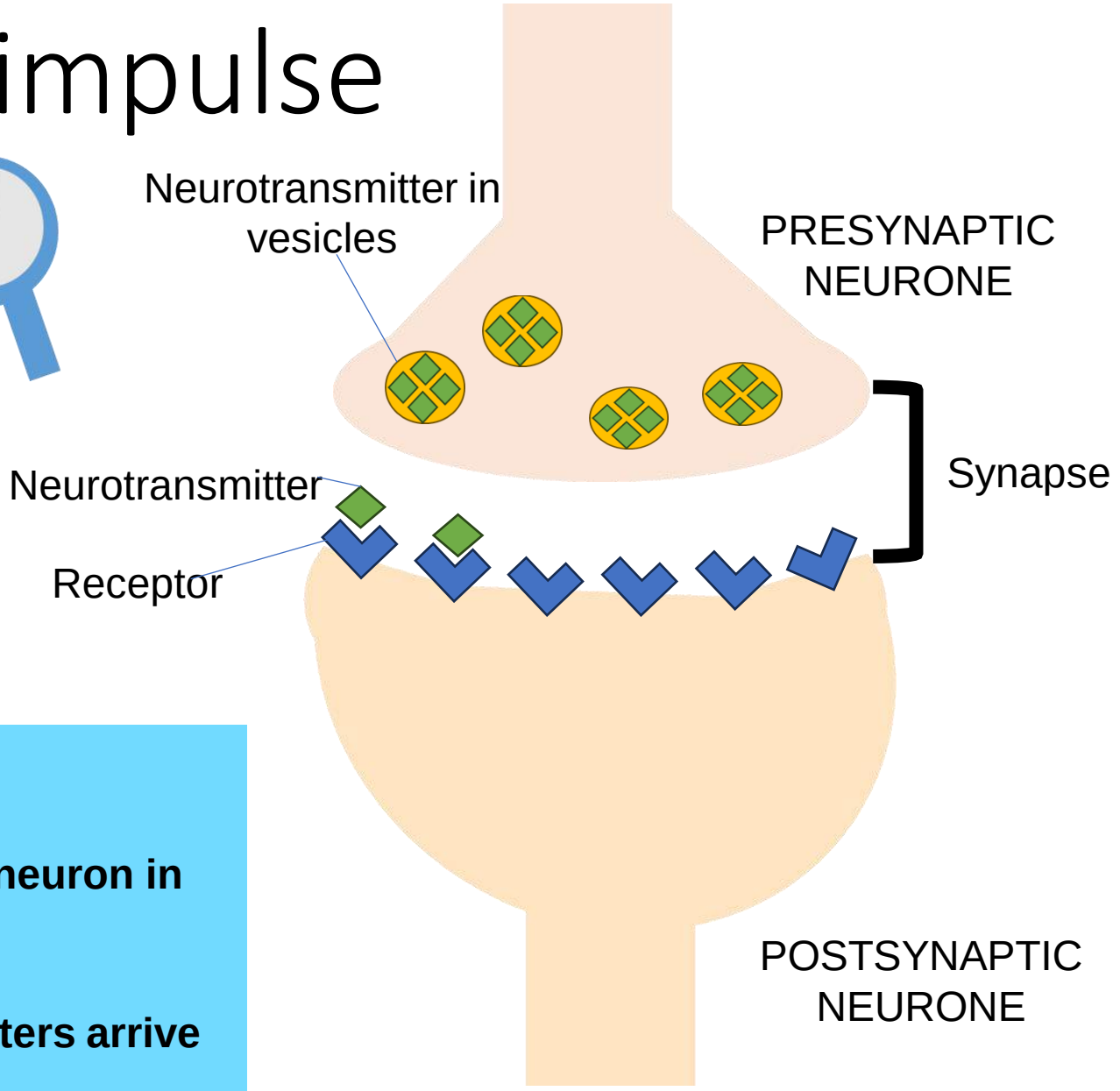
# Key Facts: Synapses




# Key Facts: The pathway

# Key Facts: Chemical impulse

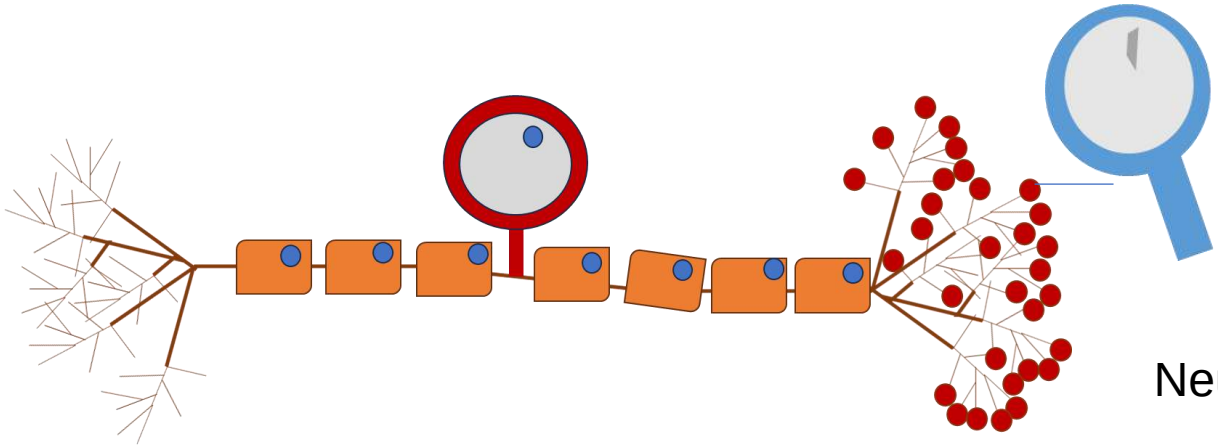


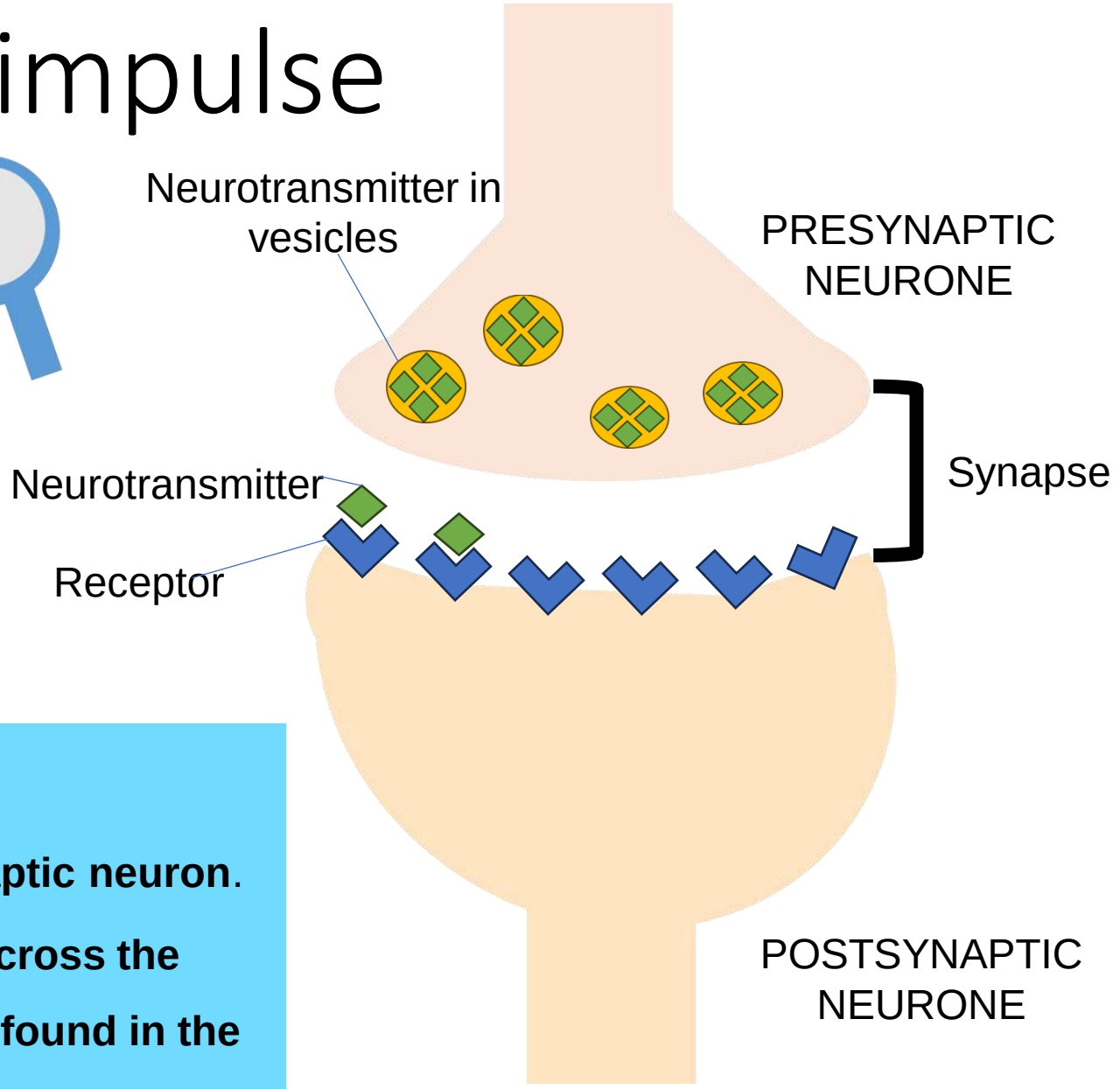



**Step 1**

- The **electrical impulse** reaches the **pre-synaptic neuron in the axon terminal.**
- **The chemical messengers called neurotransmitters arrive in small passages called vesicles.**

# Key Facts: Chemical impulse

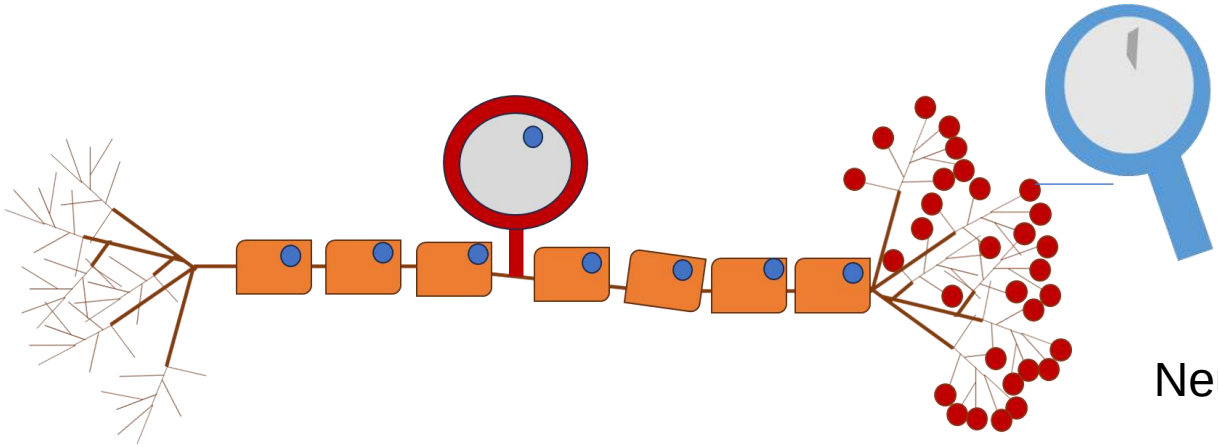


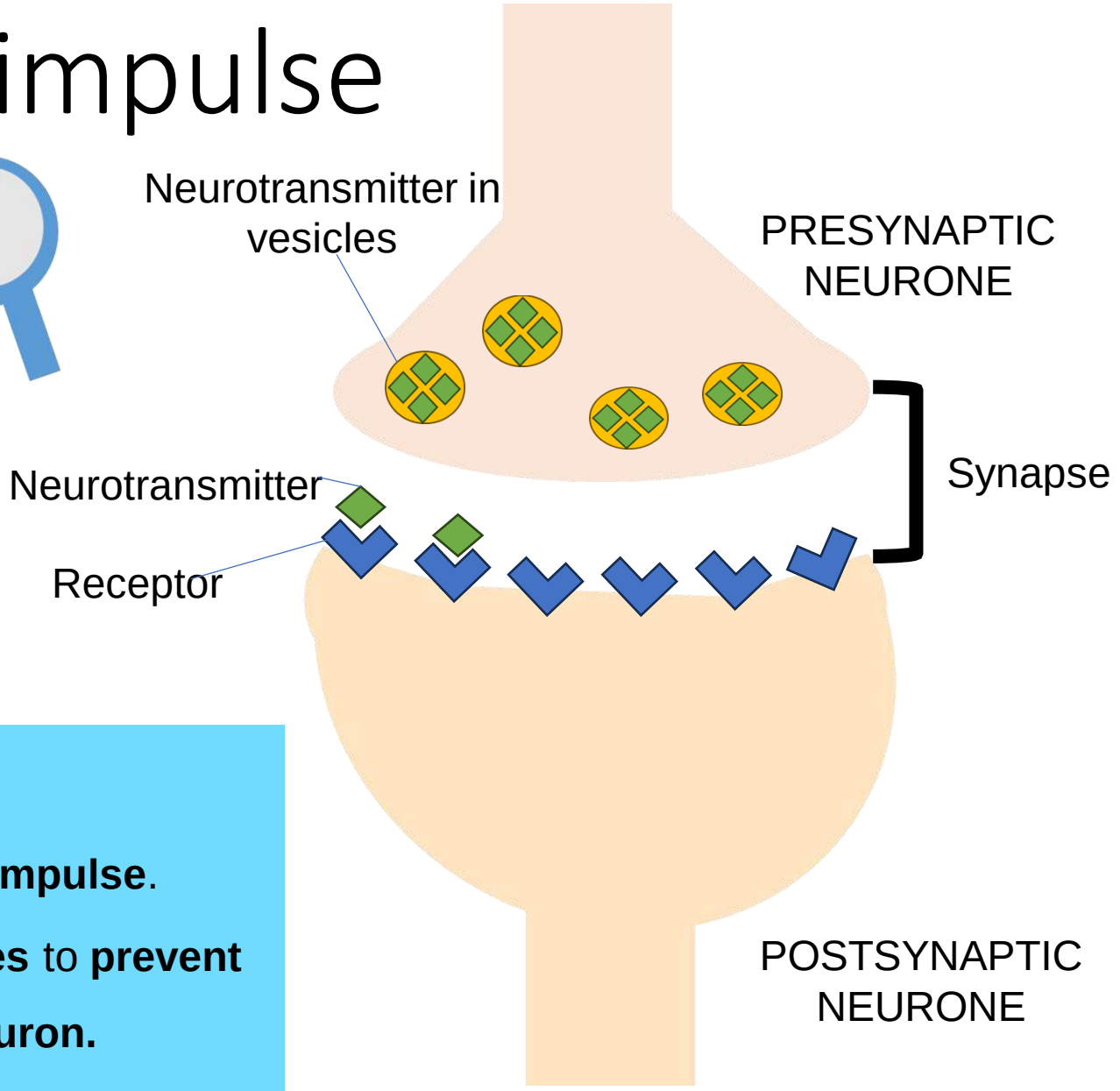



**Step 2**

- The **vesicles fuse** with the **membrane of presynaptic neuron**.
- **The neurotransmitter is released** and **diffuses across the synapse and binds specifically** with its **receptor found in the post-synaptic neuron** of the **second neuron.**

# Key Facts: Chemical impulse






**Step 3**

- The **neurotransmitters** change into an **electrical impulse**.
- The **neurotransmitters are destroyed by enzymes** to **prevent more activation of the impulse** in the **second neuron.**
- It is **reabsorbed** back into the **presynaptic neuron.**

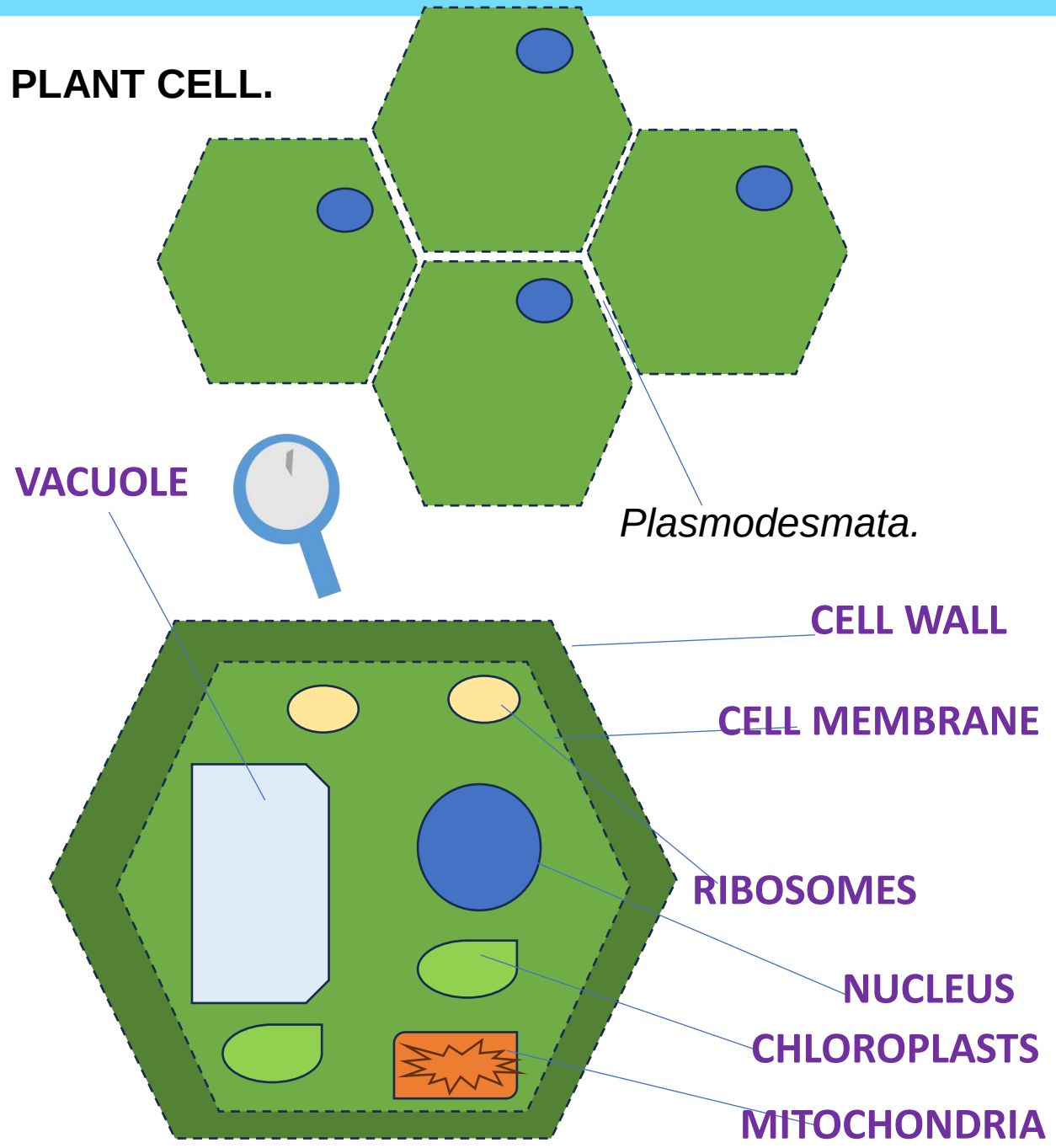
# Signalling type two: Contact dependent

# Key Facts

**Ligands bind to the cell surface of another cell via receptor**.

*Example: Plasmodesmata.*

- They are **pores** found in **plant cells.**
- They are **filled with water that connects between cell membranes of nearby cells.**
- This **helps exchange and transport small signalling molecules** and **ions through specific channels between cells.**
- **Large molecules cannot pass through** because of their **size e.g. DNA and proteins**.



# Signalling type three: Autocrine signalling

# Key Facts: Features of Autocrine signalling

**Autocrine signalling otherwise known as chemical signalling.**

**Cell secretes ligand/signalling molecules** that **binds to their own receptors on its surface**.

It can affect **nearby cells of same type**.

The **signals high due to sensitivity of density.**

It often occurs during the **early development of an organism to ensure cells develop into the correct tissues and induce function e.g. pain, immune response.**

# Key Facts: Example

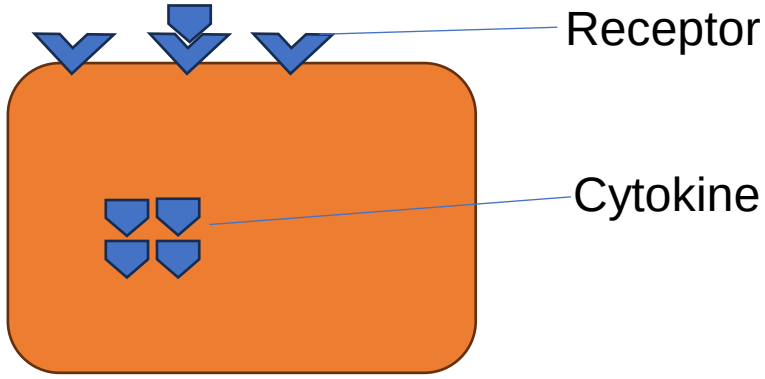
**Monocytes** are a type of **immune cell** produced in the **bone marrow.**

They produces proteins called **cytokines that affect themselves and other immune cells.**

**Cytokines** provide a **communication network where immune cells cross talk to create response.**

**Interleukin-1 (IL-1) is a type of cytokine** and is produced in **monocytes in response to external signal.**

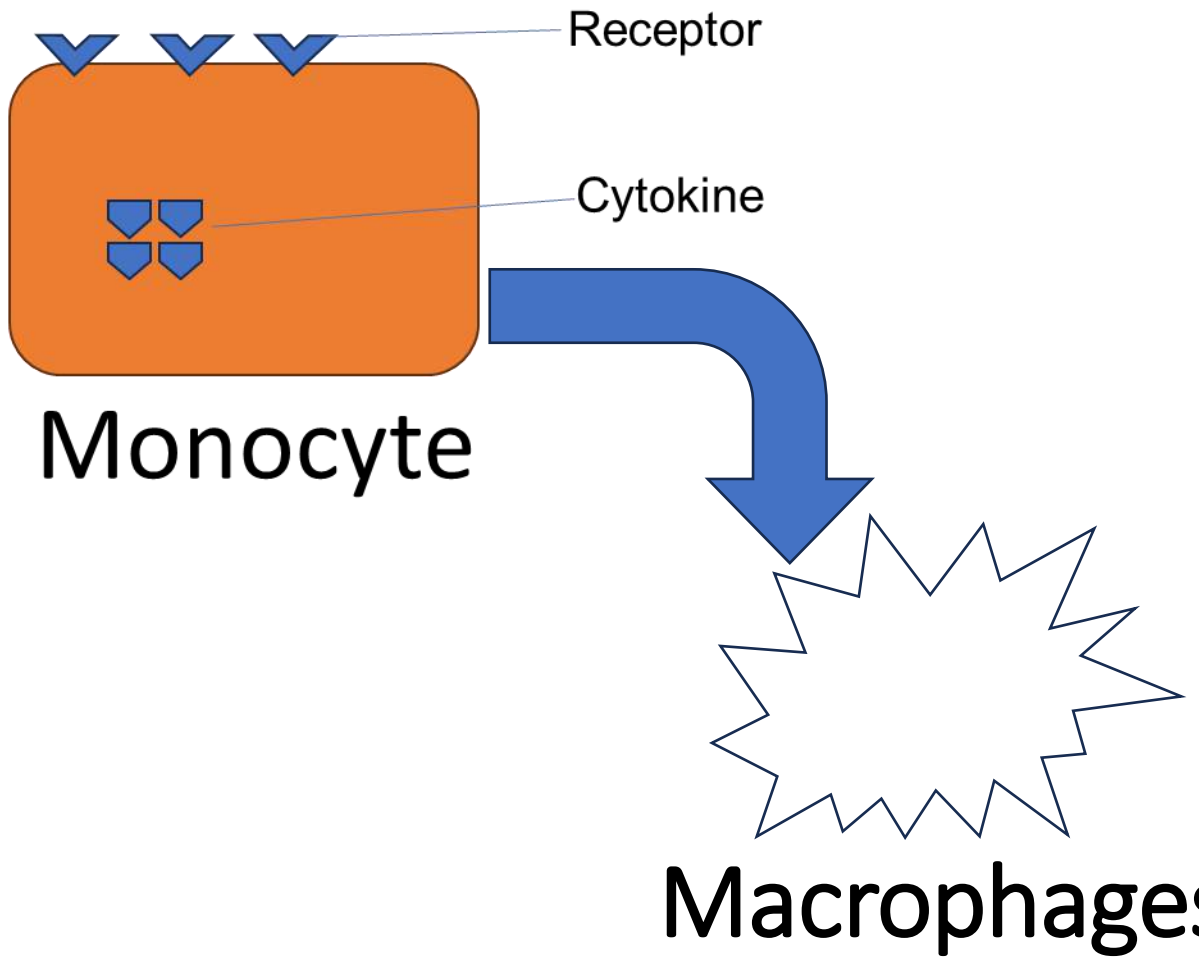
**IL-1 can bind to cell-surface receptors on the same cell that produced it.**




Monocyte

# Key Facts: Roles of Cytokines

- They regulates **mitosis for growth and repair of host cell.**
- They regulates **differentiation in monocytes to form another type of immune cell called phagocyte/macrophages to engulf bacteria and damaged organelles.**
- **Specific and non-specific immune responses.**




**Please see autophagy in Lecture 2.**

# Signalling type four: Endocrine signalling

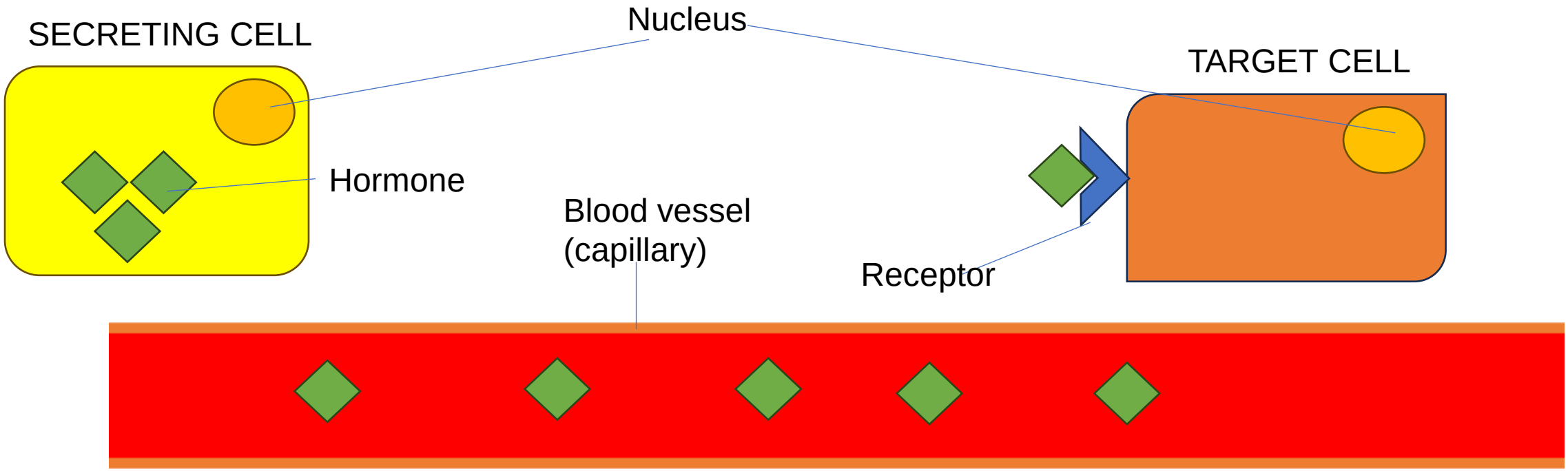
# Key Facts: Features of Endocrine signalling

The **chemical signals** begin from the **endocrine cell** and **produce hormones** in structures called **glands.**

**Hormones are chemical messengers** that travel to the target cell via **the blood.**

**Hormones get diluted and are present in low concentrations when they act on their target cells.**

**They produce a slower response and long-lasting effect than neurons**



# Key Facts: The pathway

**1) RECEPTOR ACTIVATION**

**Each hormone (signalling molecule) bind to specific receptors that have a complementary shape on their target cells.**

**2) SIGNAL TRANSDUCTION**

**A cascade of reactions that may involve enzymes and proteins occurs.**

**3) CELLULAR RESPONSE**

**Alter target enzyme or protein or gene to induce activity**

# Key Facts: Example

| Type of hormone | Features | Example |
|---|---|---|
| **Steroid hormone** | They are made from **fats/lipids via cholesterol**.<br>**They are soluble and pass through membrane.**<br>**They DO enter the cell and act on the DNA.** | **Oestrogen** |
| **Eicosanoids** | They are **lipids** produced from the **fatty acid chains of phospholipids** found in **plasma membrane**. | **Prostaglandins** |
| **Amino acid-derived** | **Amino acids are the monomers** and building blocks that join together via **peptide bonds** to **make proteins.**<br>The **amino acid is tyrosine** is used to **produce adrenaline.** | **Adrenaline, Noradrenaline** |
| Protein | They are **not soluble in the membrane.**<br>**They DO NOT enter the cell.** | **Insulin** |

# By the end of this lecture, you should understand

- **Cell-to-cell communication** consists of **direct, paracrine, contact-dependent, autocrine and endocrine signalling pathways.**
- Cell signalling has three key steps: **receptor activation, signal transduction and cellular response**.
- **Dysregulation of cellular signal transduction pathways** underlies **most of hallmarks of cancer**.
- There are **different types of signalling pathways** and vary based on the **distance** travelled to reach the **target cells.**
- **Protein-based ligands are insoluble in the membrane and does not enter the cell.**
  **Fat-based ligands are soluble and pass through membrane.**

# By the end of this lecture, you should understand

| **Feature** | **Nervous system** | **Endocrine system** |
|---|---|---|
| *Stimulus* | Yes | Yes |
| *What kind of information is transmitted?* | Electrical (electrical impulses) | Chemical (hormones) |
| *How is the information transmitted?* | Nerve cells (neurones) | Blood |
| *Organ involved?* | Yes | Yes |
| *Location of target organ* | Localised cells | Distant, many cells affected |
| *Involves a response* | Yes | Yes |
| *Type of response* | Involuntary/Automated or voluntary | Involuntary/Automated |
| *The length of the response?* | Short | Long |
| *The duration of the response?* | Quick | Slow |

# Reference list for further reading


Andrés Orellana, J., Giaume, C. and C. Sáez, J. (2011) 'Role of connexin hemichannels in neurodegeneration', *Neurodegenerative Diseases - Processes, Prevention, Protection and Monitoring* [Preprint]. doi:10.5772/28054.

Brooker, R., Widmaier, E., Graham, L., Stiling, P. (2008) '*Biology: Chemistry, Cell Biology and Genetics'*. United States of America: McGraw Hill.

King, T.C. (2007) 'Tissue homeostasis, damage, and Repair', *Elsevier's Integrated Pathology*, pp. 59–88. doi:10.1016/b978-0-323-04328-1.50009-7.

Nigerian scholars (n.d.*) Forms of Signalling* Available [online] https://nigerianscholars.com/tutorials/cell-communication/forms-of-signaling/

Nisar, S., Hashem, S., Macha, M., Yadav, S., Muralitharan, S., Therachiyil, L., Sageena, G., Al-Naemi, H., Haris, M., and Bhat, A. (2020). Exploring Dysregulated Signalling Pathways in Cancer. *Current Pharmaceutical Design*. 26(4), pp. 429–445.

Pecorino, L. (2012) '*Molecular Biology of Cancer Mechanisms, Targets, and Therapeutics'* UK: Oxford University Press.

Ranga, nr (2023) '*Cell Signaling | 5 Types with Suitable Examples'* Available [online]

https://www.studyread.com/cell-signaling/#google_vignette

SEASON 2

# Understanding Cancer

## Lecture 4
## Receptor activation

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www.hafsaabbas.com