RESTING MEMBRANE POTENTIAL

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First Semester

Week 4

Date 27/10/2025

Outline

- Electrical potential
- Membrane potential
- Resting Membrane potential
- Local potential and Action Potential
- Depolarization, repolarization and Hyperpolarization

Objectives

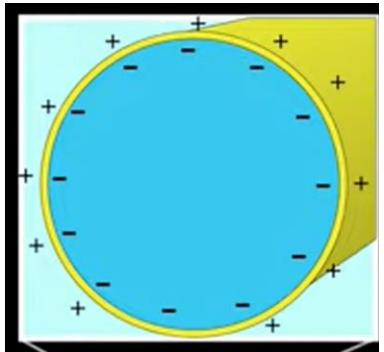
- Understanding electrical potential (Votage)
- Understanding current
- Understanding membrane potential
- Understanding the role of membrane potential
- Explaining the mechanism of action potential

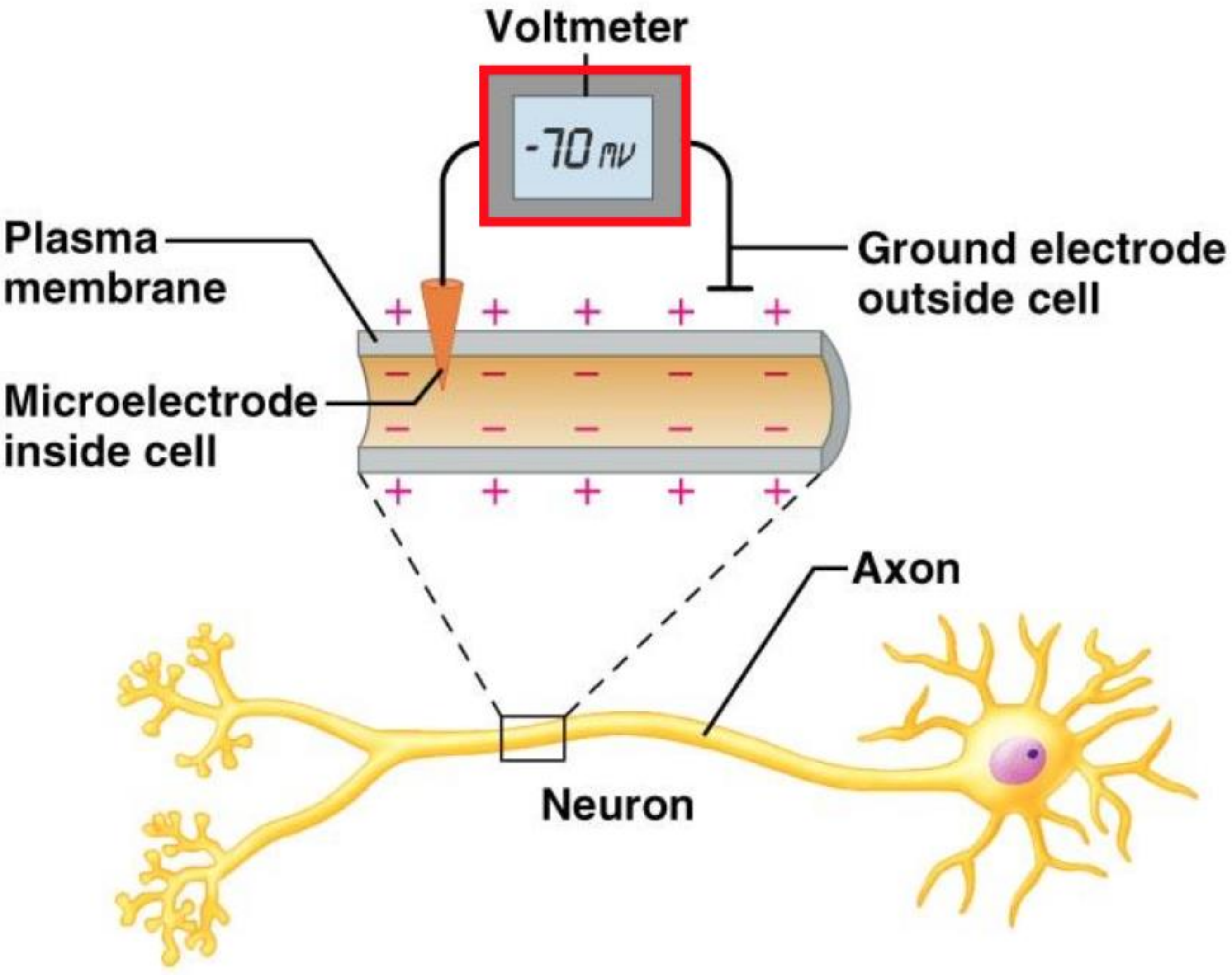
Electrical Potentials and Currents

- Difference in electrical charge from one point to another is called an **electrical potential**, or **voltage**. It typically measures 12 volts (V) for a car battery and 1.5 V for a flashlight battery
- It is a form of potential energy that, under the right circumstances, can produce a current. An electrical **current** is a flow of charged particles from one point to another.
- A new flashlight battery, for example, typically has a potential, or charge, of 1.5 volts (V). If a lightbulb and the two poles of the battery are connected by a wire, electrons flow through the wire from one pole to the other, creating a current that lights the bulb. As long as the battery has a potential (voltage), we say it is **polarized**

Cell Electrical Potentials and Currents

- Living cells are also **polarized** and **Electrical potentials** exist across the membranes of virtually all cells of the body due to **unequally** distribution of ions between the **interior** of cells and the fluid that **surrounds them**.
- The charge difference across the plasma membrane is called the **resting membrane potential (RMP).** It is much less than the potential of a flashlight battery— typically about –70 millivolts (mV) in an unstimulated, “resting” neuron.
- The negative value means there are more negatively charged particles on the **inside** of the membrane than on the **outside**.





Voltmeter
-70 mv
Plasma membrane
Ground electrode outside cell
Microelectrode inside cell
Axon
Neuron

Currents in body

We don’t have free electrons in the body as we do in an electrical circuit. Electrical currents in the body are created, instead, by the flow of ions such as Na^+ and K^+ through **gated channels** in the plasma membrane. Gated channels can be opened and closed by various stimuli, as we have seen earlier

Why we have membrane potential ?

1. **Neural communication**: In nerve and muscle cells, changes in membrane potential produce action potentials — the electrical signals that allow communication, movement, and sensation.
2. In glandular cells, macrophages, and ciliated cells, local changes in membrane activate many cellular functions including secretion, defense, and movement.

Resting membrane potential(RMP):

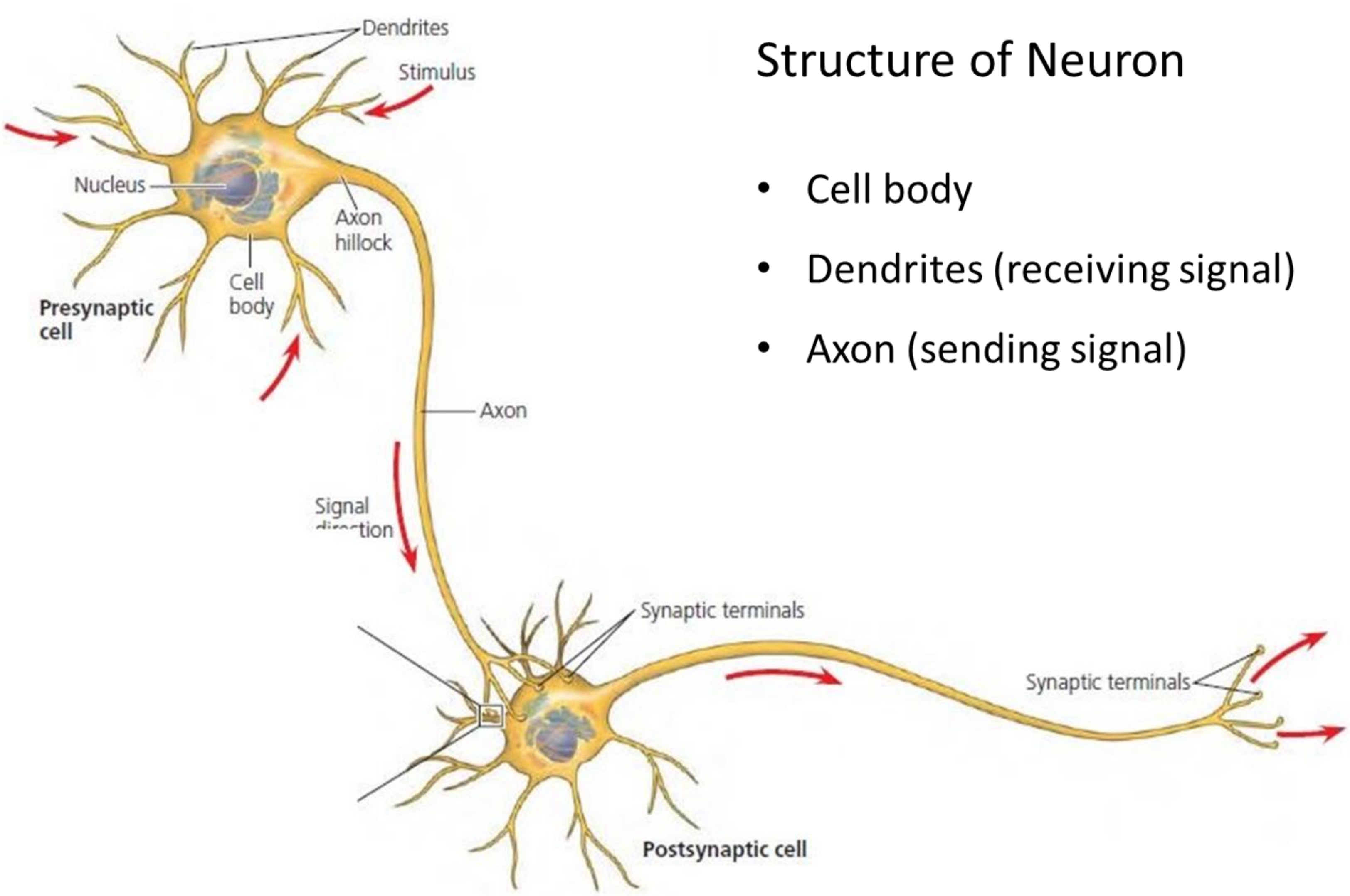
- It refers to the difference in electric charge across the cell's plasma membrane when an excitable cell is at rest, meaning it is not actively sending or receiving signals.

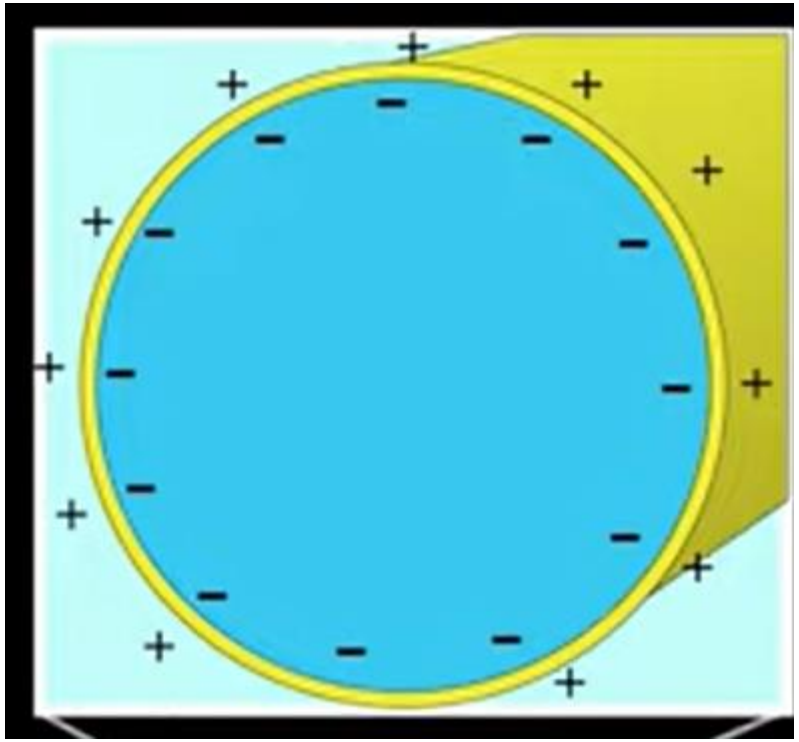
Table 5-1 Resting Membrane Potential in Different Cell Types

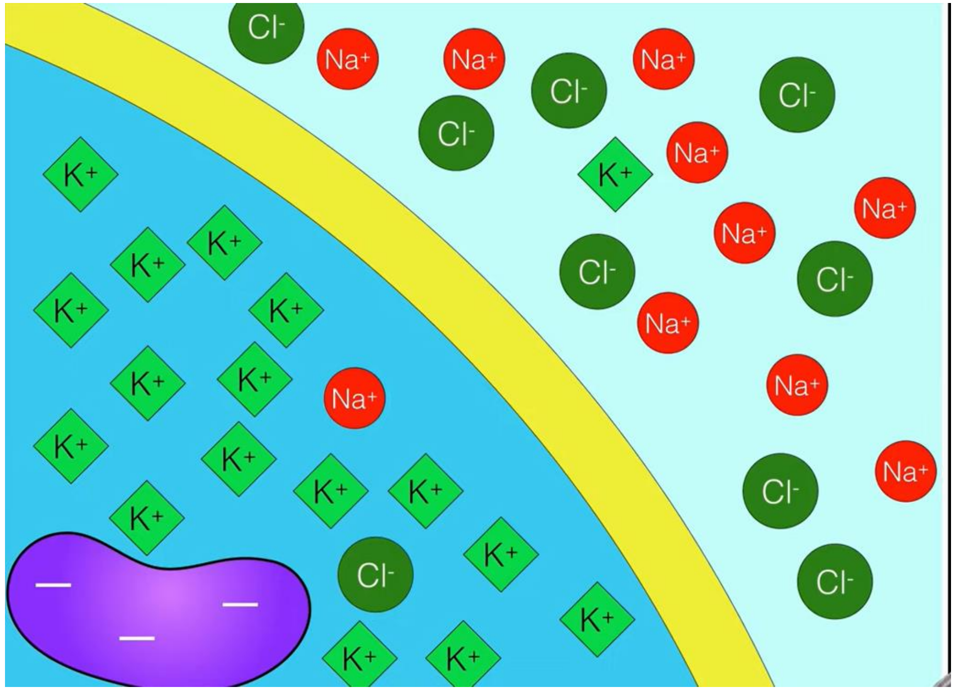
Cell Type	Resting Potential (mV)
Neurons	−60 to −70
Skeletal muscle	−85 to −95
Smooth muscle	−50 to −60
Cardiac muscle	−80 to −90
Hair (cochlea)	−15 to −40
Astrocyte	−80 to −90
Erythrocyte	−8 to −12
Photoreceptor	−40 (dark) to −70 (light)

Structure of Neuron

- Cell body
- Dendrites (receiving signal)
- Axon (sending signal)






Cl-
Na+
K+

The formation of Resting Membrane Potential

The reason a cell has a resting membrane potential is that electrolytes are unequally distributed between **the extracellular fluid (ECF) on the outside** of the plasma membrane and **the intracellular fluid (ICF) on the inside** (Due to Na^{+}-K^{+} pump)

The RMP results from the combined effect of three factors:

1. The diffusion of ions down their concentration gradients through the membrane;
2. Selective permeability of the membrane, allowing some ions to pass more easily than others;
3. The electrical attraction of cations and anions to each other.

Potassium (K^+) and sodium ions (Na^+) play an essential role in the formation of the resting potential

- **Potassium ions (K^+)** have the greatest influence on the RMP because the plasma membrane is more permeable to K^+ than to any other ion. Imagine a hypothetical cell in which all the K^+ starts out in the ICF, with none in the ECF.
- Also in the **ICF** are a number of cytoplasmic **anions** that cannot escape from the cell because of their size or charge—**phosphates**, **sulfates**, small **organic acids**, **proteins, ATP**, and **RNA.**
- Potassium ions diffuse freely through **leak channels** in the plasma membrane, down their concentration gradient and out of the cell, leaving these cytoplasmic anions behind
- As a result, the **ICF** grows more and more **negatively** charged. But as the ICF becomes more negative, it exerts a stronger attraction for the positive potassium ions and attracts some of them back into the cell

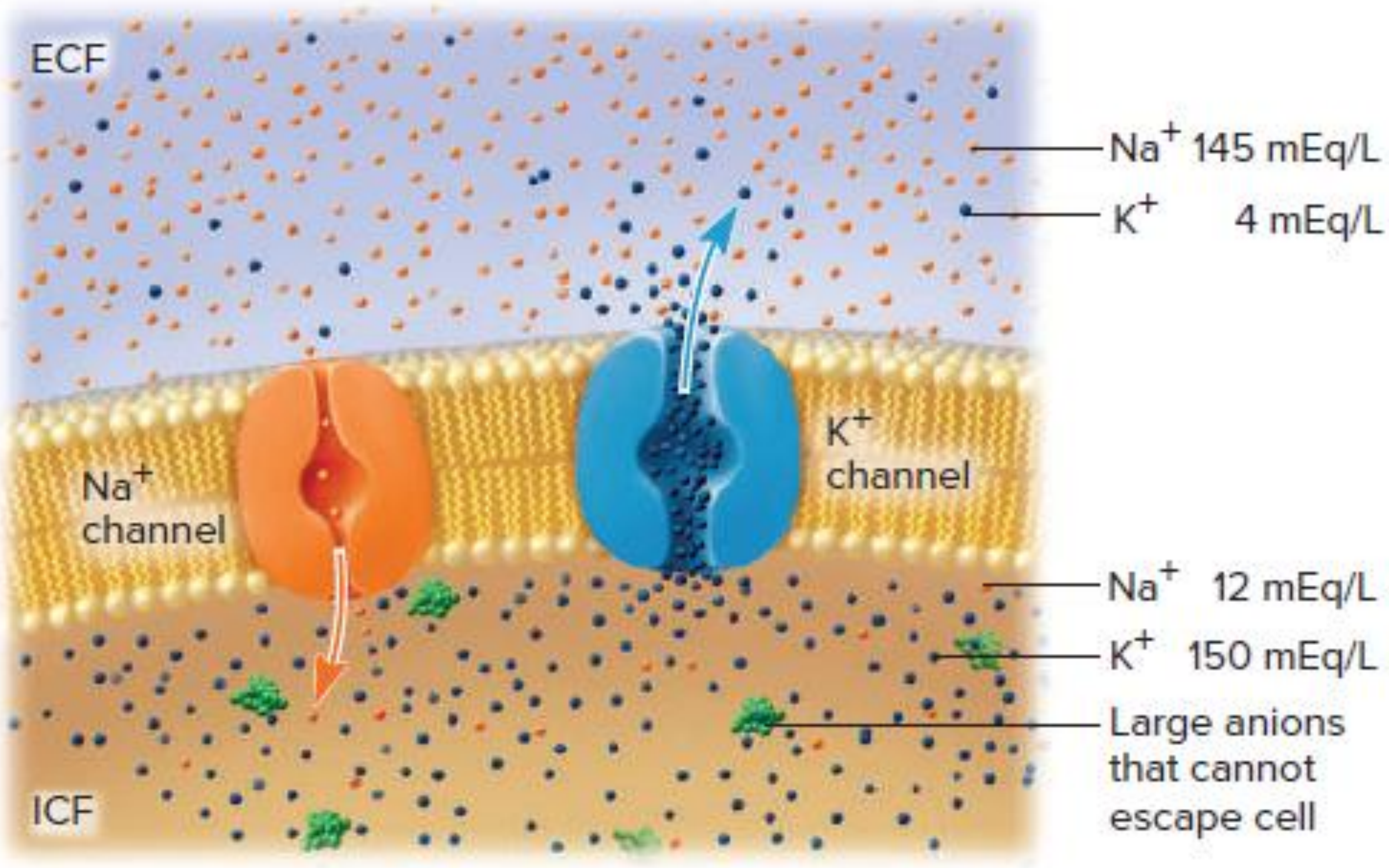
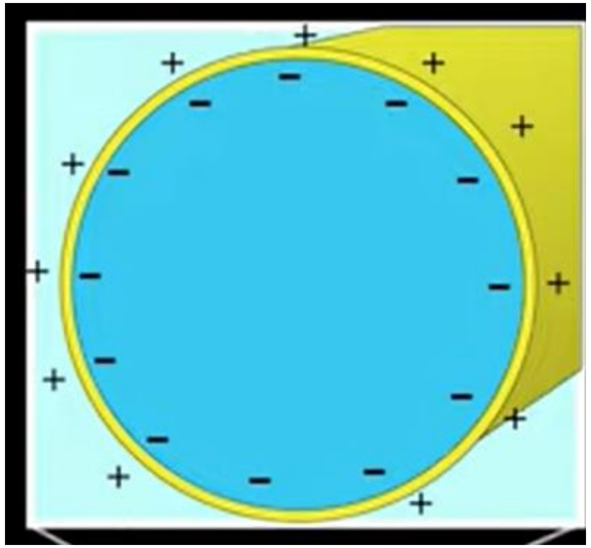
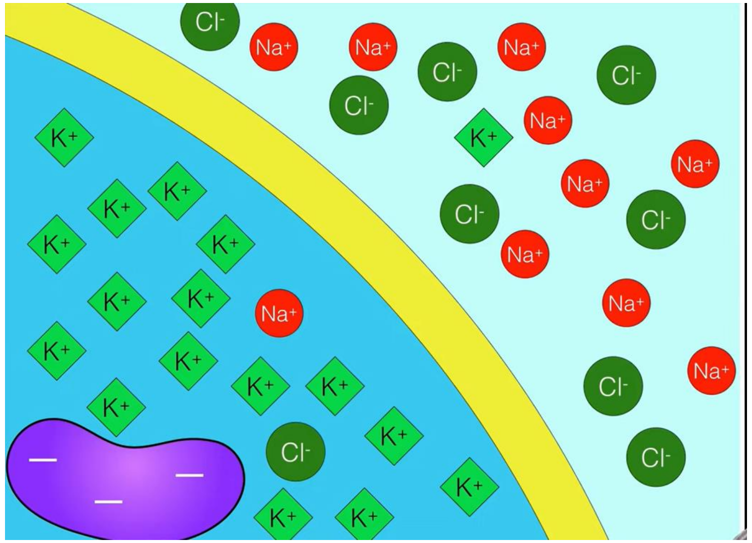


FIGURE 12.12 Ionic Basis of the Resting Membrane Potential. Note that sodium ions are much more concentrated in the extracellular fluid (ECF) than in the intracellular fluid (ICF), while potassium ions are more concentrated in the ICF. Large anions unable to penetrate the plasma membrane give the cytoplasm a

- Eventually an equilibrium is reached in which K^+ is moving out of the cell (down its concentration gradient) and into the cell (by electrical attraction) at equal rates. There is no further net diffusion of K^+. **At the point of equilibrium, K^+ is about 40 times as concentrated in the ICF as in the ECF.**



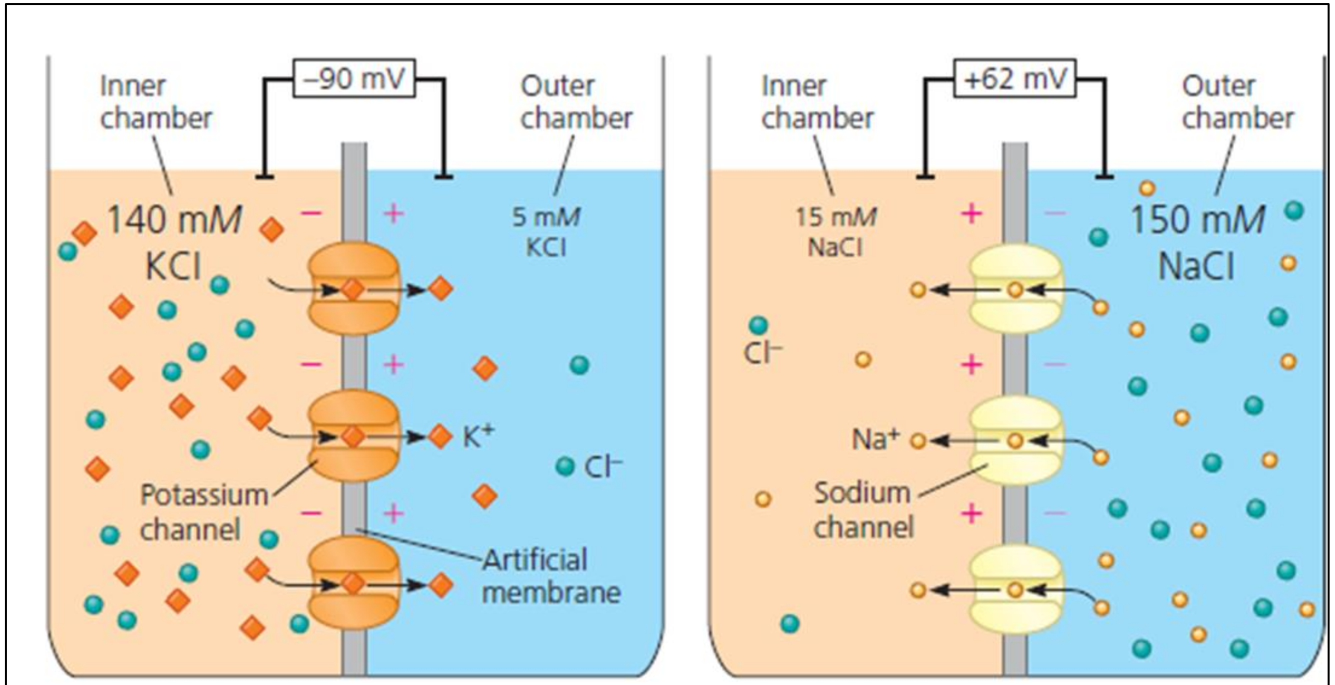


- **If K^+ were the only ion affecting the RMP, it would give the membrane potential about –90 mV.**
- However, sodium ions **(Na^+)** also enter the picture. Sodium is about 12 times as concentrated in the ECF as in the ICF. The resting plasma membrane is much **less** permeable to Na^+ than to K^+, but Na^+ does diffuse down its concentration gradient into the cell, attracted by the negative charge in the ICF.
- The resting membrane potential is close to this equilibrium potential of K^+ (around -70 mV in neurons) because K^+ has the highest permeability at rest.
- This sodium leak is only a **trickle**, but it is enough to cancel some of the negative charge and reduce the voltage across the membrane.

- **Na^+ diffuses** into the cell, making the inside of the cell less negative. **If we model a membrane in which the only open channels** are selectively permeable to Na^+, we find that a tenfold higher concentration of Na^+ in the outer chamber results in an equilibrium potential (E_{Na}) of +62 mV.

- Each molecule move down its concentration gradient, but this movement it balanced by opposite movement of ion, when electrical potential (force) is form and equal the chemical potential (equilibrium is reached)
- The magnitude of the membrane voltage at equilibrium for a particular ion is called that ion's **equilibrium potential (*E*ion)**.
- **Equilibrium potential (*E*ion), for each ion is the voltage when gradient potential is equal to electrical potential**

- **Equilibrium potential of K(EK) = -90 mV**
- **Equilibrium potential of Na(ENa) = +62 mV**
- **The sum of Equilibrium potential of K and NA is -70. which is called resting potential**



(a) Membrane selectively permeable to K^+

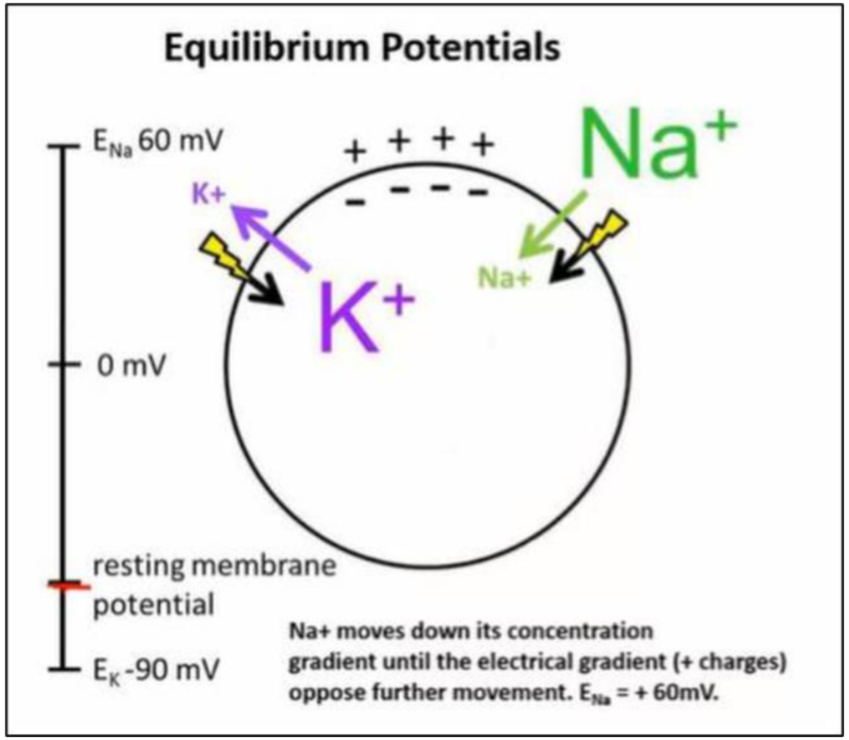
Nernst equation for K^+ equilibrium potential at 37°C:

$$E_K = 62\text{ mV}\left(\log\frac{5\text{ mM}}{140\text{ mM}}\right) = -90\text{ mV}$$

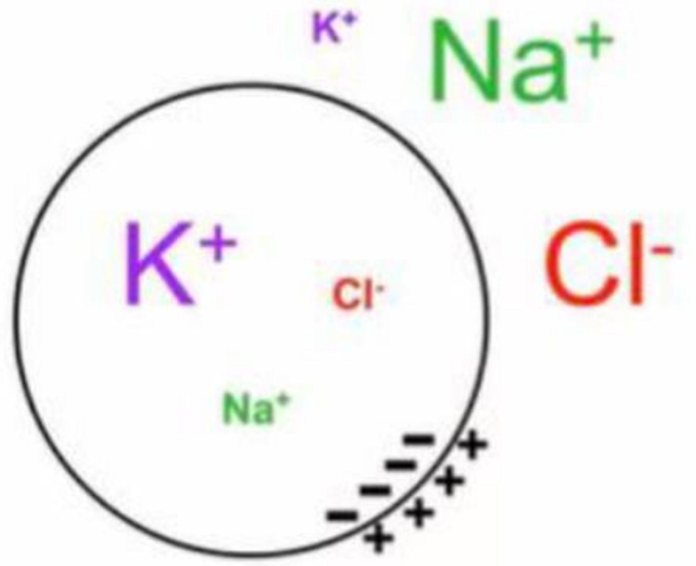
(b) Membrane selectively permeable to Na^+

Nernst equation for Na^+ equilibrium potential at 37°C:

$$E_{Na} = 62\text{ mV}\left(\log\frac{150\text{ mM}}{15\text{ mM}}\right) = +62\text{ mV}$$

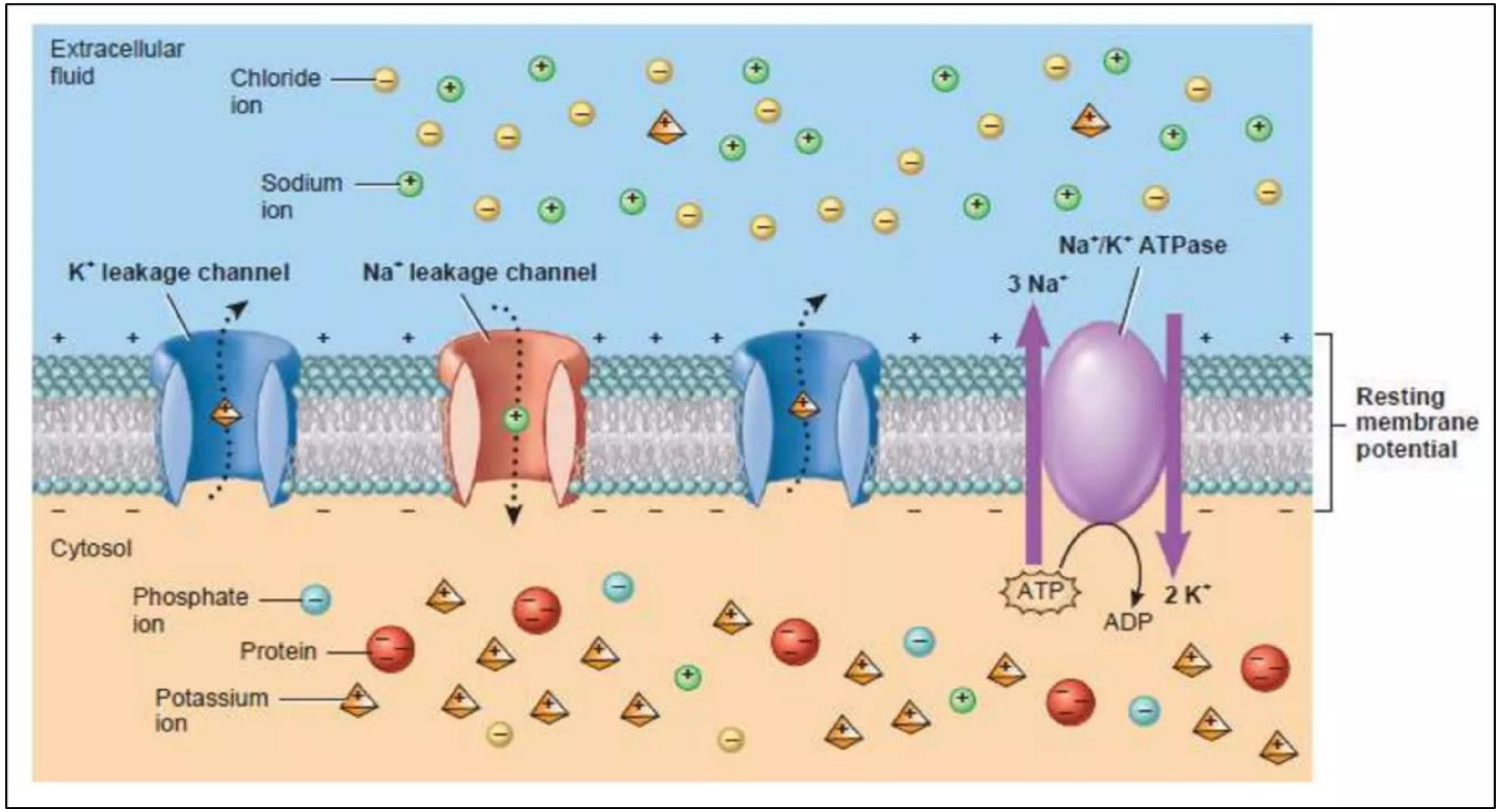


Electrochemical Gradient



Ion	ECF (mM)	ICF (mM)
Na^+	140.0	15.0
K^+	4.4	140.0
Cl^-	105.0	7.0

- **Sodium** leaks **into** the cell and **potassium** leaks **out**, but the **sodium–potassium** (Na^+–K^+) pump continually **compensates** for this leakage.
- It pumps 3 Na^+ out of the cell for every 2 K^+ it brings in, consuming 1 ATP for each exchange cycle.
- By removing more cations from the cell than it brings in, it contributes about –3 mV to the RMP.
- The resting membrane potential of –70 mV is the net effect of all these ion movements
    1. K^+ diffusion out of the cell
    2. Na^+ diffusion inward,
    3. the Na^+–K^+ pump continually offsetting this ion leakage



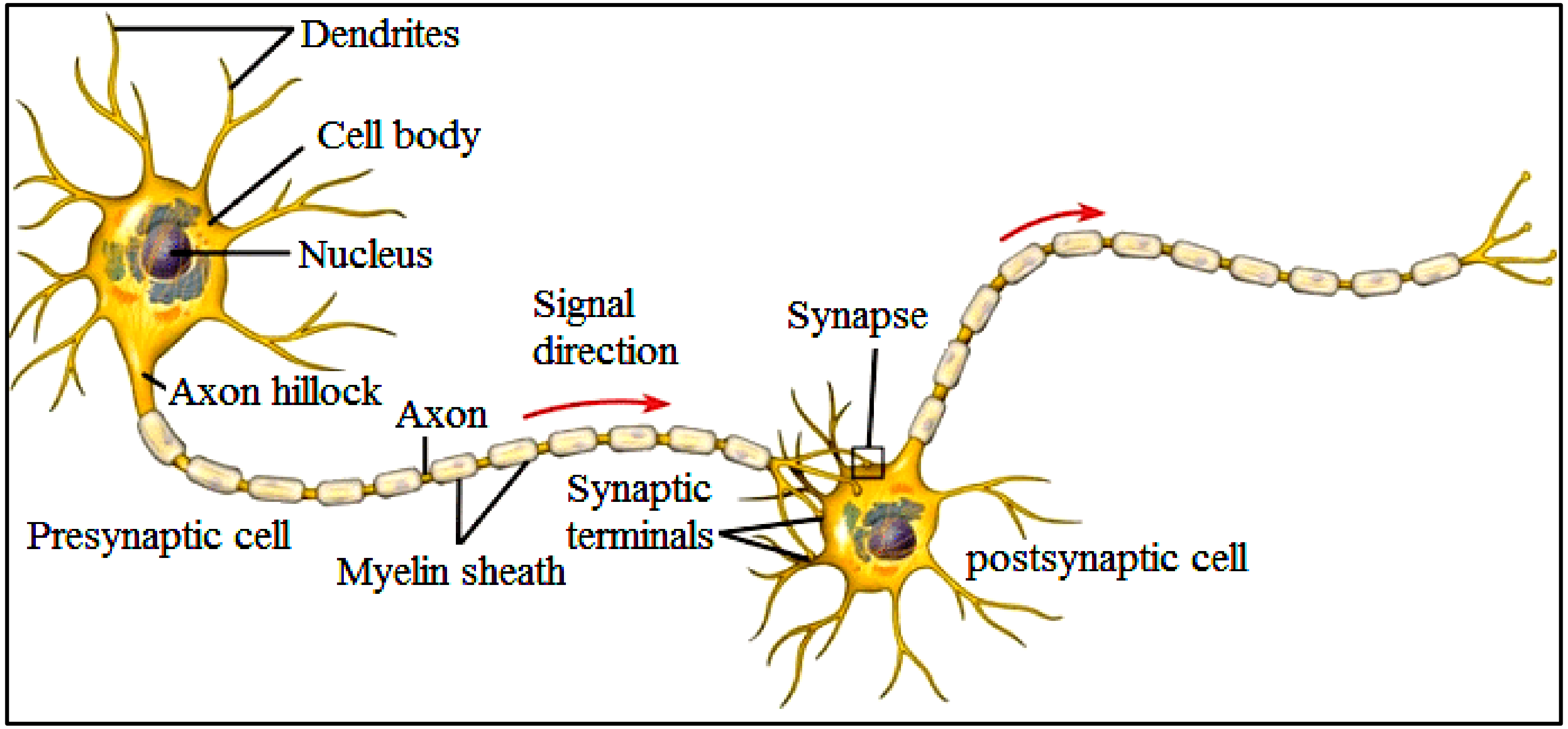
- Sodium leaks into the cell and potassium leaks out, but the **sodium–potassium (Na+–K+) pump continually establish the chemical concentration gradient for Na and K**
- **Essential for generating and sustaining the resting membrane potential**.

- **The Na^{+}–K^{+} pump accounts for about 70% of the energy (ATP) requirement of the nervous system.**
- Every signal generated by a neuron slightly upsets the distribution of Na^{+} and K^{+}, so the pump must work **continually to restore equilibrium**.
- This is why nervous has one of the highest rates of ATP consumption of any tissue in the body, and **why it demands so much glucose and oxygen.**
- **Although a neuron is said to be resting when it is not producing signals, it is highly active maintaining its RMP and "waiting," as it were, for something to happen**

LOCAL potential and ACTION potential

Local POTENTAIL

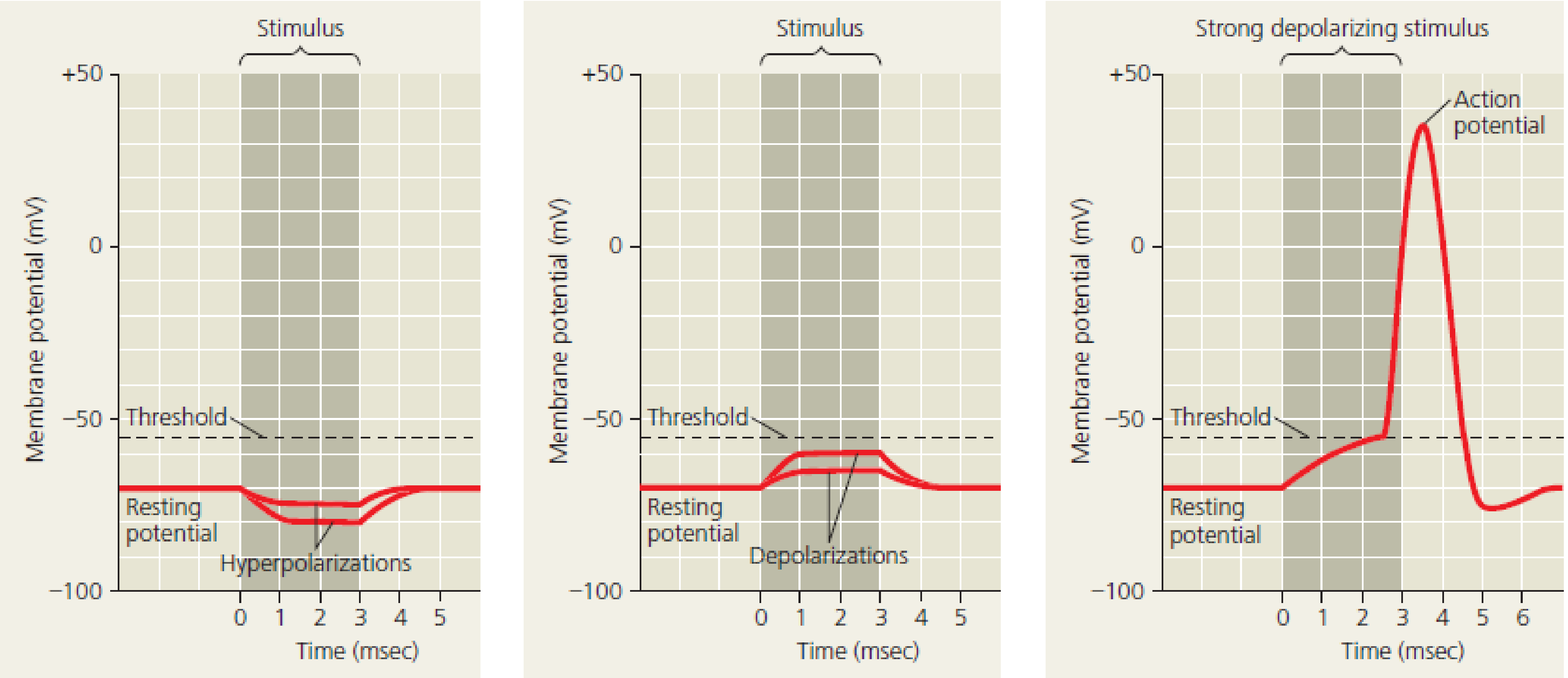
- Stimulation of a neuron causes local disturbances in membrane potential.
- Typically (but with exceptions), the response begins at a dendrite, spreads through the soma, travels down the axon, and ends at the axon terminal.



Local POTENTAIL(Graded Potential)

Local potential is mean the shortchange in membrane potential it may or **may no**t lead to action potential, if the stimulus is reaching **threshold** action potential will happens but is the strength of stimulus is not reaching the three should the action potential will not form and the change in membrane potential return to resting membrane potential (-70)

- Various neurons can be stimulated by **chemicals**, **light**, **heat**, or **mechanical forces**.
- The chemical (ligand)—perhaps a pain signal from a damaged tissue or odor molecule in a breath of air—binds to receptors on the neuron.
- **This opens ligand gated sodium channels** that allow Na^+ to flow into the cell.
- The Na^+ inflow cancels some of the internal negative charge, so the voltage across the membrane at that point drifts toward zero.
- Any such case in which the voltage shifts to a less negative value is called **depolarization**.

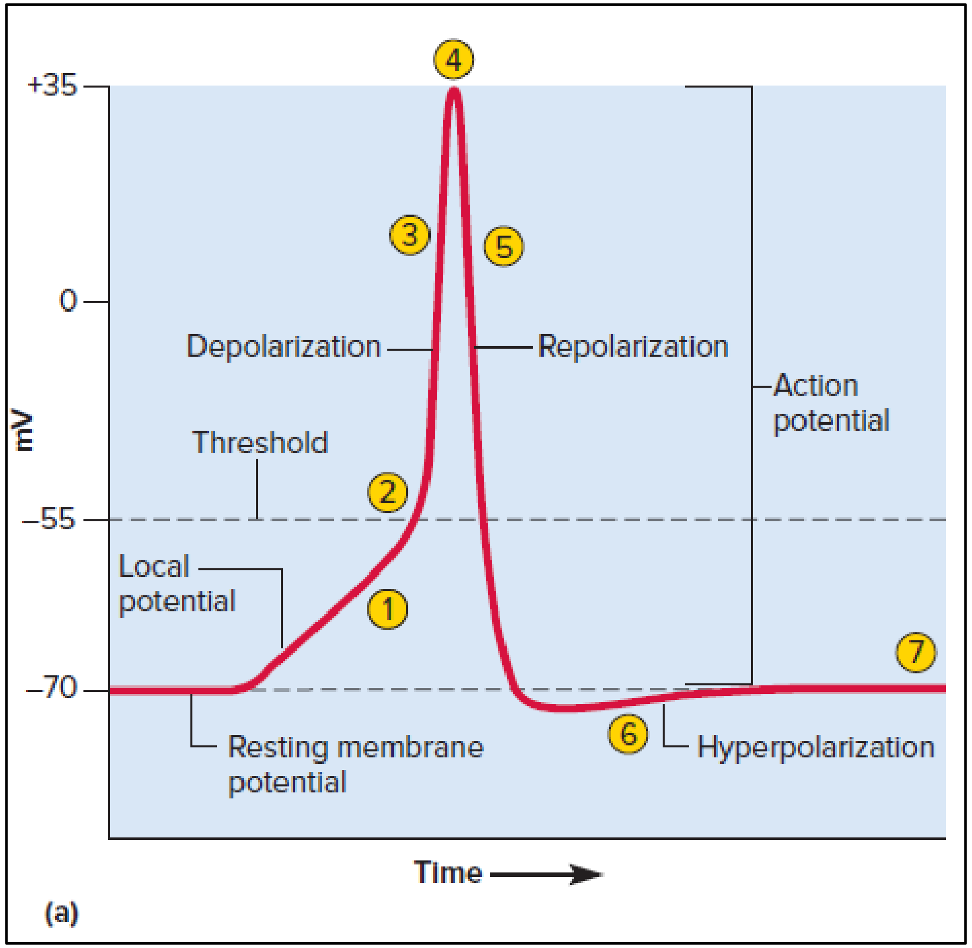


(a) Graded hyperpolarizations produced by two stimuli that increase membrane permeability to K^+. The larger stimulus produces a larger hyperpolarization.

(b) Graded depolarizations produced by two stimuli that increase membrane permeability to Na^+. The larger stimulus produces a larger depolarization.

(c) Action potential triggered by a depolarization that reaches the threshold.

The incoming Na^+ diffuses for short distances along the inside of the plasma membrane, creating a wave of excitation that spreads out from the point of stimulation, like ripples spreading across a pond when you drop a stone into it. This short-range change in voltage is called a **local potential**.



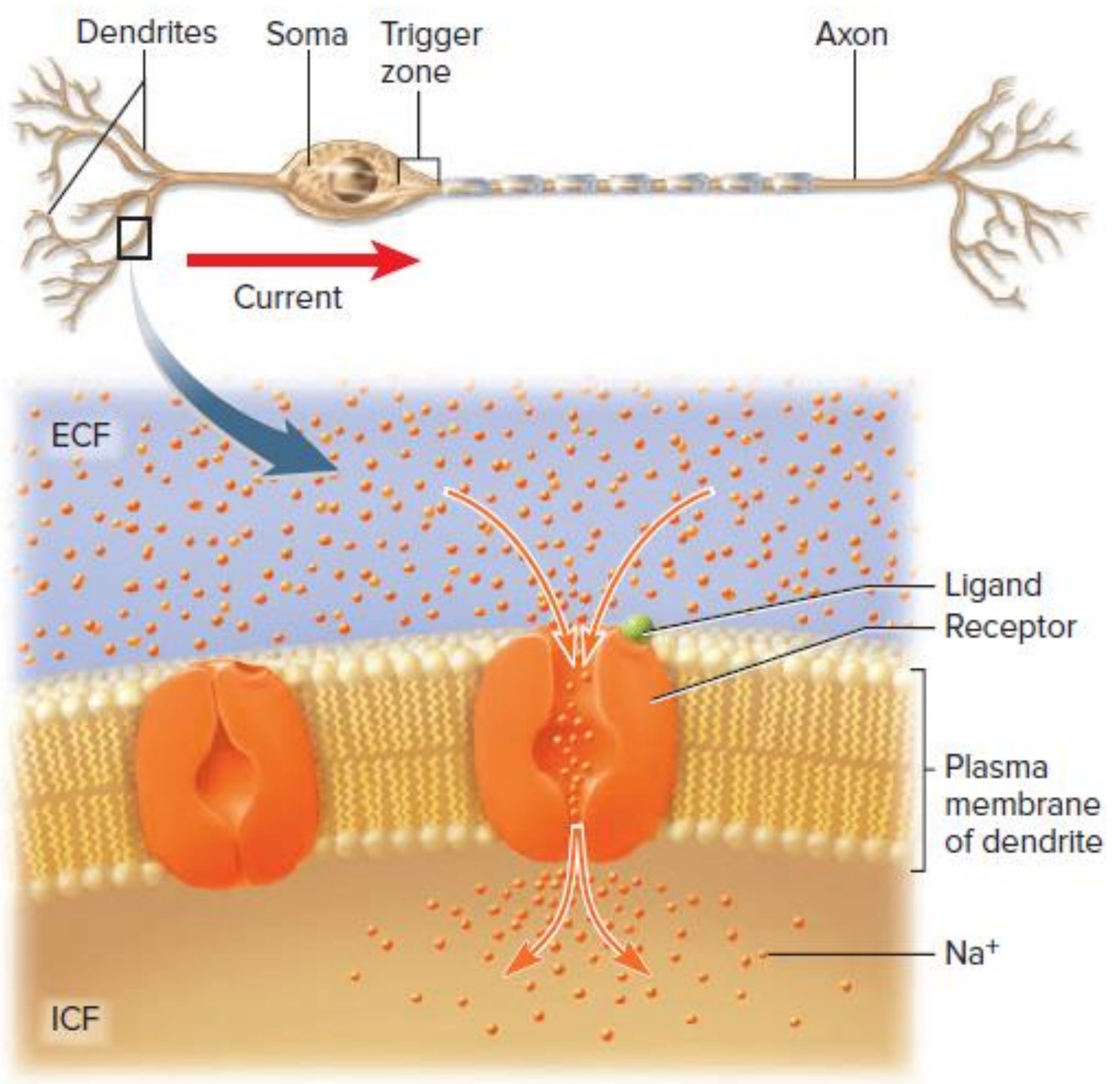
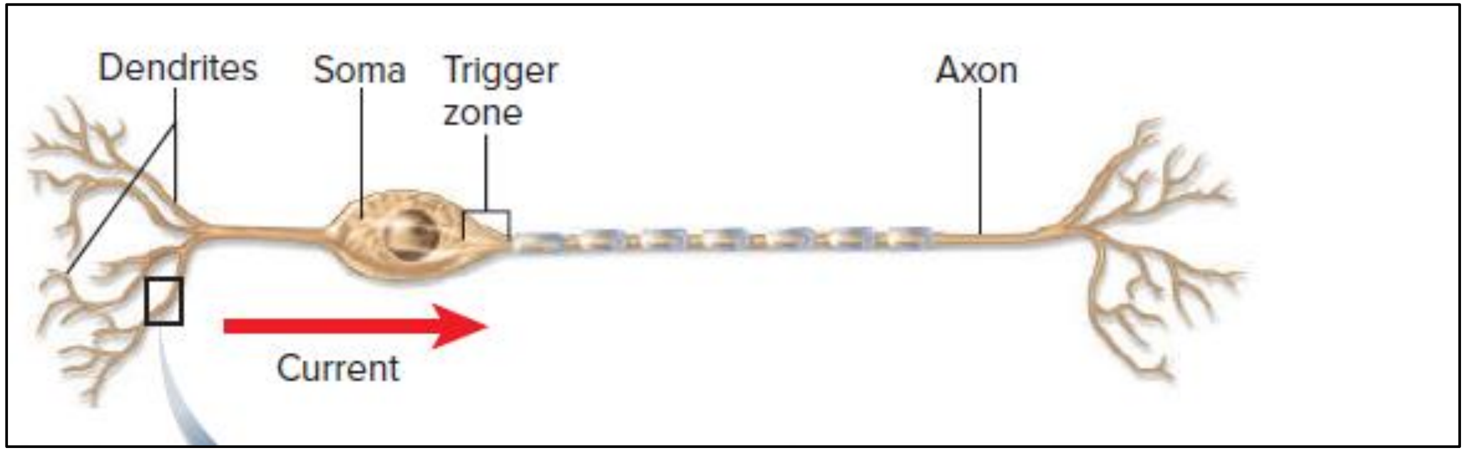


FIGURE 12.13 **Excitation of a Neuron by a Chemical Stimulus.**

Action Potentials

An **action potential** is a more dramatic change produced by voltage-gated ion channels in the plasma membrane. Action potentials occur only where there is a high enough density of voltage-gated channels. Most of the soma has only **50 to 75 channels** per square micrometer (µm2), not dense enough to generate action potentials. **The trigger zone, however, has 350 to 500 channels/µm2.**



If an excitatory local potential spreads all the way to the trigger zone and is still strong enough when it arrives, it can open these channels and generate an action potential.

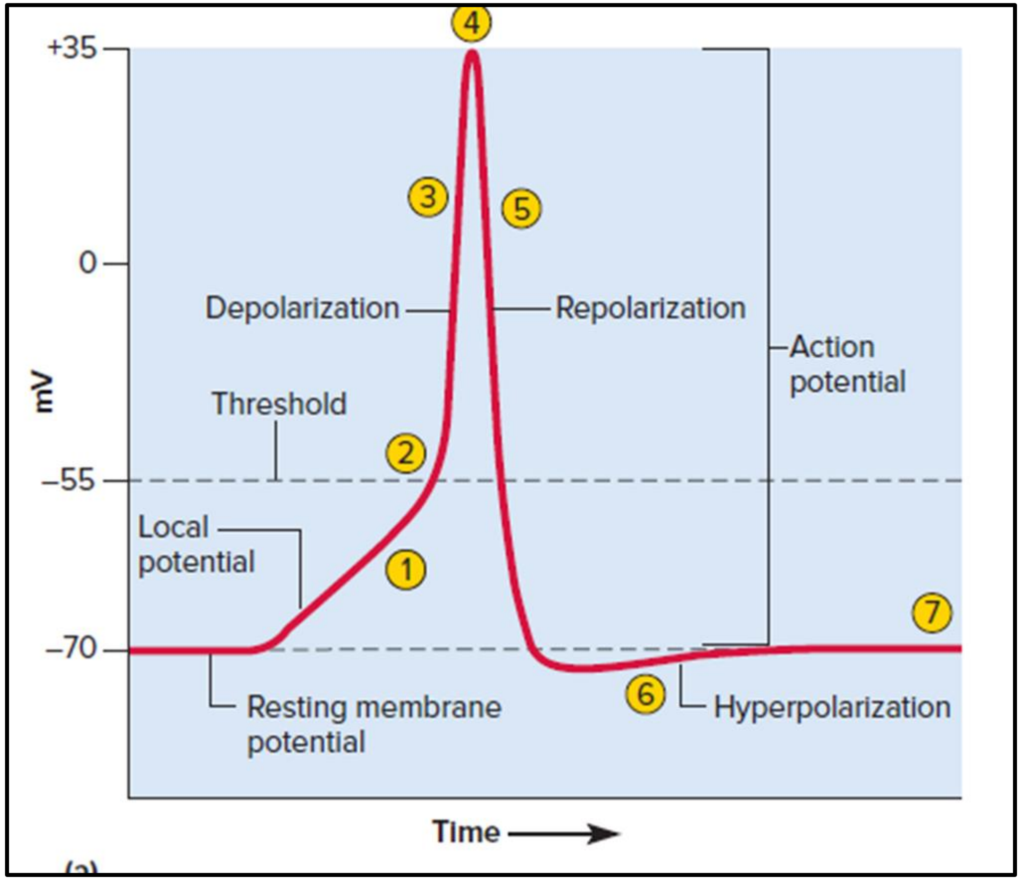
Action Potentials stages

The action potential is a rapid up-and-down shift in voltage.

- When the **local current** arrives at the axon hillock, it depolarizes the membrane at that point. This appears as a steadily rising local potential
- For anything more to happen, this local potential must rise to a critical voltage called the **threshold** (typically about –55 mV), the minimum needed to open voltage-gated channels.

1. **Depolarization Stage.** The neuron now "fires," or produces an action potential.

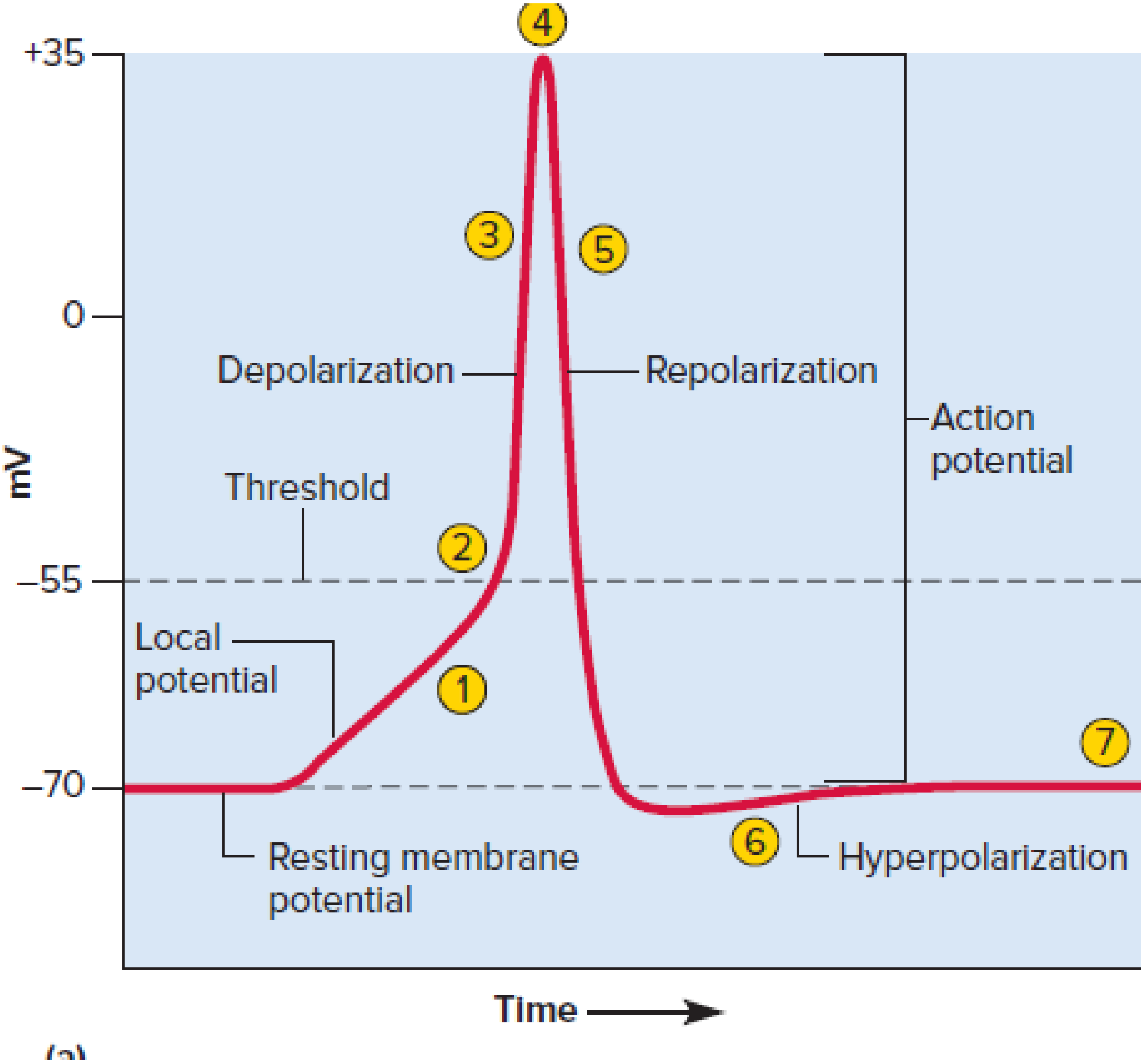
- At threshold, voltage-gated Na^+ channels open quickly, while gated K^+ channels open more slowly. The initial effect on membrane potential is therefore due to Na^+. Initially, only a few Na^+ channels open, but as Na^+ enters the cell, it further depolarizes the membrane.
- This stimulates still more **voltage- gated Na^+ channels** to open and admit even more Na^+, a positive feedback loop that causes the membrane voltage to rise even more rapidly



As the rising potential passes 0 mV, Na^+ channels are *inactivated* and begin closing. By the time they all close and Na^+ inflow ceases, the voltage peaks at approximately +35 mV. (The peak is as low as 0 mV in some neurons and as high as 50 mV in others.) The membrane is now positive on the inside and negative on the outside—its polarity is reversed compared to the RMP

2. **Repolarization Stage**.: When the voltage reach the peaks(+35 mV), the slow **K^+ gated channel**s are fully open. Potassium ions, repelled by the positive ICF, now exit the cell. Their outflow repolarizes the membrane—that is, it shifts the voltage back into the negative numbers.

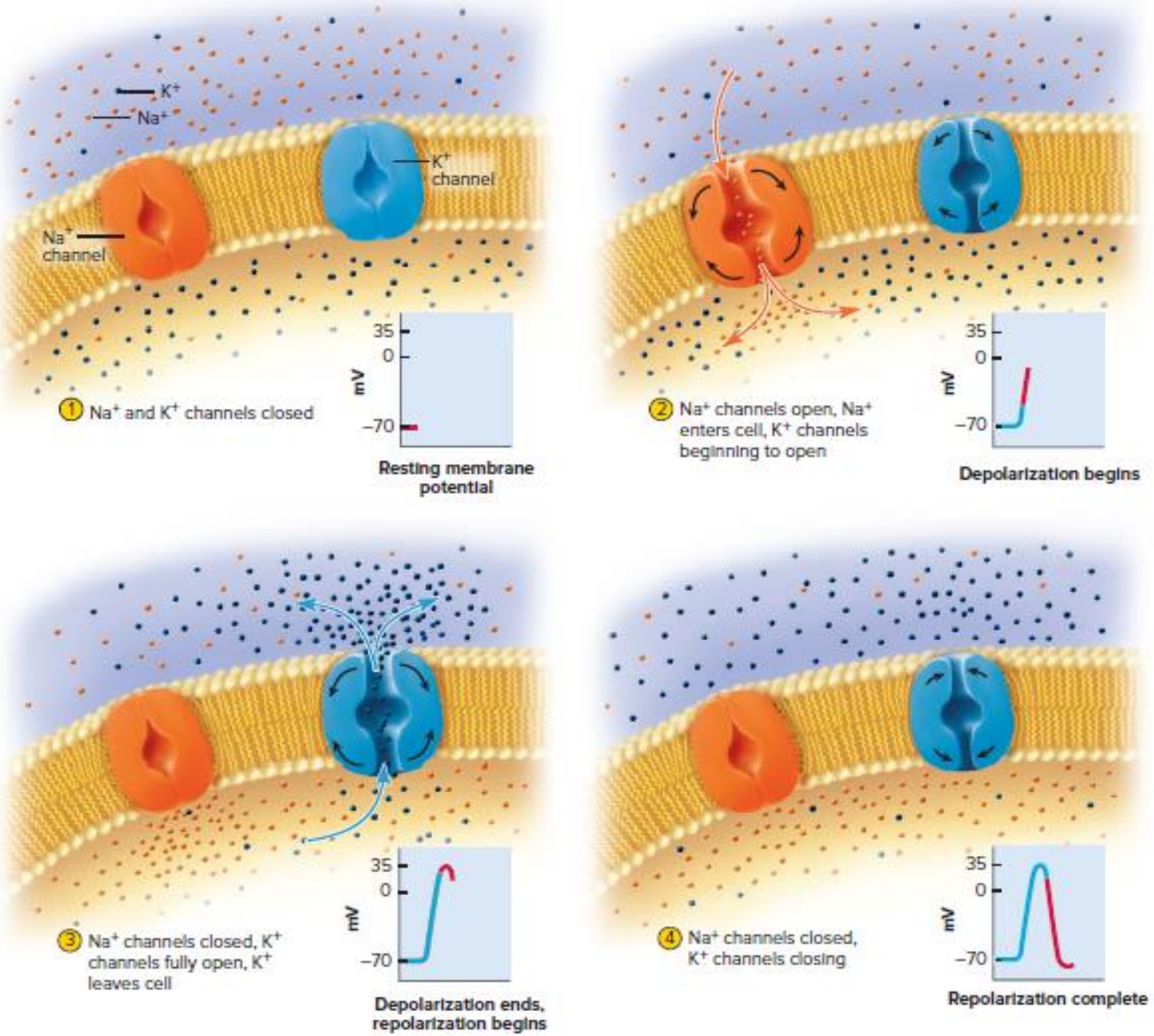
The action potential consists of the up-and-down voltage shifts that occur from the time the threshold is reached to the time the voltage returns to the RMP.

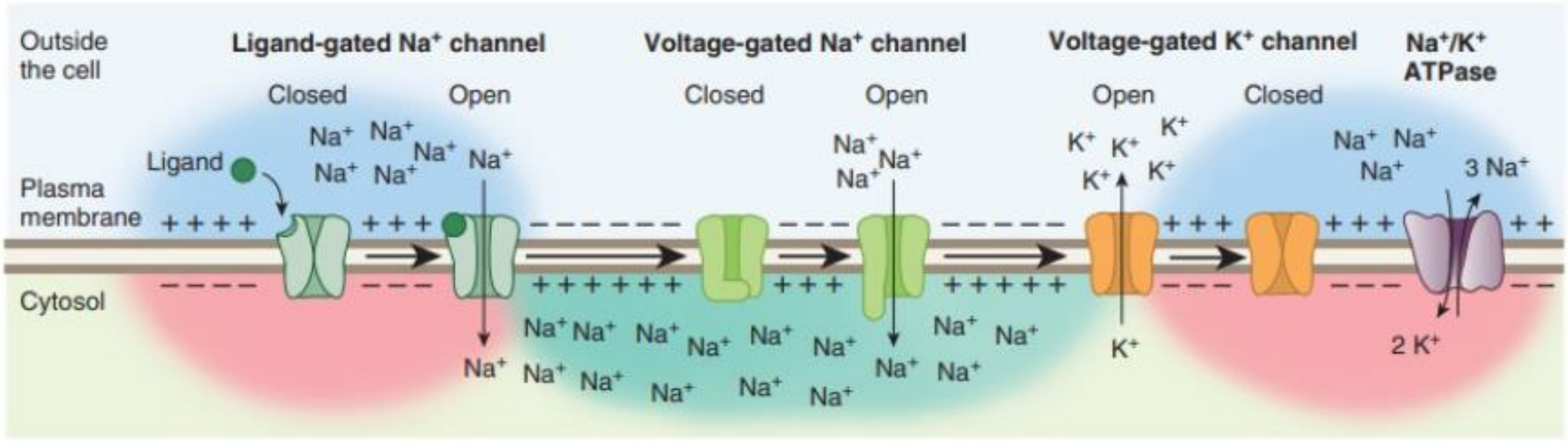


+35
0
−55
−70
mV
Depolarization
Repolarization
Action potential
Threshold
Local potential
Resting membrane potential
Hyperpolarization
1
2
3
4
5
6
7
Time

3- Hyperpolarization Stage .

Potassium channels stay open longer than Na^+ channels, so slightly more K^+ leaves the cell than the amount of Na^+ that entered. Therefore, the membrane voltage drops to 1 or 2 mV more negative than the original RMP, producing a negative overshoot called ***hyperpolarization***. During hyperpolarization, the membrane voltage gradually returns to the RMP because of Na^+ diffusion into the cell.


K+
Na+
K+ channel
Na+ channel
1 Na+ and K+ channels closed
35
0
mV
–70
Resting membrane potential
2 Na+ channels open, Na+ enters cell, K+ channels beginning to open
35
0
mV
–70
Depolarization begins
3 Na+ channels closed, K+ channels fully open, K+ leaves cell
35
0
mV
–70
Depolarization ends, repolarization begins
4 Na+ channels closed, K+ channels closing
35
0
mV
–70
Repolarization complete



Outside the cell
Ligand-gated Na⁺ channel
Voltage-gated Na⁺ channel
Voltage-gated K⁺ channel
Na⁺/K⁺ ATPase
Closed
Open
Closed
Open
Open
Closed
Ligand
Plasma membrane
Cytosol
3 Na⁺
2 K⁺

Characteristics of Action potential

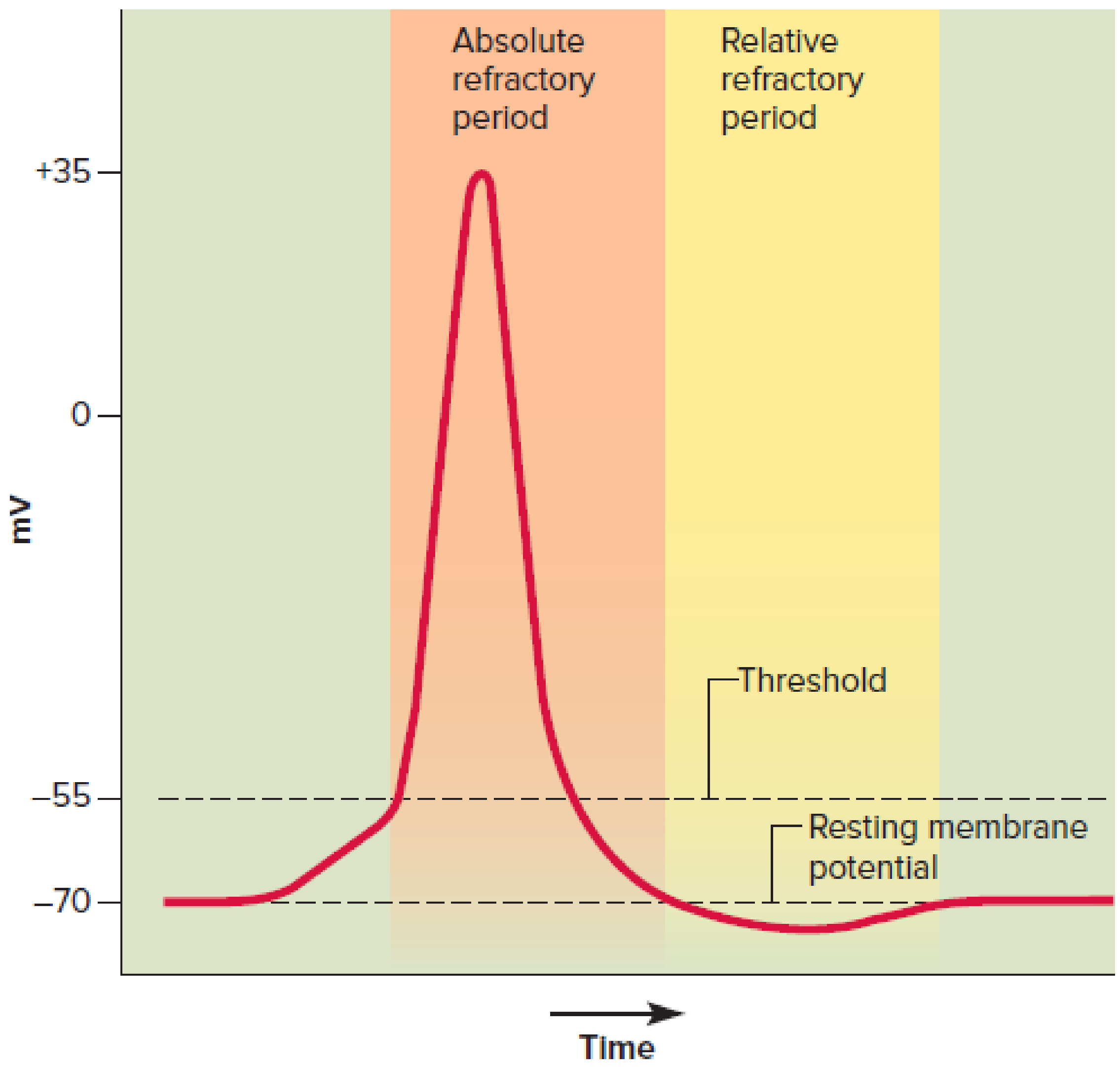
1. **Action potentials follow an all-or-none law.** If a stimulus depolarizes the neuron to threshold, the neuron fires at its maximum voltage (such as +35 mV); if threshold is not reached, the neuron doesn't fire at all. Above threshold, stronger stimuli don't produce stronger action potentials. Thus, action potentials are not graded (proportional to stimulus strength) like local potentials are.
2. Action potentials are **non-decremental.** They don't get weaker with distance. The last action potential at the end of a nerve fiber is just as strong as the first one in the trigger zone, no matter how far away—even in a pain fiber that extends from your toes to your brainstem
3. Action potentials are **irreversible.** If a neuron reaches threshold, the action potential goes to completion; it can't be stopped once it begins

The Refractory Period

During an action potential and for a few milliseconds after, it is difficult or impossible to stimulate that region of a neuron to fire again. This period of resistance to restimulation is called the **refractory period.**

It is divided into two phases:

1. **An absolute refractory** period in which no stimulus of any strength will trigger a new action potential,
2. followed by a **relative refractory** period in which it is possible to trigger a new action potential, but only with an unusually strong stimulus



https://www.youtube.com/watch?v=HYLyhXRp298

- The absolute refractory period lasts from the start of the action potential until the membrane returns to the resting potential— that is, for as long as the Na+ channels are open and subsequently inactivated.
- The relative refractory period lasts until hyperpolarization ends

Home work?

- Why a new action potential is not produced during the Absolute refractory period?
- How a new action potential can form during relative refractive period?

References

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- Saladin, K. (2020). Anatomy & Physiology: The Unity of Form and Function. McGraw-Hill Education.