Section 3

Membrane potentials and action potentials

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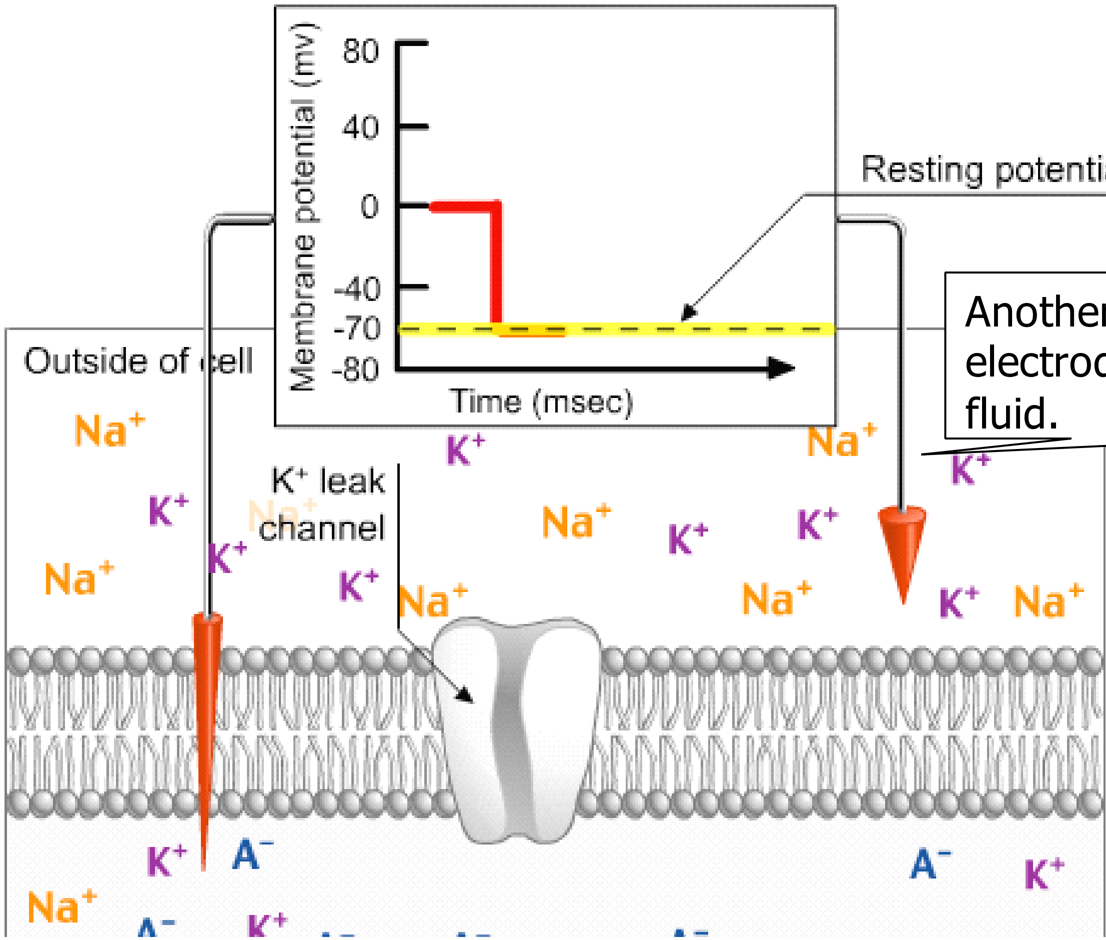
Waveform of resting potential

The potential difference between the inside and outside of the cell is measured using an appropriate voltmeter



Another electrode called indifferent electrode is placed in the extracellular fluid.

- **Inside is negative with respect to outside**

A small microelectrode filled with an electrolyte solution is impaled through the cell membrane to the interior of the cell.

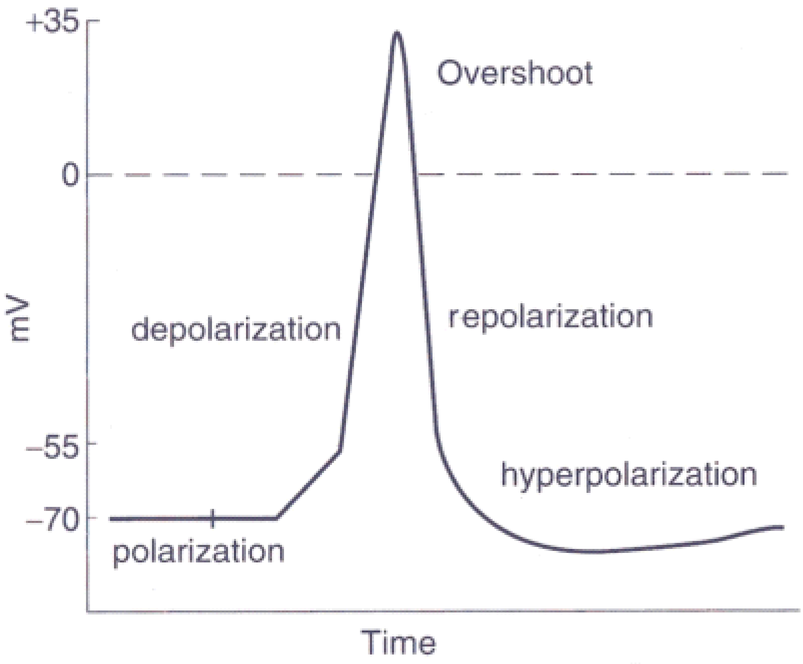
Resting potential

- **Resting potential: a constant potential difference across the plasma membrane in absence of excitatory or inhibitory stimulation, with the inside negative relative to the outside.**
- **Magnitude varies from -10~-100mV.**

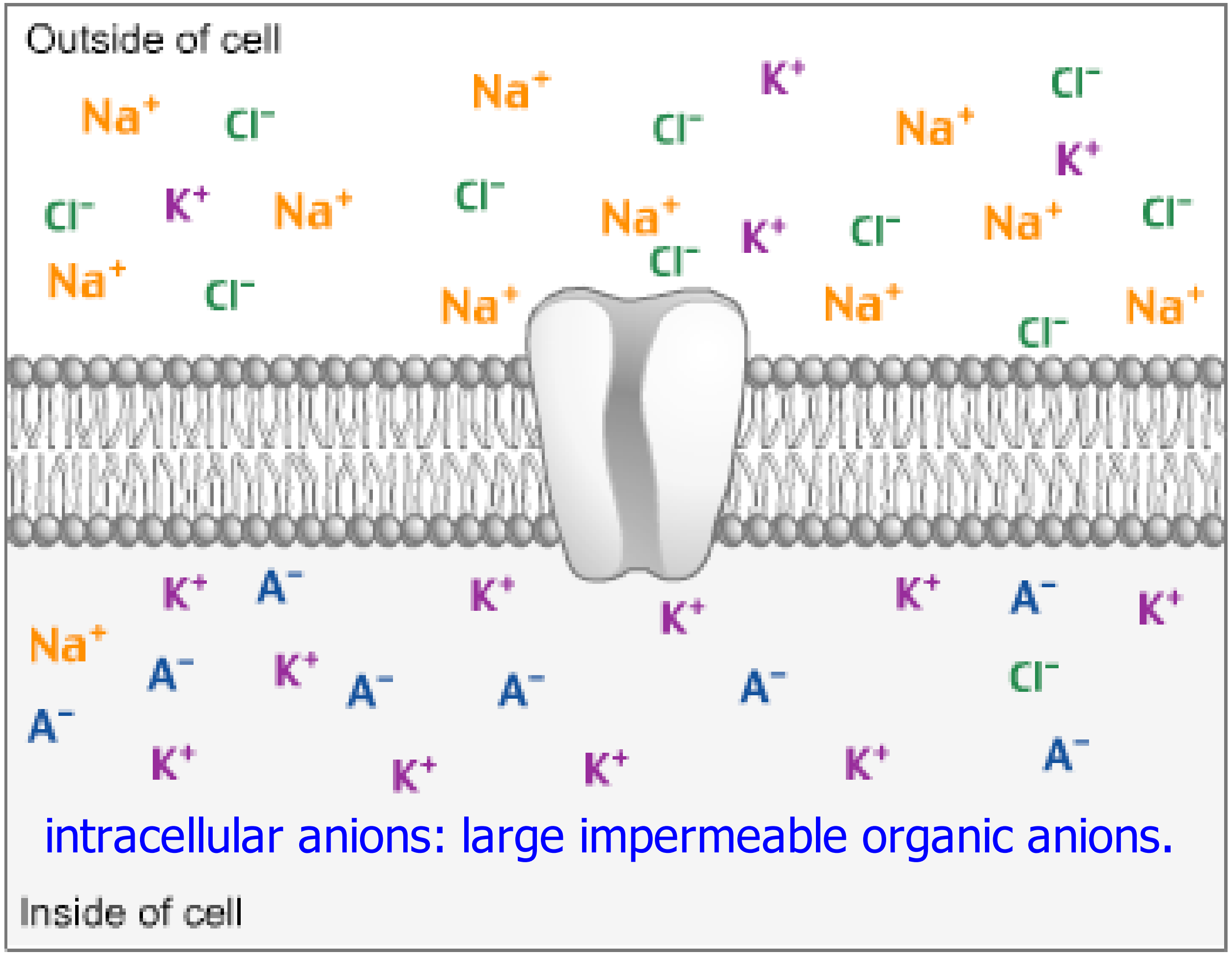
  - -70mV in neurons
  - -90mV in skeletal muscle cells
  - -55mV in smooth muscle cells
  - -10mV in red blood cells.

Recording of membrane potential

- Polarization: the steady potential difference with the inside of the cell negatively charged with respect to the outside under resting condition.
- Depolarization: the membrane potential is less negative than the resting level.
- Overshoot: refers to a reversal of the membrane potential polarity, with the intracellular positive respect to the outside.
- Repolarization: When a membrane potential that has been depolarized returns toward the resting level.
- Hyperpolarization: When the membrane potential is more negative than the resting level.



Origin of resting potential

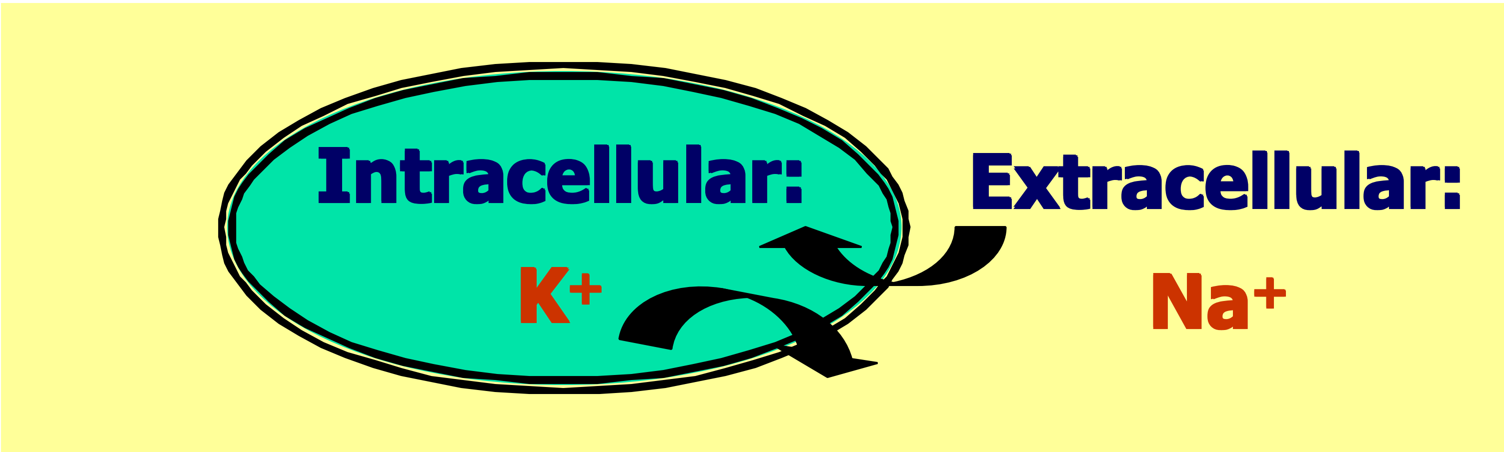


- **Concentration gradient**
- **Electrical gradient**
- **Selective permeability**

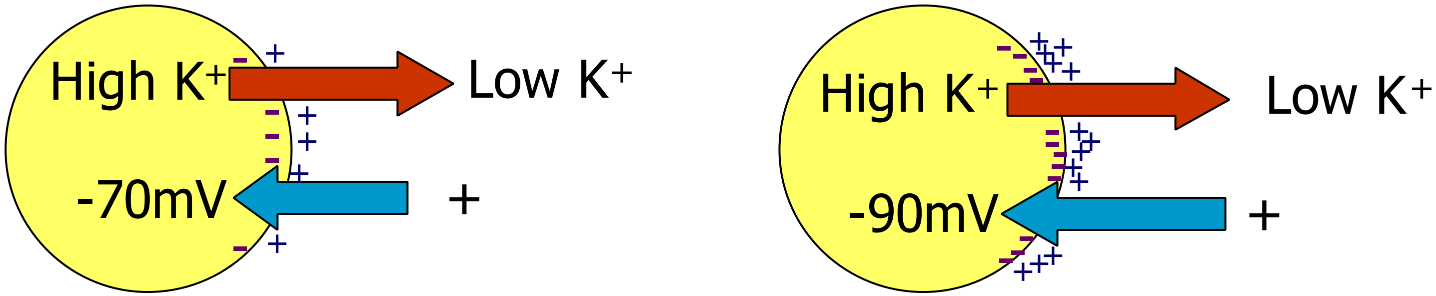
Origin of resting potential

Distribution of major ions across the plasma membrane of a typical muscle cell

Ion	Concentration, mmol/L	
	Extracellular	Intracellular
Na^+	145	12
Cl^-	120	4
K^+	4	155



Potassium movement due to electrochemical gradient



concentration difference

electrical potential difference

Equilibrium potential: voltage gradient across a membrane that is equal in force but opposite in direction to concentration force affecting a given ion species.

K^+ equilibrium potential, E_K

- **Nernst equation**

$$E_K = \frac{RT}{ZF} \ln \frac{[K^+]_o}{[K^+]_I} = 60 \log \frac{[K^+]_o}{[K^+]_i} \ (mV)$$

R: gas constant

T: absolute temperature

Z: valence of the ion

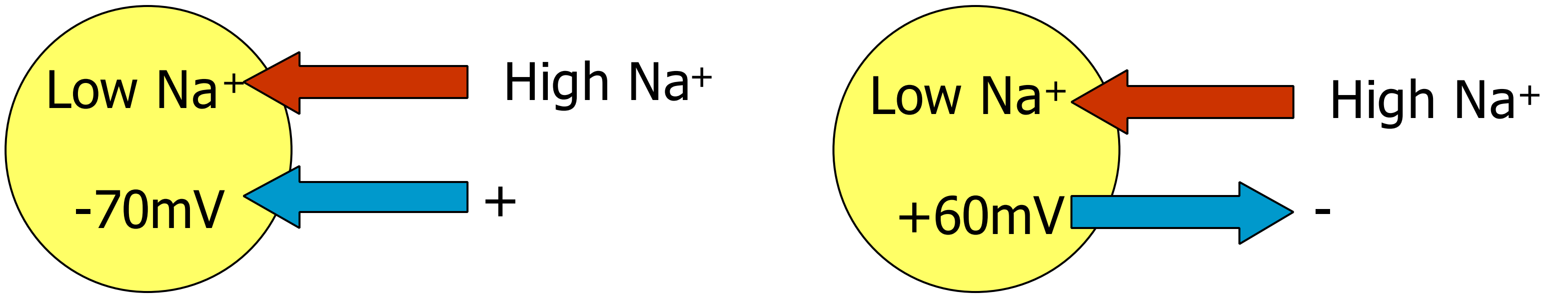
F: Faraday constant

$[K^+]_o$: concentration of potassium outside the cell

$[K^+]_i$: concentration of potassium inside the cell

$$E_K = -90 \sim -100mV$$

Na^+ equilibrium potential, E_{Na}



E_{Na} = +50 ~ +70mV

 **Ion movement due to concentration gradient**

 **Ion movement due to electrical gradient**

The equilibrium potential

- The change of the concentration gradient will change the equilibrium potential
- The larger the concentration gradient, the larger the equilibrium potential
- The greater the membrane permeability to an ion, the greater the contribution of that ion to the membrane potential

Value of resting membrane potential

There are many kinds of ions across the plasma membrane. So given the concentration gradients and membrane permeabilities for several ion species, the membrane potential permeable to these ions can be calculated by following equation.

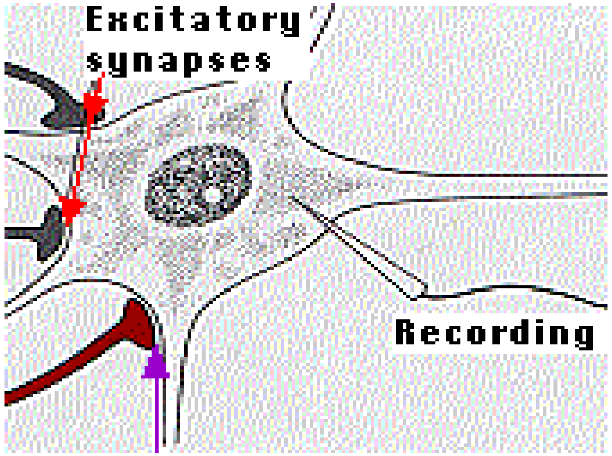
$$E_m = \frac{g_K}{\Sigma g} E_K + \frac{g_{Na}}{\Sigma g} E_{Na} + \frac{g_{Cl}}{\Sigma g} E_{Cl}$$

gK, gNa, gCl: conductance of K+, Na+ and Cl- respectively. Σg: sum.

Because the Cl- equilibrium potential is very close to the resting potential, the resting potential primarily depends on the permeability of K+ and Na+.
Therefore, the equation is simplified as:

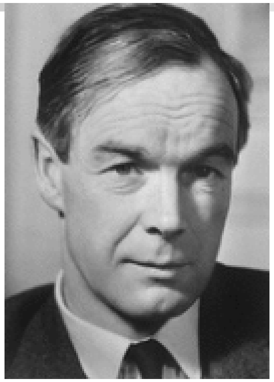
$$\rightarrow \quad E_m = \frac{g_K}{g_K + g_{Na}} E_K + \frac{g_{Na}}{g_K + g_{Na}} E_{Na}$$

Hodgkin and Huxley

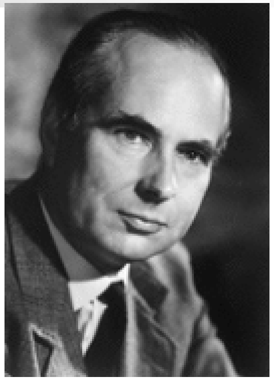


E_m=-60mV

E_K=-75mV



Hodgkin

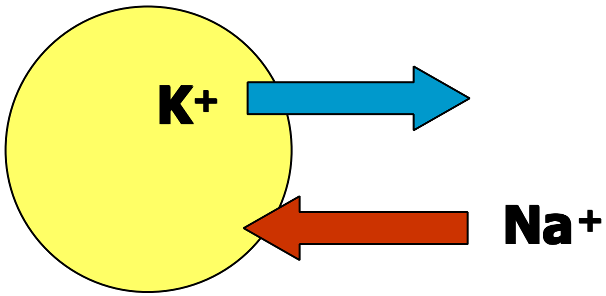


Huxley

- The value of Em is very closer to Ek, which means that the resting potential is largely generated by the movement of K out of the cell down its concentration gradient.
- The resting membrane potential is less than Ek. The reason is that, under resting condition, the plasma membrane also has permeability to Na. Some Na continually move into the cell, therefore reduce the value of Ek.

Ionic basis of resting potential

$$E_m = \frac{g_K}{g_K + g_{Na}} E_K + \frac{g_{Na}}{g_K + g_{Na}} E_{Na}$$

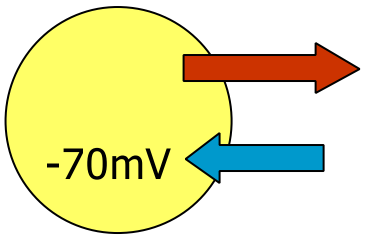


E_K = -75 mV **E_m=-60mV**

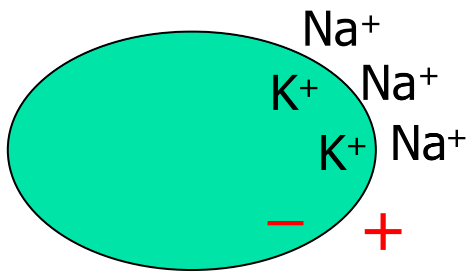
E_{Na} = +50mV **E_m=-60mV**

Factors affecting the level of resting membrane potential

- **Concentration of extracellular K^+**
- **Permeability to K^+ and Na^+**
- **Activity of Na^+- K^+ pump (contribution for resting membrane potential is about 4mV)**

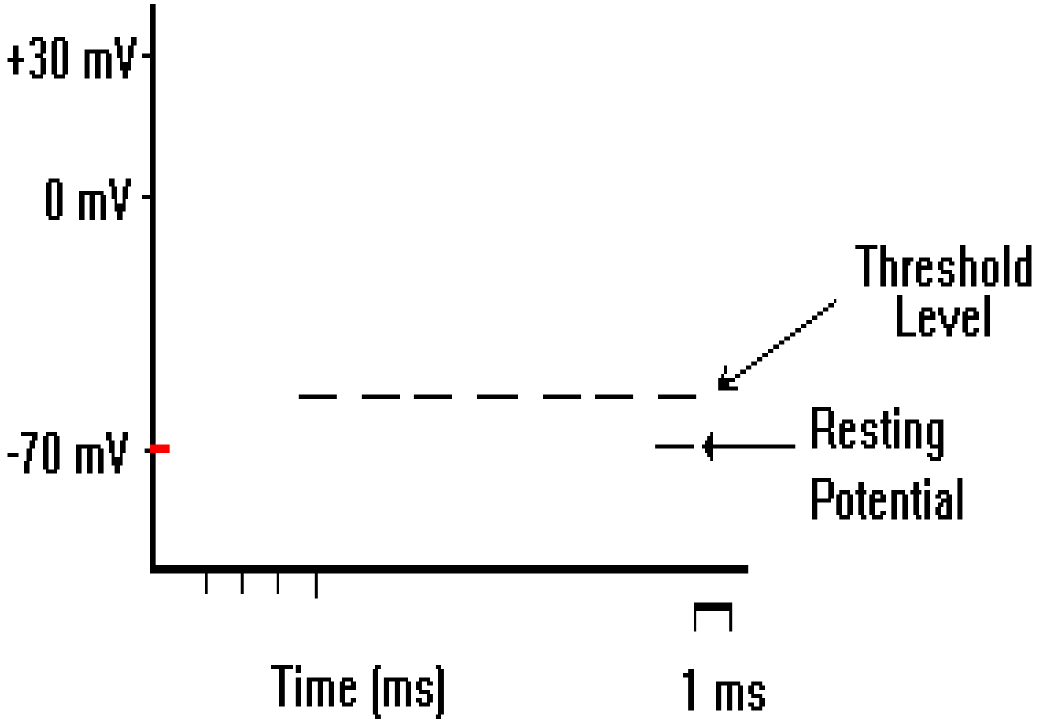


$$E_m = \frac{g_K}{g_K+g_{Na}} E_K + \frac{g_{Na}}{g_K+g_{Na}} E_{Na}$$



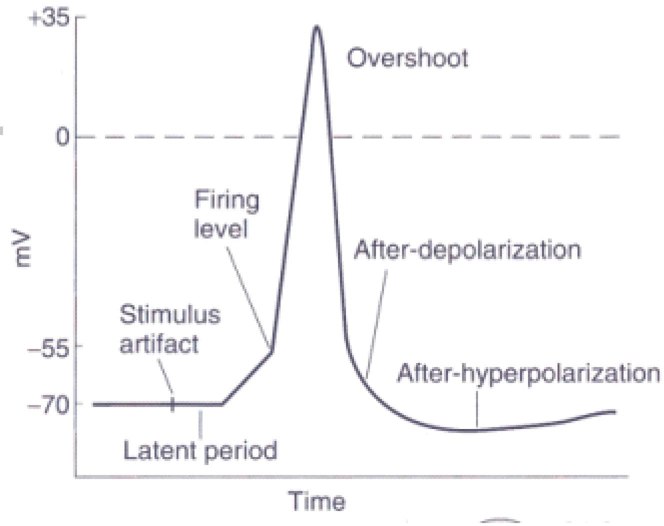
Electrogenic pump

Action potential and its origin



Action potentials are rapid, large alterations in the membrane potential that spread rapidly along the whole cell membrane

Waveform of typical action potential

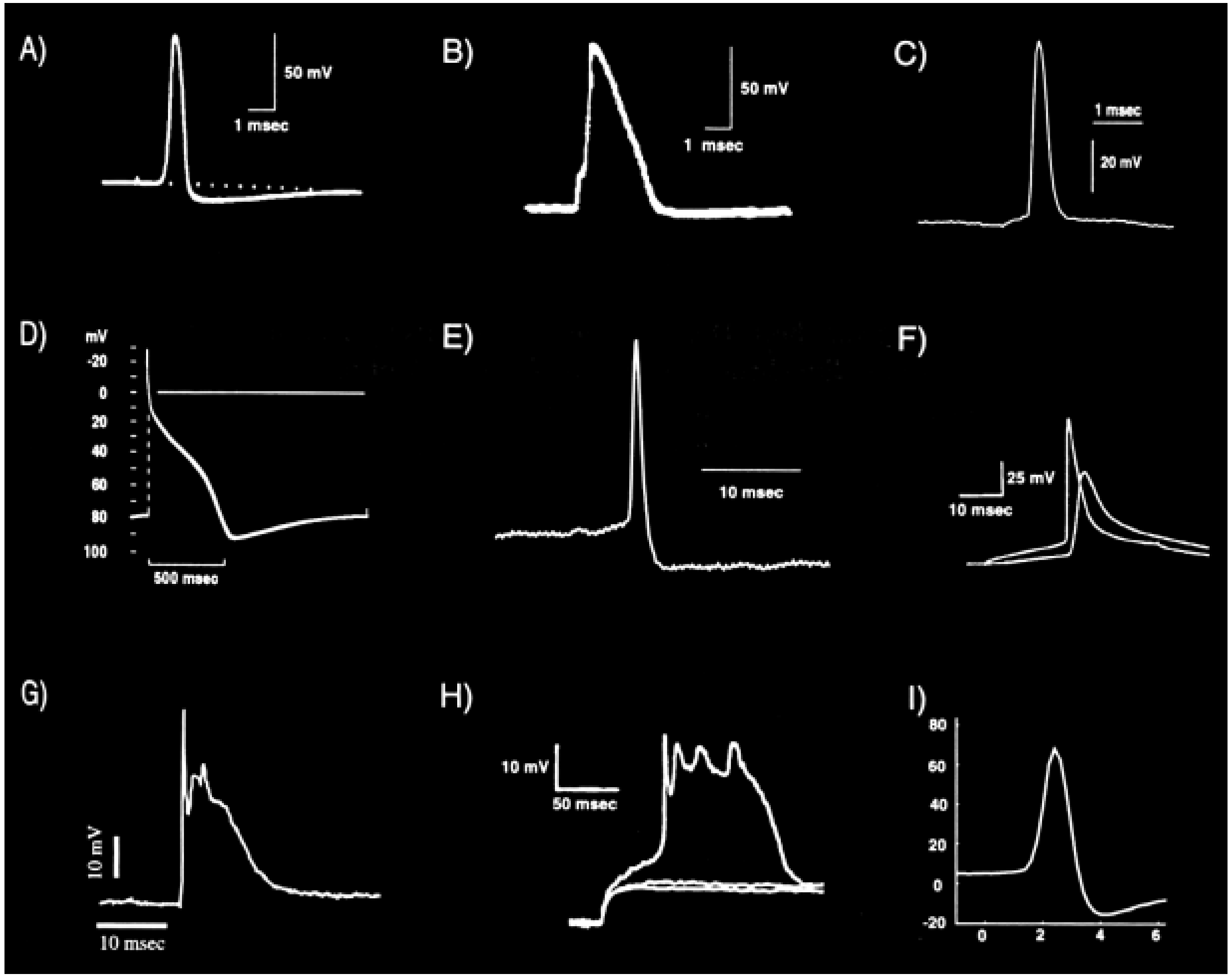


- **Action potential**
  - **Spike potential:**

Both rapid rising part and rapid failing part of the action potential.

  - **After-potential**
    - **Negative after-potential**
    - **Positive after-potential**

Action Potentials

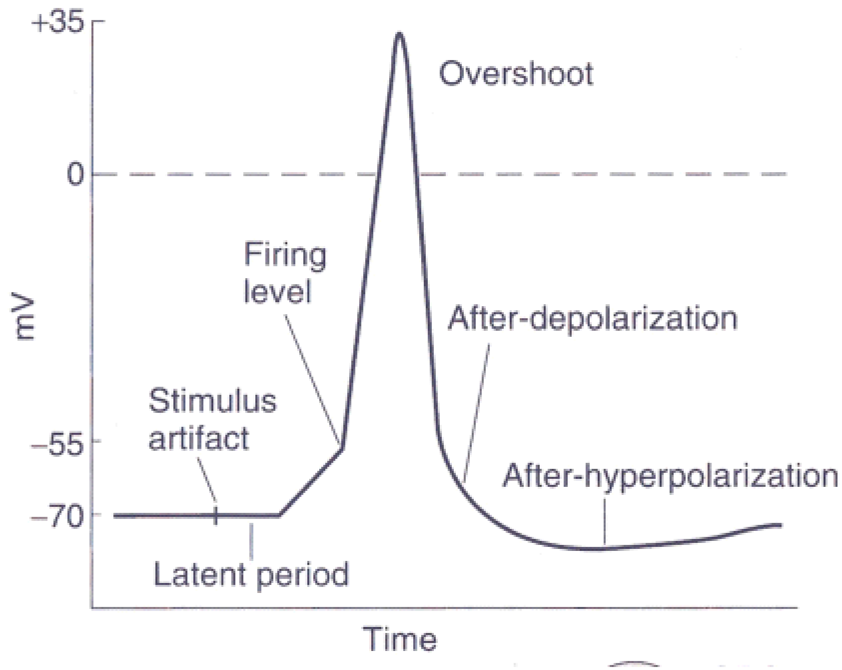


(*A*) Giant squid axon at 16°C (*B*) Axonal spike from the node of Ranvier in a myelinated frog fiber at 22°C (*C*) Cat visual cortex at 37°C (*D*) Sheep heart Purkinje fiber at 10°C (*E*) Patch-clamp recording from a rabbit retinal ganglion cell at 37°C (*F*) Layer 5 pyramidal cell in the rate at room temperatures, simulataneuous recordings from the soma and apical trunk (*G*) A complex spike consisting of several large EPSPs superimposed on a slow dendritic calcium spike and several fast somatic spikes from a Purkinje cell body in the rat cerebellum at 36°C (*H*) Layer 5 pyramidal cell in the rat at room temperature - three dendritic voltage traces in response to three current steps of different amplitudes reveal the all-or-none character of this slow event. Notice the fast superimposed spikes. (*I*) Cell body of a projection neuron in the antennal lobe of the locust at 23°C

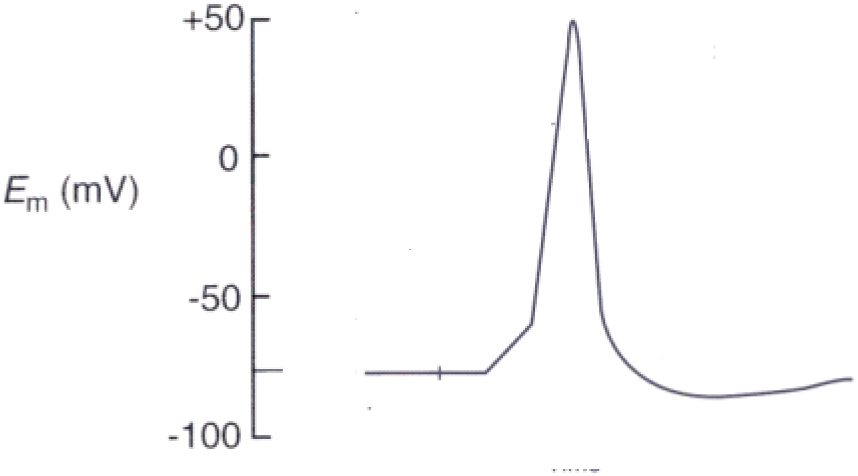
Characteristics of action potential

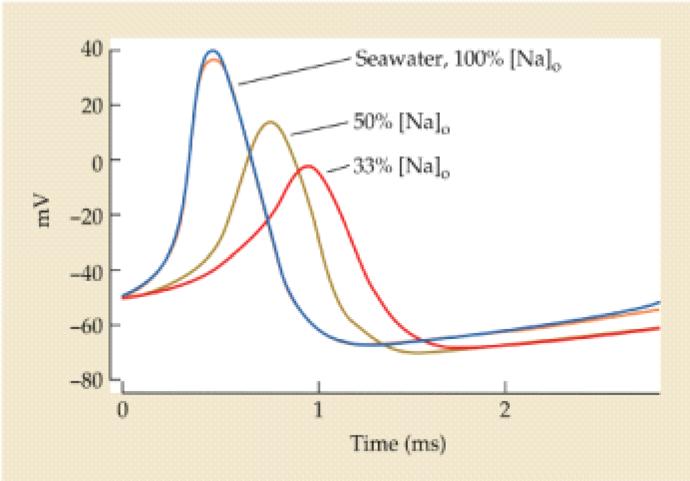
- **All-or-none principle: event that occurs maximally or not at all**

- **Can propagate long distances**

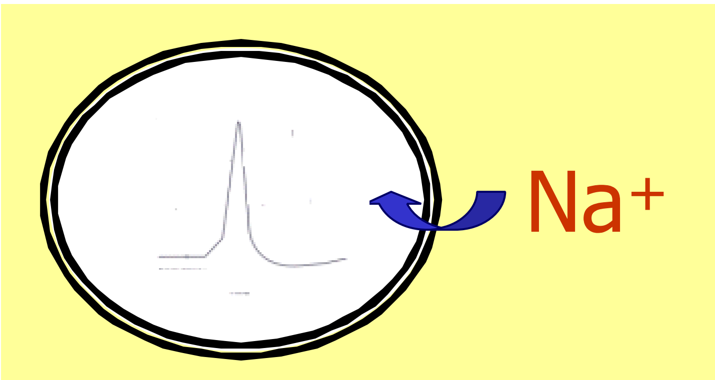


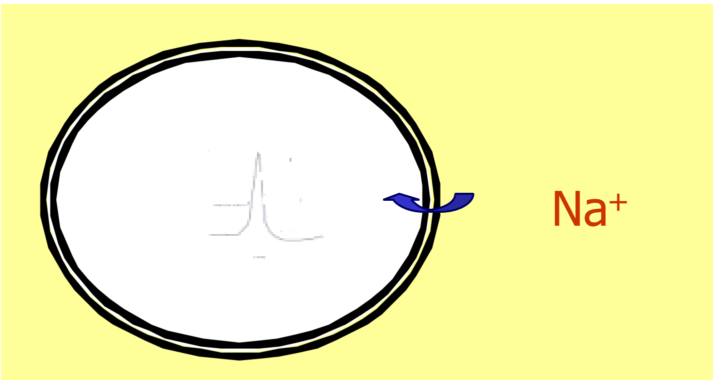
Ionic basis of action potential



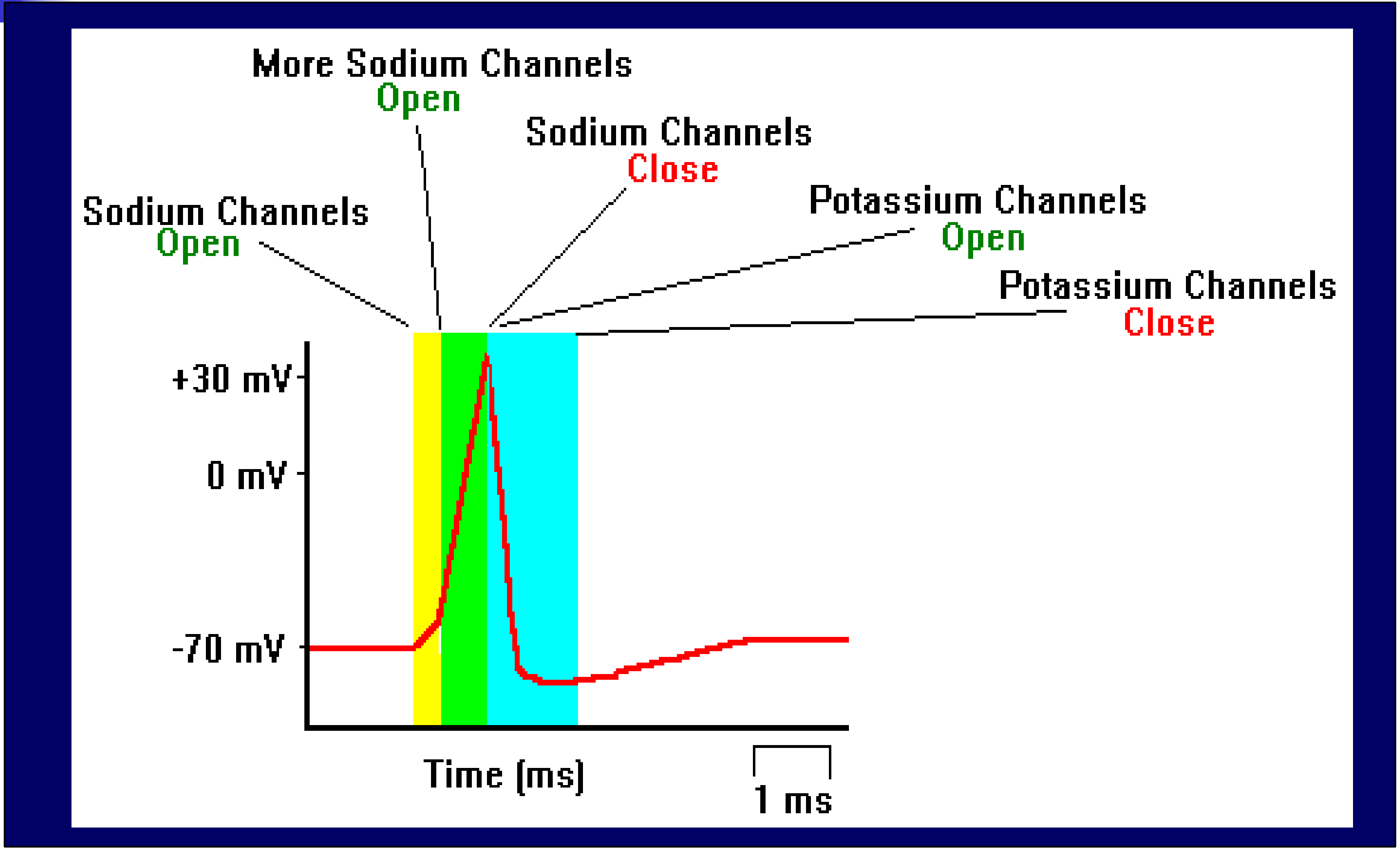


E_{Na} = +50 ~ +70mV





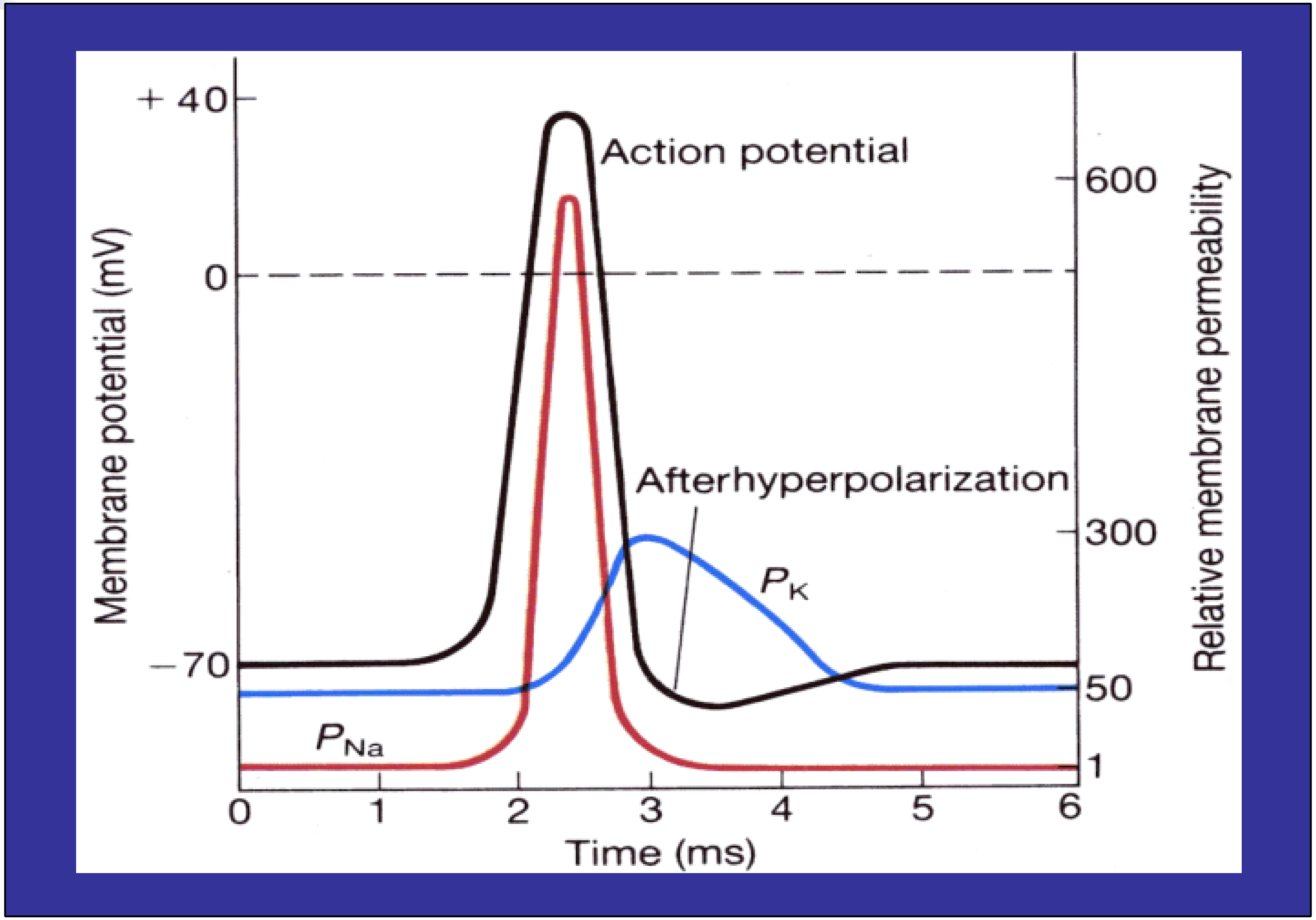
Change in membrane conductance during an action potential



Ionic basis of action potential

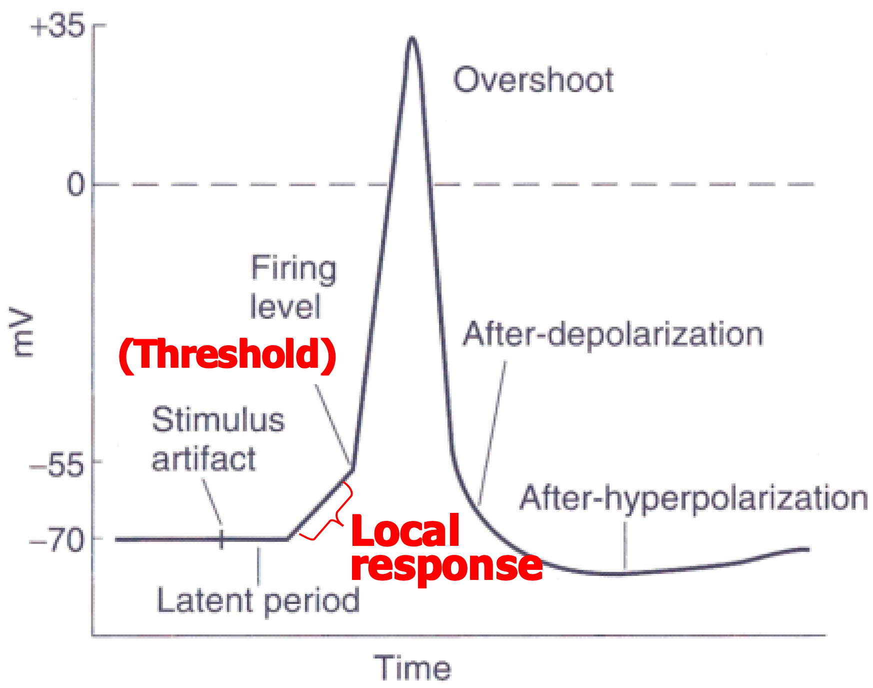
- The action potential begins with depolarization of the membrane in response to a stimulus.
- This initial depolarizaiton opens voltage gated Na channels
- At the peak of the action potential, Na permeability abruptly decreases and voltage gated K channels open.
- The membrane potential begins to repolarize rapidly to its resting level.
- After the Na channels have closed, some of the voltage gated K channels are still open, there is generally a small hyperpolarization of membrane potential beyond the resting level called the afterhyperpolarization.
- Once the voltage gated K channels close, the resting membrane potential is restored.

Changes in membrane potential and changes in membrane permeability to Na^+ and K^+



Ionic basis of action potential

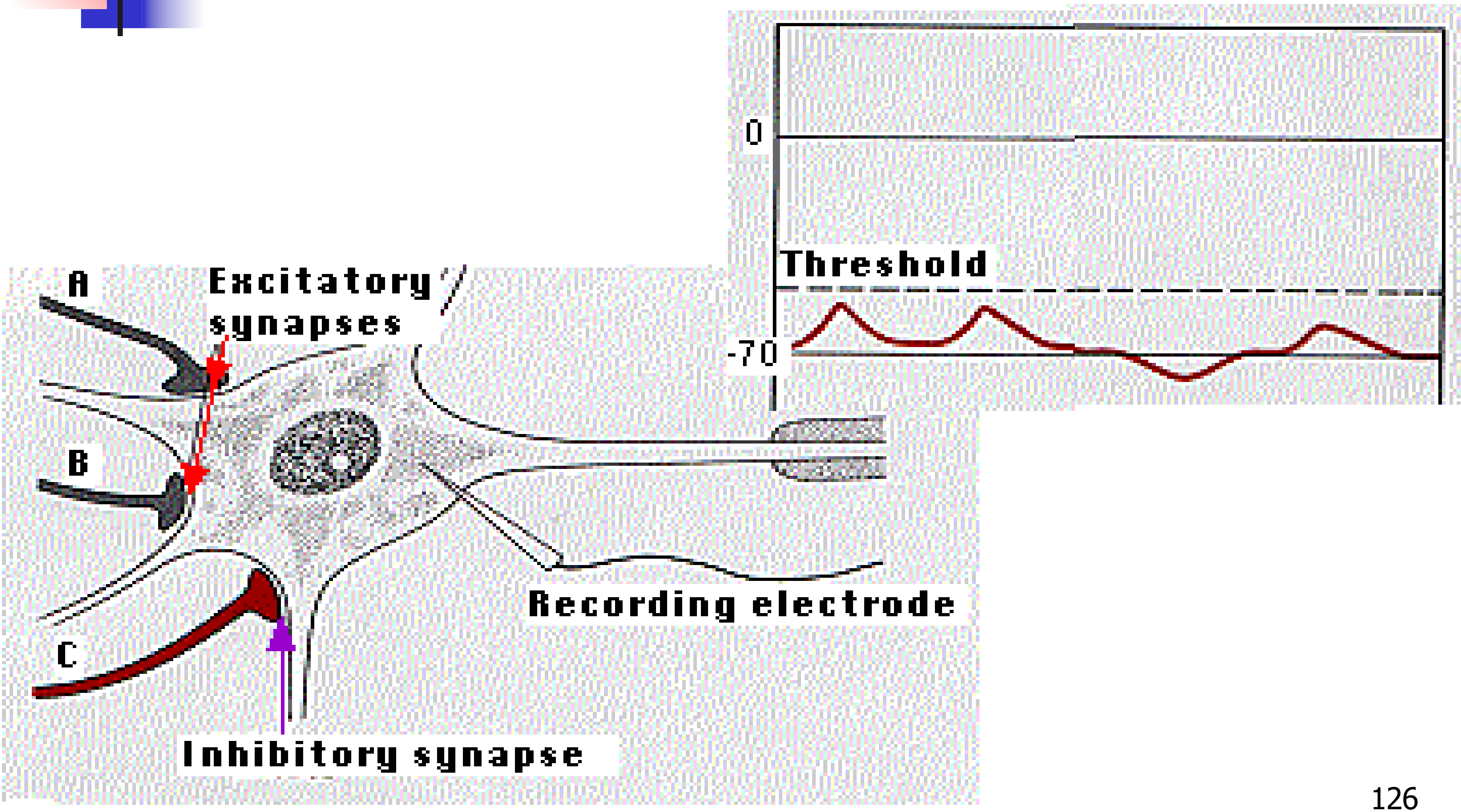
- **Threshold potential:** membrane potential to which excitable membrane must be depolarized to initiate an action potential.



Graded potentials (local response)

- **Graded potentials** are changes in membrane potential that are confined to a relatively small region of the plasma membrane.

Graded potentials (local response)



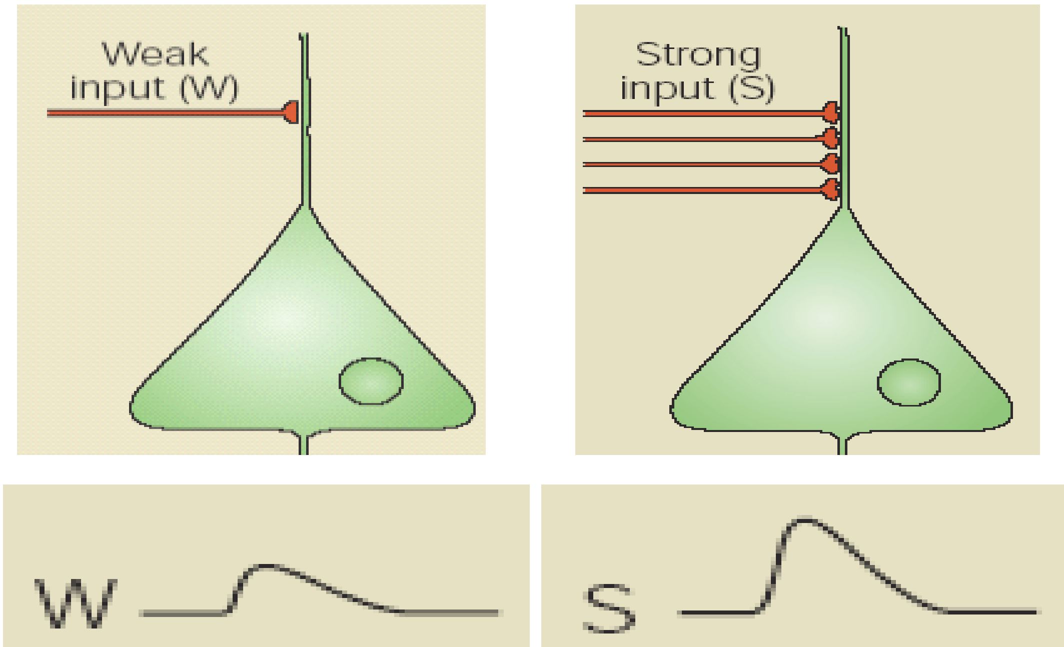
Graded potentials (local response)

Characteristics of local response

- Graded magnitude (No "all-or-none")
- Summation
- Electrotonic propagation

Graded magnitude

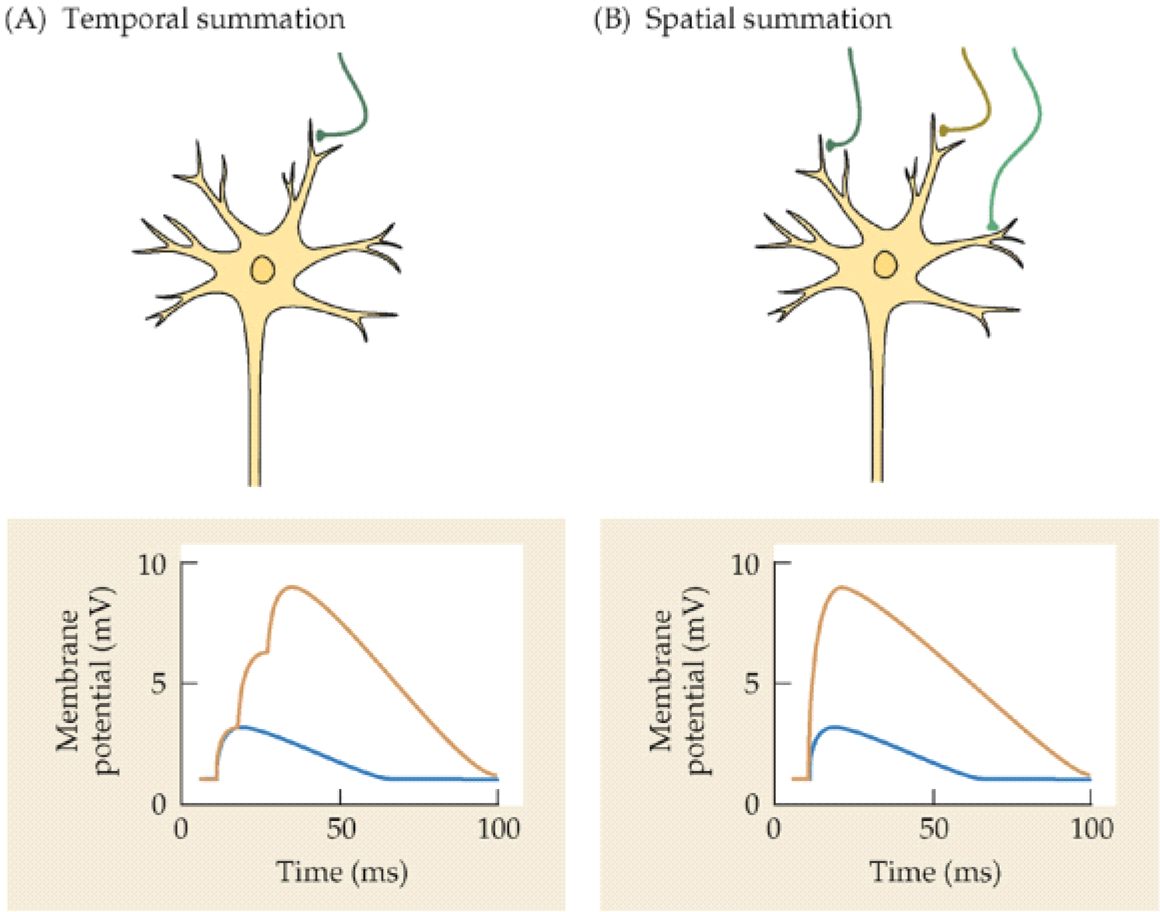
- **Graded magnitude depends upon the initiating stimulus**



Spatial summation and temporal summation

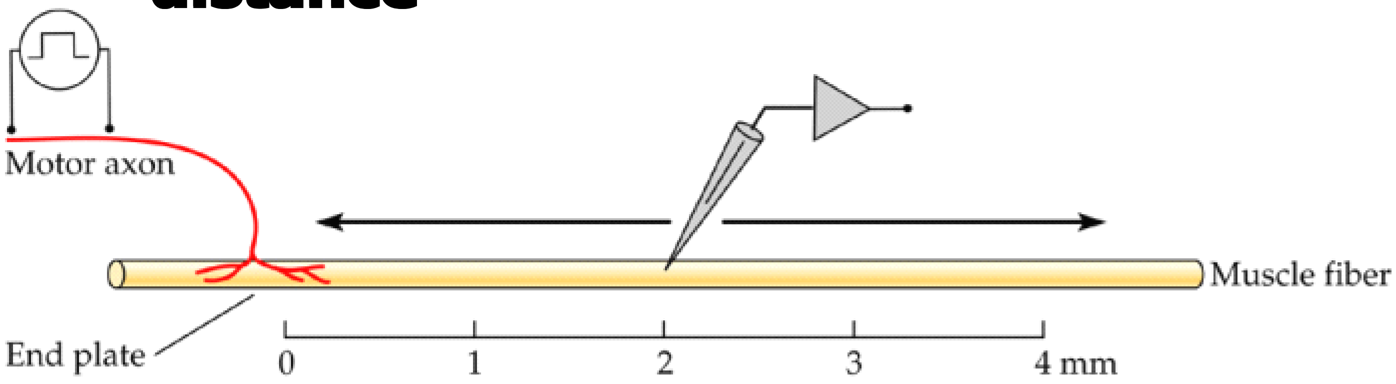
- **Summation: if additional stimuli occur before the graded potential has died away, these can be added to the depolarizaiton from the first stimulus.**
  - **Temporal summation: occurs if repeated afferent stimuli cause new graded response before previous one has decayed.**
  - **Spatial summation: occurs when activity is present in more than one points at the same time.**

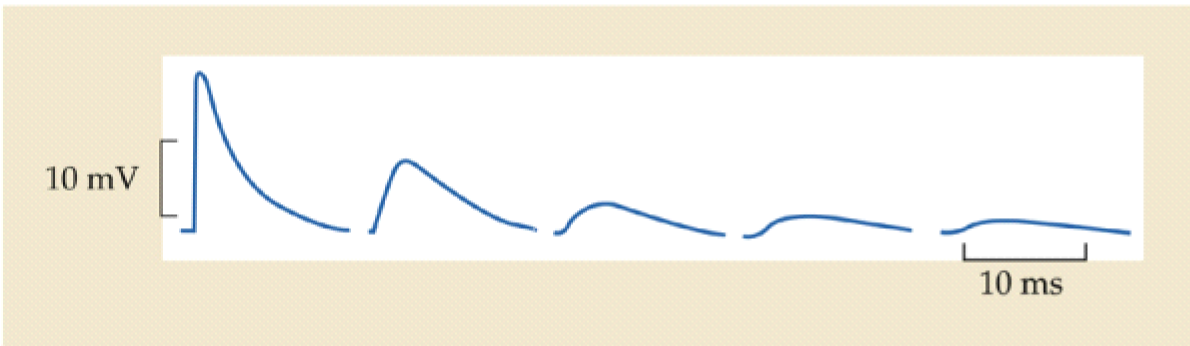
Spatial summation and temporal summation

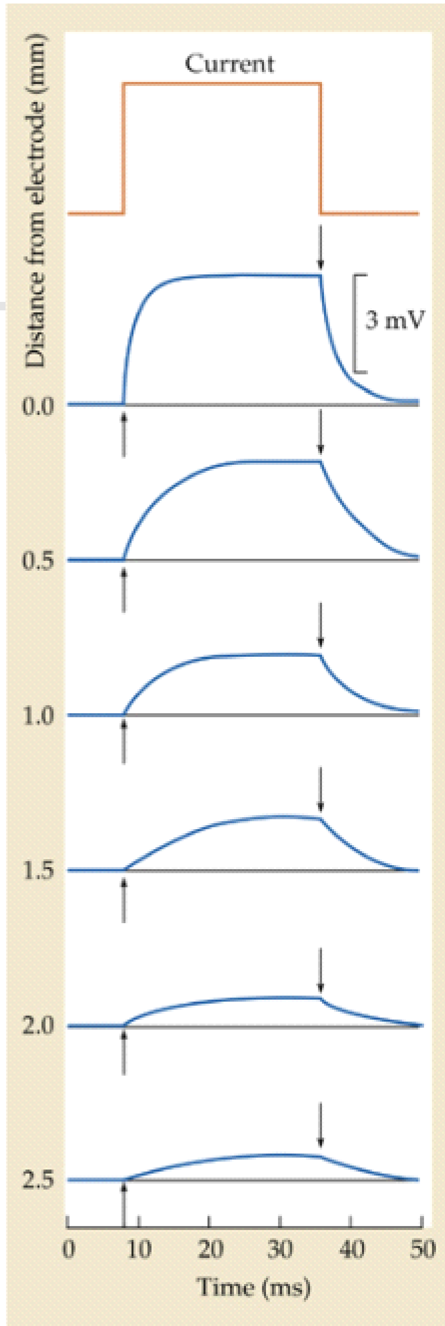


Electrotonic propagation

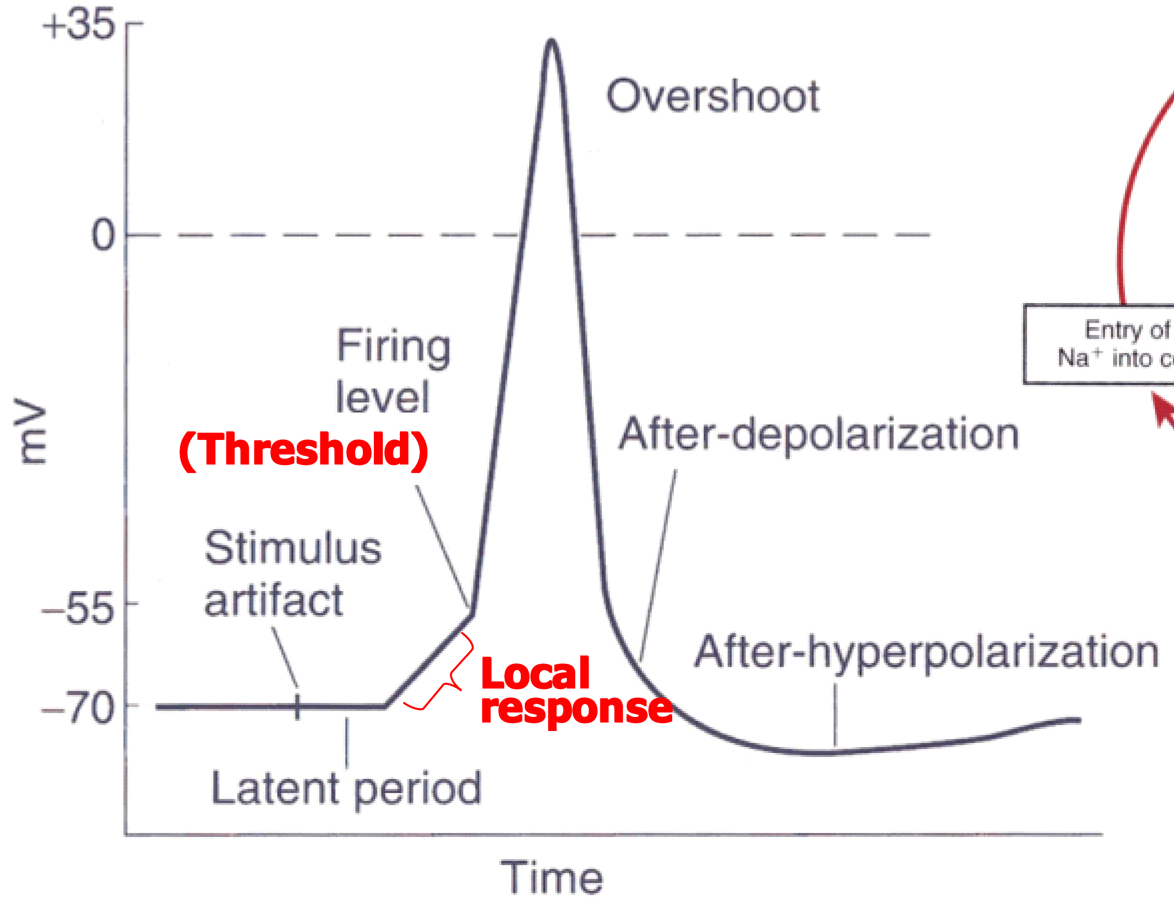
- The graded potential decreases with distance

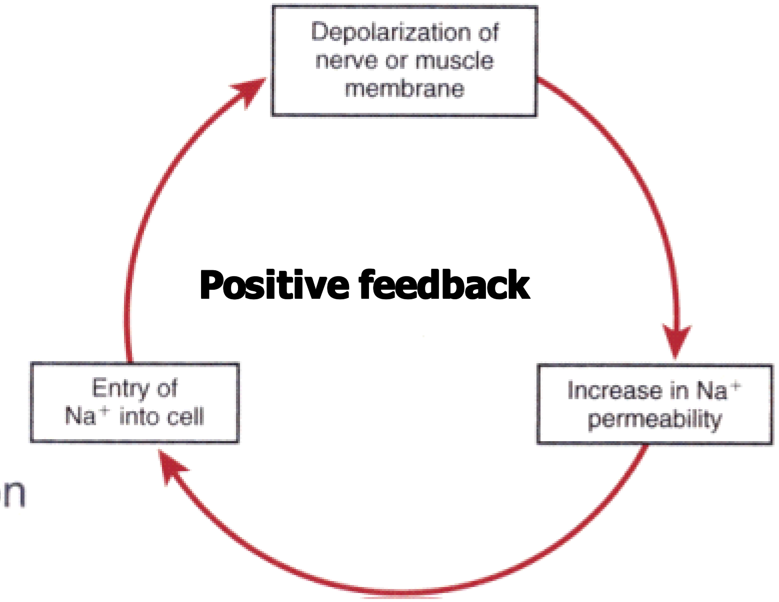






Initiation of action potential

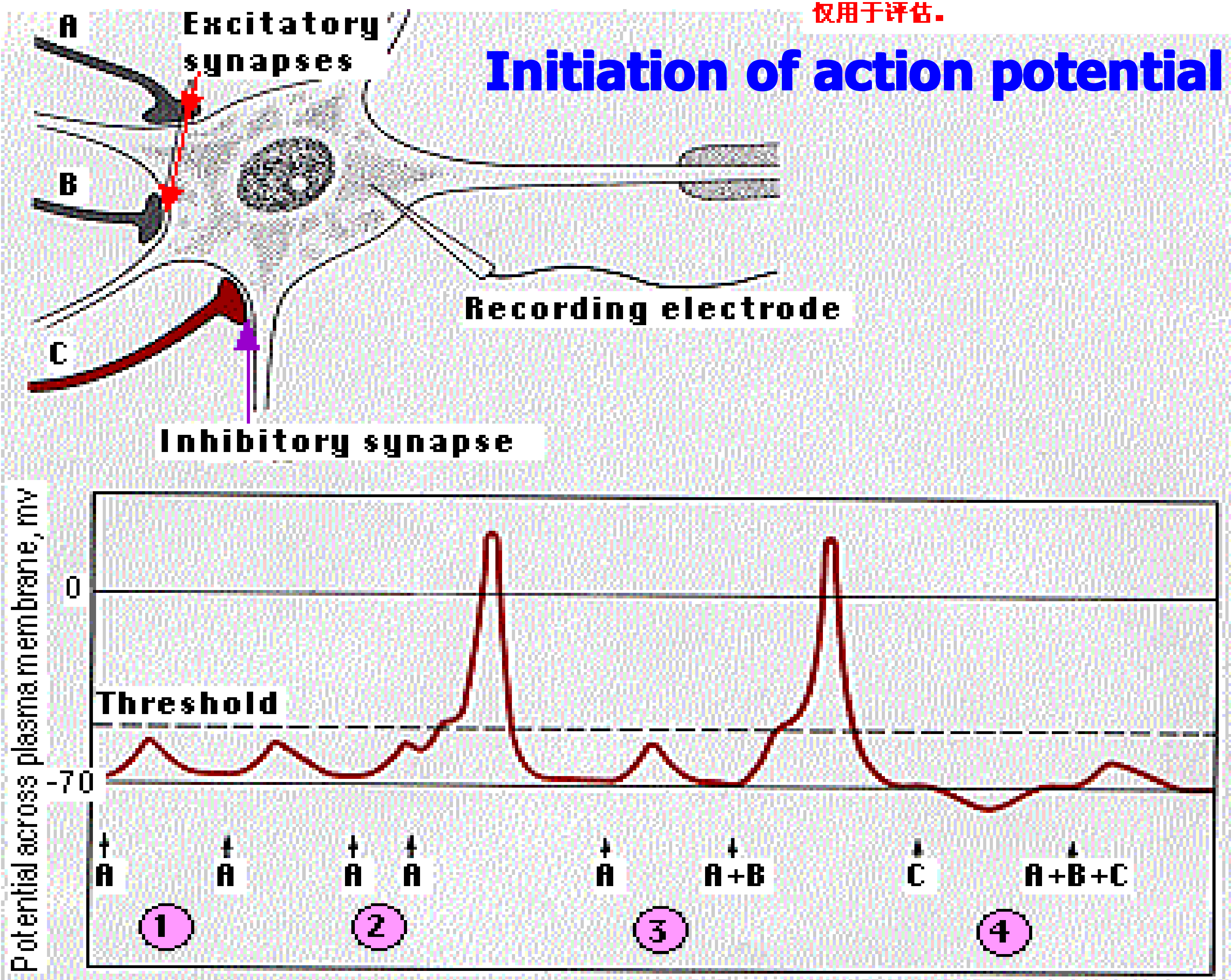




Threshold potential:

10~20mV depolarized from RMP

Initiation of action potential

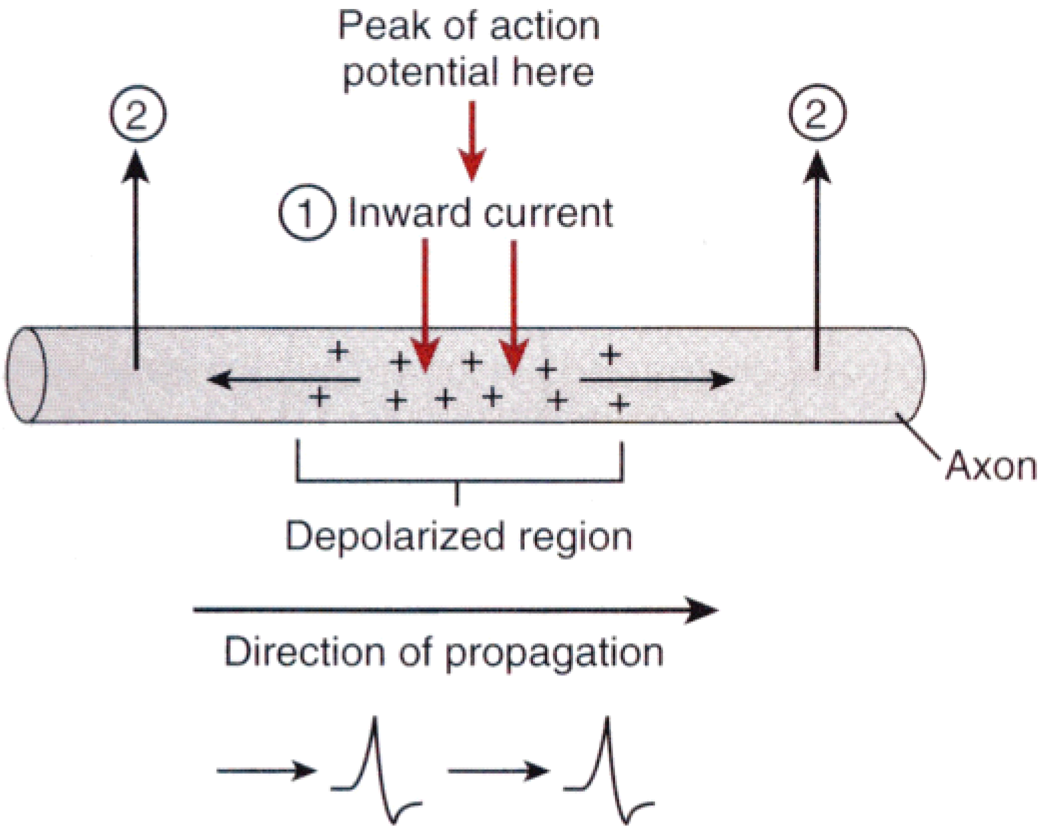


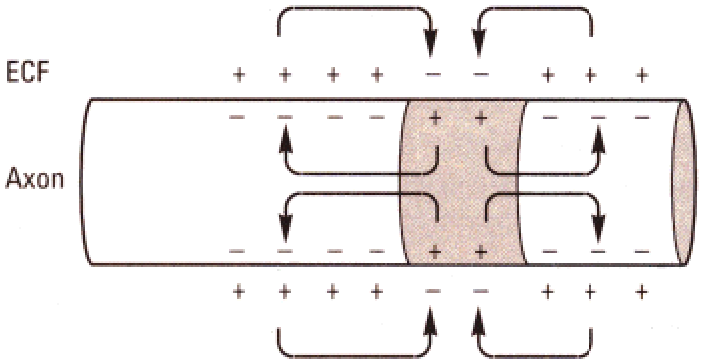
Propagation of action potential

- **An action potential elicited at any one point on an excitable membrane usually excites adjacent portion of the membrane, resulting in the propagation of the action potential over the membrane.**

Propagation of action potential

- The propagation of an action potential in an **unmyelinated** axon

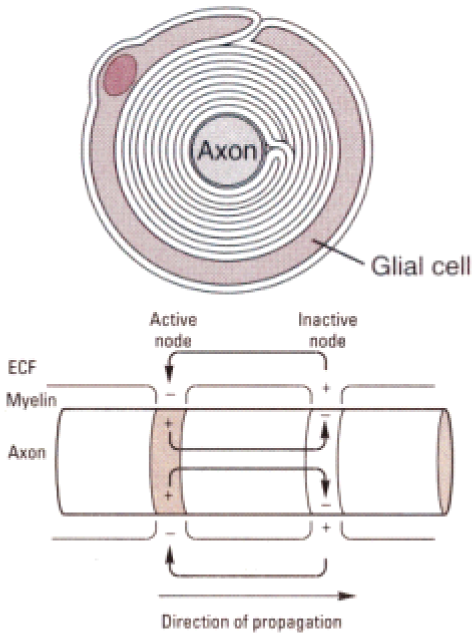


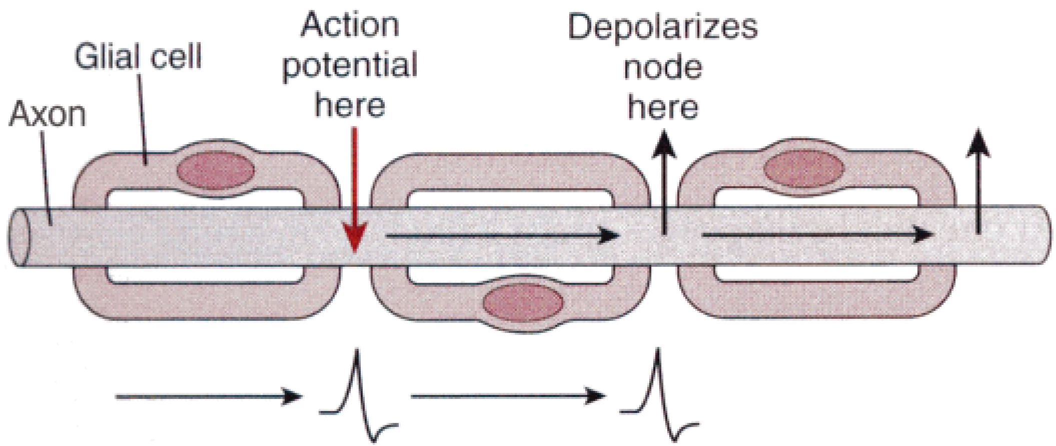


Local current

Propagation of action potential

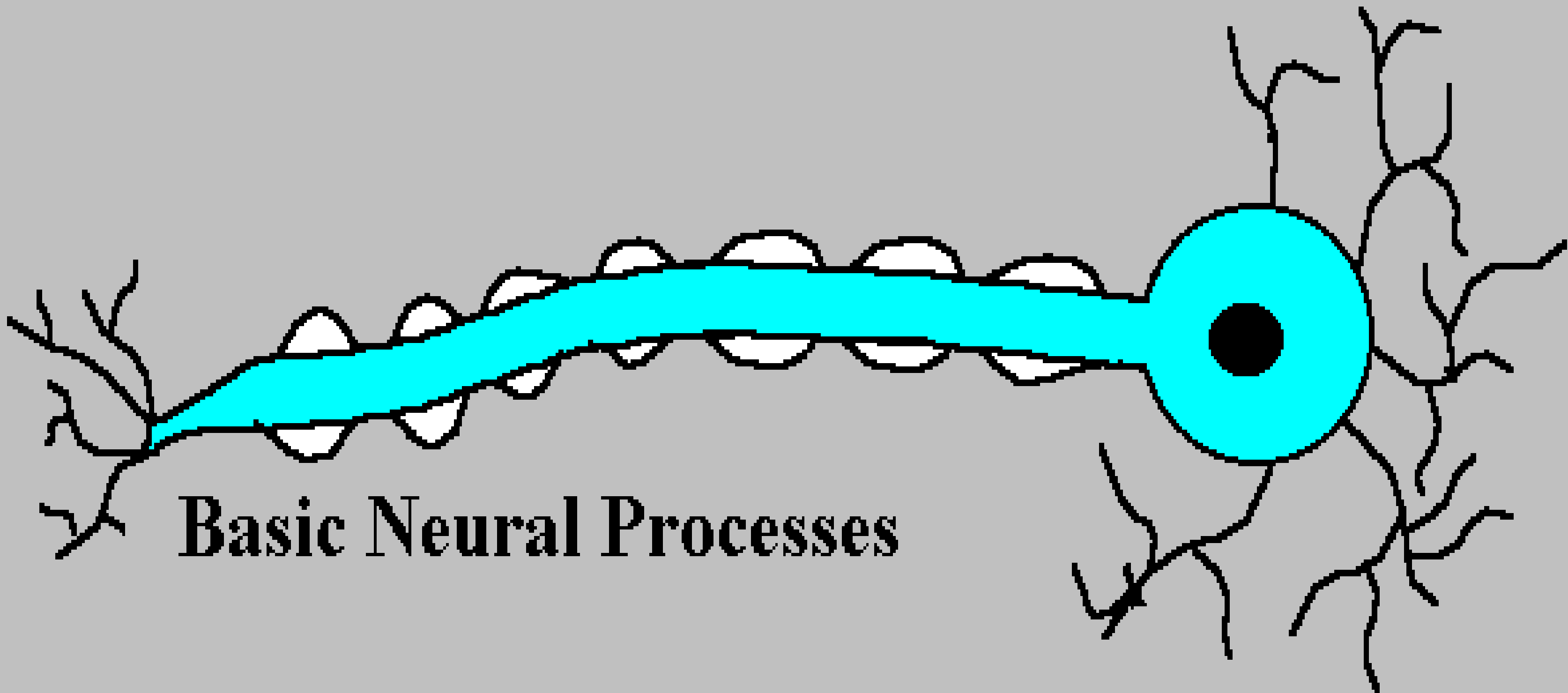
- **Propagation of an action potential in a myelinated axon.**





- **Myelin is an insulator that makes it more difficult for charge to flow between intracellular and extracellular fluid compartments.**

Saltatory conduction



- **Saltatory conduction: The initiation of an action potential in one node of Ranvier depolarizes the next node. Jumping from one node to the next.**

Excitation and excitability

- Excitation and excitable cell
- Excitability and threshold stimulus
- Change in excitability

Excitation and excitable cell

- **Excitation: action potential**
- **Excitable cell: cells that can produce action potential.**

Nerve and muscle cells as well as some endocrine, immune, and reproductive cells

- **Excitation-contraction coupling**
- **Excitation-secretion coupling**

Excitability and threshold stimulus

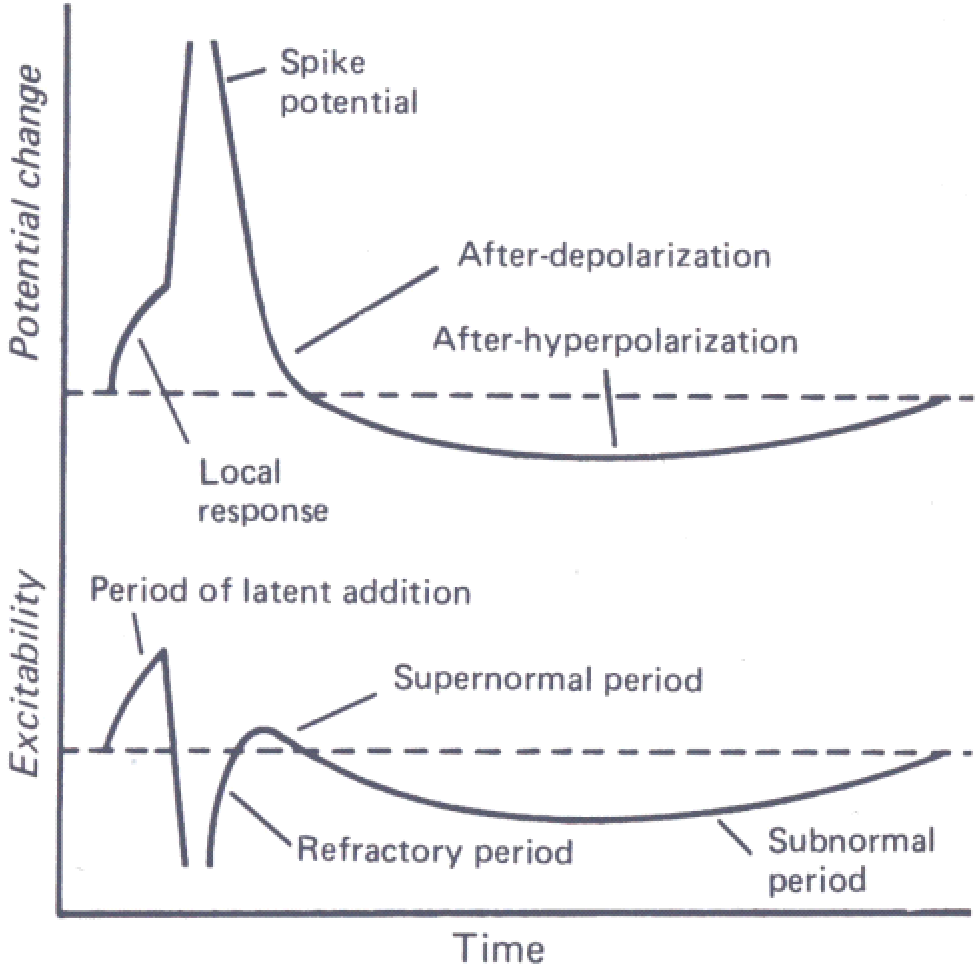
- **Excitability: ability to produce action potential**
- **Stimulus: detectable change in environment**
- **Three parameters of a stimulus:**
  - **Intensity of stimulus**
  - **Duration of stimulus**
  - **Rate of change**

Excitability and threshold stimulus

- **Threshold stimulus: the minimal intensity of stimulus to cause action potential of cells**
- **Threshold stimulus could be used to evaluate excitability:**

  The larger the threshold stimulus, the lower the excitability.

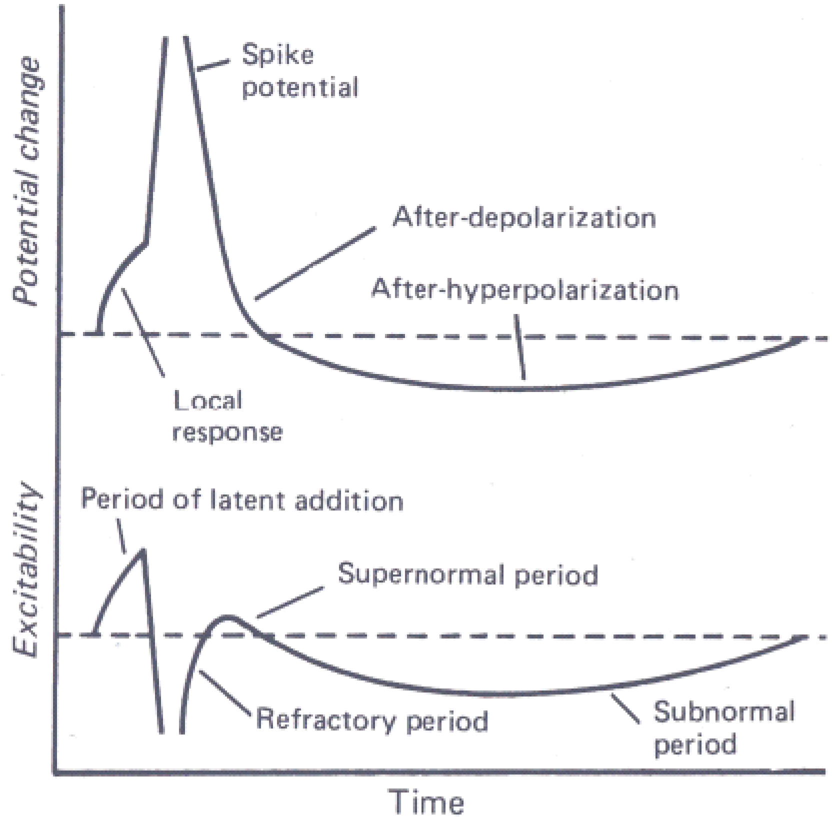
A series of excitability alteration after excitation



- **Absolute refractory period**
- **Relative refractory period**
- **Supranormal period**
- **Subnormal period**

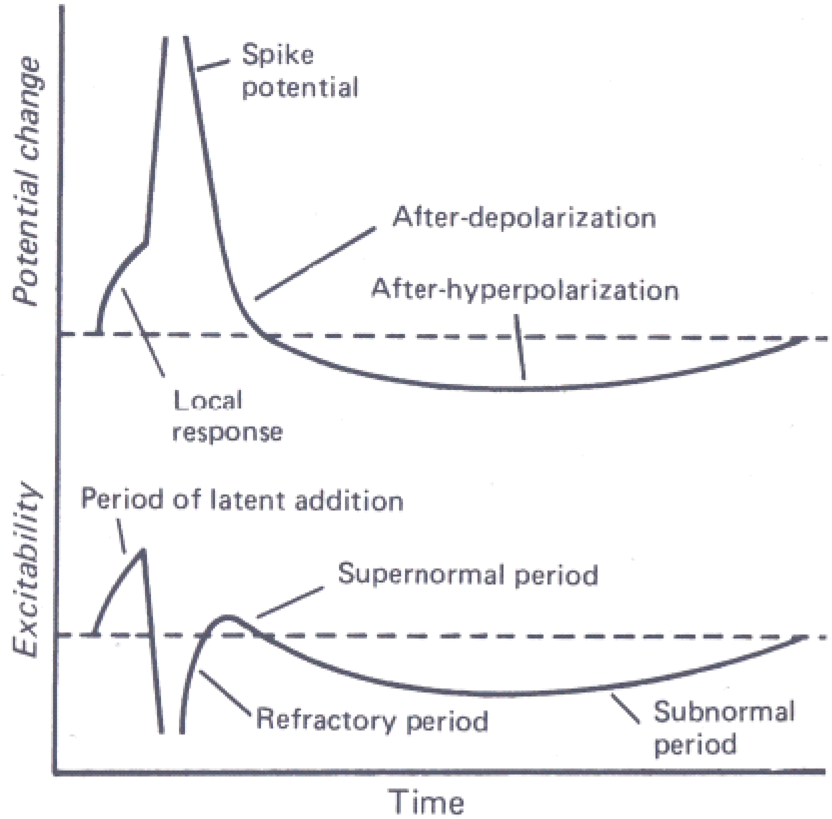
Change in excitability during an action potential

- **Absolute refractory period: time during which an excitable membrane cannot generate an action potential in response to any stimulus.**



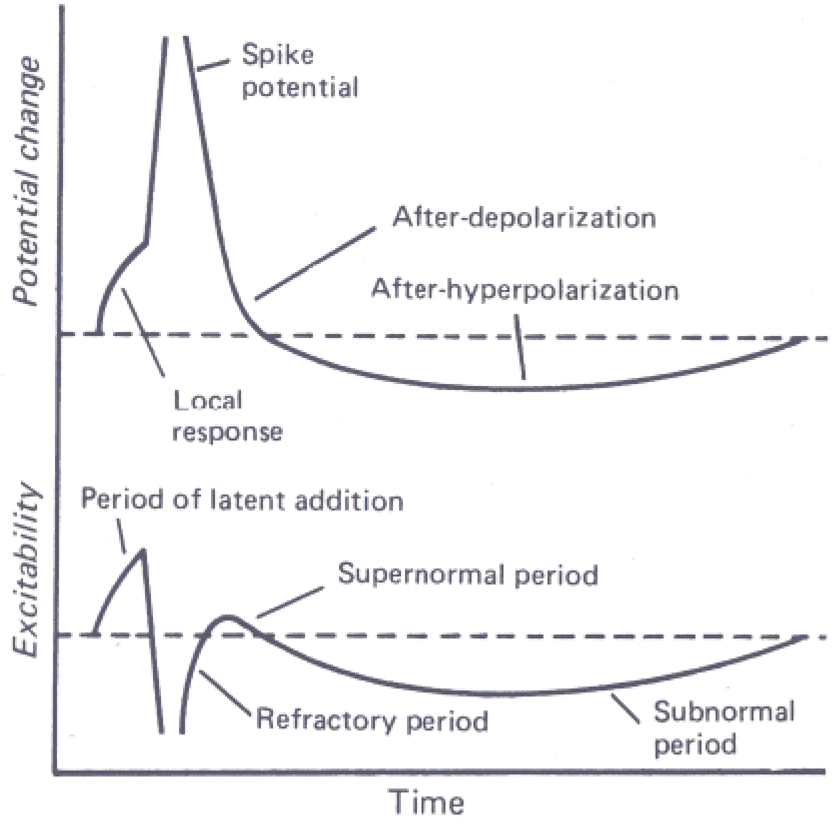
Change in excitability during an action potential

- **Relative refractory period**: time during which excitable membrane will produce action potential only to a stimulus of **greater strength** than the usual threshold strength.



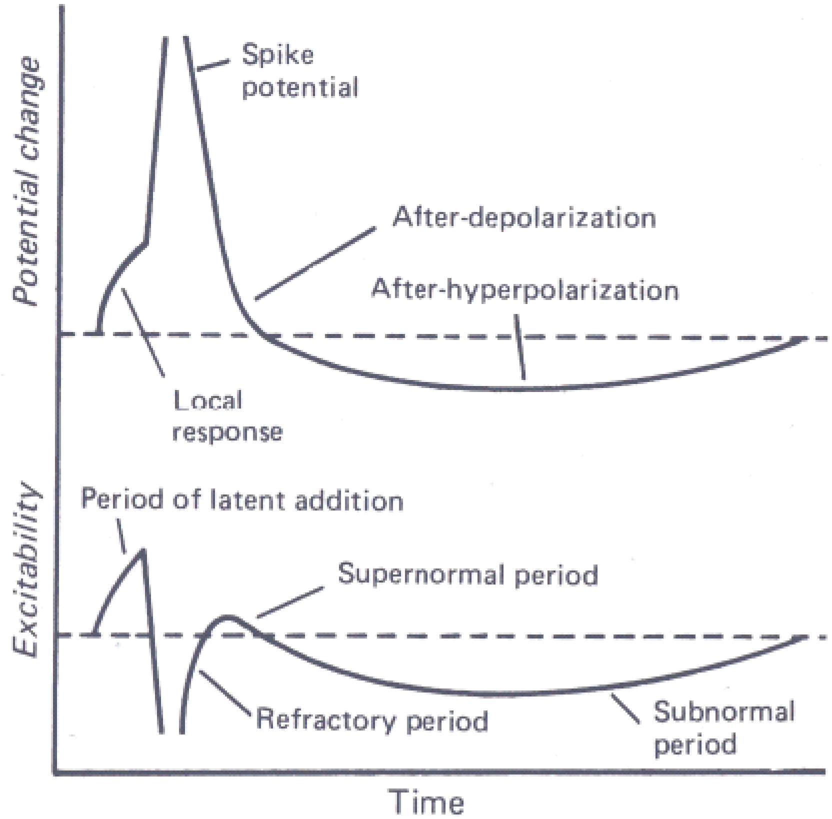
Change in excitability during an action potential

- **Supranormal period**: time during which excitable membrane will produce action potential in response to subthreshold stimuli.



Change in excitability during an action potential

- **Subnormal period: time during which excitable membrane will produce action potential in response to suprathreshold stimuli.**



Summary

- **RMP, ionic basis, factors affecting RMP**
- **AP, ionic basis, characteristics**
- **Characteristics of local response**
- **Excitation, Excitable cell, Excitability, Stimulus, Threshold stimulus**
- **Change in excitability during an action potential**