Bioelectrical Phenomenon

電生理現象

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General guide of bioelectric signals

- Originate from electrochemical activity across the cell membrane
  - Electrophysiology (電生理學)
- Membrane potential can be measured in excitable cells (e.g., neurons, muscle cells).
  - Range: -70 mV (resting) → +40 mV (action)

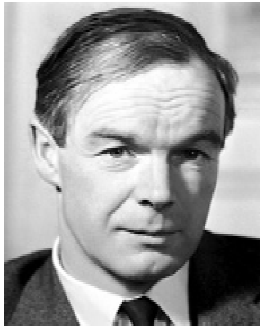
Bioelectric signals

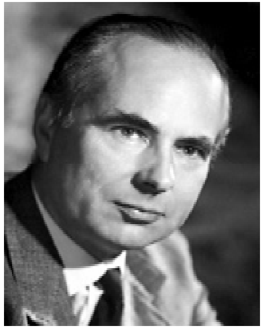
- The change of electric current and potential across a specialized tissue, organ, or cell system.
  - Electrocardiogram (ECG or EKG)
  - Electroencephalogram (EEG)
  - Electromyogram (EMG)
  - and more…

Investigation of membrane potential

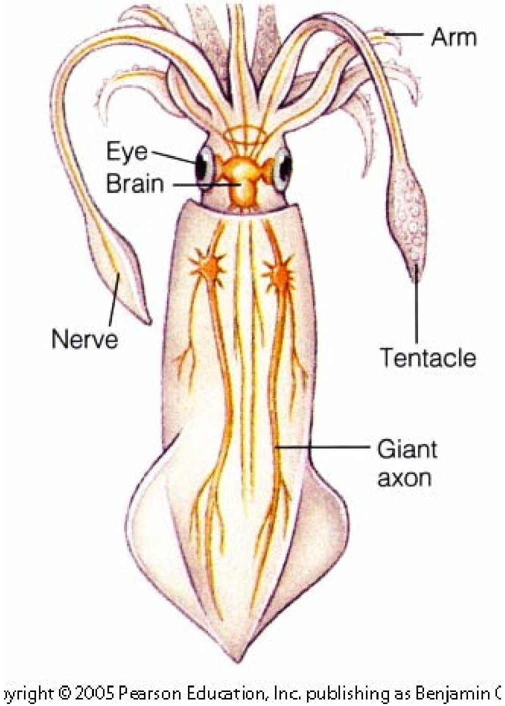
- Experiments using the squid giant axon
  - First demonstrated by J.Z. Young in 1930s
  - 0.5-1.5 mm in diameter
  - Axon in humans: 20 µm (largest), mostly < 2 µm
- Hodgkin AL & Huxley AF, 1963 Nobel Prize

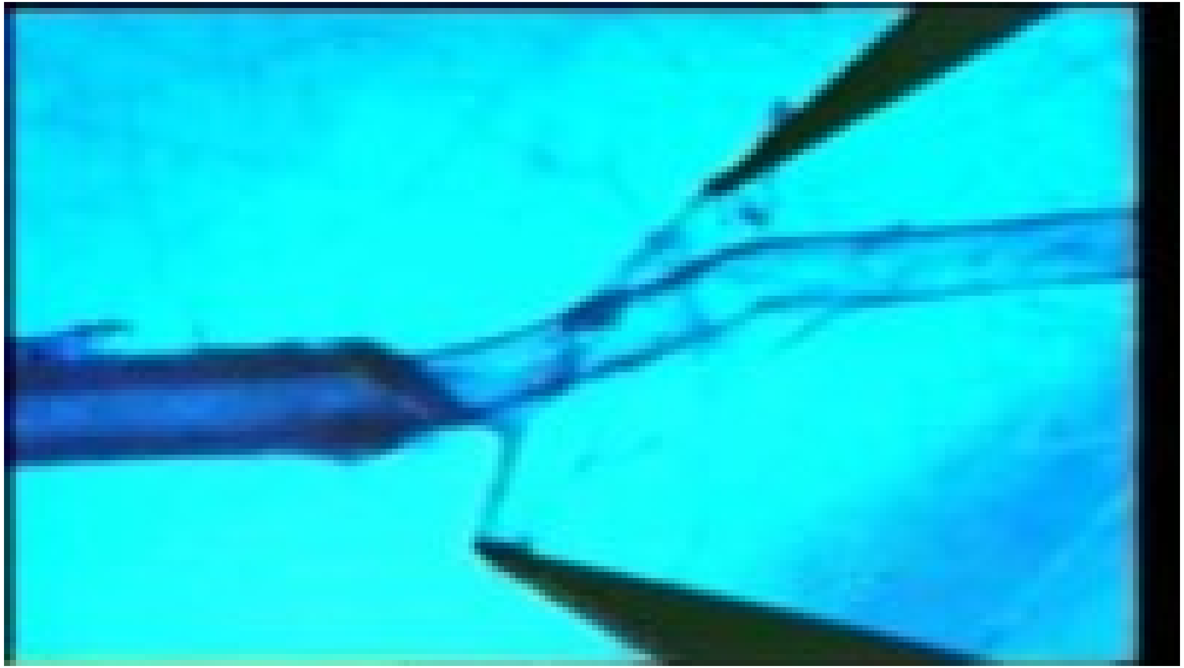
"It's the squid that really ought to be given the Nobel Prize." by Dr. Hodgkin.





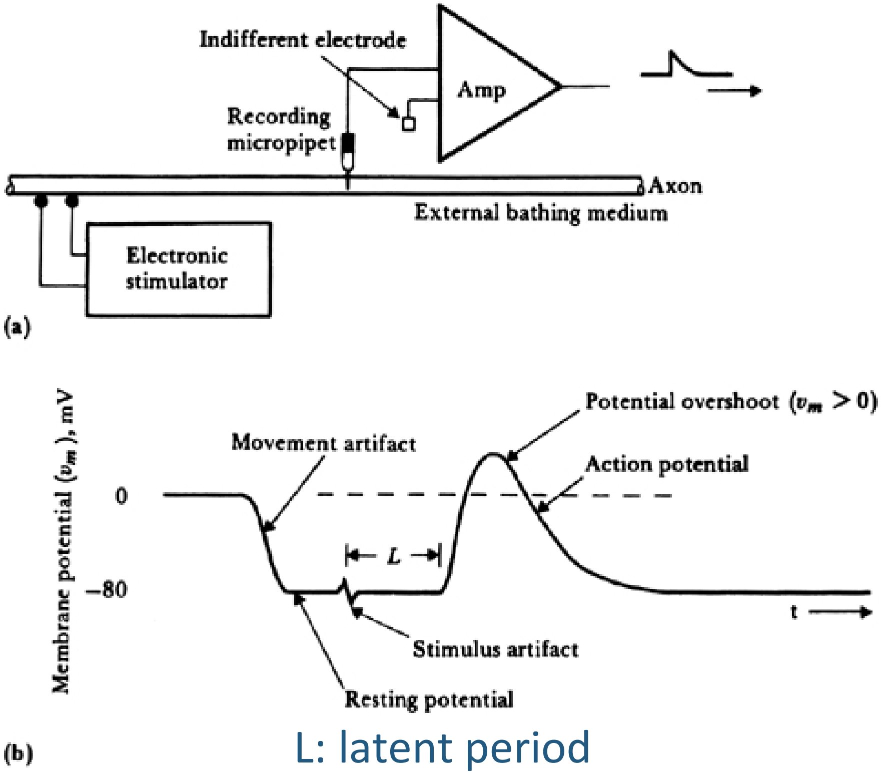
Squid giant axon





Filmed in the 1970s at Plymouth Marine Laboratory in England

Recording of action potential on an axon



L: latent period

Formation of electric signals

- Neuron cell is enclosed by a semi-permeable membrane and surrounded by water solution rich of electrolytes.

- Electric potential would be induced once the ion concentration is imbalanced inside and outside the cell membrane.
  - Termed as membrane potential

Resting potential with K^+

Fick's Law

$$J_K(diffusion) = -D\frac{d[K^+]}{dx}$$

D : diffusion coefficient or diffusivity constant (m^2/sec)

$$D = \frac{kT\mu}{q}$$

Ohm's Law

$$J_K(drift) = -\mu Z[K^+]\frac{dv}{dx}$$

μ : mobility ($m^2/sec/V$)

Z : ionic valence

$[K^+]$: ionic concentration of K^+

Steady state of K^+

$$J_K(diffusion) + J_K(drift) = 0$$

Resting potential with K^+

Fick's Law

$$J_K(diffusion) = -D\frac{d[K^+]}{dx}$$

$$D = \frac{kT\mu}{q}$$

Ohm's Law

$$J_K(drift) = -\mu Z[K^+]\frac{dV}{dx}$$

$$J_K(diffusion) + J_K(drift) = 0$$

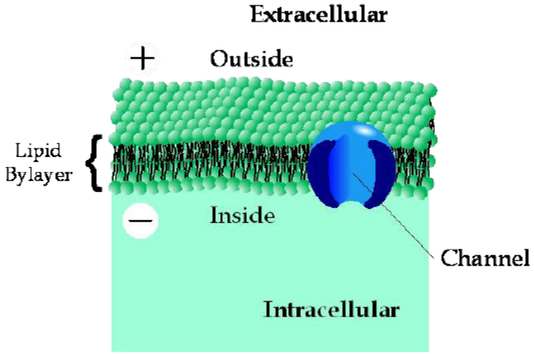
$$-\frac{kT}{q}\mu\frac{d[K^+]}{dx} - \mu Z[K^+]\frac{dV}{dx} = 0 \Rightarrow dV = -\frac{kT}{q}\frac{d[K^+]}{[K^+]}$$

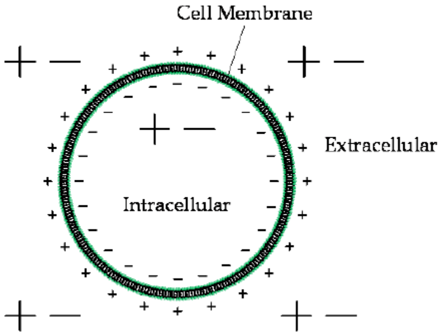
Nernst Eq: $$E_K = V_i - V_o = \frac{kT}{q}\ln\frac{[K^+]_o}{[K^+]_i} = 0.0615\log_{10}\frac{[K^+]_o}{[K^+]_i} \text{ at 37 °C}$$

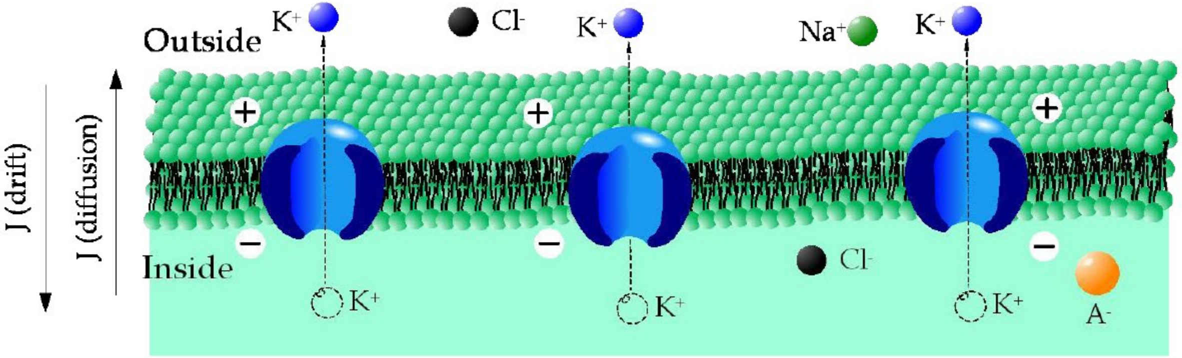
Resting state with K^+

- Typically, $[K^+]$ is much higher inside the cell membrane (e.g., 120 mM in cytosol) than outside (4 mM).
  - Diffusion gradient drives K^+ ion outward.
  - The negative Nernst potential keeps the drift flux inward.
  - Resting state: a result of thermodynamic equilibrium

Potassium ion channel

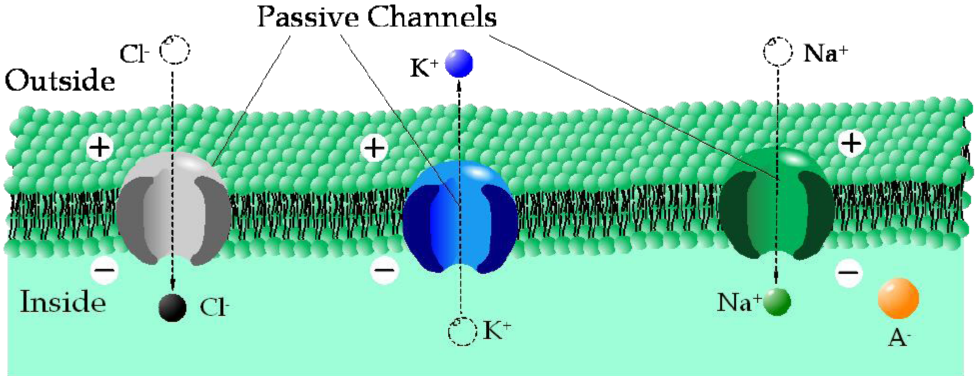






Other ions and their ion channels

- The Nernst potential can be determined by the distribution across the membrane of any permeable ion.
  - Ex: Cl^-, Na^+, …



Nernst potential: giant squid axon

Ion	Cytoplasm (mM)	Extracellular fluid (mM)	Nernst potential (mV)
K^+	400	20	- 74
Na^+	50	440	+ 55
Cl^-	52	560	- 60

- Which one is the membrane potential?

Membrane potential

- All permeable ions contribute to the membrane potential.
- Principle ions: K^+, Cl^-, and Na^+
- Goldman equation of membrane potential (E_m)

$$E_m = \frac{kT}{q}\ln\left(\frac{P_K[K^+]_o + P_{Cl}[Cl^-]_i + P_{Na}[Na^+]_o}{P_K[K^+]_i + P_{Cl}[Cl^-]_o + P_{Na}[Na^+]_i}\right)$$

  - *P*: permeability

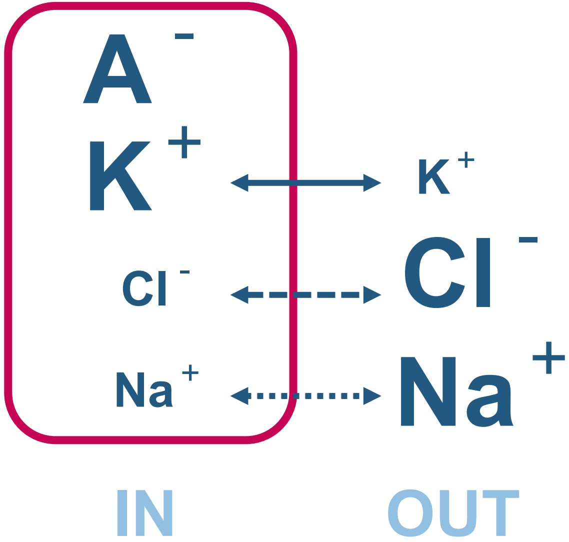
Membrane potential: giant squid axon

Ion	Cytoplasm (mM)	Extracellular fluid (mM)	Nernst potential (mV)	Permeability ratio
K^+	400	20	- 74	1
Na^+	50	440	+ 55	0.04
Cl^-	52	560	- 60	0.45

- Membrane potential of giant squid axon -60 mV

Resting membrane model

- Membrane potential is dominated by the ions with the highest permeability
  - Permeability: $P_K > P_{Cl} >> P_{Na}$
  - A^-: impermeable molecules

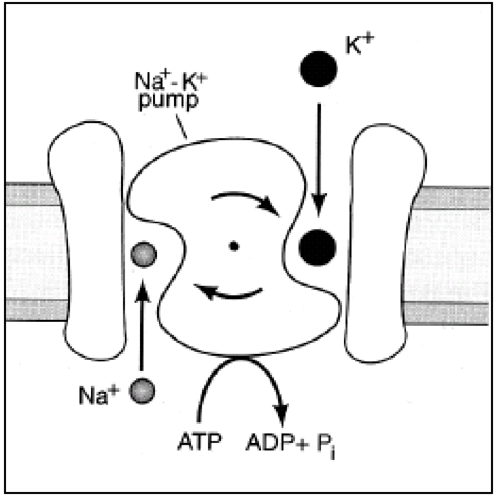


Direction of the ion flux

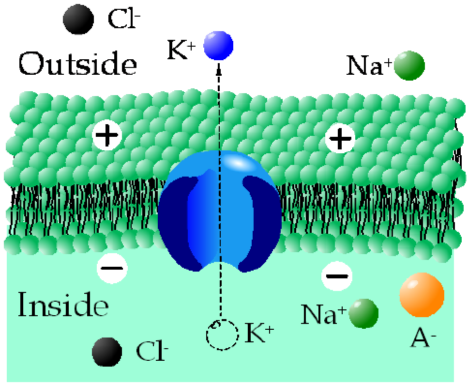
- Two driving forces: diffusion and drift
- K^+: diffusion out and drift in → balanced
- Cl^-: diffusion in and drift out → balanced
- Na^+: diffusion in and drift in → imbalanced?
  - Reaching balance with the relatively low permeability and active transport

Active transport

- The movement of ions across the cell membrane against the concentration gradient (from low to high concentration)
  - Cost energy (ATP)
  - Na^+-K^+ ion pump: 3 Na^+ out, 2 K^+ in
- Diffusion and drift are passive transport.



Represent an ion channel by circuit model



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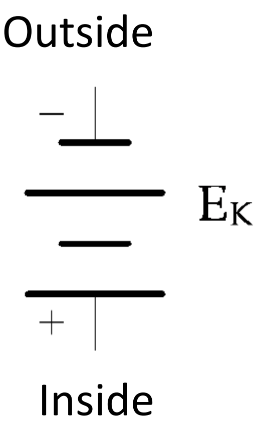
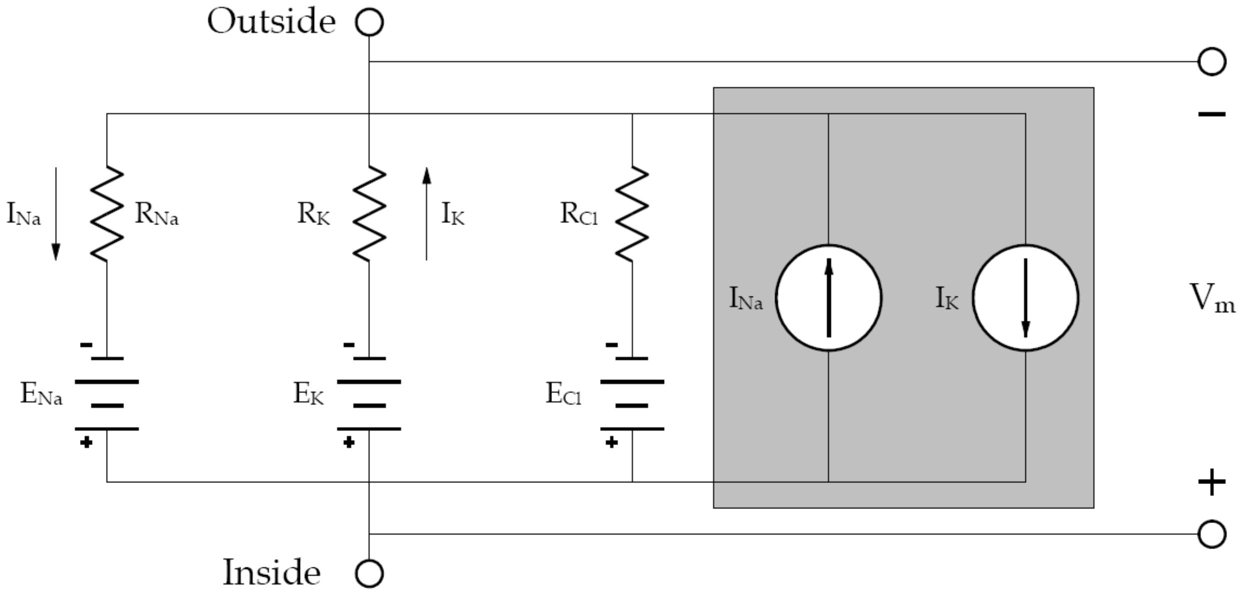


Nernst potential of an ion (E) = DC voltage

Equivalent circuit of cell membrane



V_m: membrane potential

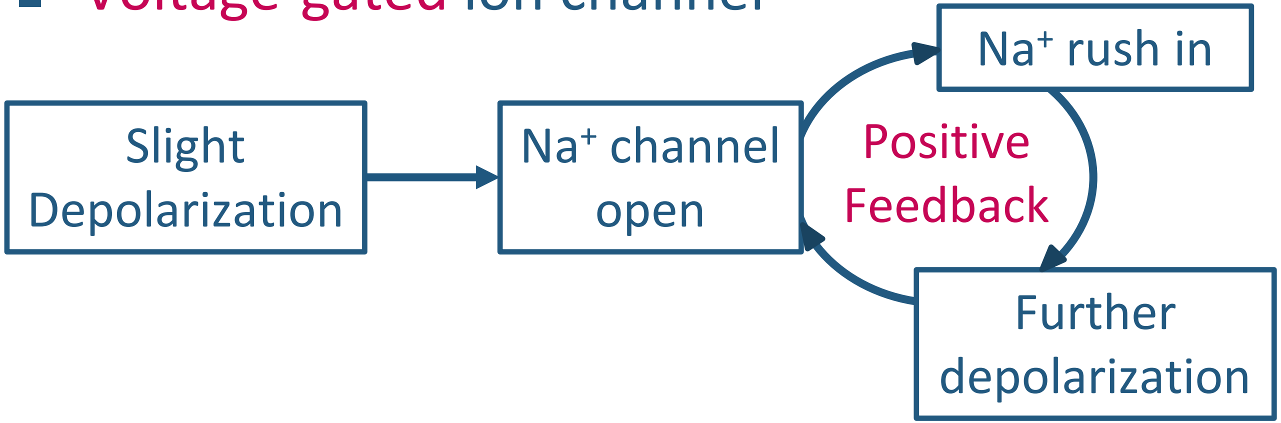
Action potential

Generation of action potential

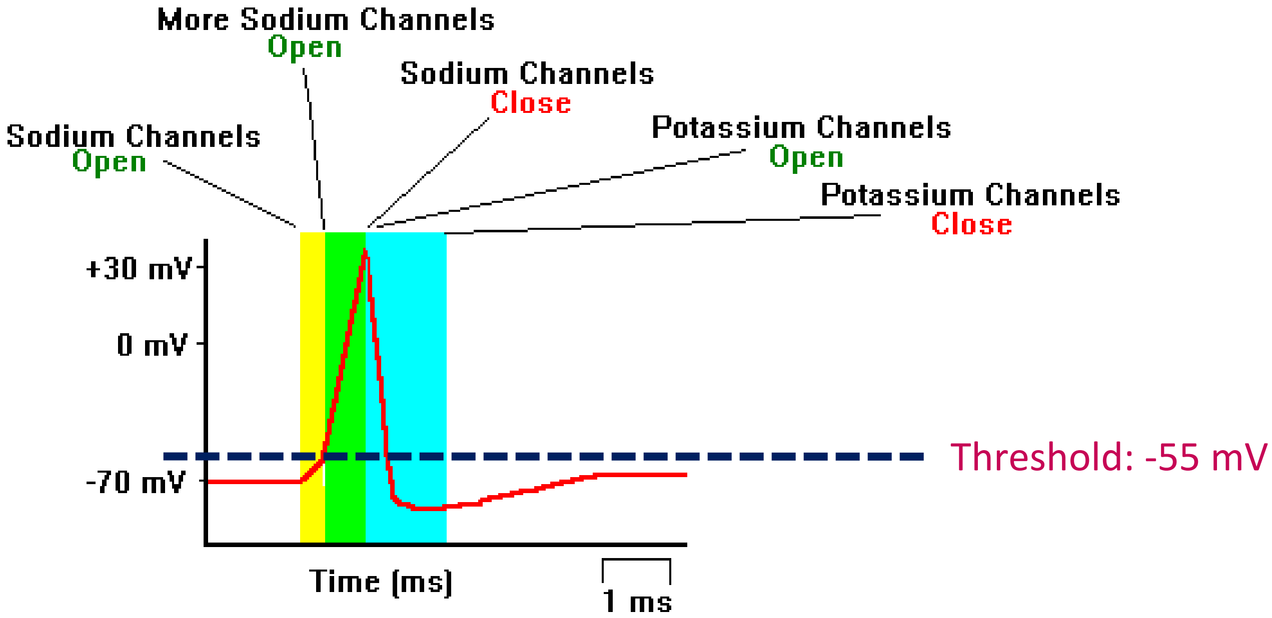
- Purpose: to signal (at cell level)
  - Nerve stimulation, muscle contraction
- How to change the membrane potential?
  - Increase the permeability of Na^+ channel dramatically
  - Na^+ flows inward rapidly, enhancing the membrane potential (depolarization)

Depolarization

- Permeability of Na^+ ion channel (P_{Na}) is very sensitive to membrane potential, which means it can be triggered by increased potential.
  - Voltage-gated ion channel

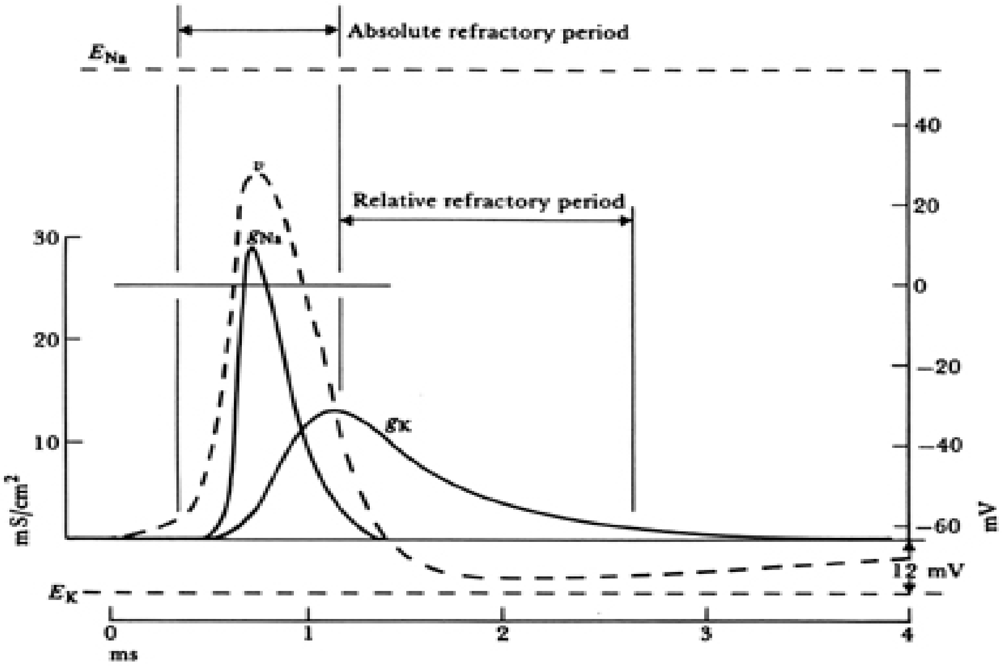


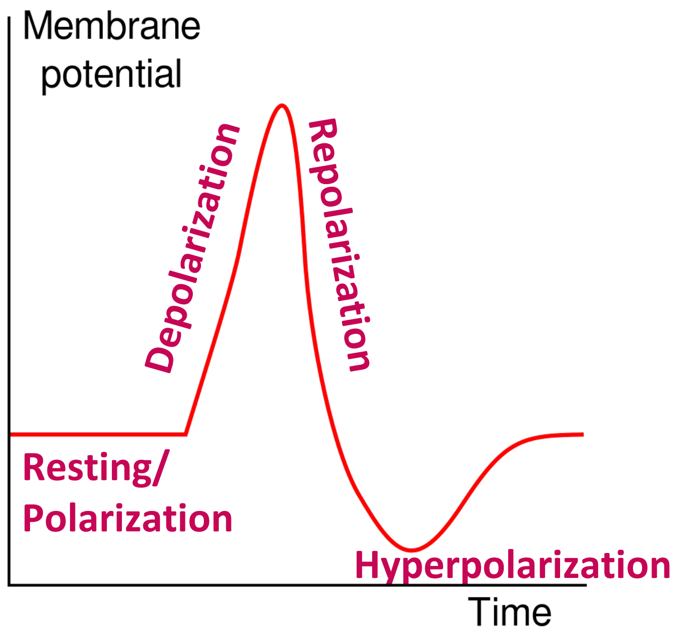
Action potential (simplified)



Opening and closing of ion channels creates action potential (AP)

Action potential and ion permeability

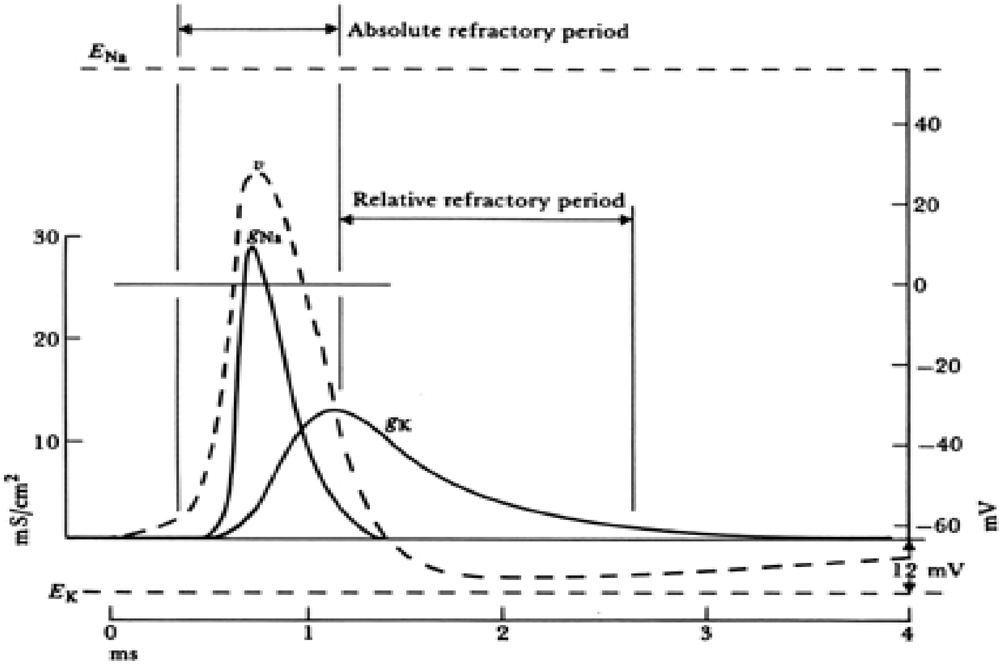




v (dash line): membrane potential (right axis)

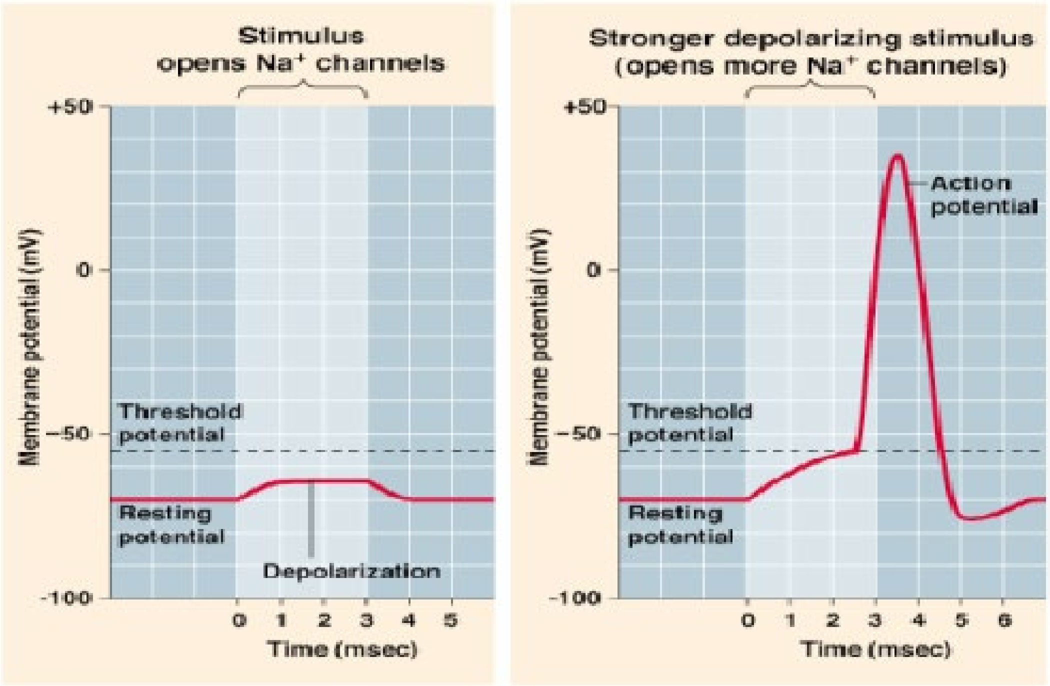
g (solid lines): membrane ionic conductance (left axis)

Refractory period



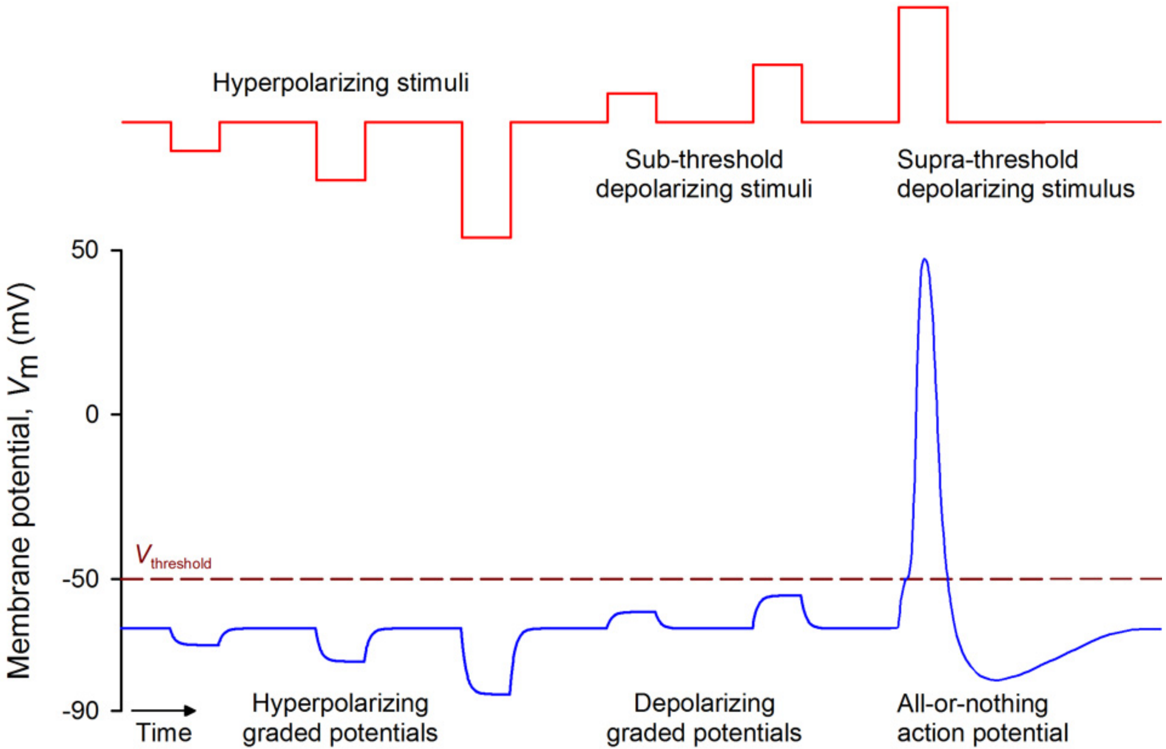
Absolute refractory period: membrane can not respond to any stimulus.
Relative refractory period: membrane can respond to intense stimulus.

All-or-None law

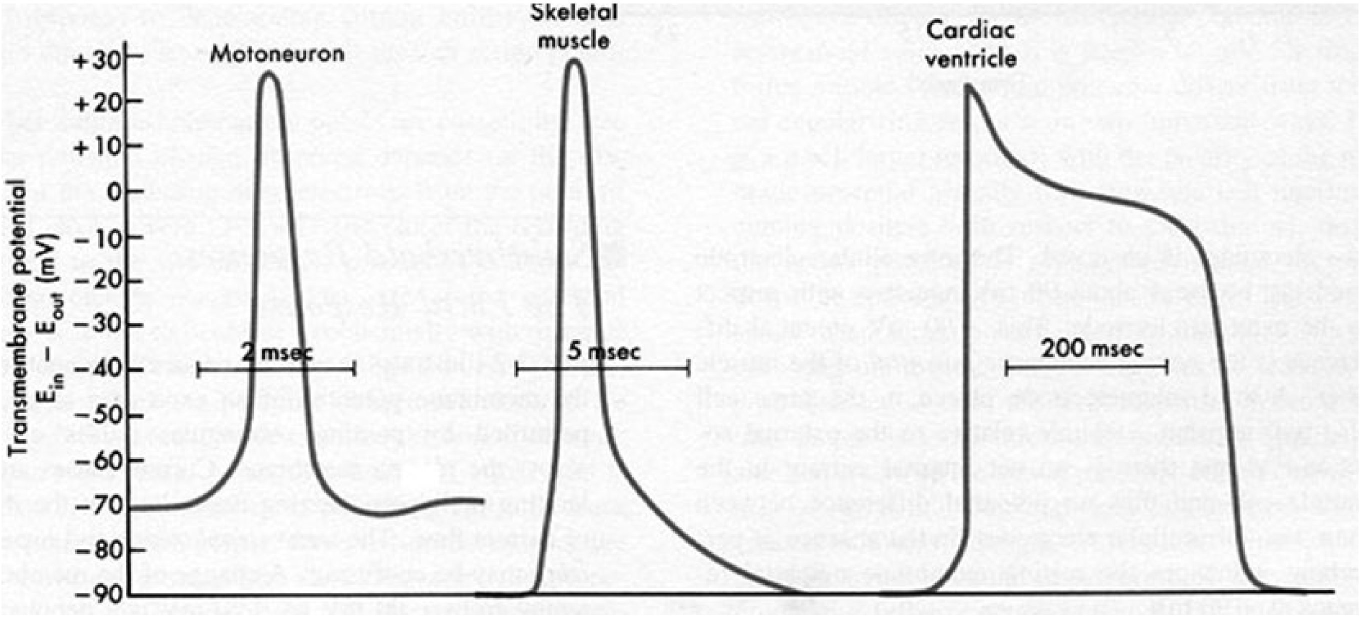


AP fires only when stimulus reaches over the threshold potential

Electrical stimulation of neurons



Action potential of different cells



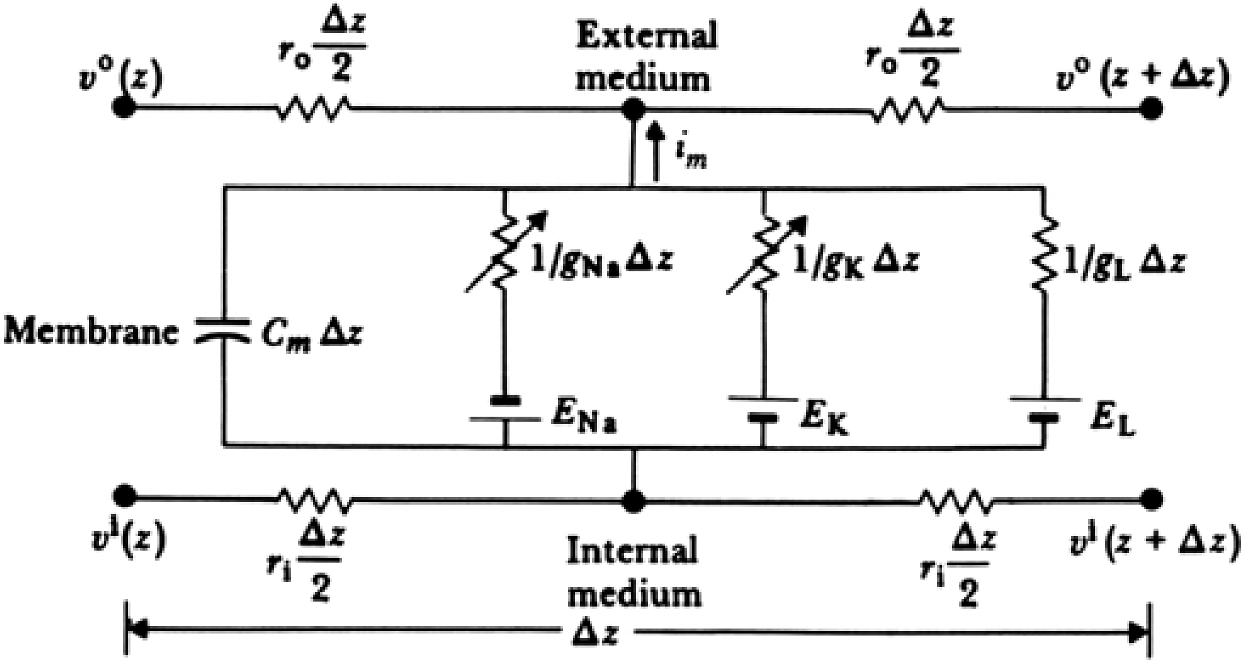
Action potential

- Action potential, rapidly rising and falling of membrane potential, occurs when cell membrane is stimulated to induce rapidly and dramatically change of ion permeability.
  - Electrical (cell membrane) or chemical (synapse) stimulus
  - Rapid: in several milli-seconds
  - Dramatic: $P_{Na}/P_K = 0.03 \rightarrow 15$ (squid axon)

Adjustable ionic permeability

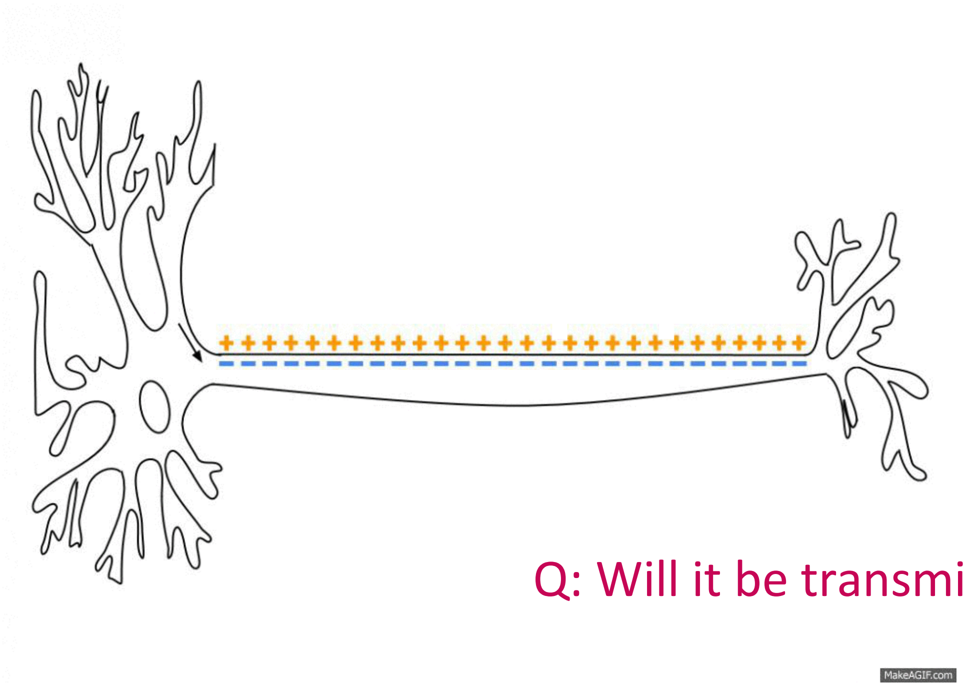
- Related to the structure of ion channel, which is integral proteins embedded in the membrane.
  - Cell physiology
- Modeled as a variable resistor

Equivalent circuit



Equivalent circuit of a piece of neural fiber

Propagation of action potential



Q: Will it be transmitted backward?

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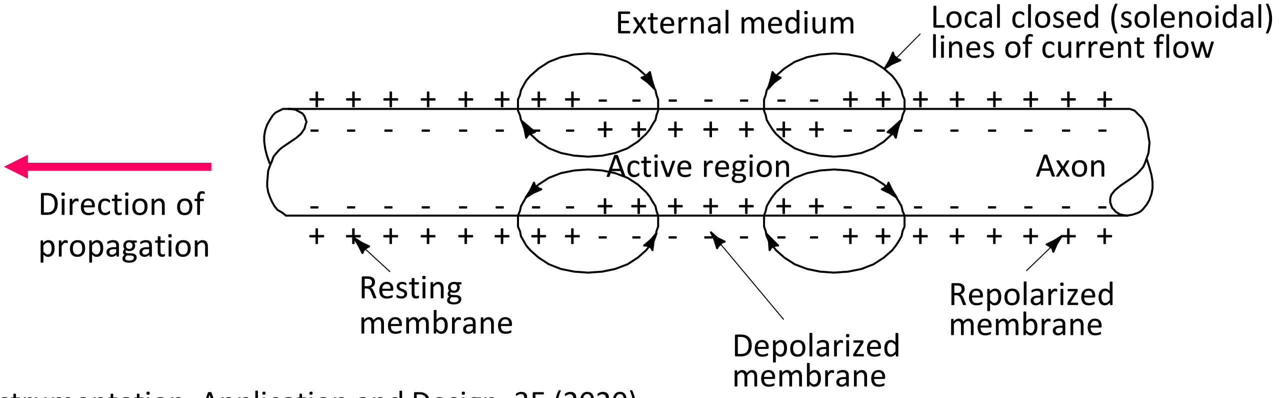
Propagation of action potential

- Resting potential is restored after repolarization.
- Entering absolute/relative refractory period
  - Inactivation of Na^+ channel
  - Ensure that AP moves in one direction

Absolute refractory period

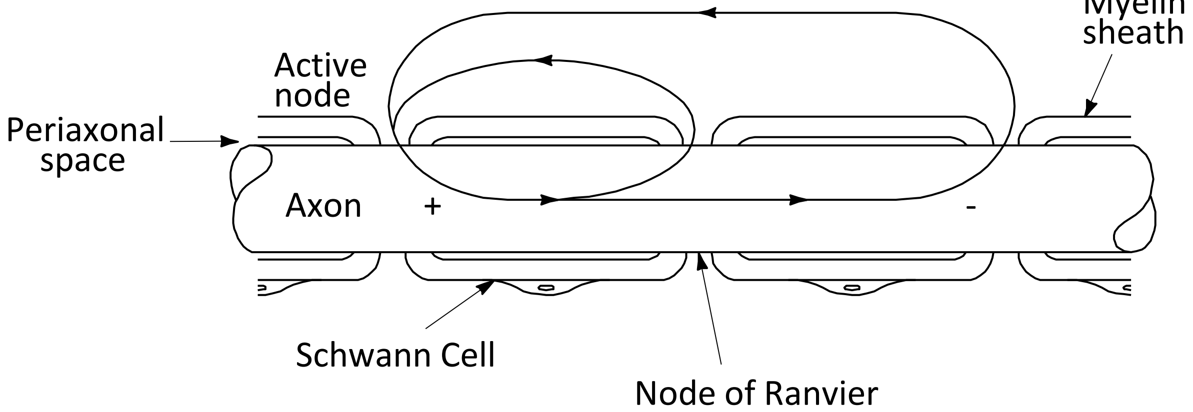
- Responsible for unidirectional transmission of AP
- Restrict the minimal interval of repeated stimuli
  - Absolute refractory period ~ 1 ms
  - Maximal firing rate: 1 kHz



Webster et al. Medical Instrumentation: Application and Design, 3E (2020)

Myelin around the axons

- Insulator: reducing leakage of currents
- Accelerate the nerve conduction velocity (several tens times faster)



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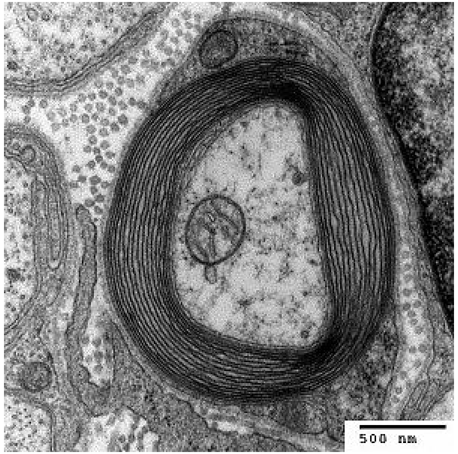
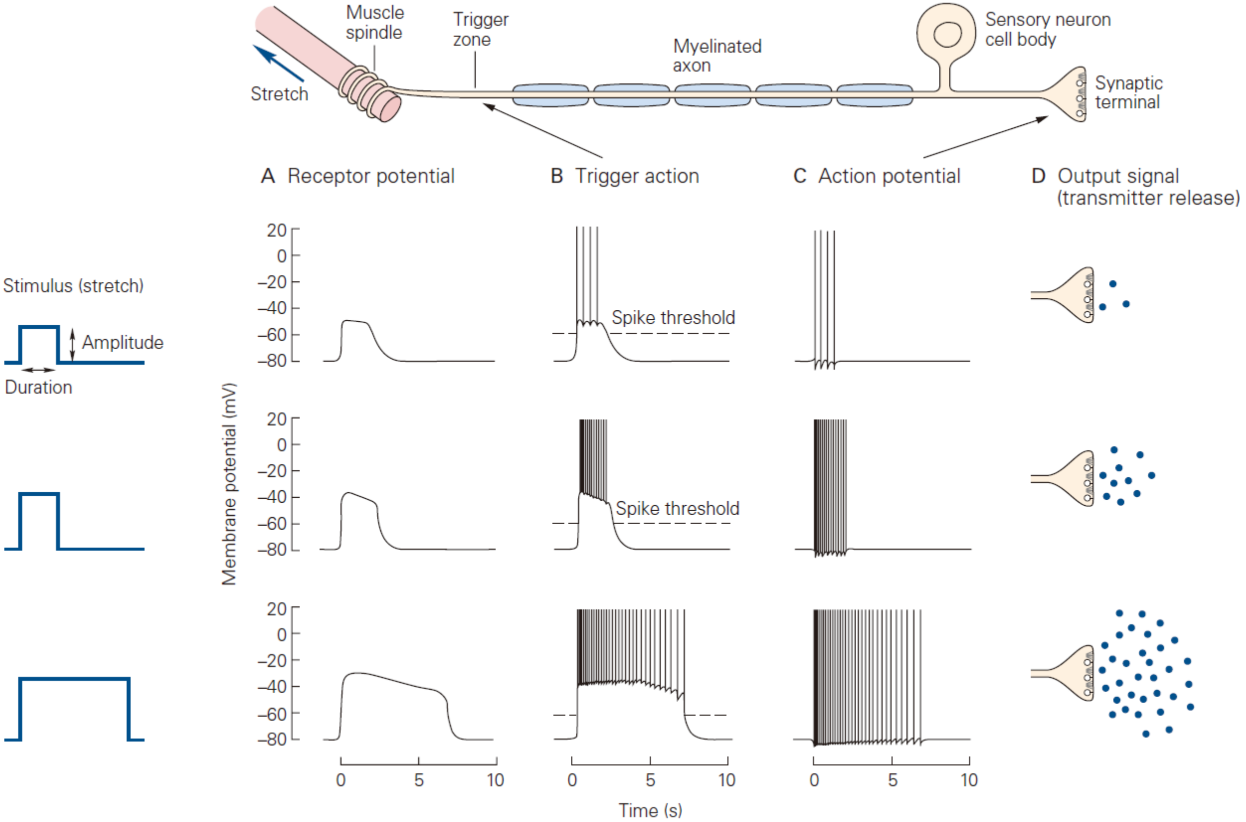


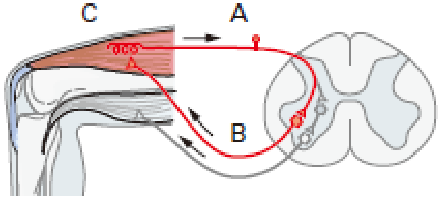
https://en.wikipedia.org/wiki/File:Myelinated_neuron.jpg

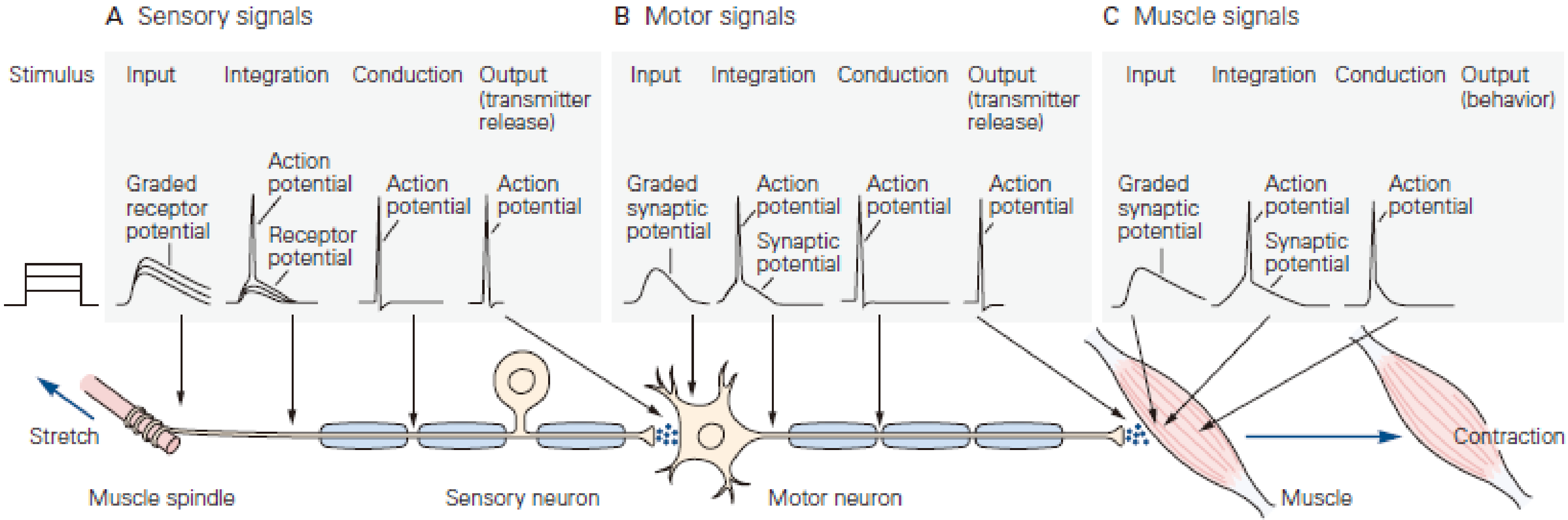
Response to stimulus: a sensory neuron



Kandel et al. Principles of Neural Science, 6E (2021)

Sequence of a reflex action





Kandel et al. Principles of Neural Science, 6E (2021)

Summary

- Formation of membrane potential
  - Distribution of permeable ions (K^+, Cl^-, and Na^+)
- Induction of action potential
  - Permeability of ion channel
- Transmission of the neural signal

生醫工程導論：電生理現象

Reference chapters:

Chapter 11: Bioelectric phenomena, “Introduction to Biomedical Engineering”, John Enderle, Susan Blanchard, and Joseph Bronzio.

Chapter 4.1: The origin of biopotentials, “Medical Instrumentation: Application and Design”, John G. Webster.