An Introduction to Neural Computing

CMP3751 – Neural Computing

Week 1

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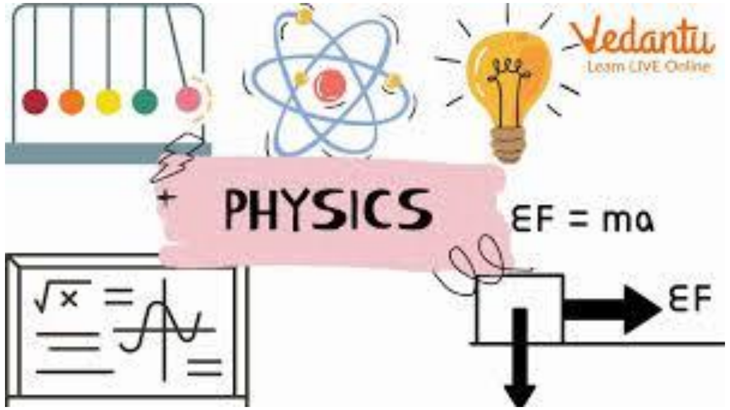
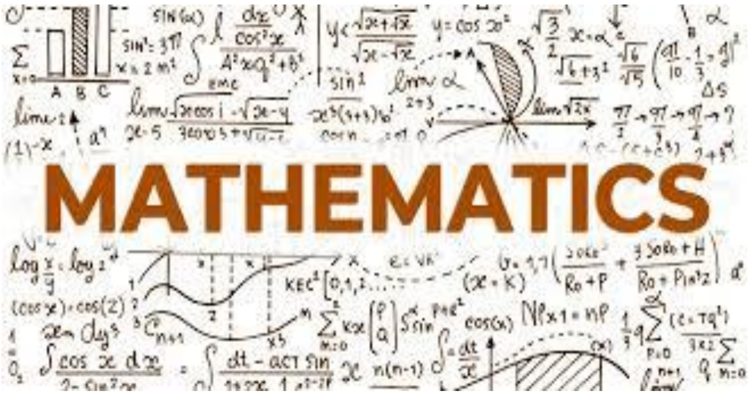
Access Code:

What is computational neuroscience?

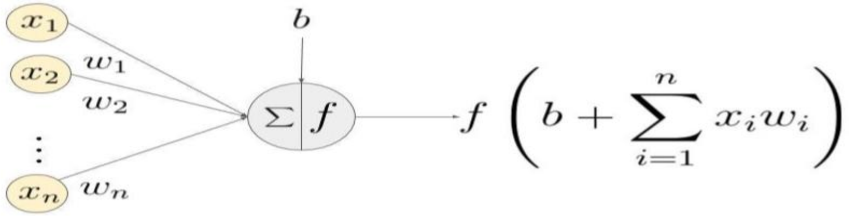
It is a field that combines elements of neuroscience, computer science, mathematics and physics to understand how the brain processes information.



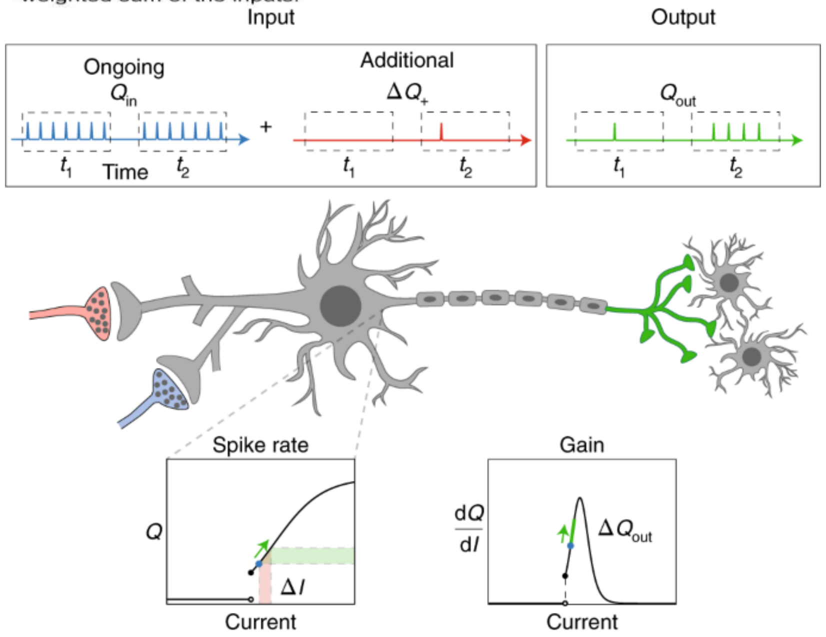


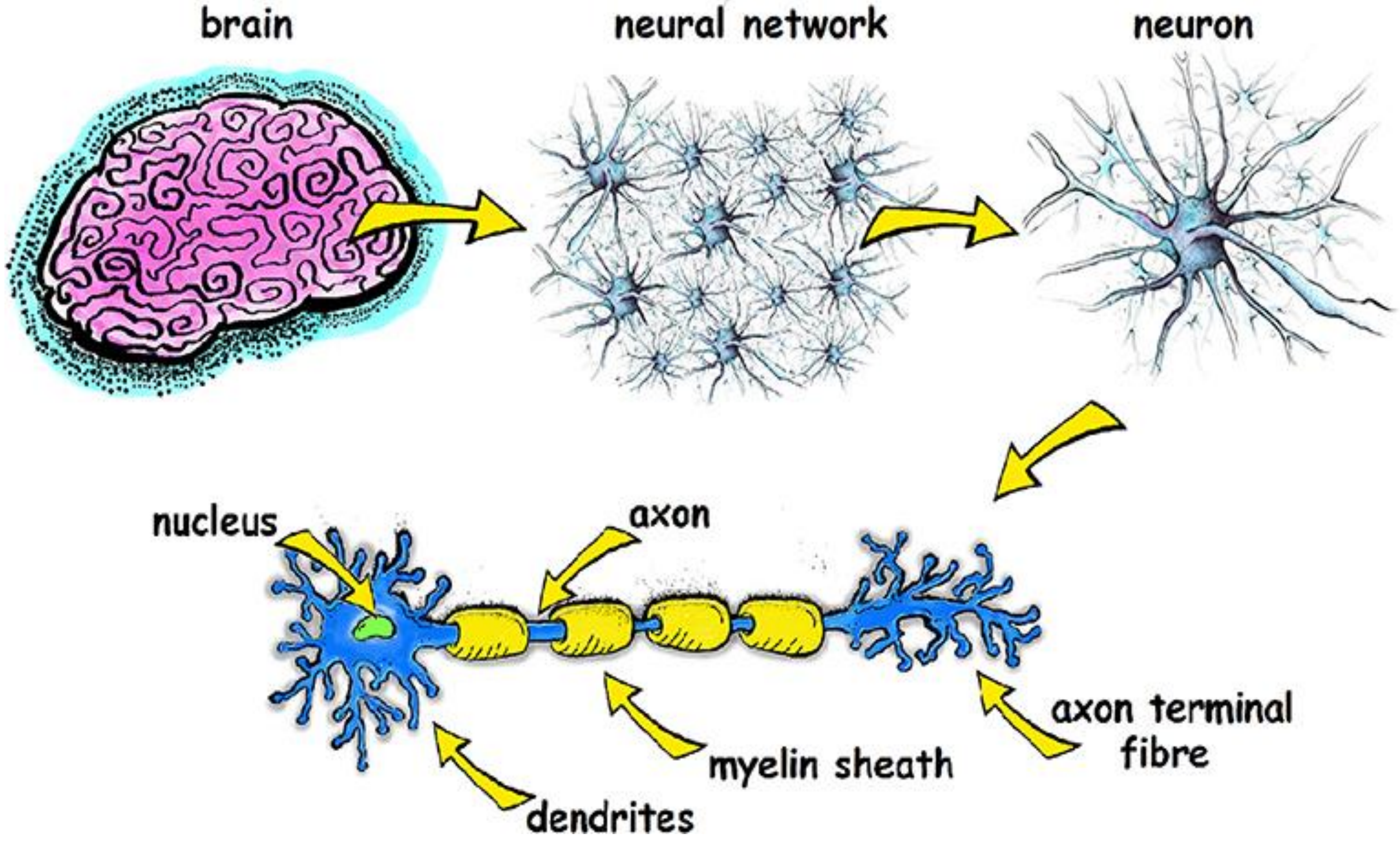
What does it involve?

It involves creating mathematical models, simulations and algorithms to represent and analyze the complex functions of the nervous system, from individual neurons to entire neural networks.

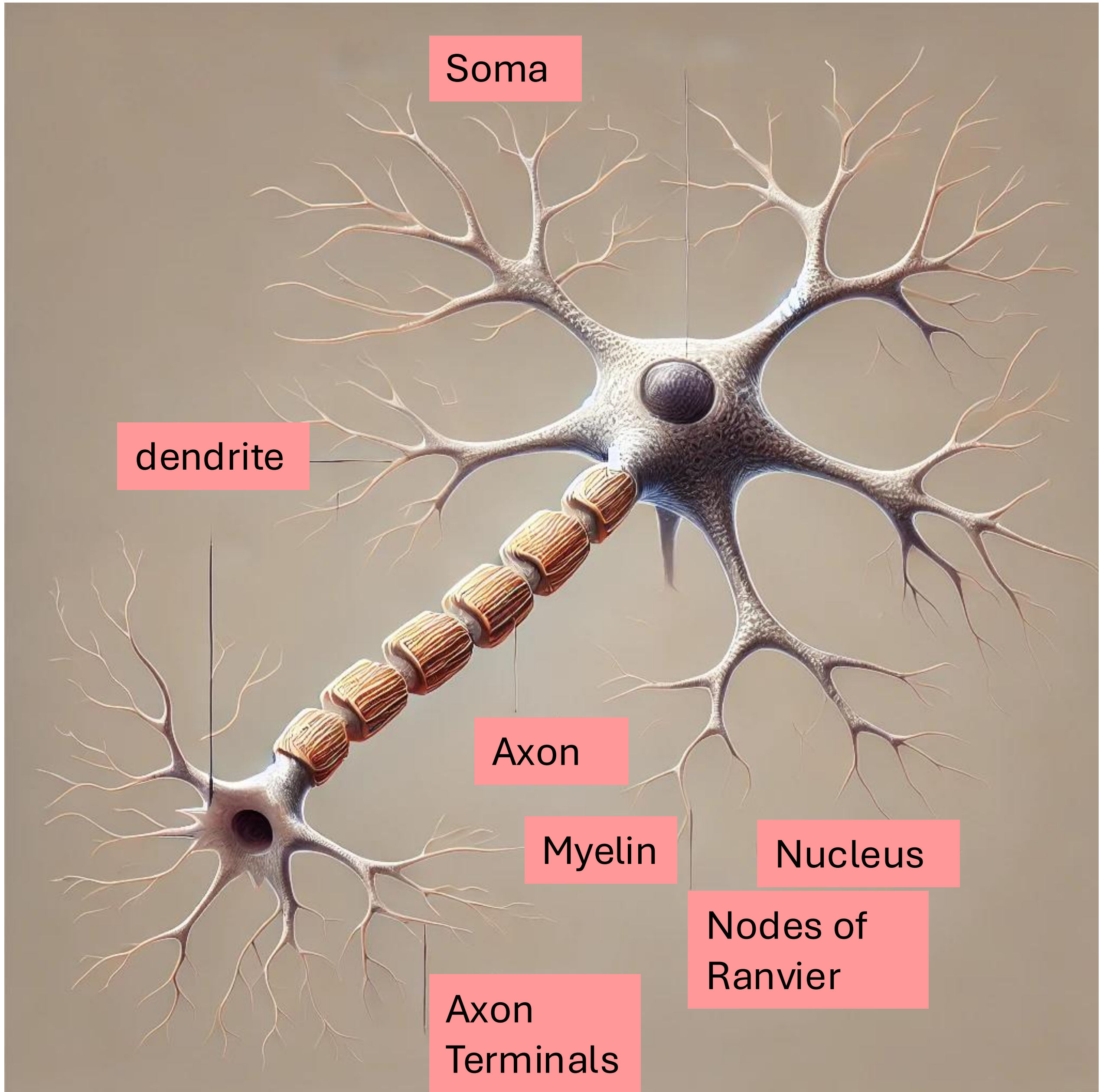


An example of a neuron showing the input (x_1 - x_n), their corresponding weights (w_1 - w_n), a bias (b) and the activation function f applied to the weighted sum of the inputs.





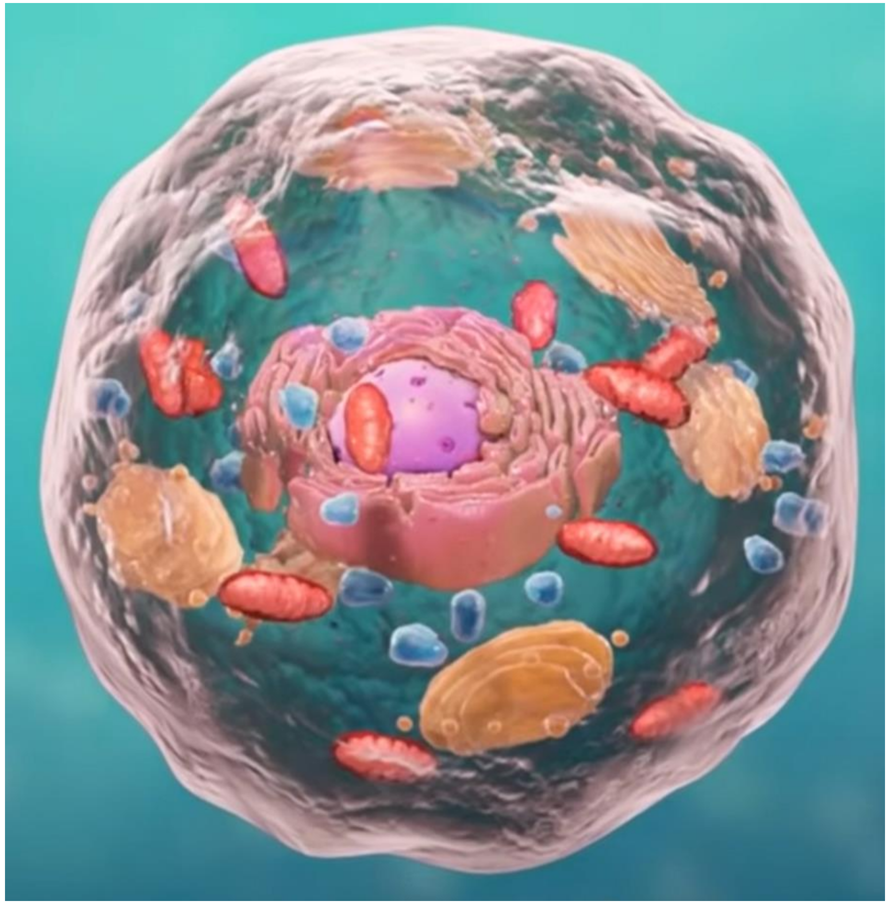
The basic neuron structure



1. Cell Body (Soma)
2. Dendrites
3. Axon
4. Myelin Sheath
5. Nodes of Ranvier
6. Axon Terminals
7. Synapse

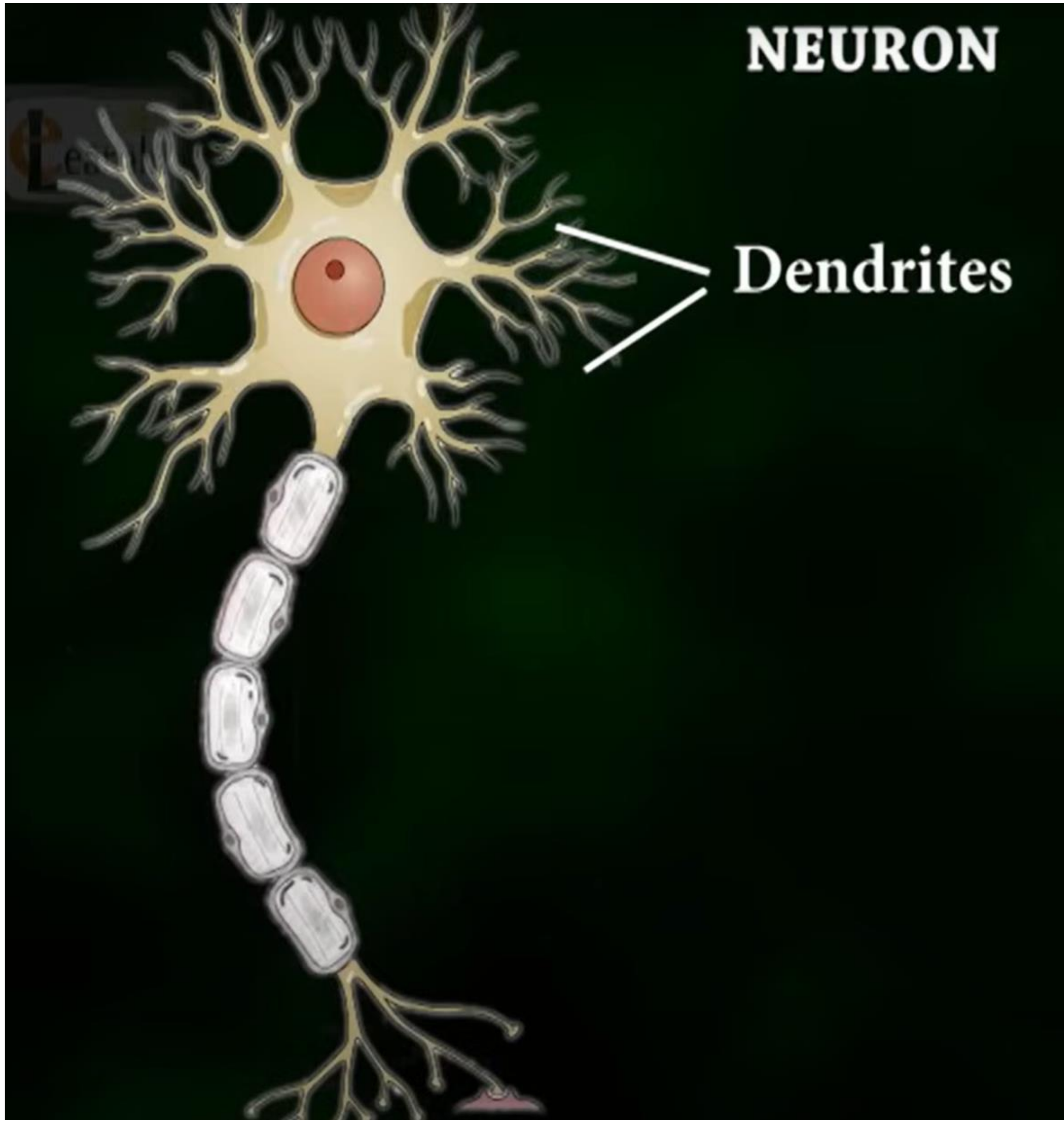
1. Cell Body (Soma)

- It is the central part of the neuron.
- It contains the nucleus and most of the cell's organelles.
- It is responsible for maintain the cell's health and metabolism.
- It integrates the signals received from the dendrites.
- It may generate an action potential if the signals are strong enough.
- The nucleus contains the neuron's DNA.
- The nucleus controls the neuron's activities, including protein synthesis.
- The cytoplasm contains typical cell organelles like mitochondria for energy production.
- It also contains the endoplasmic reticulum and Golgi apparatus, involved in cellular processes like energy metabolism and protein production.



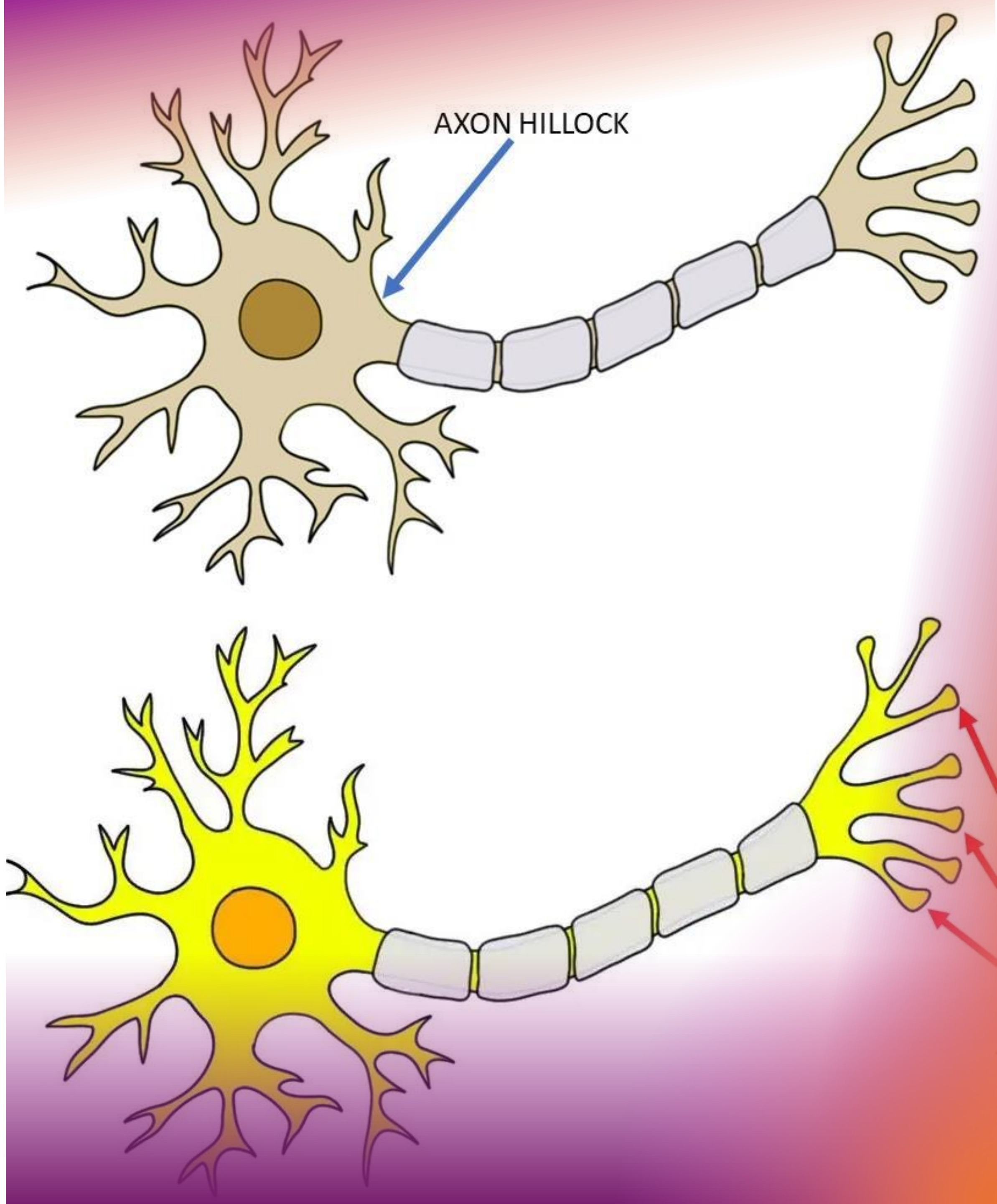
2. Dendrites

- They are tree-like extensions from the neuron’s cell body.
- They receive signals from other neurons or sensory receptors.
- They act as the input region, collecting information that will be sent to the soma.
- They have many branches, which allows them to receive signals from multiple neurons at once.
- These signals are usually in the form of neurotransmitters binding to receptors on the dendrite’s surface, leading to small electrical changes in the neuron.



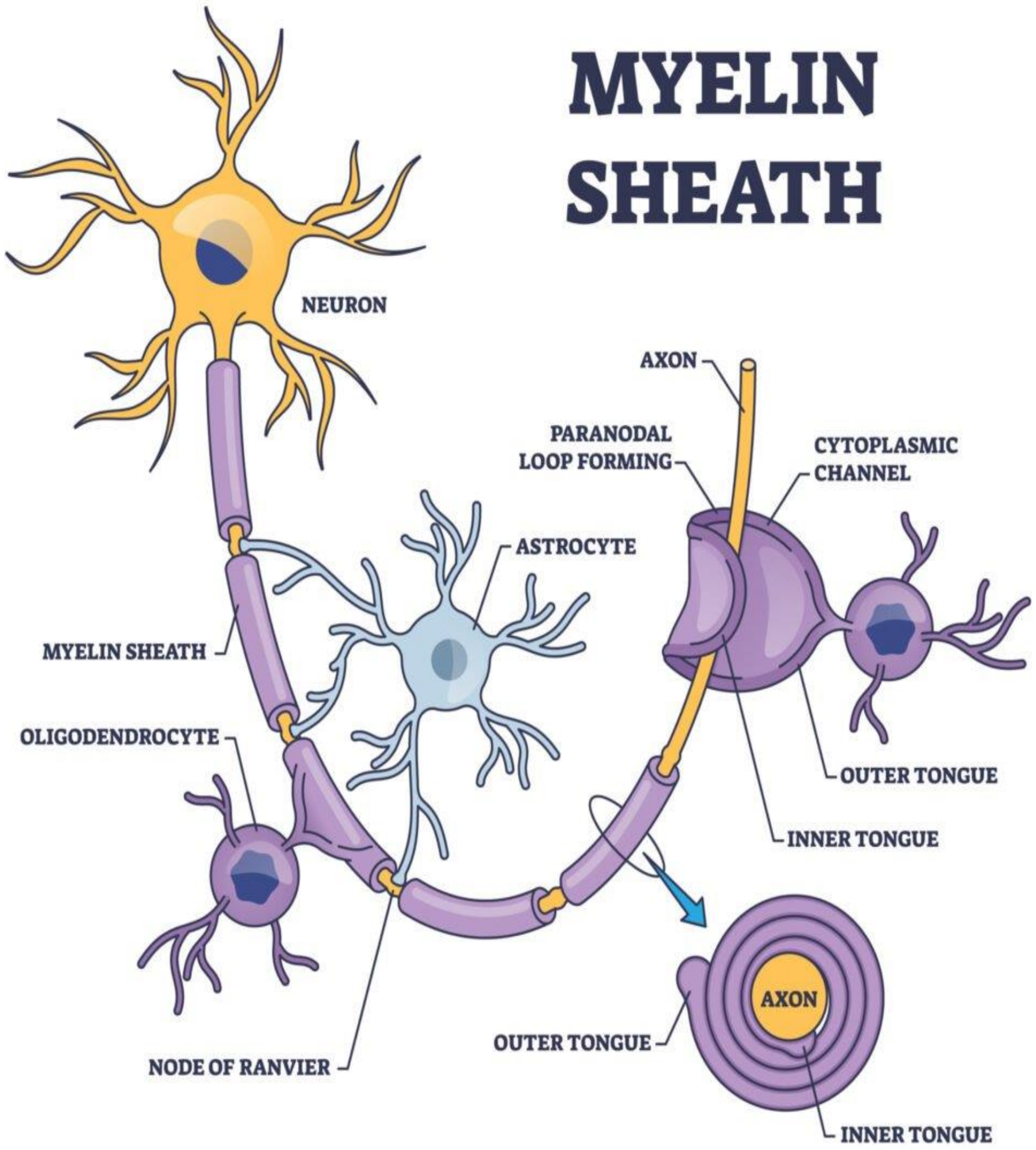
3. Axon

- The axon is the long, thin extension that transmits electrical signals (action potentials) away from the cell body toward other neurons or effectors (muscles, glands).
- It functions as the neuron’s output pathway.
- The axon hillock is the region where the axon connects to the cell body.
- The axon hillock is where the action potentials are generated if the incoming signals from the dendrites and soma reach a certain threshold.
- The axon (synaptic) terminals is the end of the axon branches, where neurotransmitters are released to communicate with target cells (other neurons, muscles or glands)



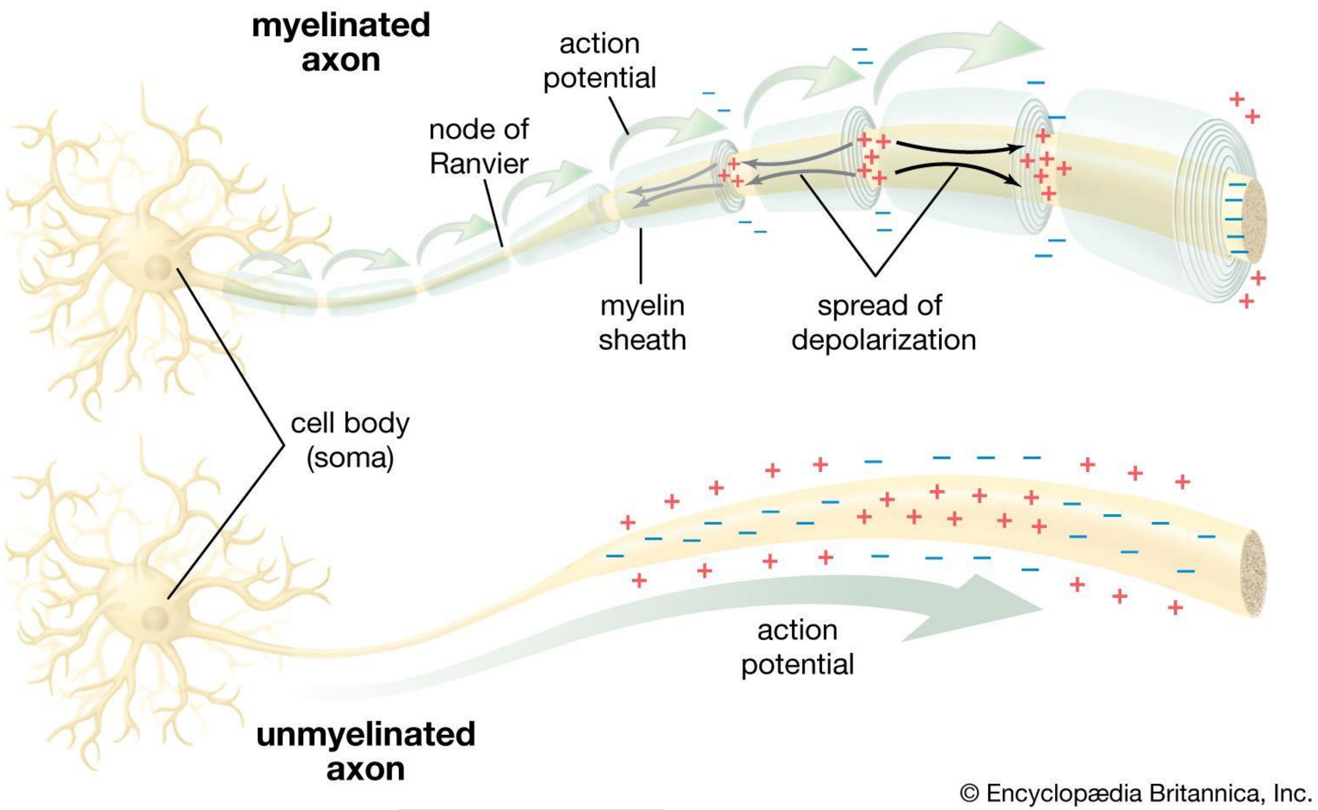
4. Myelin Sheath

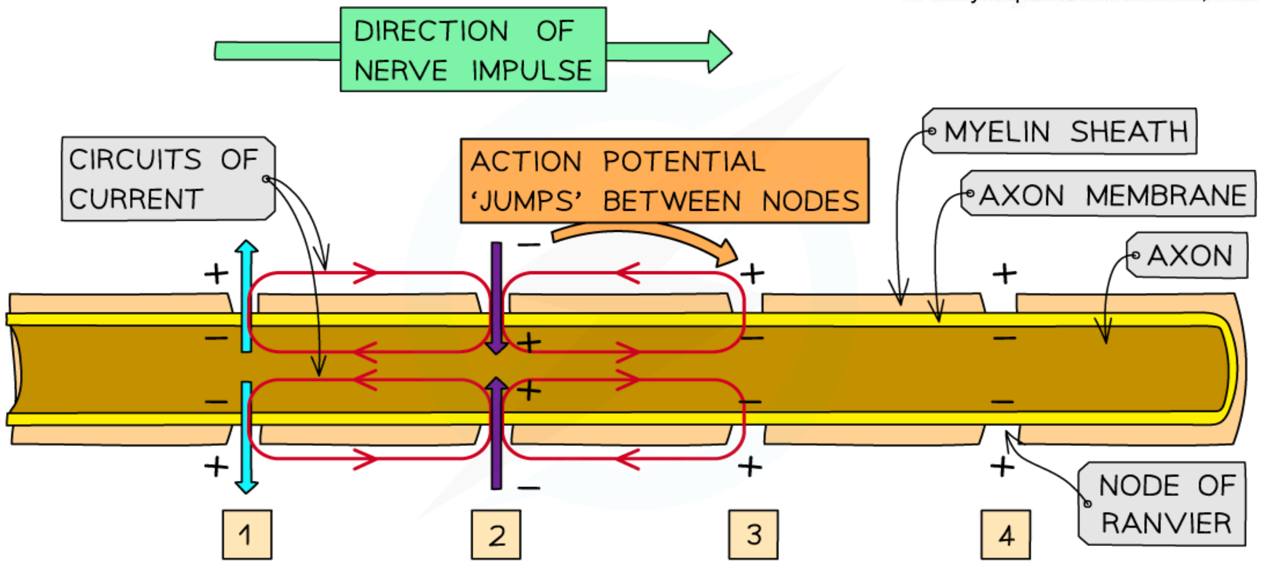
- It is an insulating layer that covers the axon.
- It allows faster transmission of electrical signals.
- It helps prevent signal loss and increases the speed at which action potentials propagate along the axon.
- It is made of glial cells, specifically **Schwann** cells in the peripheral nervous system and **oligodendrocytes** in the central nervous system.
- The myelin sheath is not continuous.
- There are small gaps called **Nodes of Ranvier**.



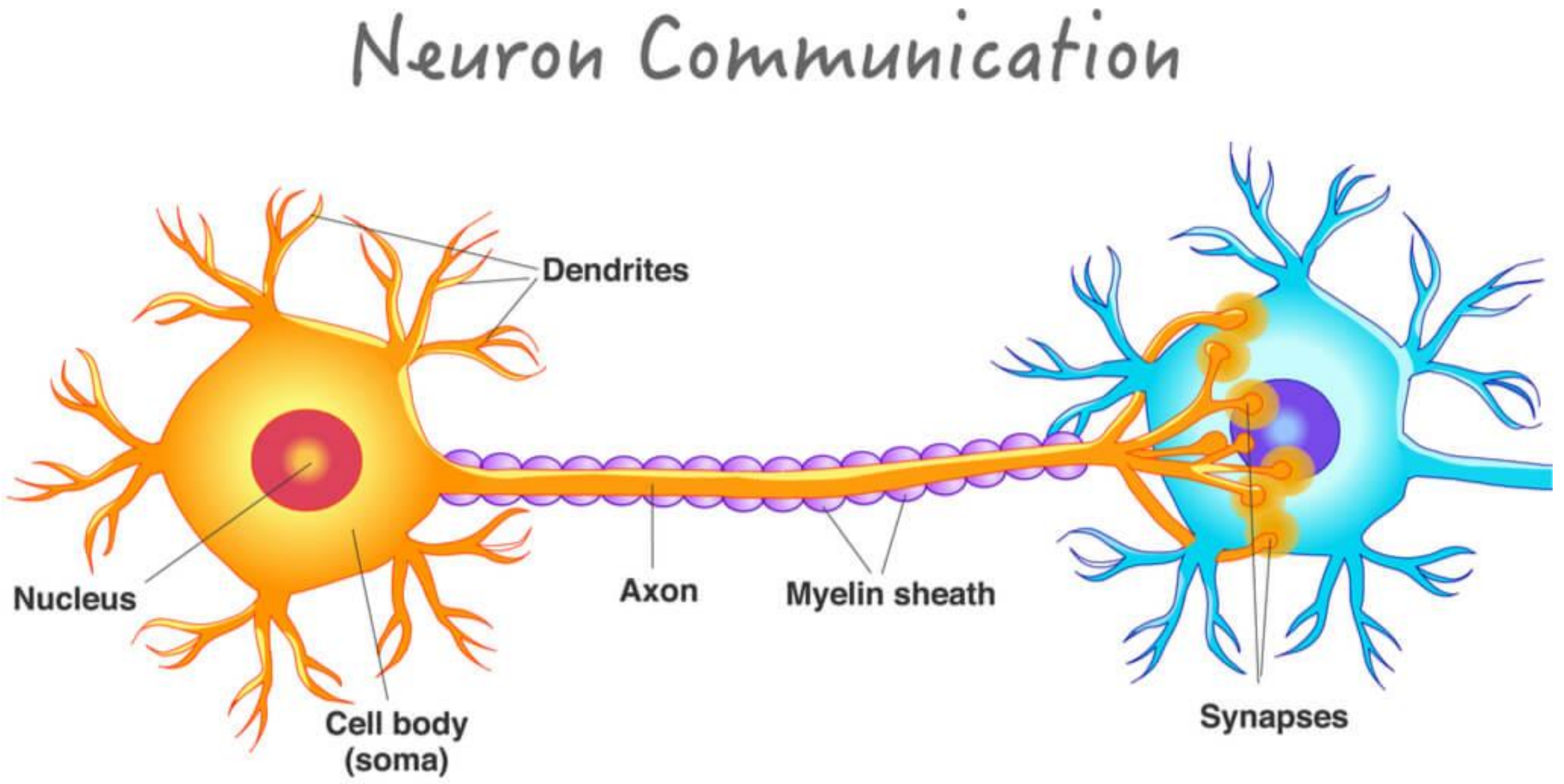
5. Nodes of Ranvier

- These are small gaps between segments of the myelin sheath.
- They play a key role in **saltatory conduction**, which allows action potentials to “jump” from one node to the next.
- This greatly increases the speed of signal transmission.
- The **nodes of Ranvier** are structured as bare regions of the axon membrane where ion channels are concentrated, enabling the rapid propagation of action potentials.





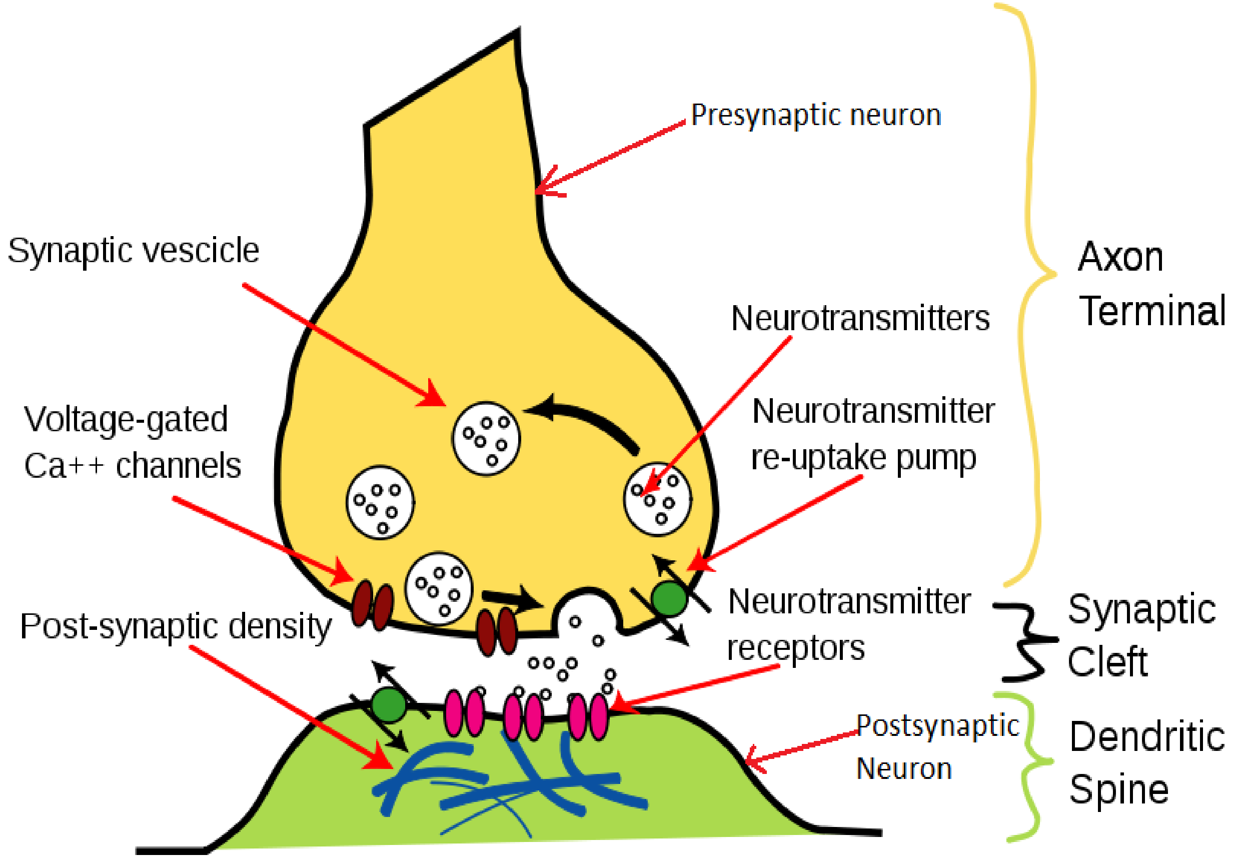
6. Axon Terminals



- They are small branches at the axon's end, each with a bulb-like ending called a synaptic knob or bouton, which contains vesicles filled with neurotransmitters.
- At the end of the axon, axon terminals form connections (synapses) with other neurons, muscles or glands.
- When an action potential reaches the terminal, it triggers the release of neurotransmitters into the synaptic cleft, which then binds to receptors on the postsynaptic cell, influencing its activity.

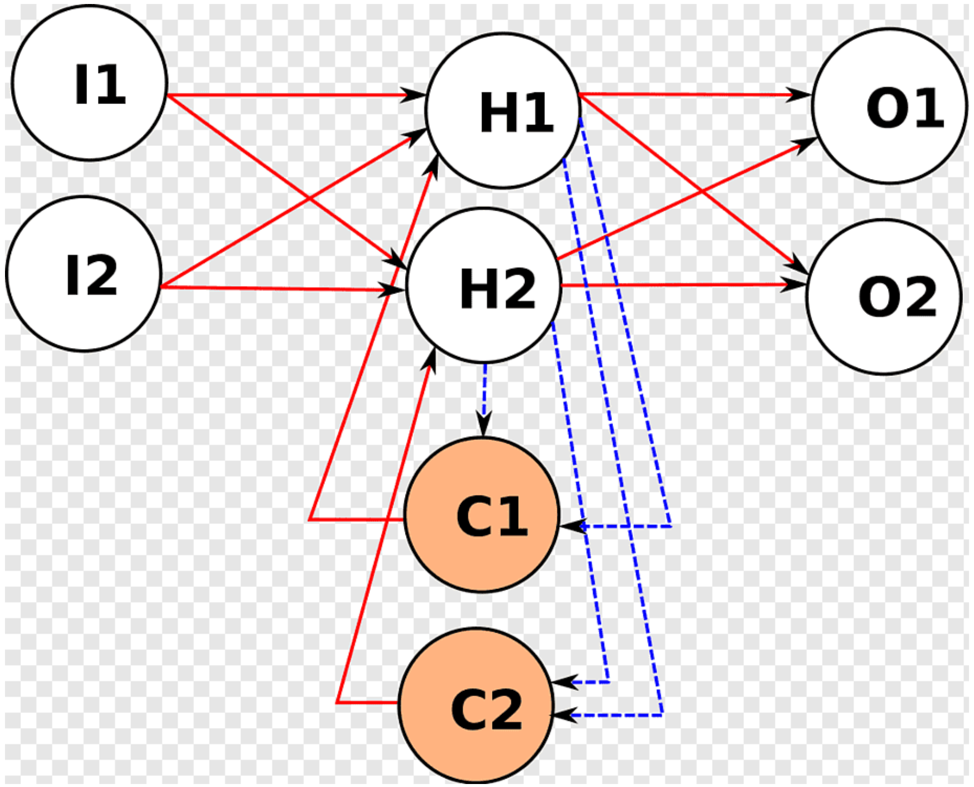
7. Synapse

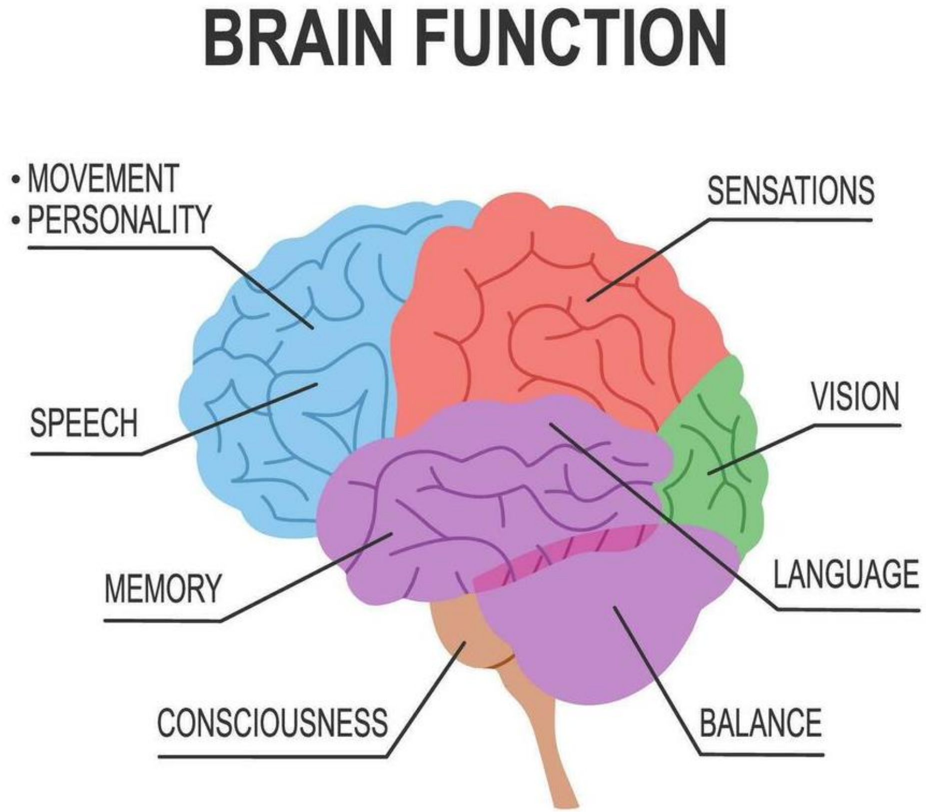
- The synapse is the point of communication between two neurons or between a neuron and its target (like a muscle or gland).
- It allows the transmission of signals from one cell to the next.
- The presynaptic neuron is the one which sends the signal and releases neurotransmitters.
- The postsynaptic neuron is the one that receives the signal, which contains receptors for the neurotransmitters.
- The synaptic cleft is the small gap between the presynaptic and postsynaptic cells through which neurotransmitters diffuse.



What is its goal?

1. To understand brain function in terms of its underlying physical and biological mechanisms.
2. To predict the behavior of neural systems under various conditions.

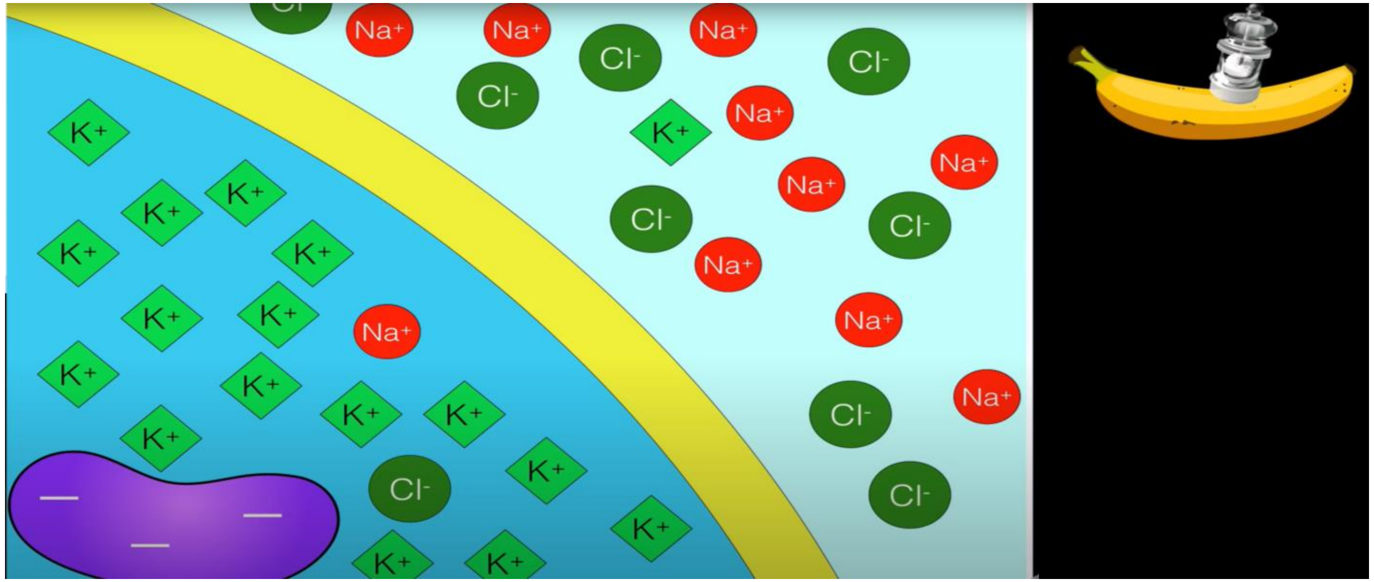




The Resting Membrane Potential

Definition

- It refers to the electrical charge difference across the membrane of a neuron when it is not actively sending signals.
- Then, the neuron is in a resting state.
- In most neurons, the resting potential is about -70 mV.



Two key ions involved in setting the resting membrane potential are:

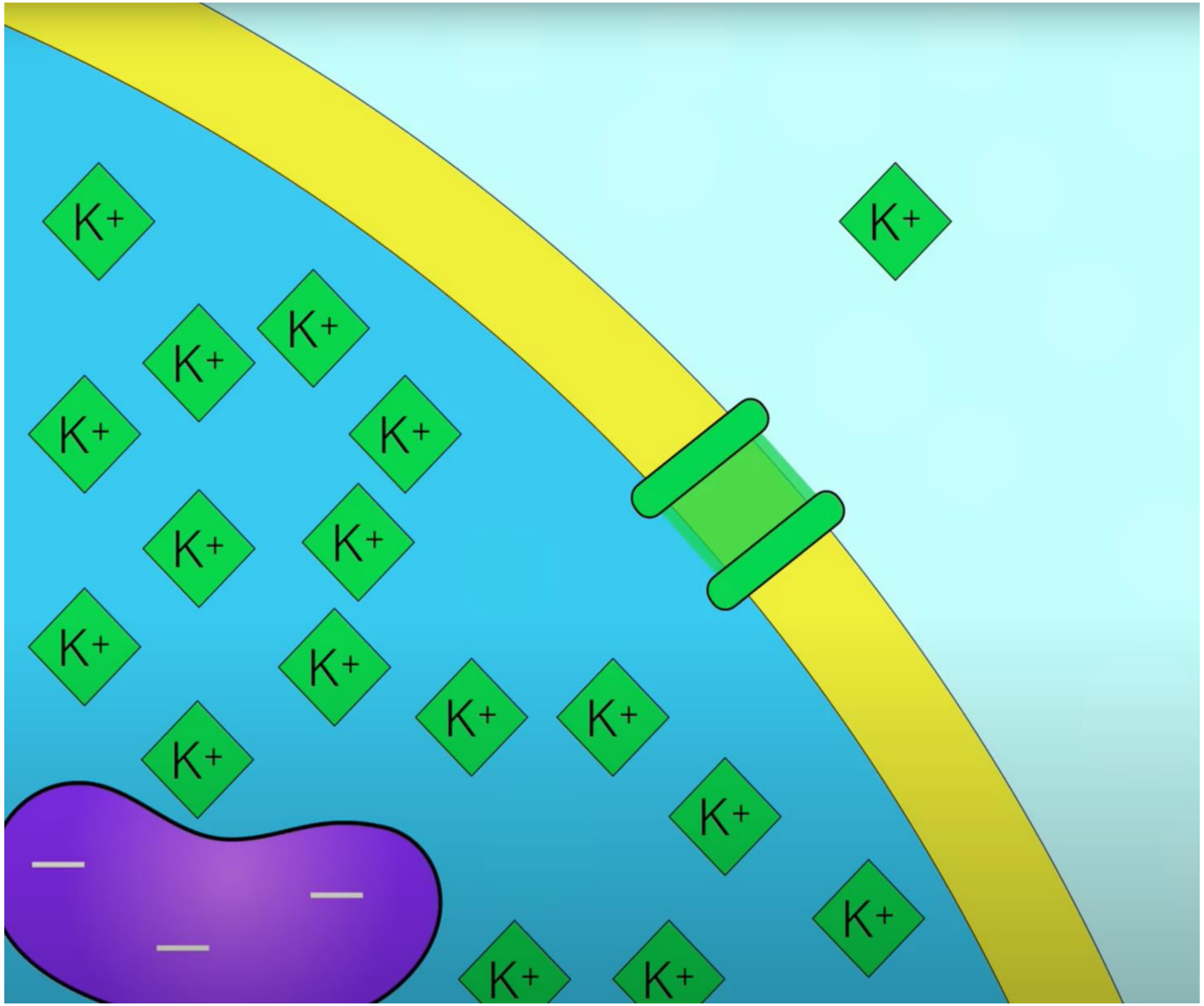
1. Potassium (K^+): There is a high concentration of K^+ **inside** the neuron.
2. Sodium (Na^+): There is a high concentration of Na^+ **outside** the neuron.

The resting membrane potential exists because:

1. There are different **concentrations of ions** such as sodium / Na^+, potassium / K^+, chloride Cl^- and other ions) inside and outside the neuron.
2. The cell membrane is selectively permeable, allowing some ions to pass more easily than others.

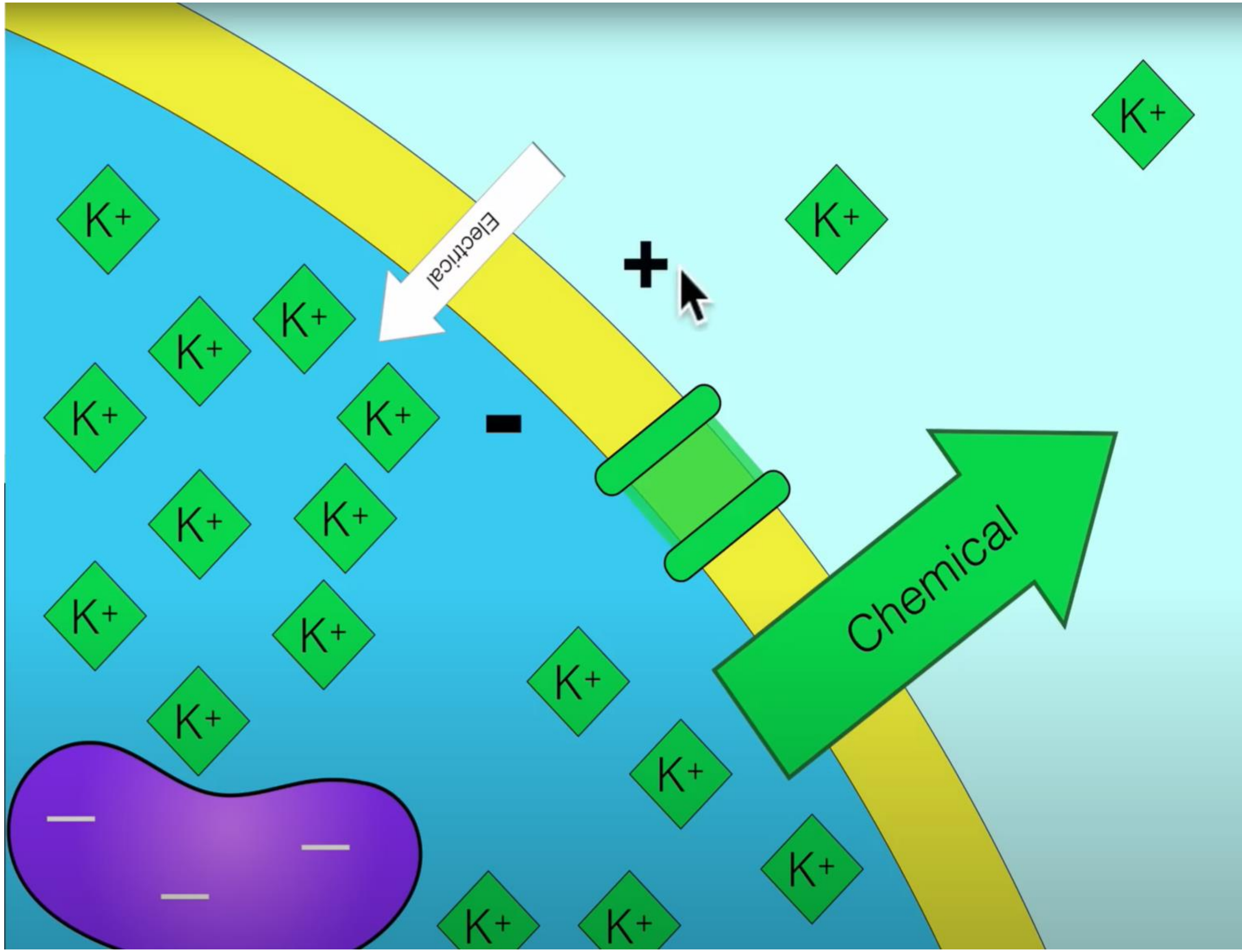
Ion Channels & Permeability (1)

- There are the potassium channels, which are "**leaky**" allowing some K^+ ions to flow out of the cell.
- There are very few sodium channels open at rest, so Na^+ ions cannot enter the cell easily.



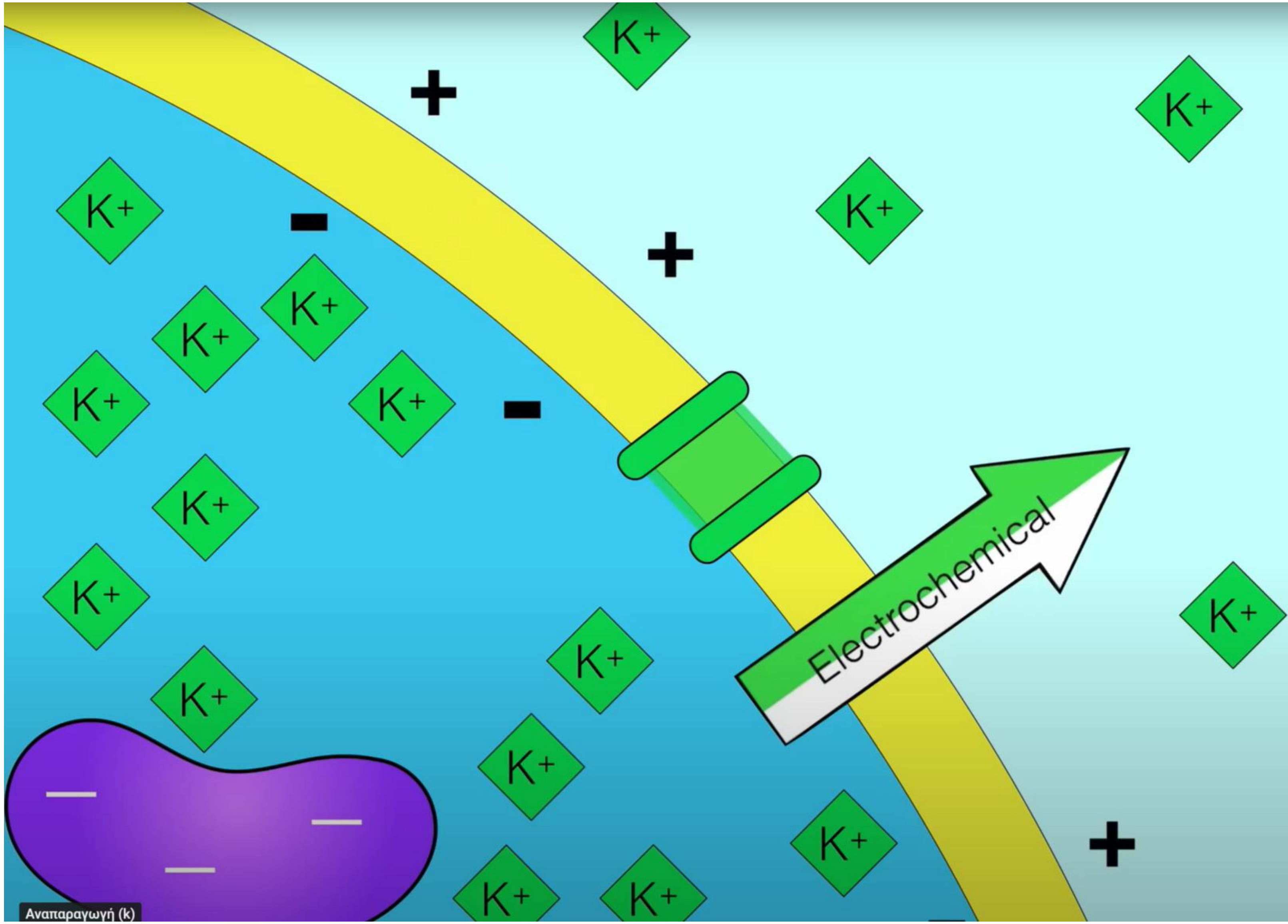
Ion Channels & Permeability (2)

- As K^+ ions leave the neuron through leak channels, they carry positive charge out of the cell.
- Since Na^+ ions are mostly kept outside the cell, this negative charge remains inside.
- This creates a chemical gradient from the inside to the outside.
- As the potassium moves out, a separation in charge is being created.
- So, now there is a relatively negative charge on the inside.
- This creates an electrical gradient.



Ion Channels & Permeability (3)

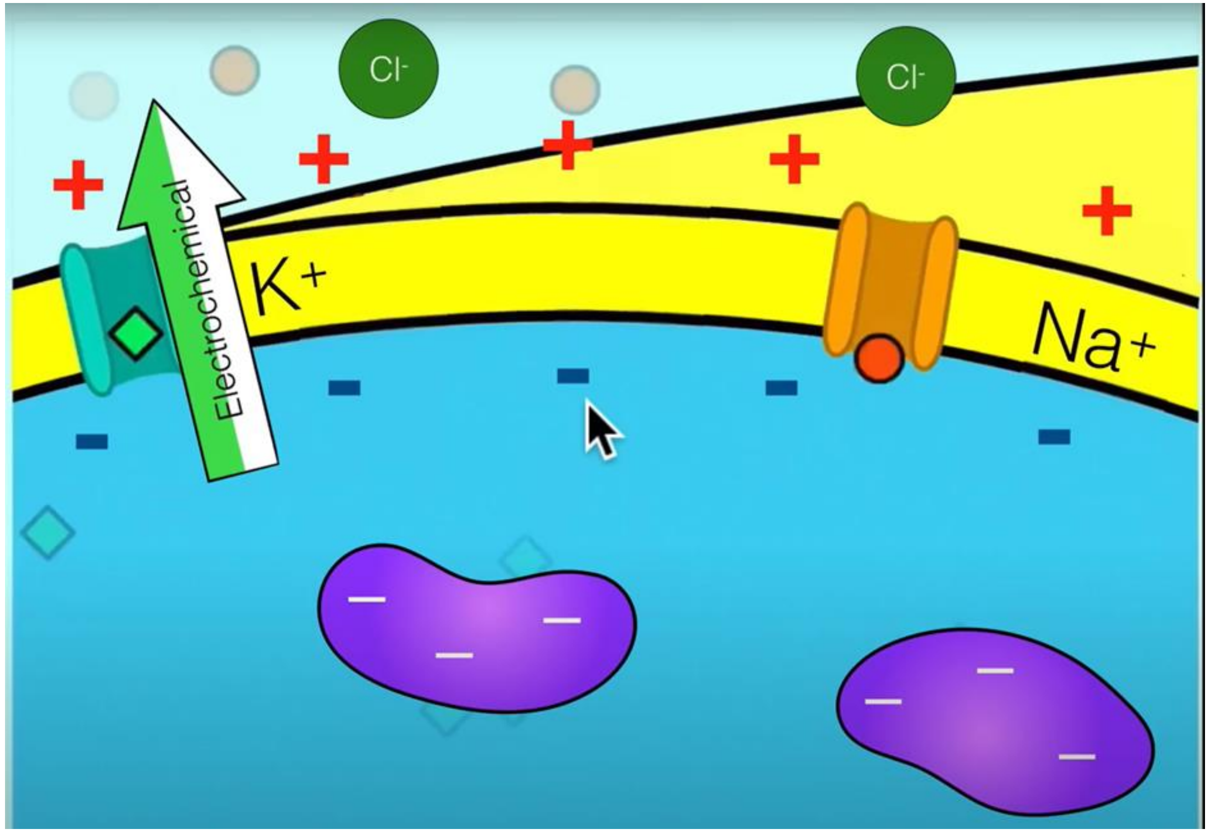
- As more potassium leaves, the electric chare is increasing.
- Eventually, this starts a flow back in.
- Now there is potassium movement inside and outside.
- The leak channels do not allow much of the potassium to flow out.



https://phet.colorado.edu/sims/html/neuron/latest/neuron_all.html

The Sodium Channel

- Mostly, they are voltage-sensitive and open in response to changes in the membrane potential.
- They are typically closed at the resting membrane potential.
- They open when the membrane potential becomes more positive (depolarized).
- At rest (around -70 mV), the sodium channels prevent Na^+ ions from entering the neuron.



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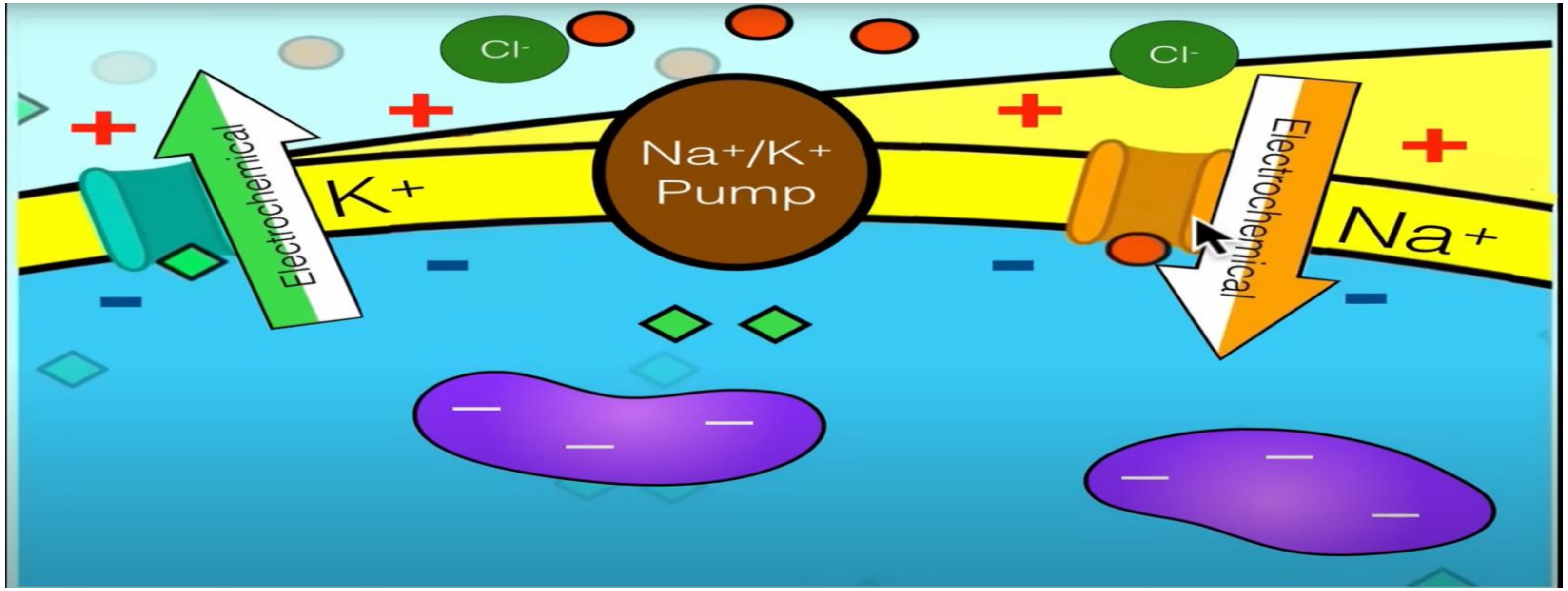
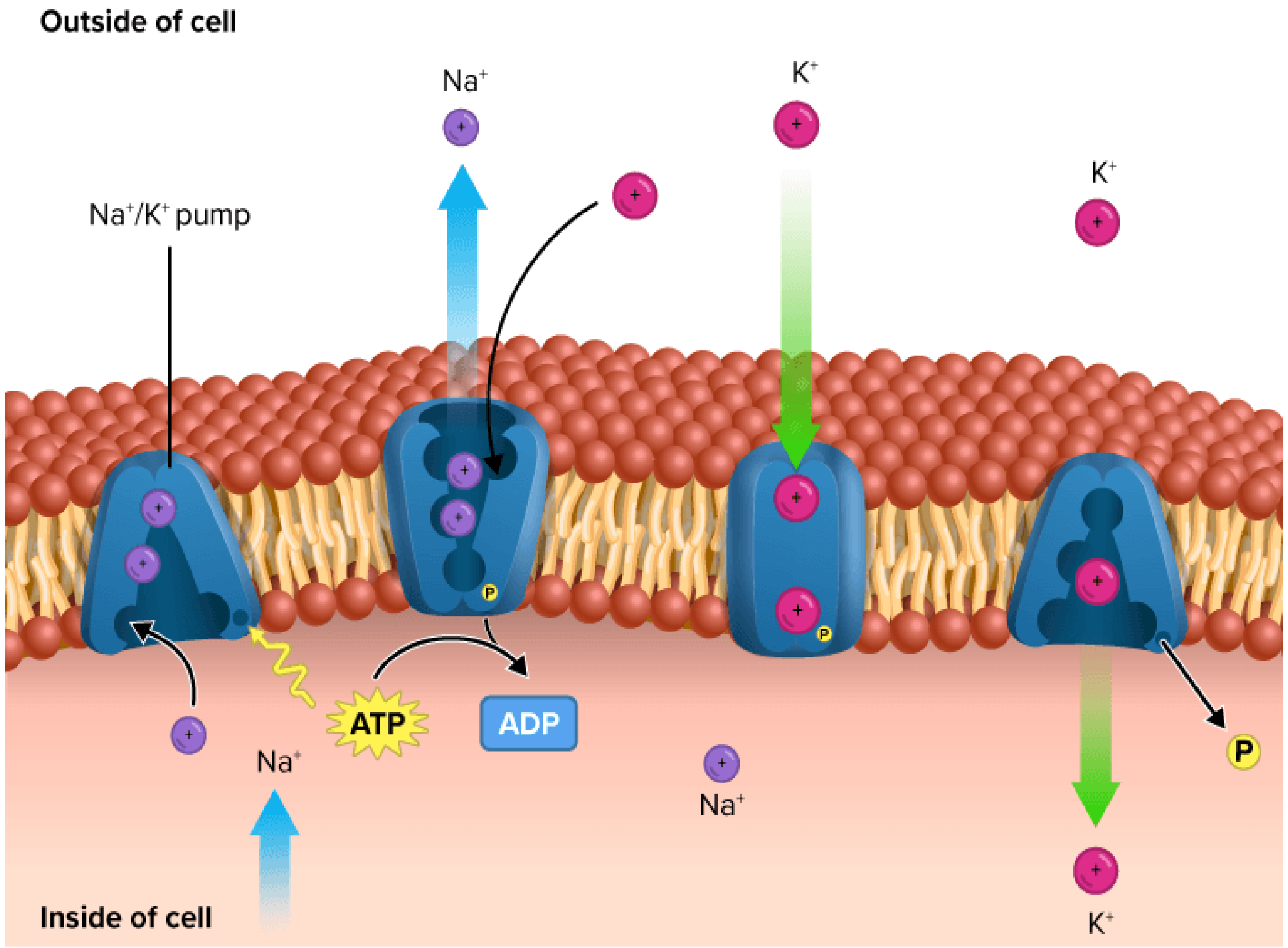
The Sodium – Potassium Pump



- If we were to just let this go, eventually we would lose that potential because all the sodium would come in.
- So, we have the sodium-potassium pump which moves 3 Na+ ions out of the neuron and brings 2 K+ ions in to the neuron.
- The pump moves ions against their concentration gradients.
- This requires energy which comes from the adenosine triphosphate (ATP)

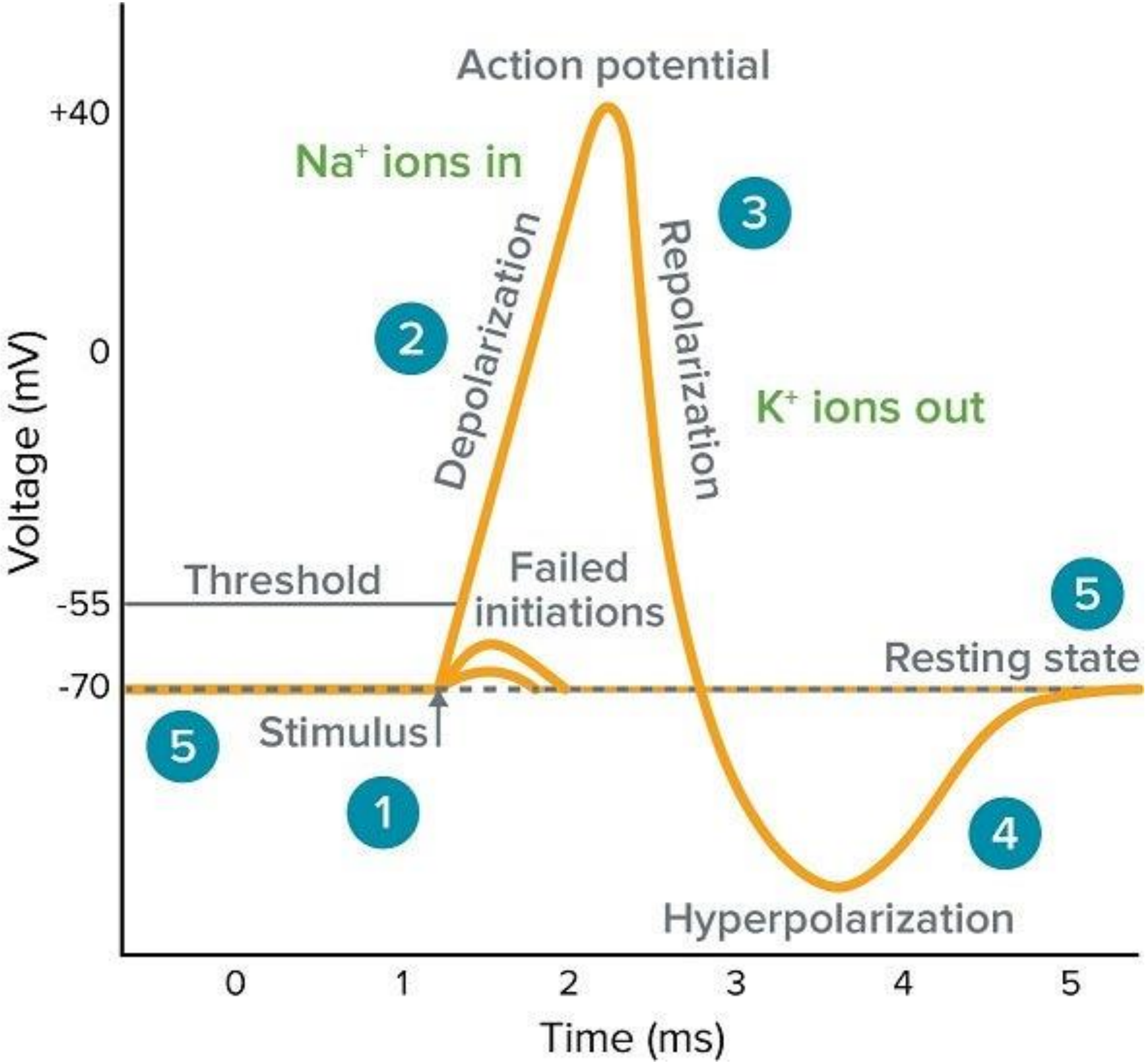
The importance of the sodium - potassium pump

- It maintains the concentration gradients of Na+ and K+, which are crucial for the resting membrane potential and the generation of action potentials.
- By keeping more Na+ outside and more K+ inside the neuron, the pump ensures that the neuron stays polarized (with the inside more negative).
- Without this pump, the neuron would gradually lose its membrane potential, as Na+ would build up inside the cell and K+ would leak out.
- The pump is energy intensive, using up a significant portion of the ATP produced by the neuron.
- This reflects how critical ion balance is for proper neuron function.



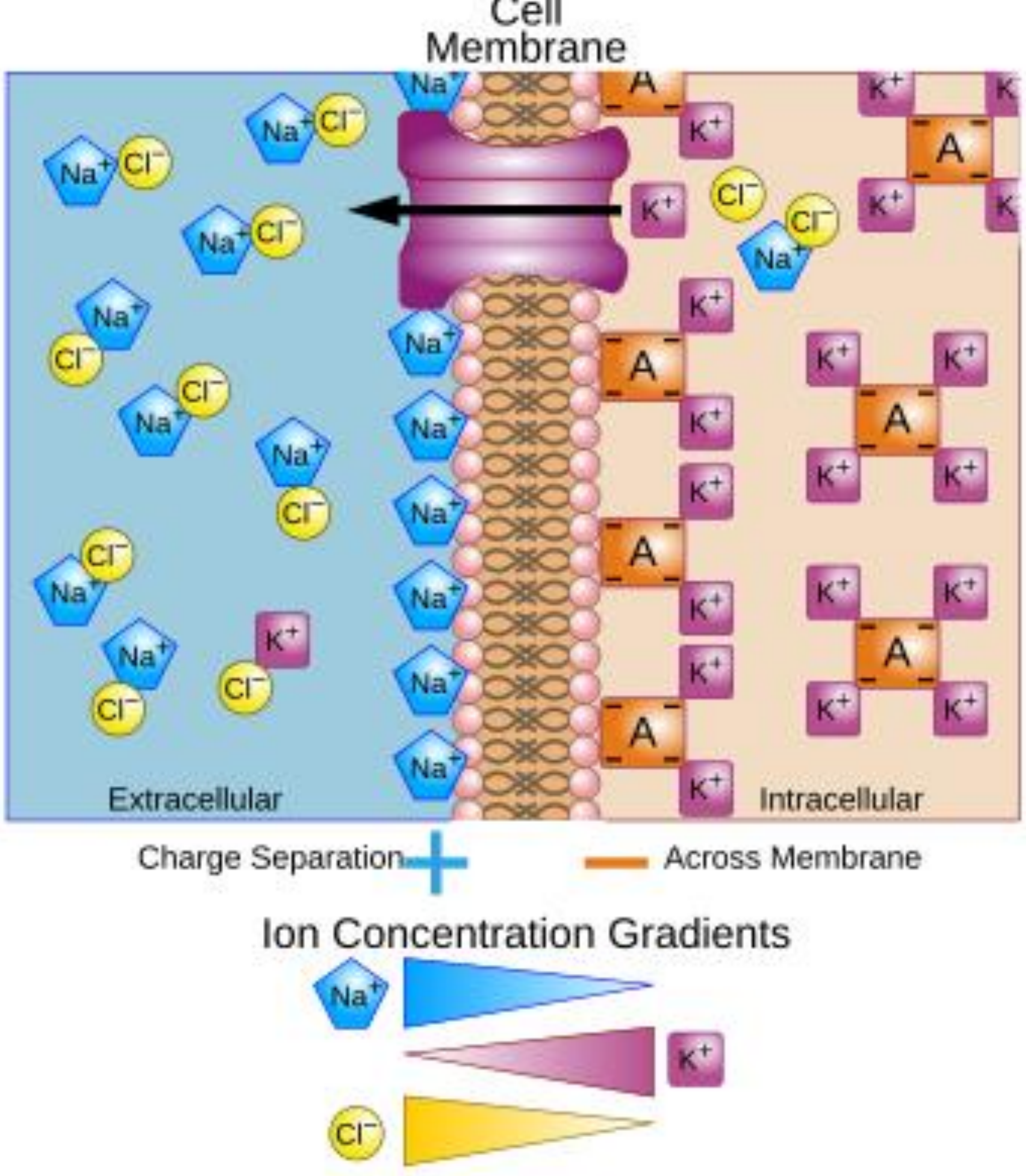
The Action Potential

- It is a rapid, temporary change in the electrical membrane potential of a neuron or other excitable cell (such as a muscle cell), which allows it to transmit signals.
- It is the fundamental mechanism by which neurons communicate and send information over long distances.
- The following five steps describe a detailed breakdown of what an action potential is and how it works.



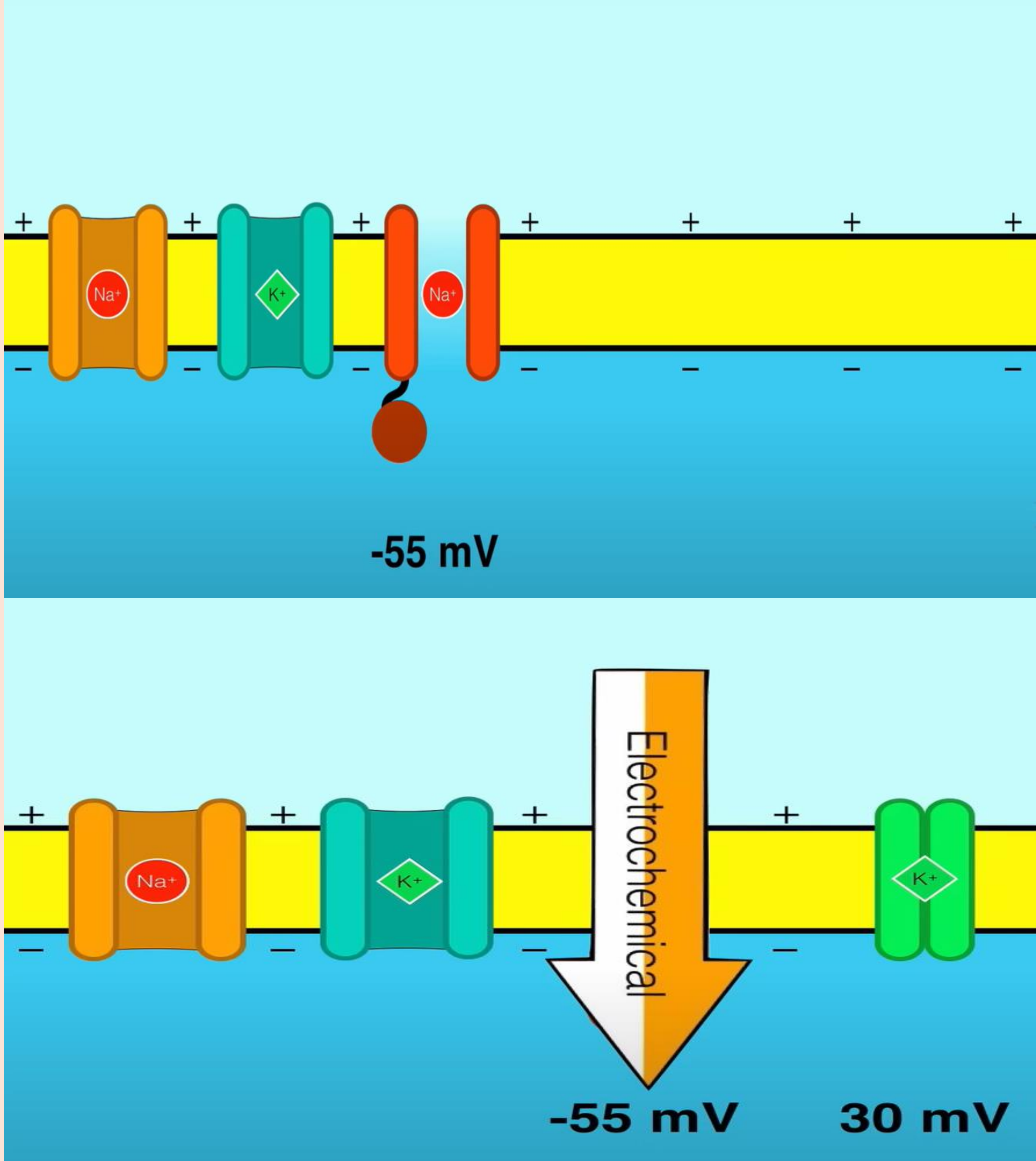
1. Resting Membrane Potential

- Before the action potential, the neuron is at its resting membrane potential, typically around -70 mV.
- Inside of the neuron is more negative than the outside.
- This resting potential is maintained by the sodium-potassium pump and leak channels, which maintain the concentration gradients of ions (Na^+, K^+) across the membrane.
- There is more Na^+ (sodium) outside the cell.
- There is more K^+ (potassium) inside the cell.



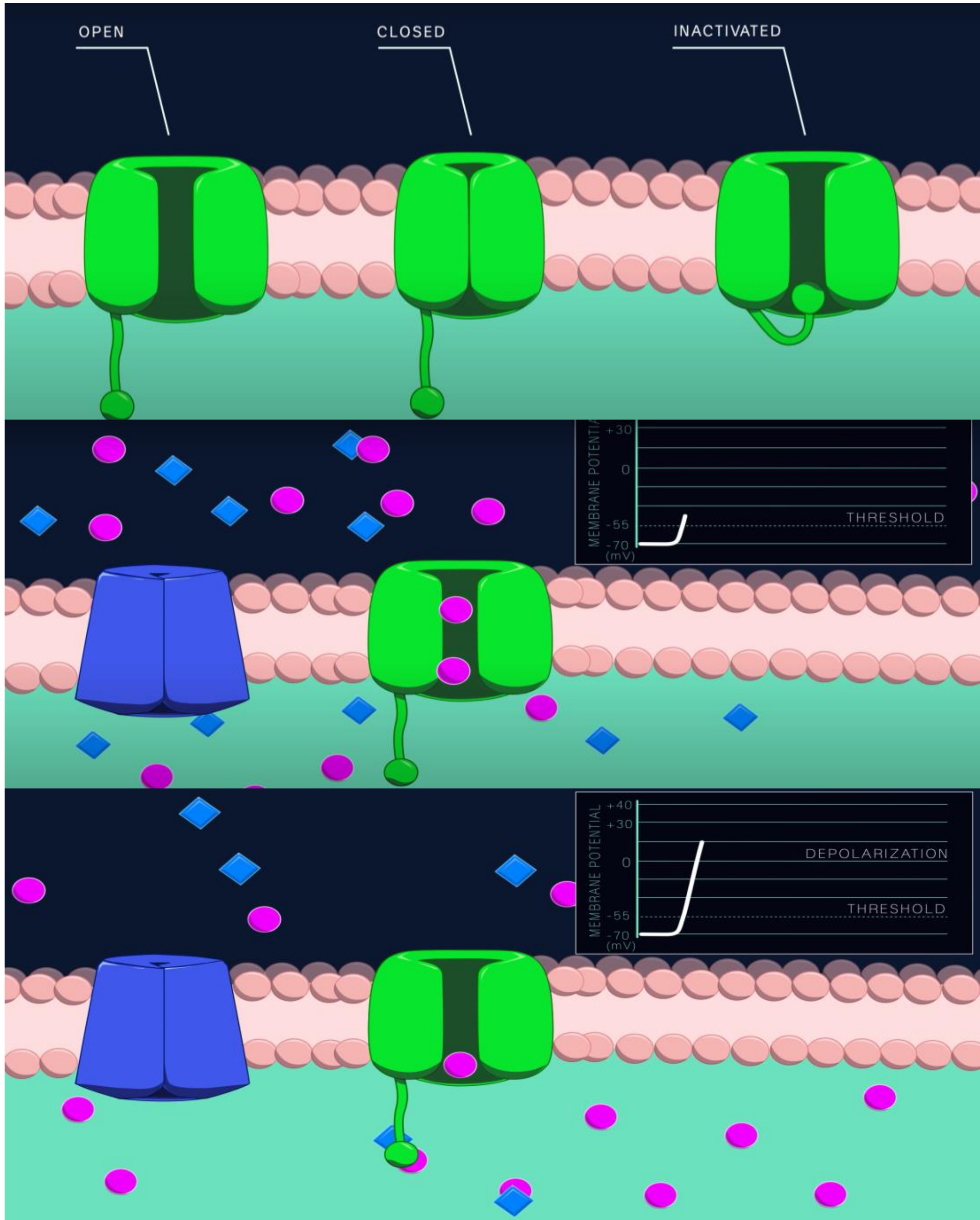
2. Initiation (Threshold)

- An action potential is initiated when the membrane potential becomes less negative (depolarizes) to reach a threshold potential, usually around -55 mV.
- Depolarization can be triggered by inputs from other neurons or sensory stimuli that cause excitatory postsynaptic potentials.



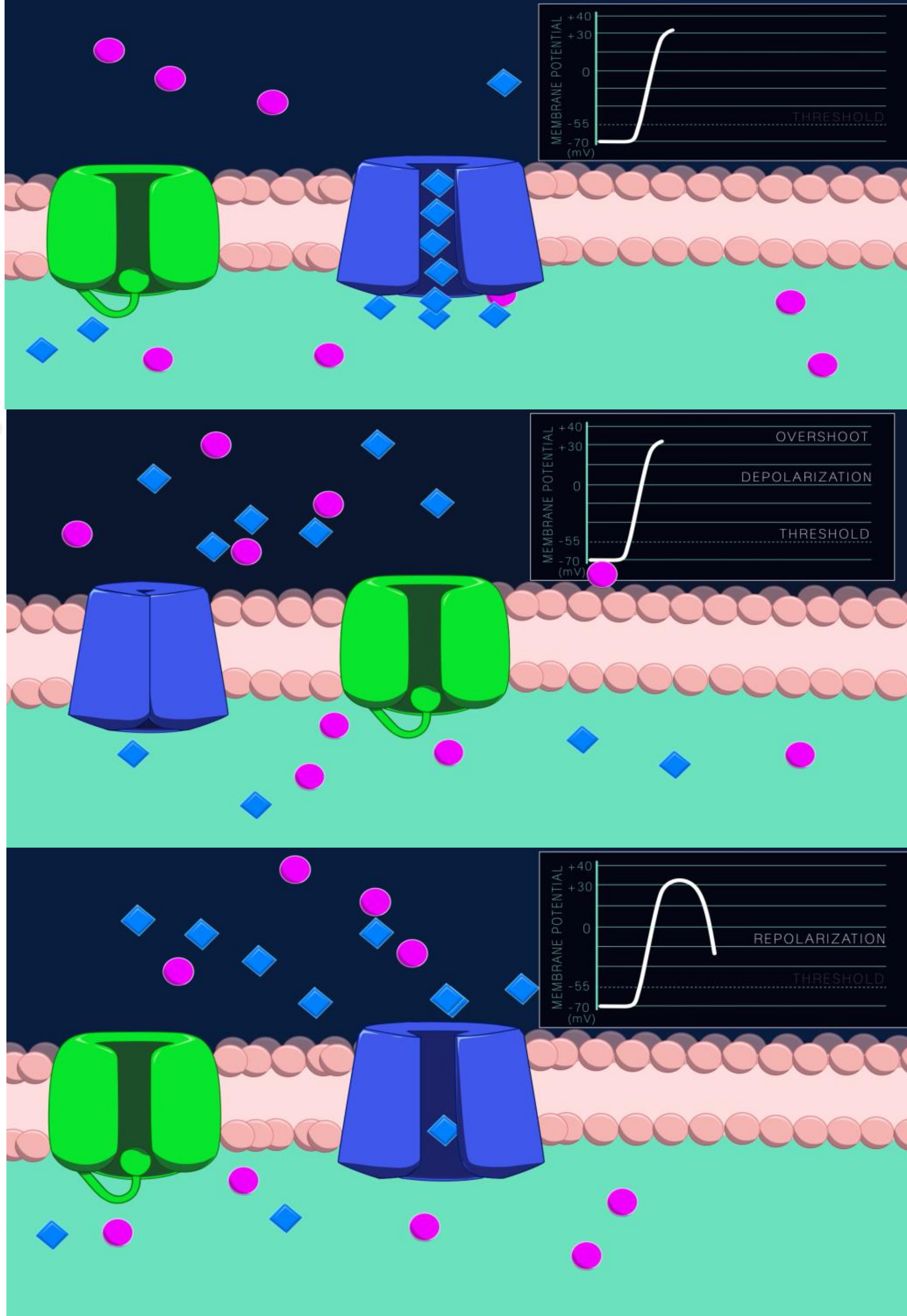
3. Depolarization Phase

- Once the threshold is reached, voltage-gated sodium (Na+) channels open, and Na+ ions rapidly flow into the neuron due to their concentration and electrical gradient.
- This influx of positive ions causes the membrane potential to rapidly become more positive, moving towards +30 to +40 mV.



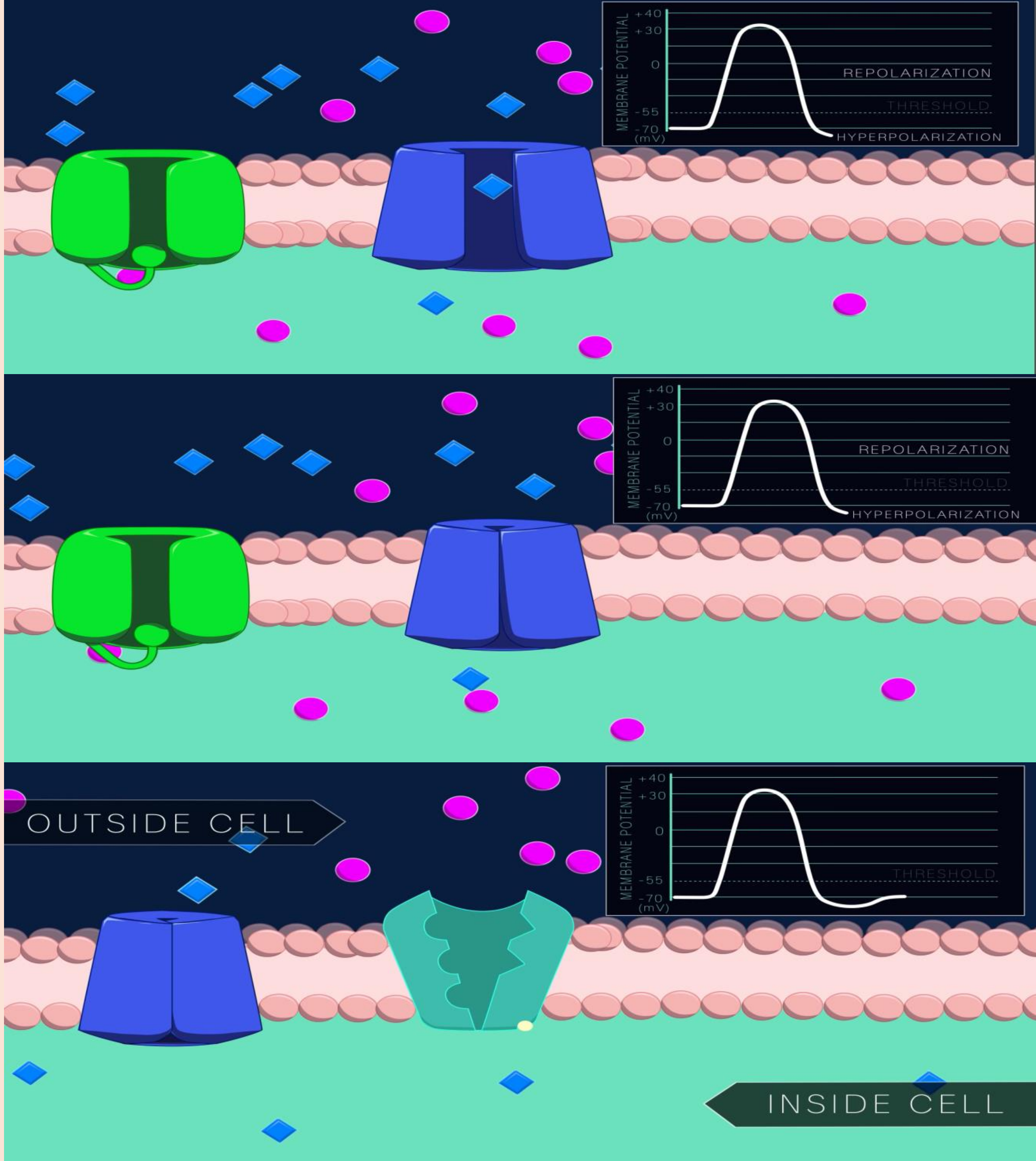
4. Repolarization Phase

- Shortly after the Na^+ channels open, they quickly become inactivated, **stopping** the influx of Na^+ ions.
- At the same time, voltage-gated potassium channels **open**, and K^+ ions **flow out** of the neuron, driven by their concentration gradient.
- The **efflux** of K^+ brings the membrane potential back toward the negative resting level, which is known as **repolarization**.



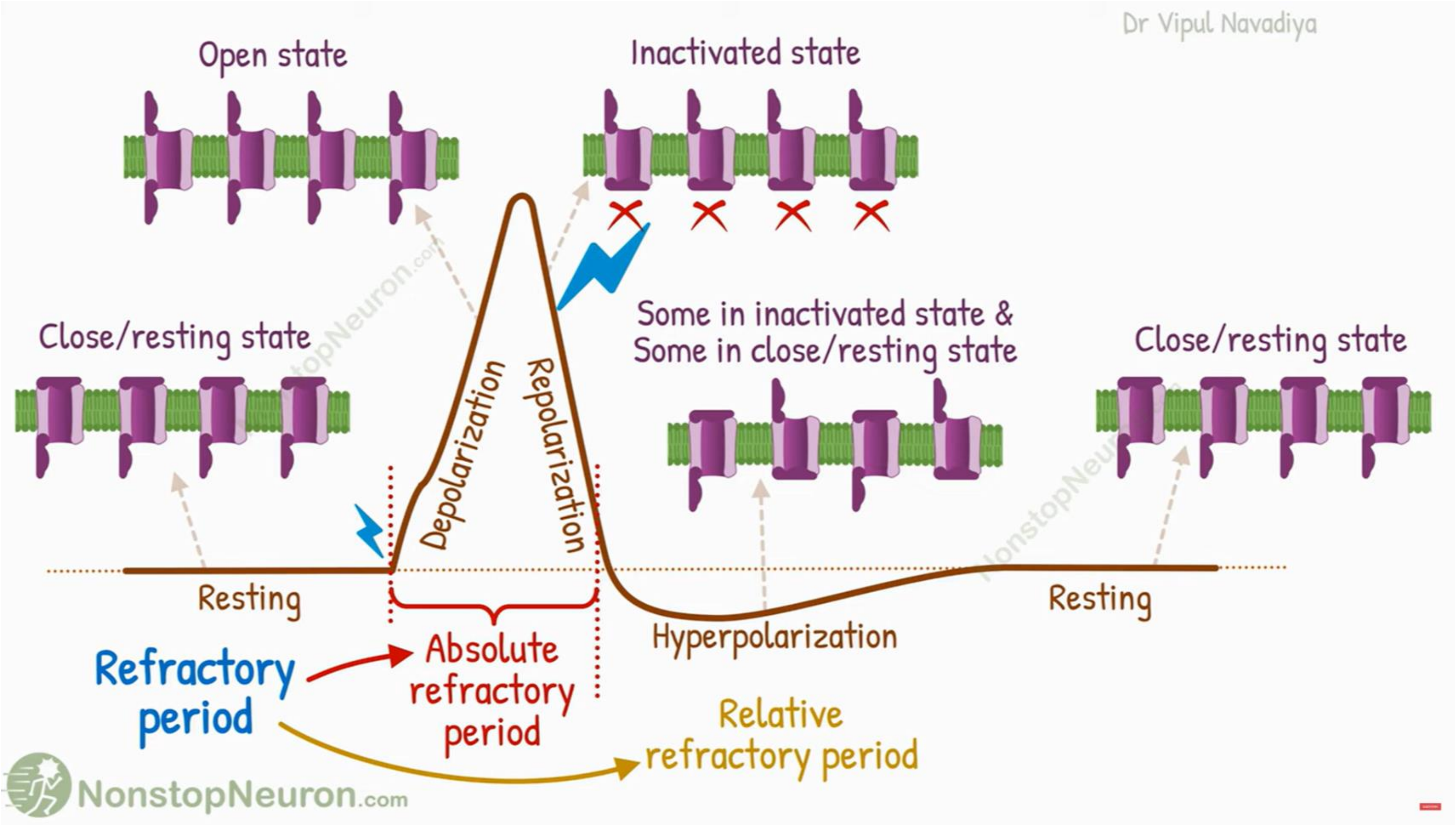
5. Hyperpolarization (Afterpotential)

- The K^+ channels remain open for a short period after the neuron repolarizes, allowing more K^+ to exit the cell than necessary.
- This causes the membrane potential to become more negative than the resting membrane potential, typically around -80 mV.
- This phase is called **hyperpolarization** or the **afterpotential**.
- Eventually the K^+ channels close, and the sodium-potassium pump restores the neuron to its resting membrane potential.



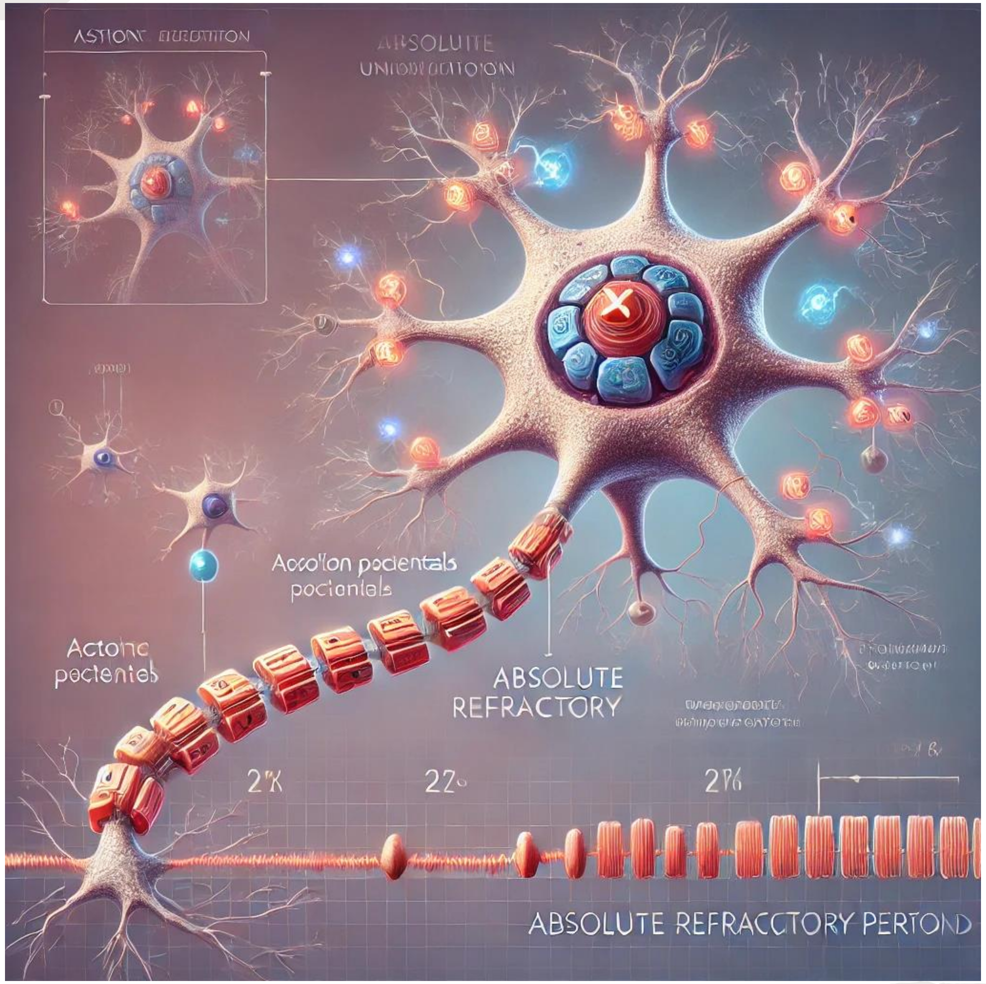
6. Refractory Period

- **Absolute refractory period**: During this phase, the neuron **cannot fire** another action potential because the Na^+ channels are inactivated.
- **Relative refractory period**: After the absolute refractory period, the neuron can fire another action potential, but a **stronger – than – normal** stimulus is needed because the membrane is **hyperpolarized**.



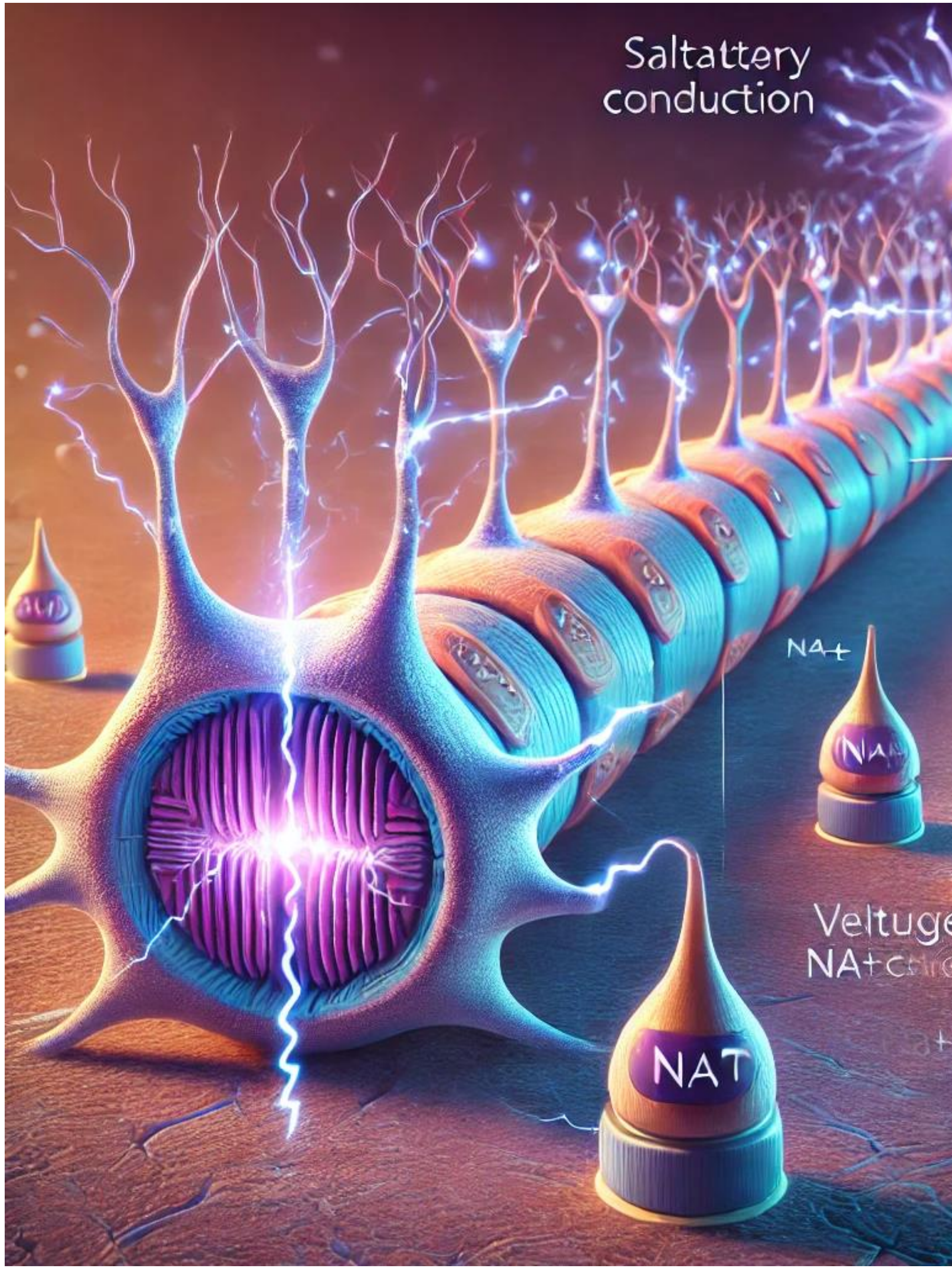
The biological significance of the absolute refractory period

1. The absolute refractory period is crucial for unidirectional propagation, discrete action potentials and frequency control.
2. It prevents backward movement of the action potential, ensuring proper signal transmission.
3. It sets an upper limit on firing frequency, enabling neurons to properly encode information through the modulation of action potential frequency.
4. It protects neurons from becoming over-excited or entering a state of continuous firing which could lead to cellular damage or dysfunction.



Propagation of Action Potentials

- The action potential does not remain in one place but propagates along the length of the neuron's **axon**.
- As the membrane potential in on region of the axon depolarizes, it triggers adjacent voltage-gated Na^+ channels to open, propagating the action potential down the axon toward the **axon terminals**.
- In **myelinated neurons**, the action potential "**jumps**" between gaps in the myelin sheath called the **Nodes of Ranvier**.
- This is called **saltatory conduction**, and it greatly increases the speed of signal transmission.



Summary of Mathematical Knowledge Needed

- ODEs for describing voltage changes over time.
- PDEs (cable equation) for modeling signal propagation along an axon
- Exponential functions for modeling ion channel dynamics (activation / inactivation)
- Circuit theory for understanding the neuron's behavior as an RC circuit.
- Numerical methods for solving the differential equations (e.g. Runge-Kutta)
- Probability theory for modeling stochastic ion channel behavior
- Fourier transforms for analyzing neuronal responses to ifferent frequencies.
- Conductance models (e.g. Hodgkin – Huxley) for ion channel behavior.

Ordinary Differential Equations (ODEs) for describing voltage changes over time in neurons

- The membrane potential of a neuron changes over time as ions flow in and out of the cell.
- This dynamic change can be mathematically described by **Ordinary Differential Equations** (ODEs).
- The most common approach for modelling the voltage change in neurons is based on the principles of electrostatics and current balance.
- It is often conceptualized through the **Hodgkin-Huxley** model or its simplified derivatives (**Leaky Integrate-and-Fire** model).
- At the heart of these models is the equation governing the membrane potential (**V**).
- It is the difference in electric potential inside versus outside the neuron.
- The voltage changes due to the flow of ions across the membrane through various channels.
- This movement of ions is captured by ODEs.

Current Balance Equation

- The voltage change across the neuronal membrane can be described using the current-balance equation.
- It is based on the law of conservation of charge: $Cm\frac{\mathrm{d}v(t)}{\mathrm{d}t} = I_{tot}$
- $\mathbf{C_m}$ is the membrane capacitance (measured in Farads per square centimetre).
- It represents the cell membrane's ability to store charge.
- $\frac{\mathbf{d}\boldsymbol{v}(\boldsymbol{t})}{\mathbf{d}\boldsymbol{t}}$ is the rate of charge of the membrane potential V(t) over time
- $\boldsymbol{I_{tot}}$ is the total ionic current flowing across the membrane.

Ionic Currents & Total Current

- The total current ($\mathbf{I_{tot}}$) is made up of different ionic currents flowing through channels specific to various ions.
- These are sodium ($\mathbf{I_{Na}}$), potassium ($\mathbf{I_K}$) and a "leak" current ($\mathbf{I_{leak}}$) that accounts for other small ions.
- Additionally, there may be an external input current ($\mathbf{I_{ext}}$), which represents external stimuli applied to the neuron.
- We have $\mathbf{I_{tot}} = \mathbf{I_{ext}} - (\mathbf{I_{Na}} + \mathbf{I_K} + \mathbf{I_{leak}})$
- External Current $\mathbf{I_{ext}}$: Applied externally, such as from a stimulus or an electrode.
- Sodium Current $\mathbf{I_{Na}}$: Driven by sodium ions flowing through voltage-gated sodium channels.
- Potassium Current $\mathbf{I_K}$: Driven by potassium ions flowing through voltage-gated potassium channels.
- Leak Current $\mathbf{I_{leak}}$: Represents the constant, passive flow of ions through non-gated channels.

Current - Voltage Relationship: Ohm’s Law

- For each ion current, the relationship between the current and voltage can be described by a variation of **Ohm’s Law**.
- This law relates the current to the conductance of the channel and the difference between the membrane potential V and the ion’s reversal / equilibrium potential.
- For each current we have: $I_{\text{ion}} = gi_{on}(V - Eion)$
- The conductance of the ion channel (g_m) is measured in Siemens.
- It may be a function of time or voltage (especially in voltage-gated channels).
- The reverse potential of that ion (E_{ion}) is the voltage at which there is no net flow of that ion across the membrane.
- Foe example, we have $I_{\text{Na}} = gN_a(V - ENa)$

1. Parameter Initialization

- The membrane capacitance $\mathbf{C_m}$ represents how easily the membrane stores charge.
- It is measured in microfards per square centimeter.
- It affects how fast or slow the membrane potential changes in response to currents.
- Higher $\mathbf{C_m}$ means the membrane potential changes slower.
- Lower $\mathbf{C_m}$ leads to **faster** changes.

- The **Leak Reversal Potential $\mathbf{E_L}$** is the voltage (milli-volts) at which the leak current reverses direction.
- This means that no net flow of ions occur through the leak channels.
- In this case, it's -54.4 mV.
- The leak current drives the membrane potential toward this value when no external current is applied.

- The leak conductance $\mathbf{g_L}$ is measured in milli-siemens per square centimeter.
- It represents how easily ions leak across the membrane through passive (non-voltage-gated) channels.
- Higher $\mathbf{g_L}$ means ion flow more easily, **driving** the membrane potential back towards the **leak reversal potential** faster.

```
% Parameters
C_m = 1.0;    % Membrane capacitance, uF/cm^2
g_L = 0.3;    % Leak conductance (mS/cm^2)
E_L = -54.4;  % Leak reversal potential (mV)
V_rest = -65; % Resting membrane potential (mV)
```

- The **Resting Membrane Potential $\mathbf{V_{rest}}$** is the baseline voltage of the neuron when no stimulation is applied.
- Here, it's set to -65 mV, which is a typical value for many neurons.

2. Time Setup

Time Step (dt):

- The time increment (in milliseconds) for each step of the stimulation.
- Smaller time steps give more accurate simulations but take longer to compute.
- Here, the time step is 0.01 ms

Total Time (T):

- The duration of the stimulation.
- In this case, the simulation runs for 100 ms

Time Vector (time):

- This creates an array of time points from 0 to 100 ms in increments of 0.01 ms
- The time array will have 10,000 points in total
- It represents the simulation over time

```
% Time parameters
dt = 0.01;  % Time step (ms)
T = 100;    % Total time (ms)
time = 0:dt:T;
```

3. External Current Injection

```
% External current (stimulation)
I_ext = zeros(size(time));
I_ext(500:600) = 10;  % Inject current between 5 and 6 ms (in microamps)
```

External Current (I_{ext}):

- This array stores the **external current applied to the neuron** at each time step.
- Initially, it is set to zero at all time points.
- This means **no current** is applied.
- Between time steps 500 and 600 (which corresponds to 5 – 6 ms), a current of **10 microamperes** is injected into the neuron.
- This is a brief pulse of external current.
- It will trigger a temporary change in the membrane potential.

4. Initial Conditions

```
% Initialize membrane potential (starting at resting potential)

V = V_rest * ones(size(time));  % Membrane potential (mV)
```

Initial Membrane Potential (V):

- The array V stores the membrane potential at each time point.
- Initially, the membrane potential is set to V_rest = -65 mV at all time points.
- This means the neuron starts at its resting potential.
- It will change based on the injected and leak currents during the simulation.

5. Simulation Loop

```
for t = 2:length(time)
    % Leak current
    I_leak = g_L * (V(t-1) - E_L);

    % Update membrane potential using Euler's method
    V(t) = V(t-1) + dt * (I_ext(t) - I_leak) / C_m;
end
```

- The Euler's method is used to numerically solve the differential equation governing the membrane potential.
- The equation we are solving is: $$C_m \frac{dV(t)}{dt} = I_{\text{ext}} - I_{\text{leak}}$$
- Using the Euler's method, the membrane potential at time t is updated as follows:
- The leak current I_{leak} is calculated using the Ohm's law: $$V(t) = V(t-1) + \frac{\Delta t}{C_m} \times (I_{\text{ext}}(t) - I_{\text{leak}}(t))$$
- The leak current pulls the membrane potential toward the **Leak Reversal Potential** E_L
- The membrane potential (V(t)) is updated by applying the current balance equation at each time step.
- The membrane potential is influenced by both the external current I_{ext} and the leak current I_{leak}.

6. Visualization

- This part of the code generates a plot showing the membrane potential V over time.
- The time points (in milliseconds) are plotted on the x-axis.
- The corresponding membrane potential (in millivolts) is plotted on the y-axis
- The plot shows:
    1. A steady membrane potential at -65 mV (the resting potential) before stimulation.
    2. A rise in membrane potential during the current injection (between 5 ms and 6 ms).
    3. A return to the resting potential after the current injection stops, driven by the leak current.

```
% Plot membrane potential over time
figure;
plot(time, V, 'LineWidth', 2);
title('Simplified Neuron Model: Membrane Potential');
xlabel('Time (ms)');
ylabel('Membrane Potential (mV)');
grid on;
```

This simple model shows how neurons respond to external current and how they return to equilibrium due to the leak channels.