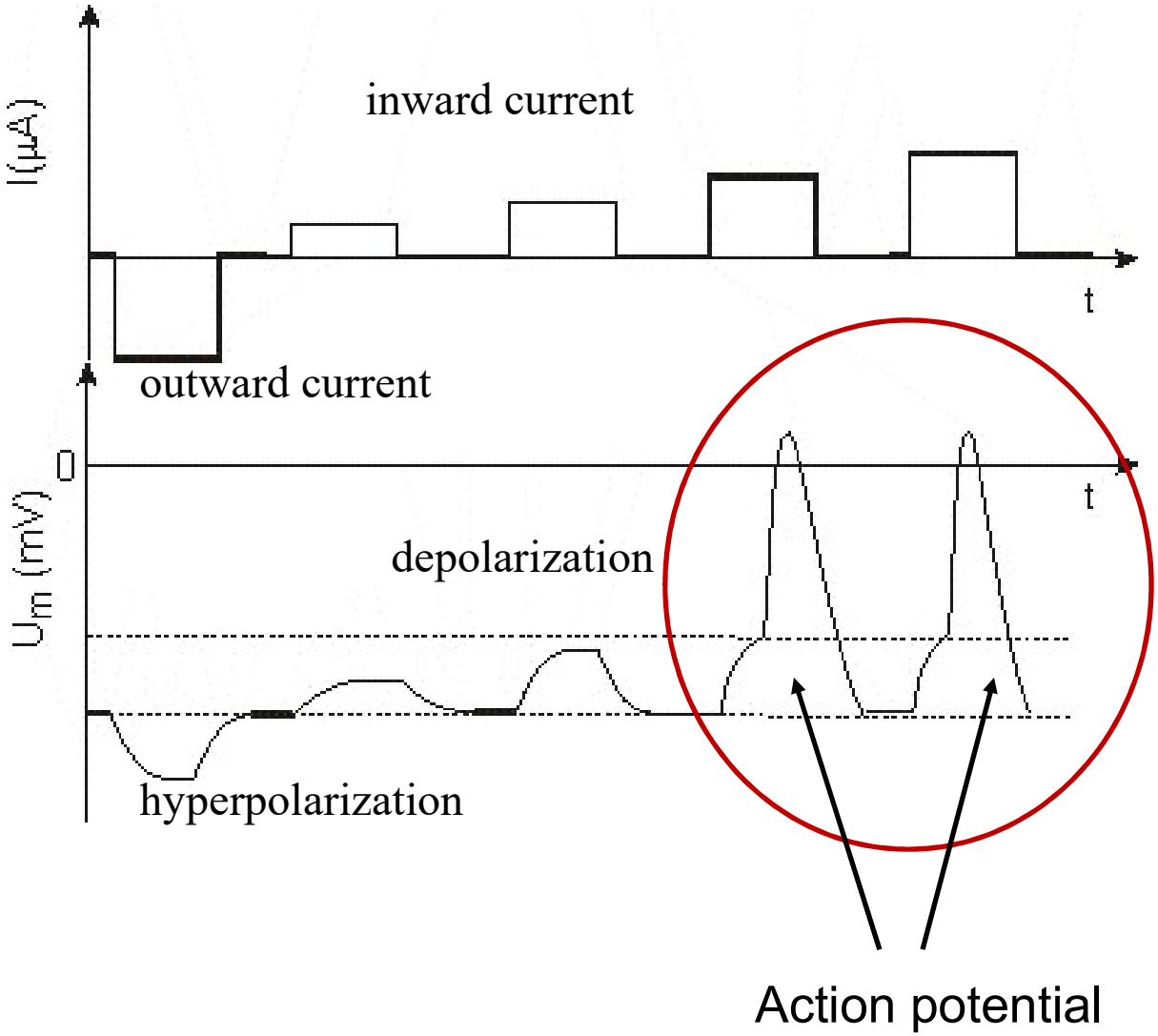
Alteration of resting membrane potential

2. “active” electric properties of the membrane in excited state

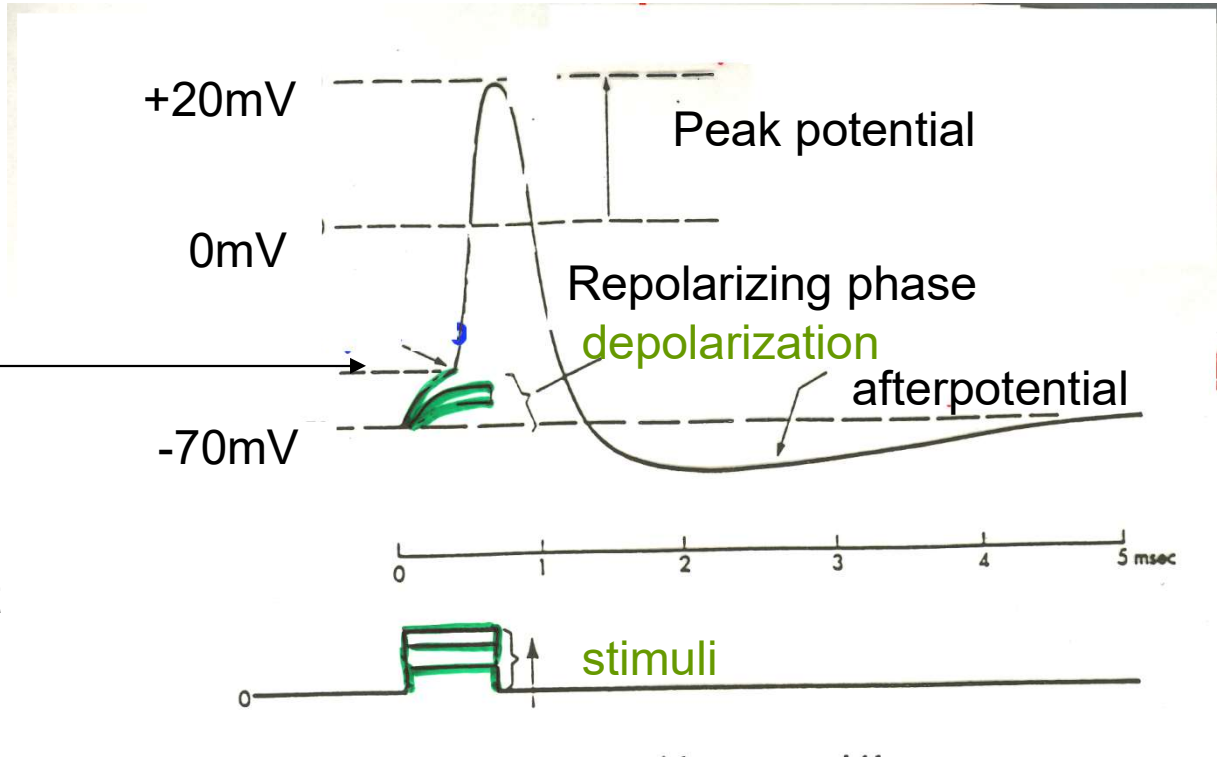
Observation



Phases and landmark of the action potential

Threshold potential

critical membrane potential level at which an action potential can occur



facultative

"All-or-none" amplitude

conducted with constant amplitude

Hodgkin-Katz hypothesis of action potential generation

Voltage-gated, potential sensitive ion channels

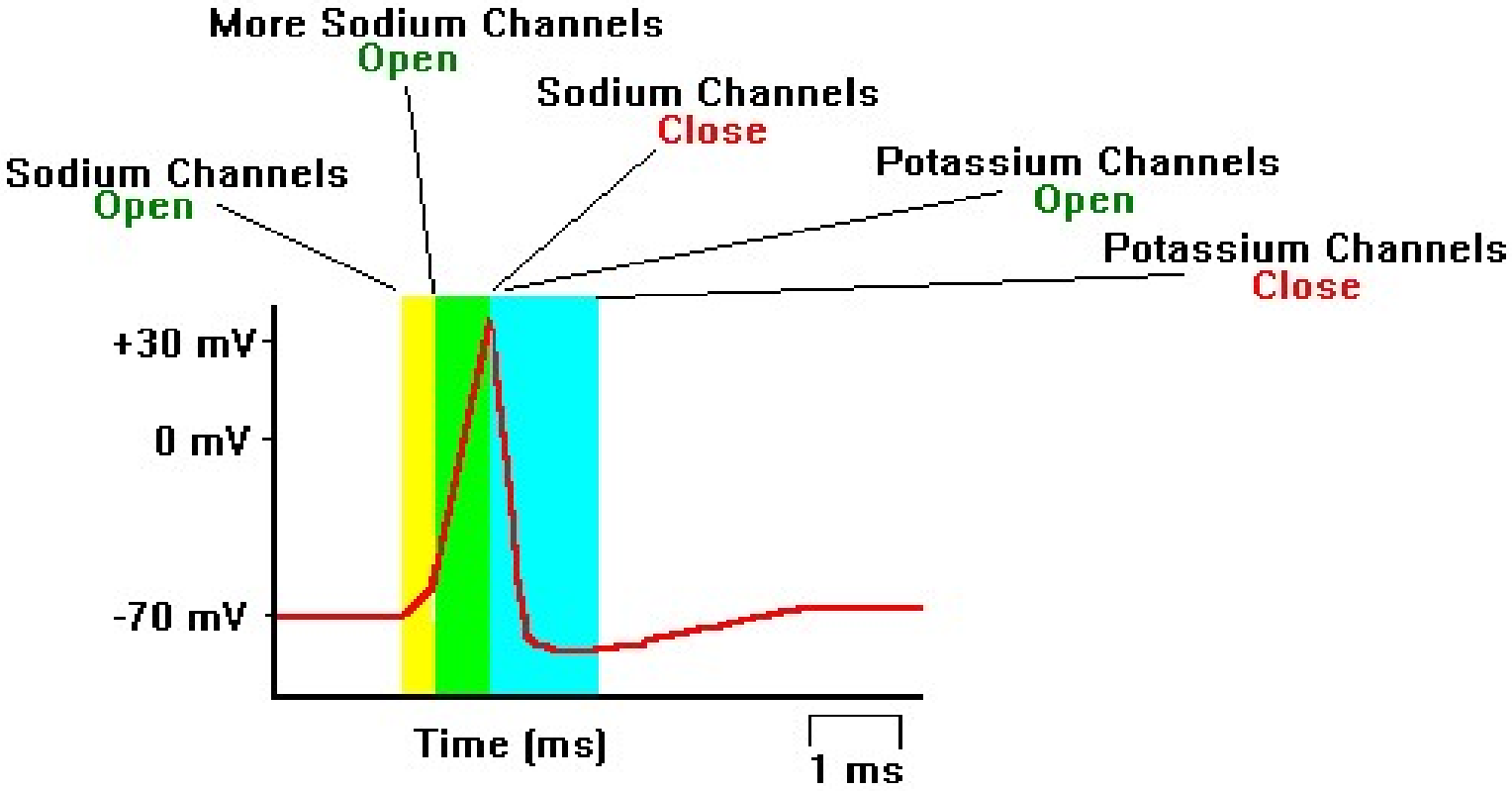
$$\varphi_e - \varphi_i = -\frac{RT}{F} \ln \frac{\Sigma p_k^+ c_{ke}^+ + \Sigma p_k^- c_{ki}^-}{\Sigma p_k^+ c_{ki}^+ + \Sigma p_k^- c_{ke}^-}$$

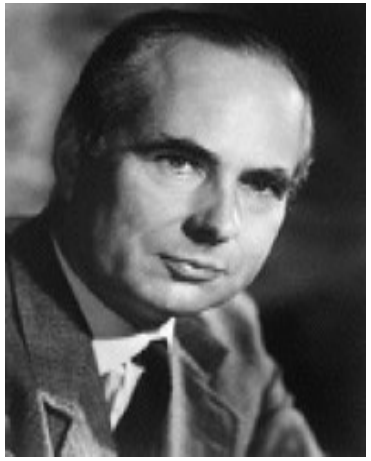
depolarization

p_{Na} (g_{Na}) increases

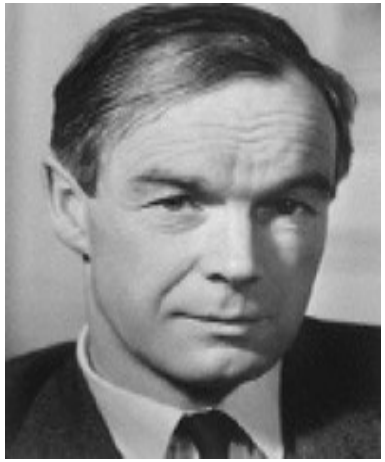
inward Na^+ current

Hodgkin-Katz hypothesis of action potential sequence





Andrew Fielding Huxley
(1917-2012)

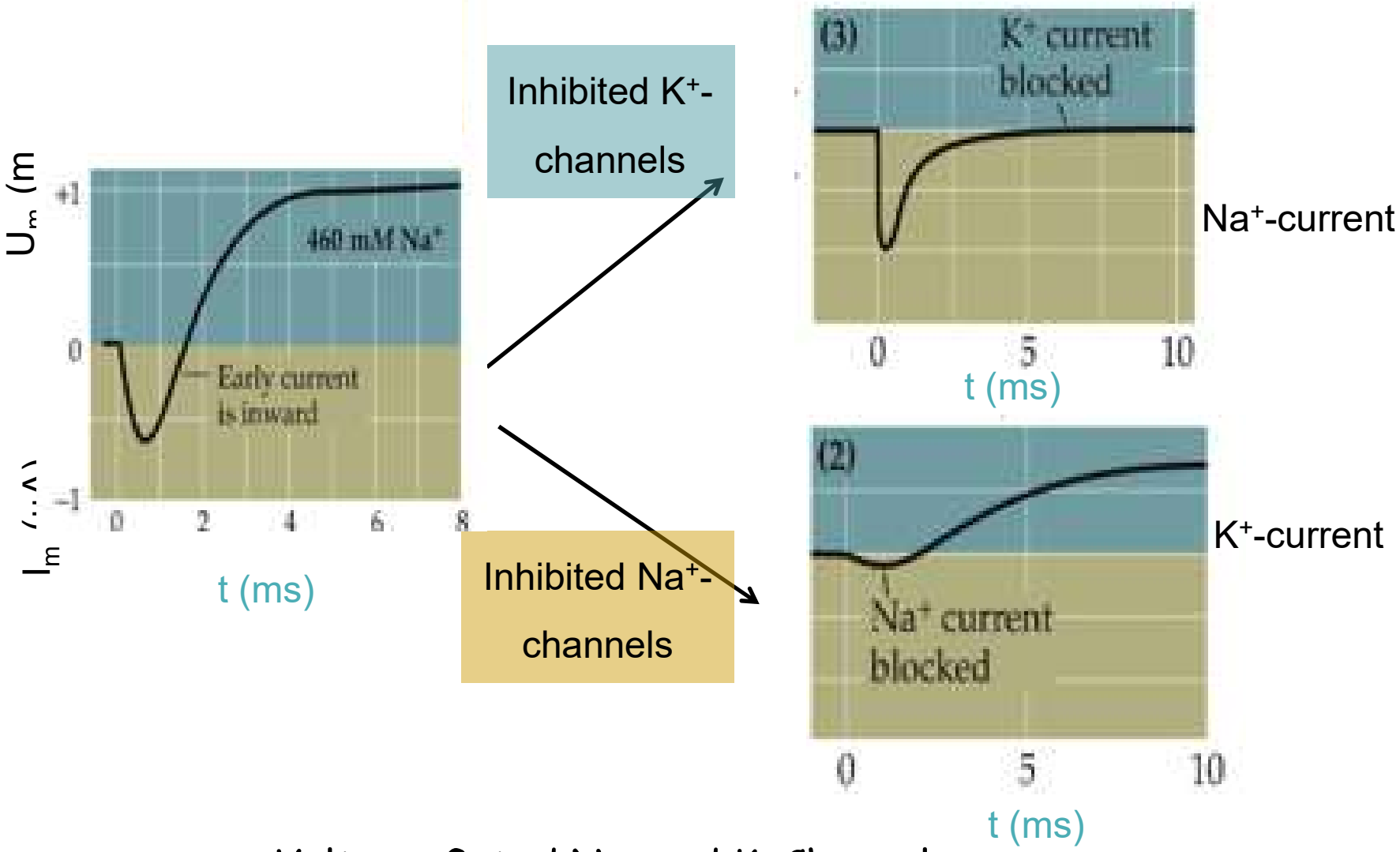


Alan Loyd Hodgkin
(1914-1998)

The Nobel Prize in Physiology or Medicine
1963

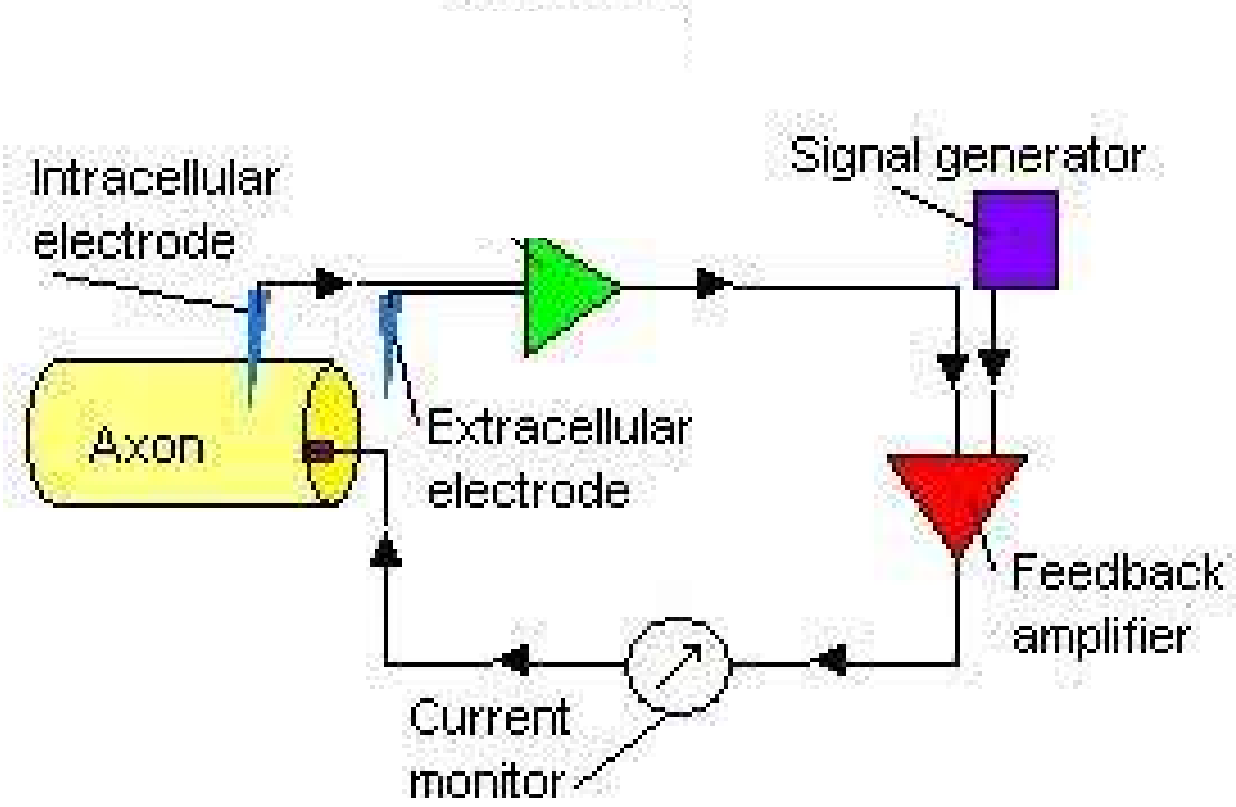
“for their discoveries concerning the ionic mechanisms involved in excitation and inhibition in the peripheral and central portions of the nerve cell membrane"

Measurement of separated ionic currents



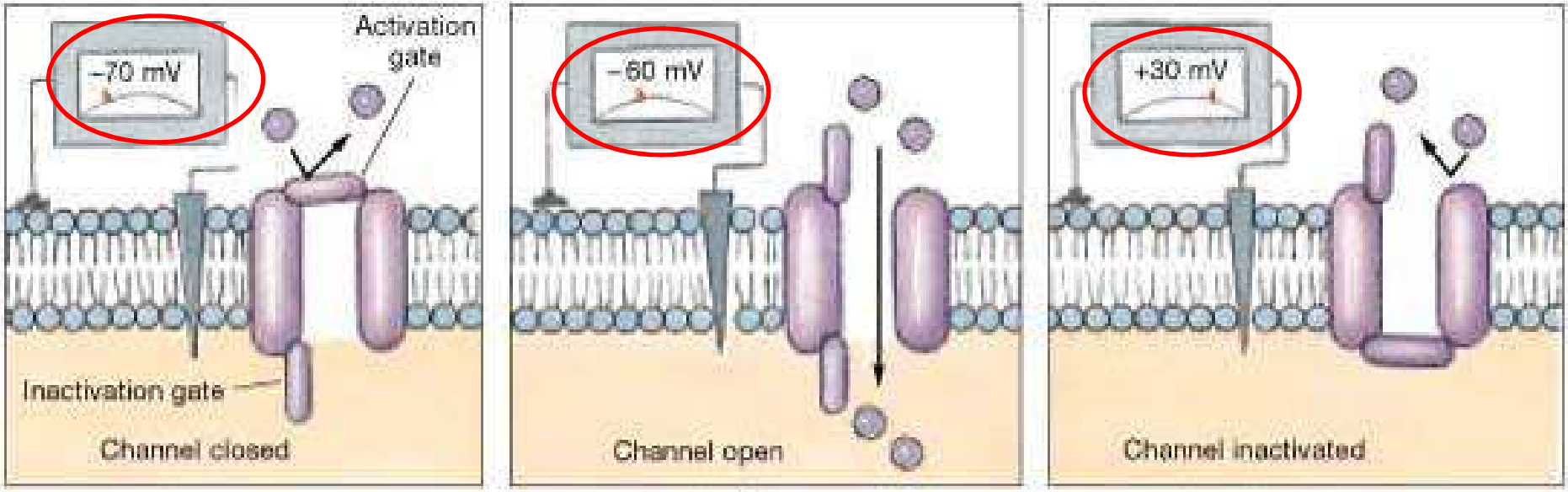
Voltage-Gated Na^+ and K^+ Channels

Voltage Clamp



- Membrane potential is kept constant
- ion-current is monitores

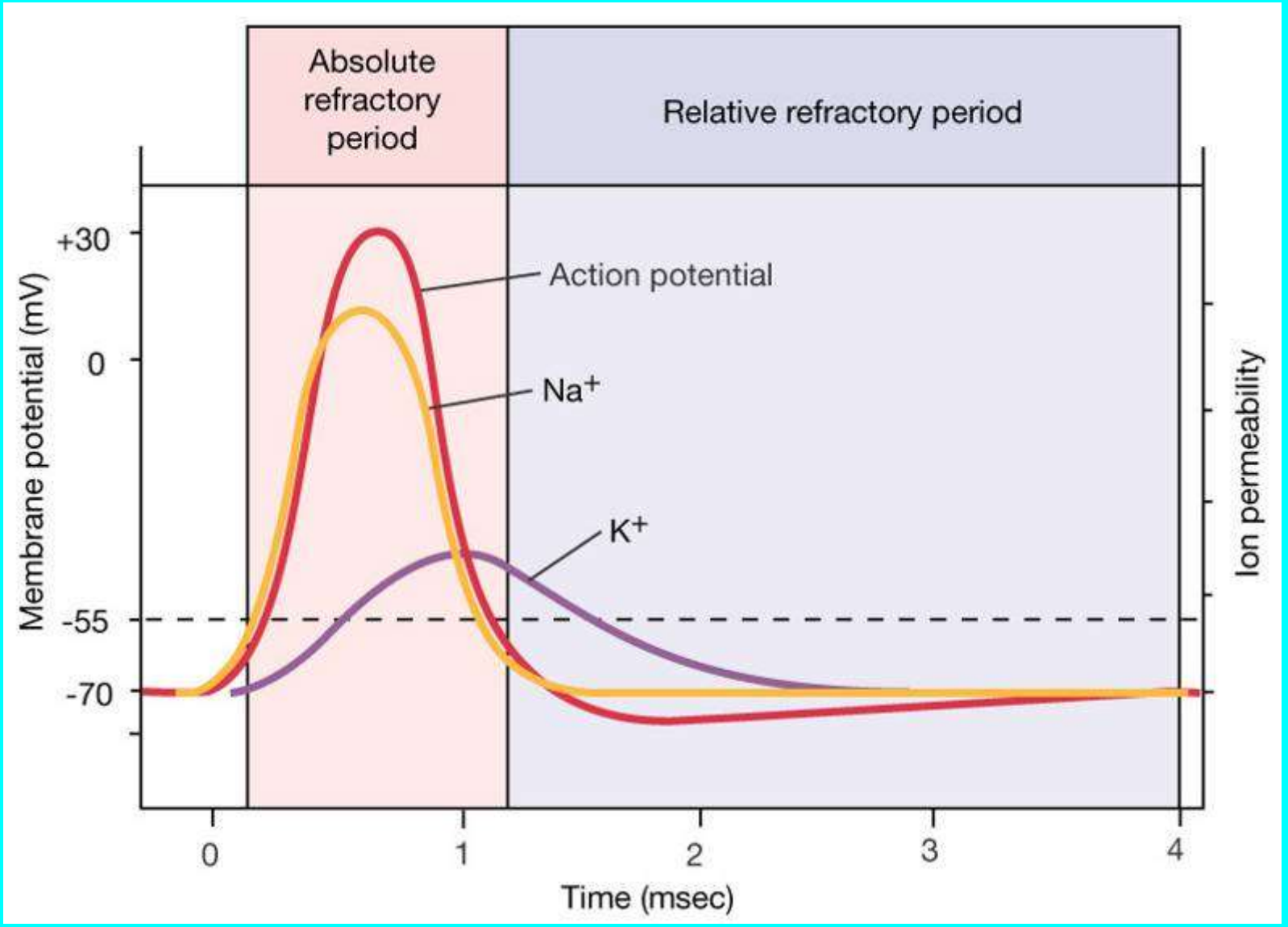
States of voltage-gated sodium channels



(c)

at depolarization threshold

Conductivities during action potential

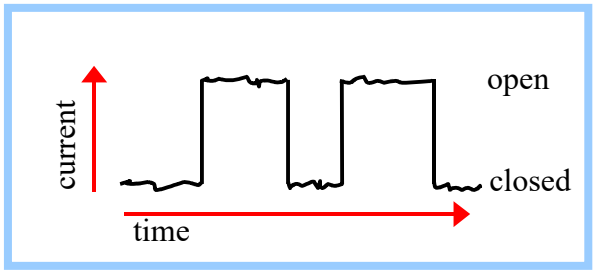


Patch-Clamp technika

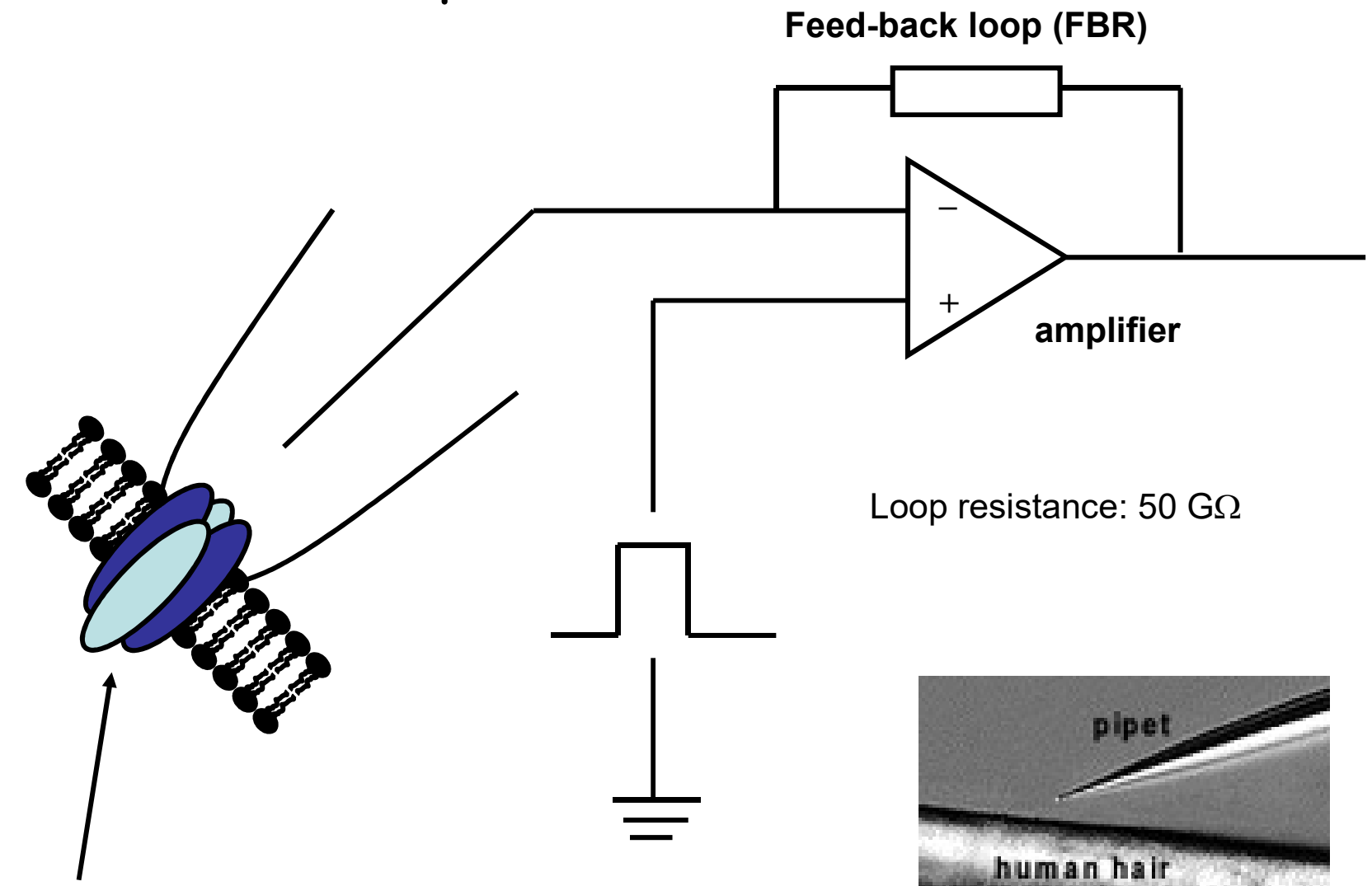
Ion current in single membrane channel (10^{-12} A)

The Nobel Prize in Physiology or Medicine 1991 was awarded jointly to Erwin Neher (1944-) and Bert Sakmann (1942-)

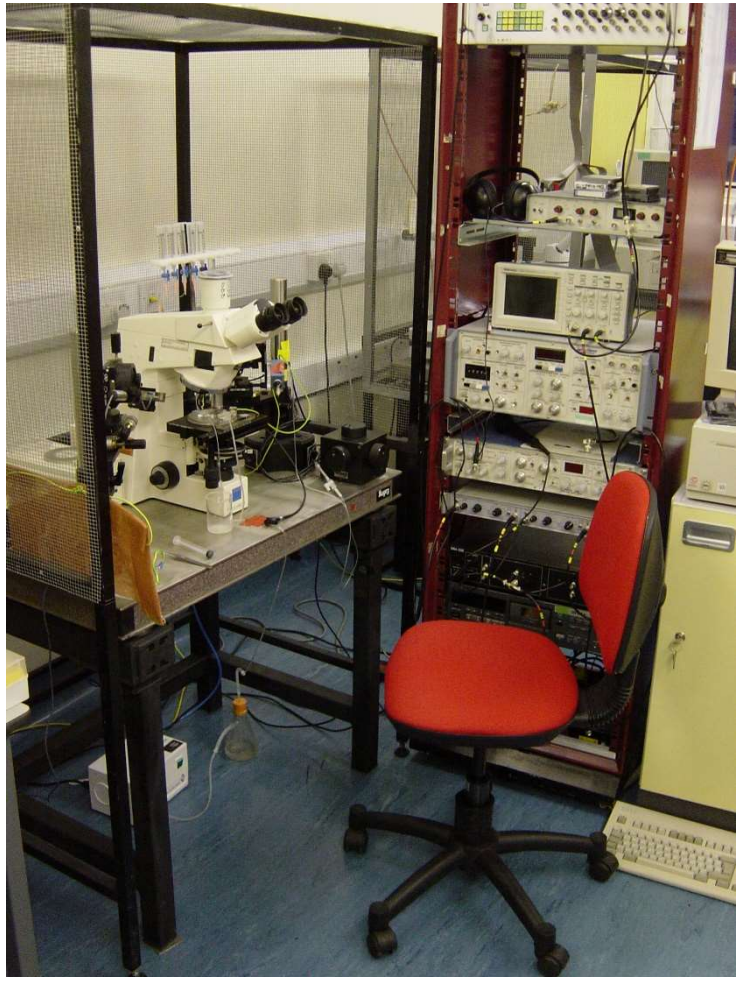
"for their discoveries concerning the function of single ion channels in cells"

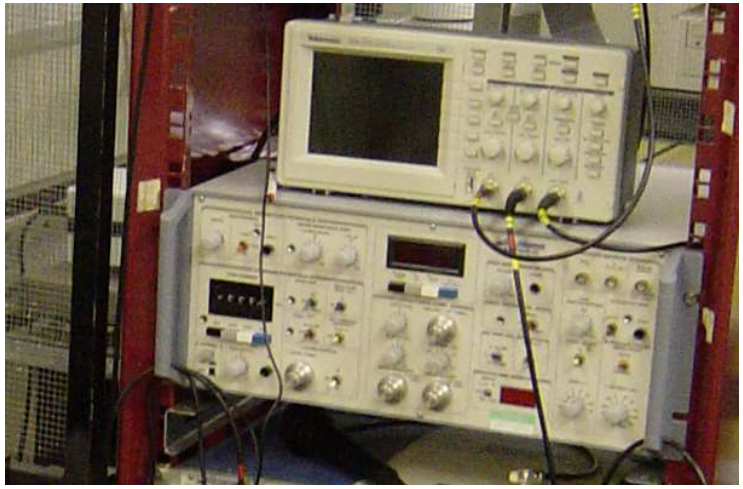


Patch-Clamp circuit



Patch-Clamp device





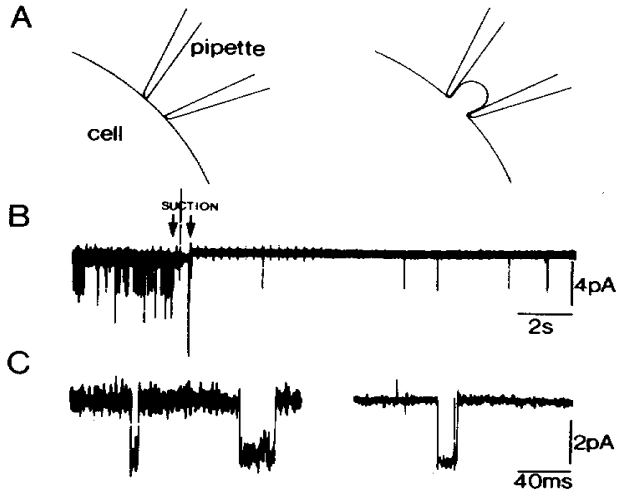
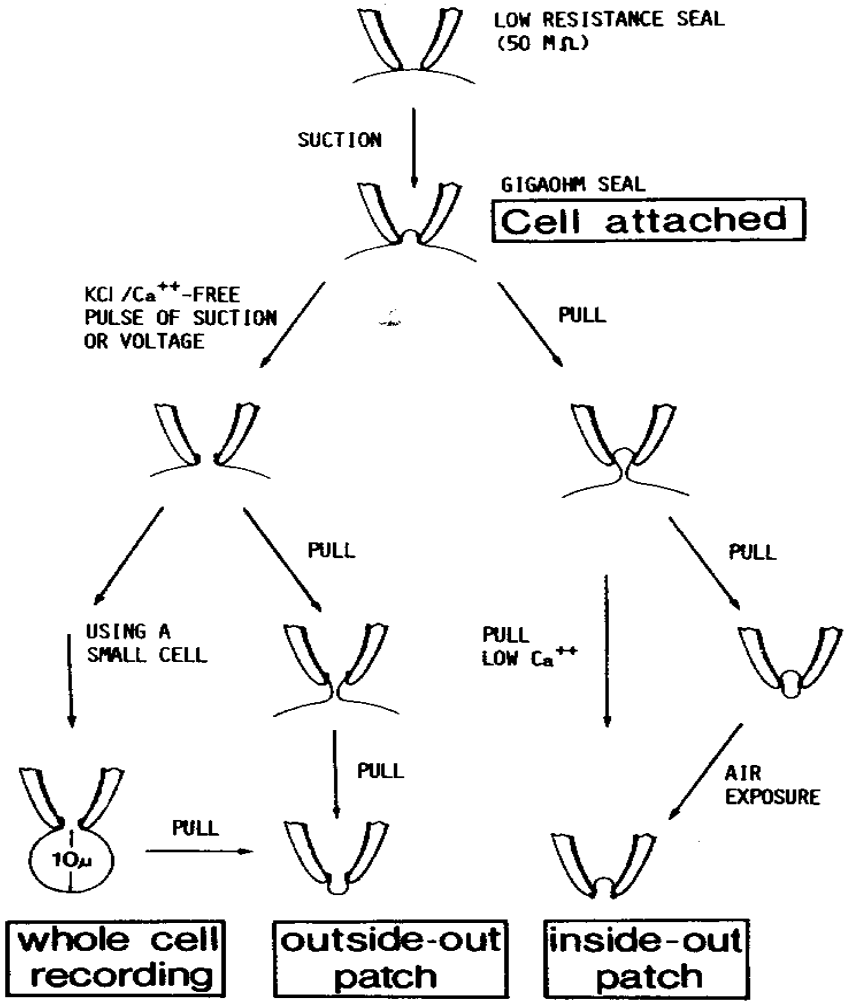
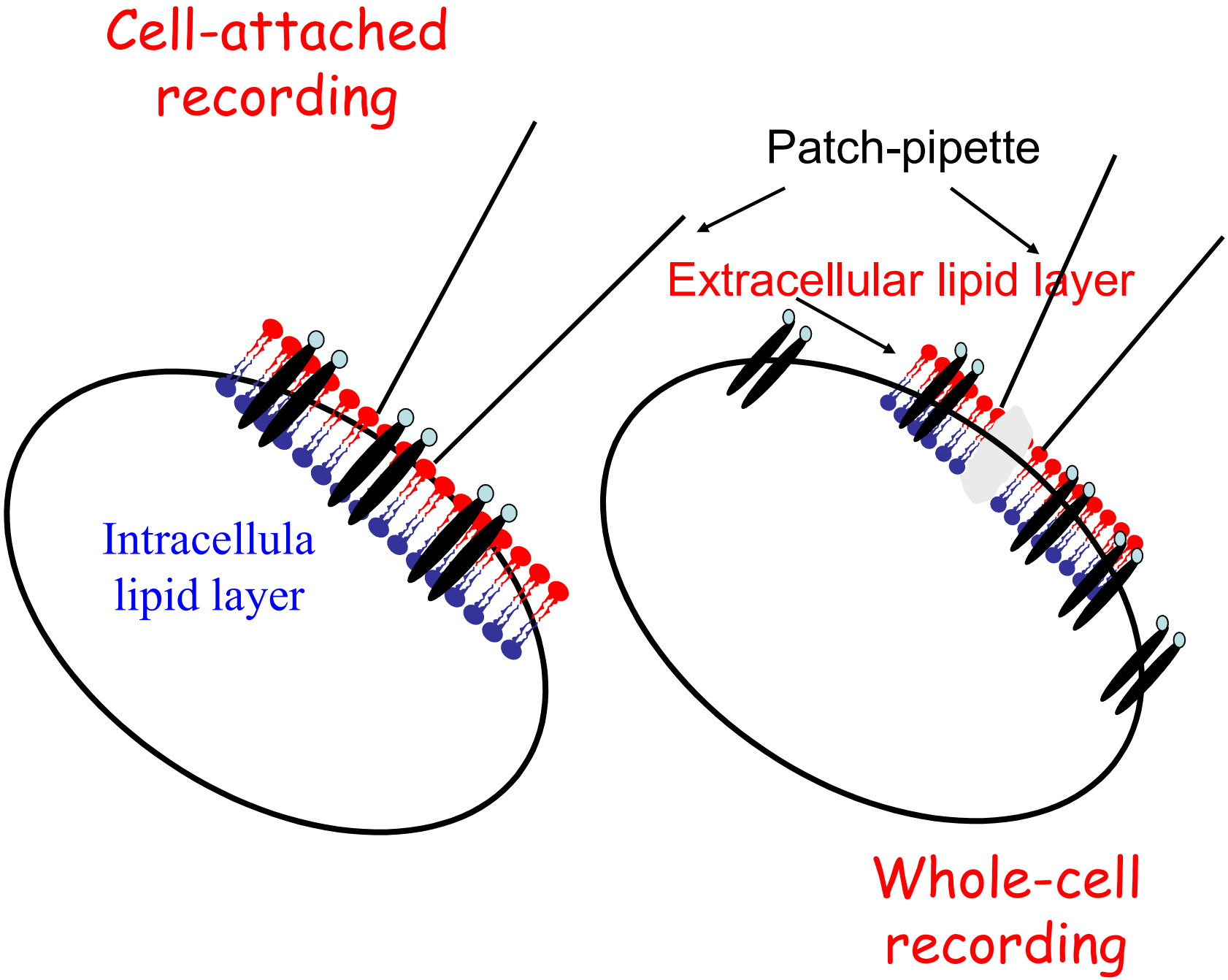


Fig. 6A—C. Giga-seal formation between pipette tip and sarcolemma of

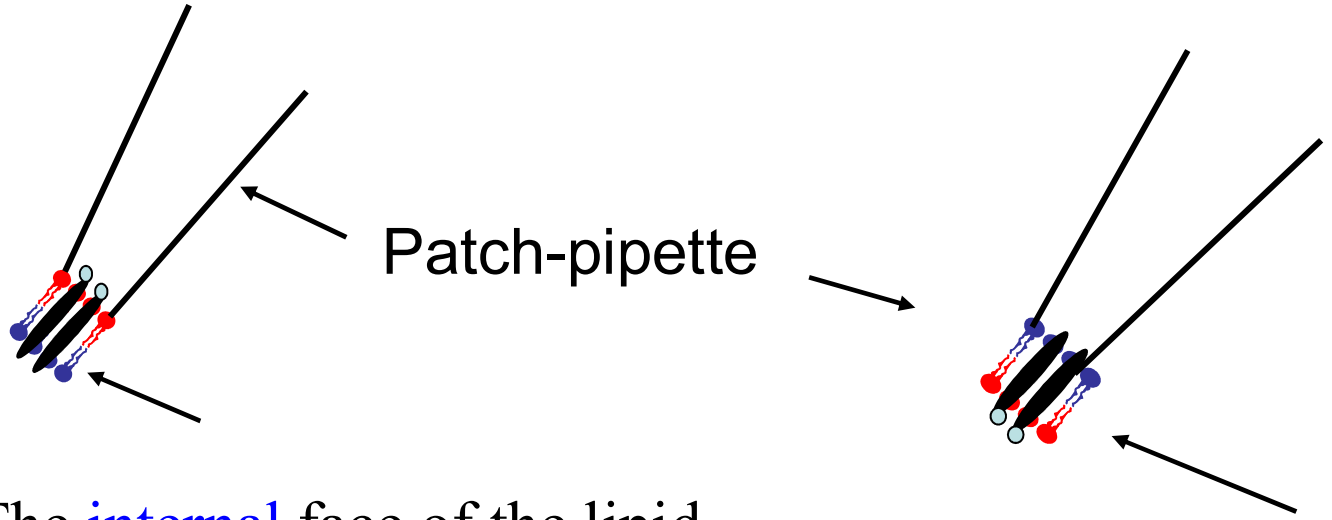
Patch-Clamp arrangements



From Hamill *et al* 1981


Cell-attached recording
Patch-pipette
Extracellular lipid layer
Intracellula lipid layer
Whole-cell recording

Inside-out recording

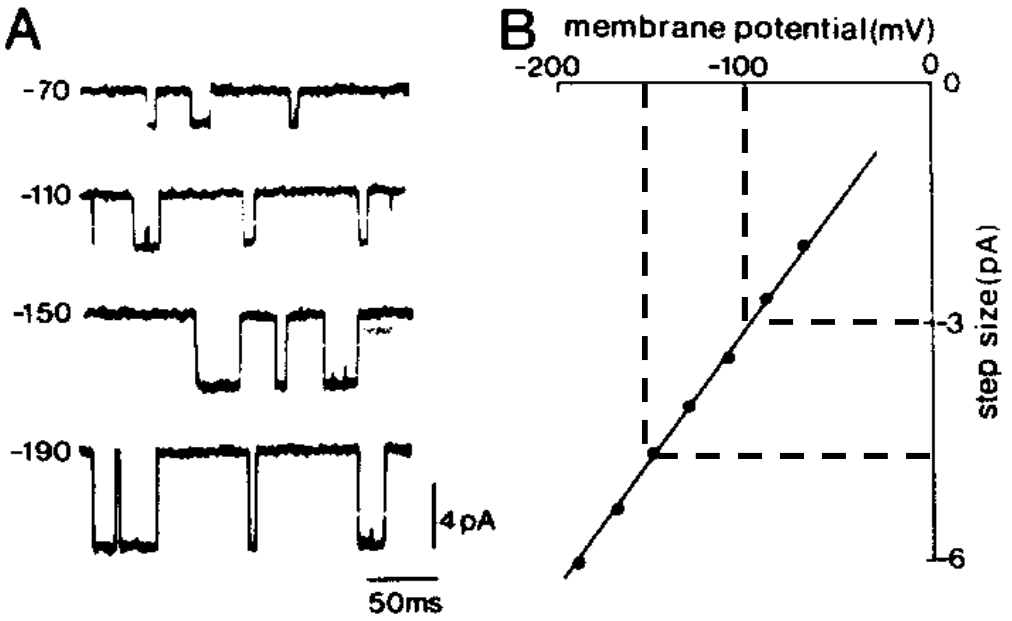


The internal face of the lipid bi-layer faces the bath solution

The external face of the lipid bi-layer faces the bath solution

Outside-out recording

Single-channel I/V function



$g_{csatorna} = \Delta I \div \Delta V$

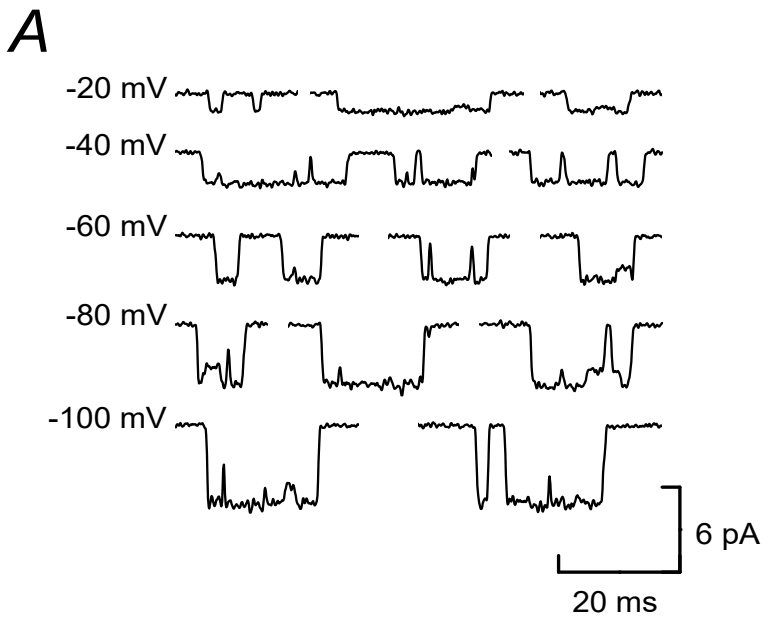
$= 1.6 \times 10^{-12}\,A \div 50 \times 10^{-3}\,V$

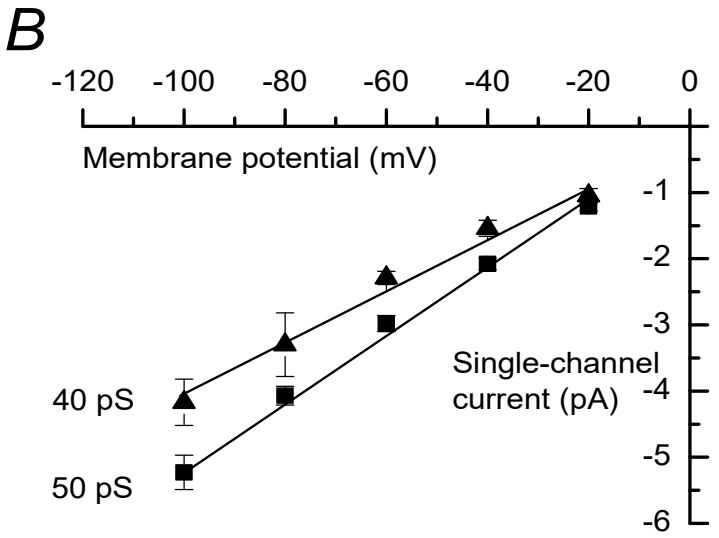
$= 32 \times 10^{-12}\,S$

$= 32\,pS$

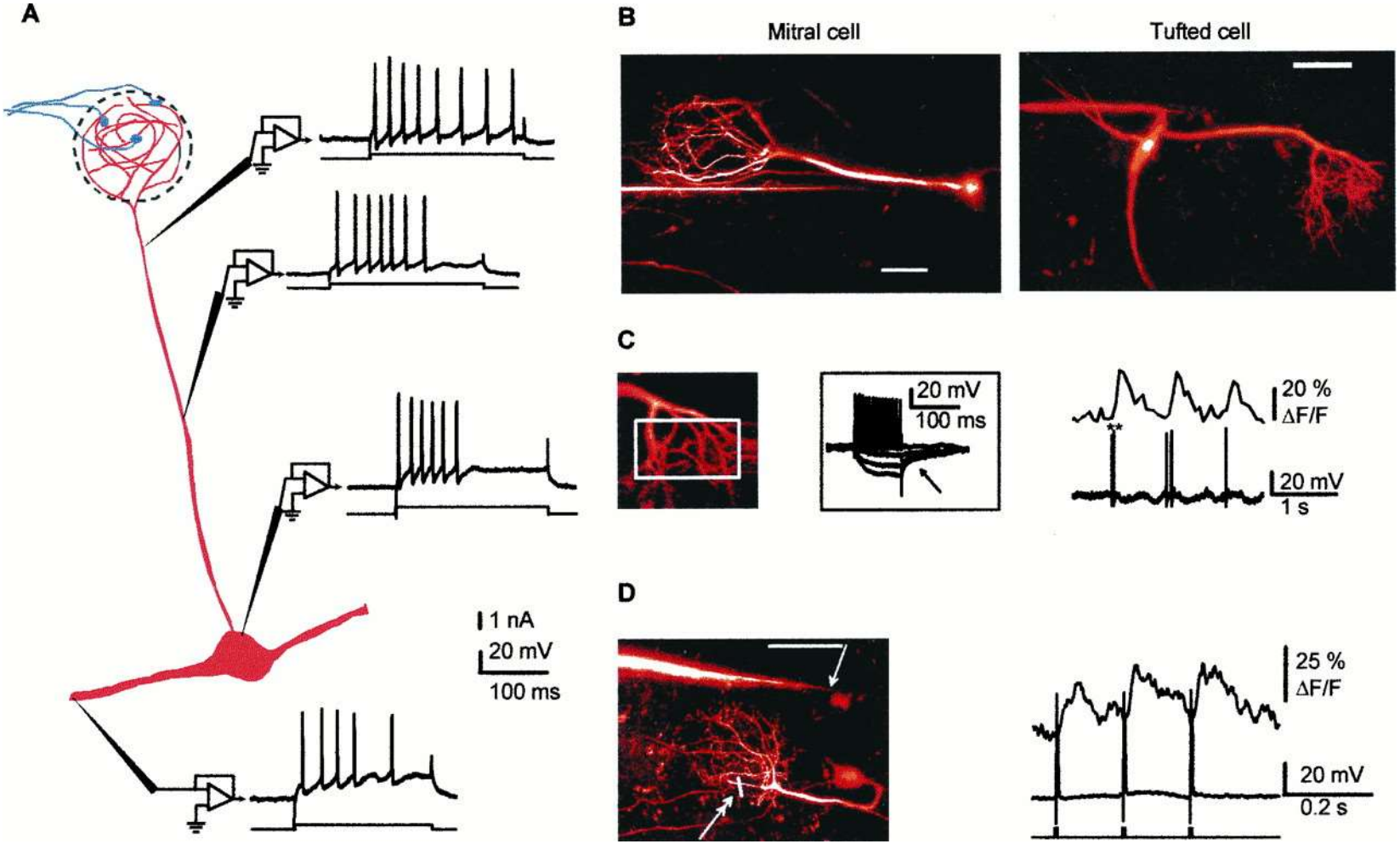
From Hamill *et al* 1981

Multi-state single channel





Sodium action potentials synchronize [Ca2+] transients in all dendritic compartments of mitral cells in the olfactory bulb of anesthetized rats.

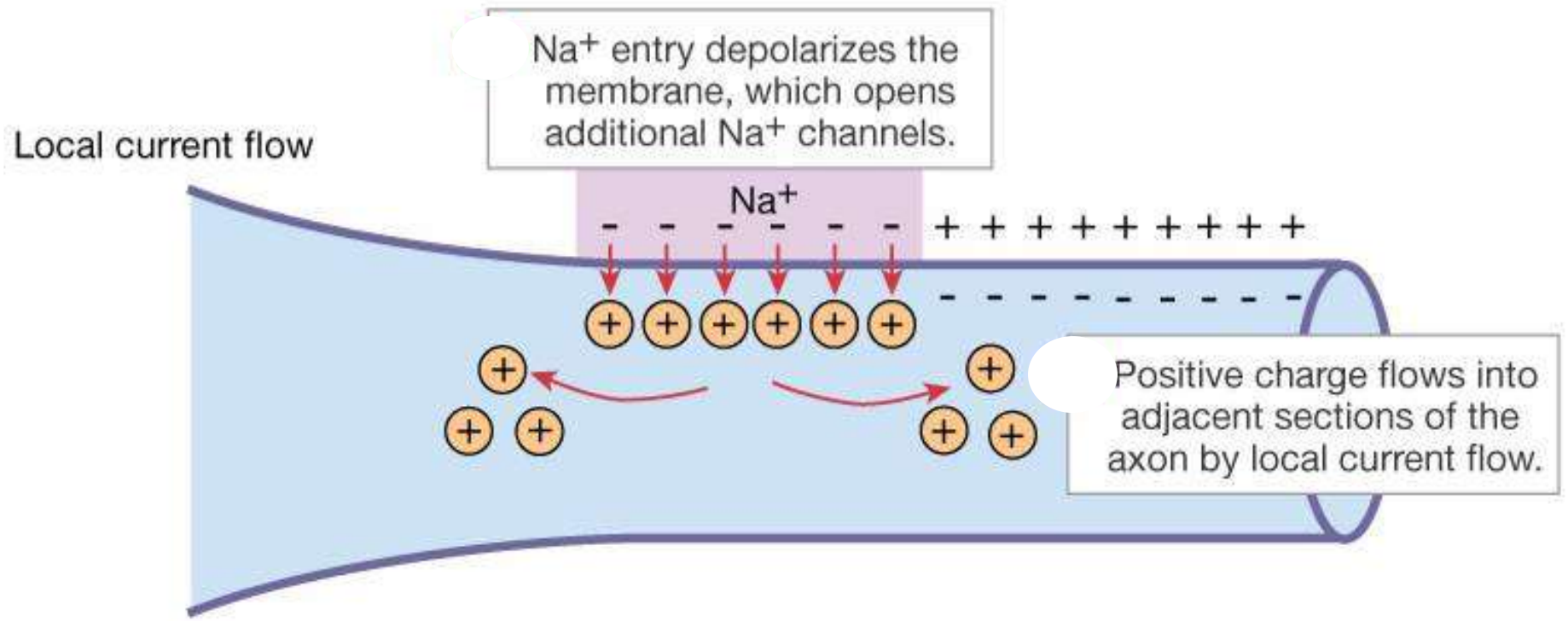


Charpak S et al. PNAS 2001;98:1230-1234

Factors Influencing Conduction Direction and Velocity

The evolutionary need for the fast and efficient transduction of electrical signals

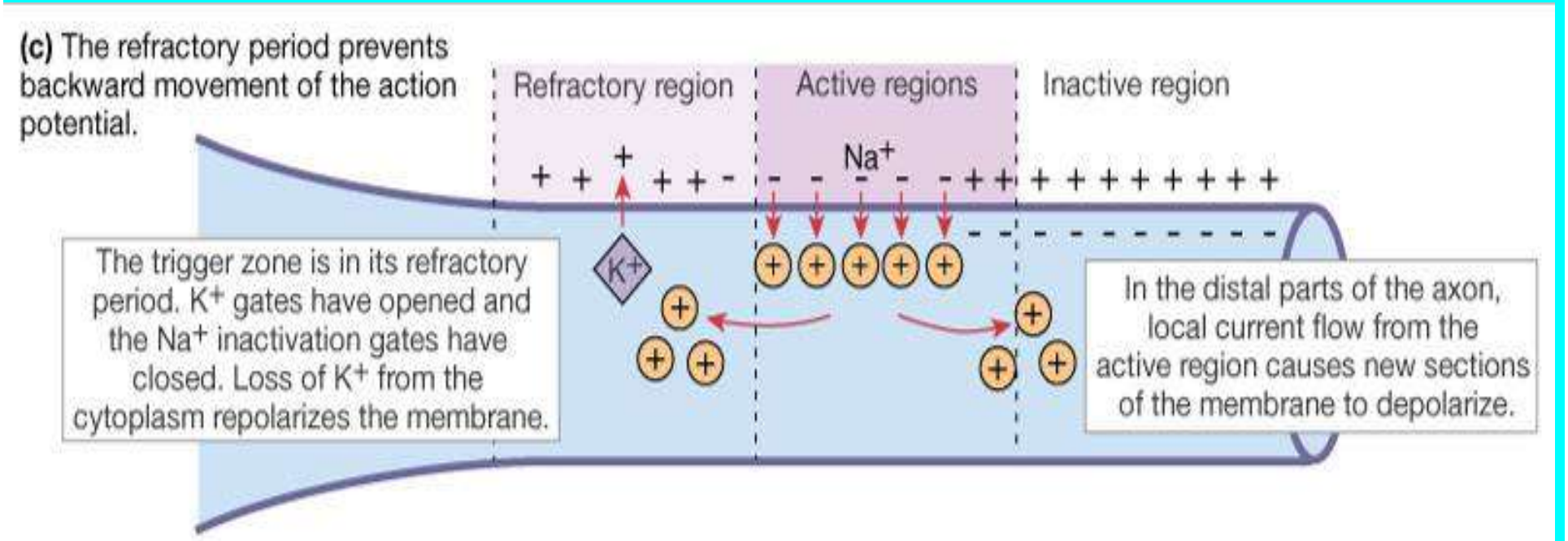
Propagation of action potential (1)



based on local current flow and depolarization of

adjacent membrane area

Propagation of action potential (2)

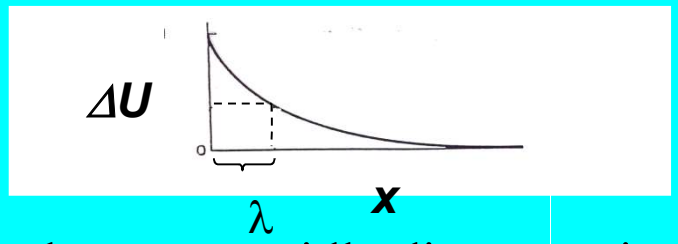


Speed and distance of propagation?

How are the ***time constant*** and the ***space constant*** related to propagation velocity of action potentials

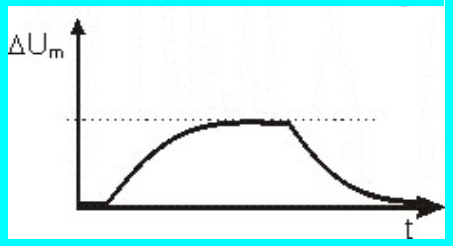
Generation of the next peak potential

Where?



The greater the space constant, the more rapidly distant regions will be brought to threshold and the more rapid will be the propagation velocity

When?



The smaller the time constant, the more rapidly a depolarization will affect the adjacent region.

Velocity is the function of passive properties – τ and λ – of membranes

***Effect of axon diameter*:**

$$\tau = C_m R_m$$

$$\lambda \sim \sqrt{\frac{R_m}{R_i}}$$

r↑ ⇒ R_i↓ (~1/r^2) ⇒ τ↓

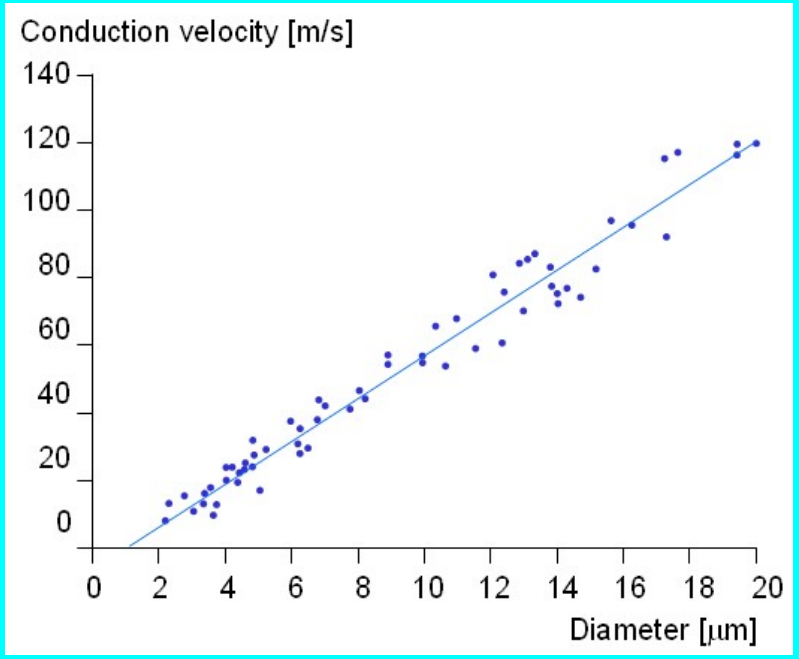
R_m↓ (~1/r) λ↑

Squid giant axon r=250μm

v=25m/s

human nerve cell r= 10 μm

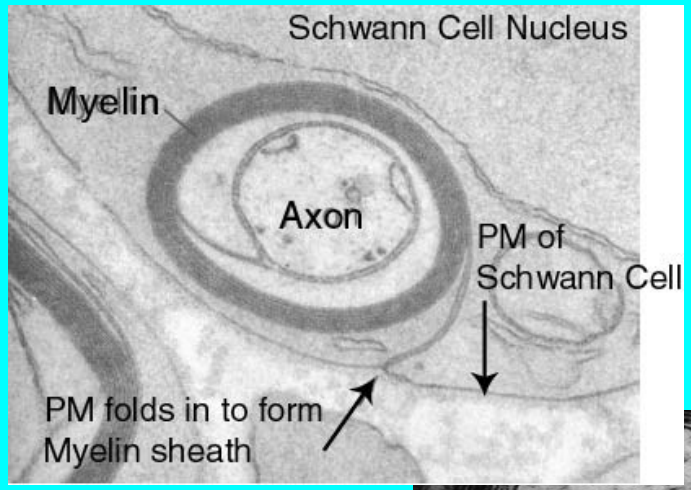
v≠0.5m/s ?

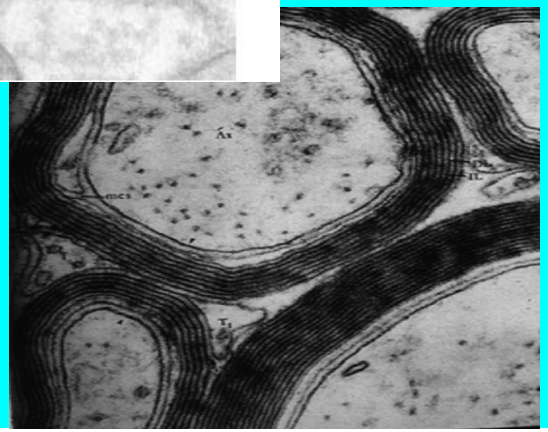


Myelination!

R_m – very high ⇒ big space constant

C_m – very small ⇒ small time constant

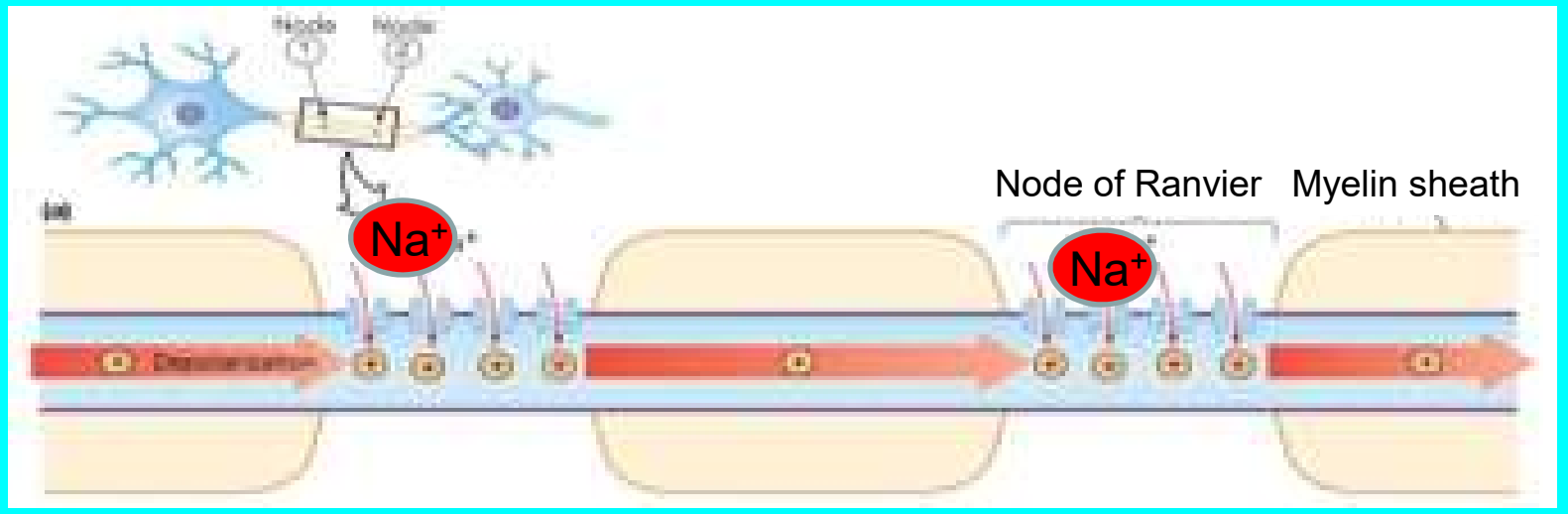




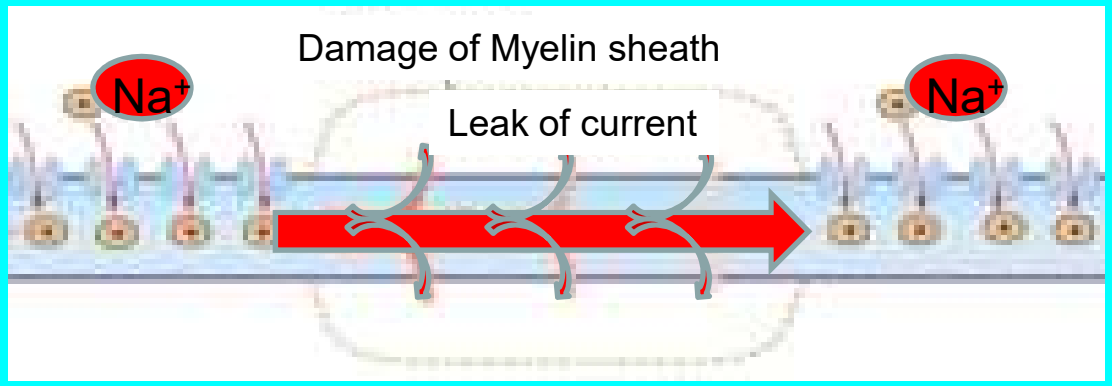
human nerve cell r= 10 μm

v~ 100 m/s

Saltatory conduction – quick, energy saving



Myelin prevents ions from entering or leaving the axon along myelinated segments.



Effect of axon diameter and Myelination

The diameter of frog axons and the presence or absence of myelination control the conduction velocity.

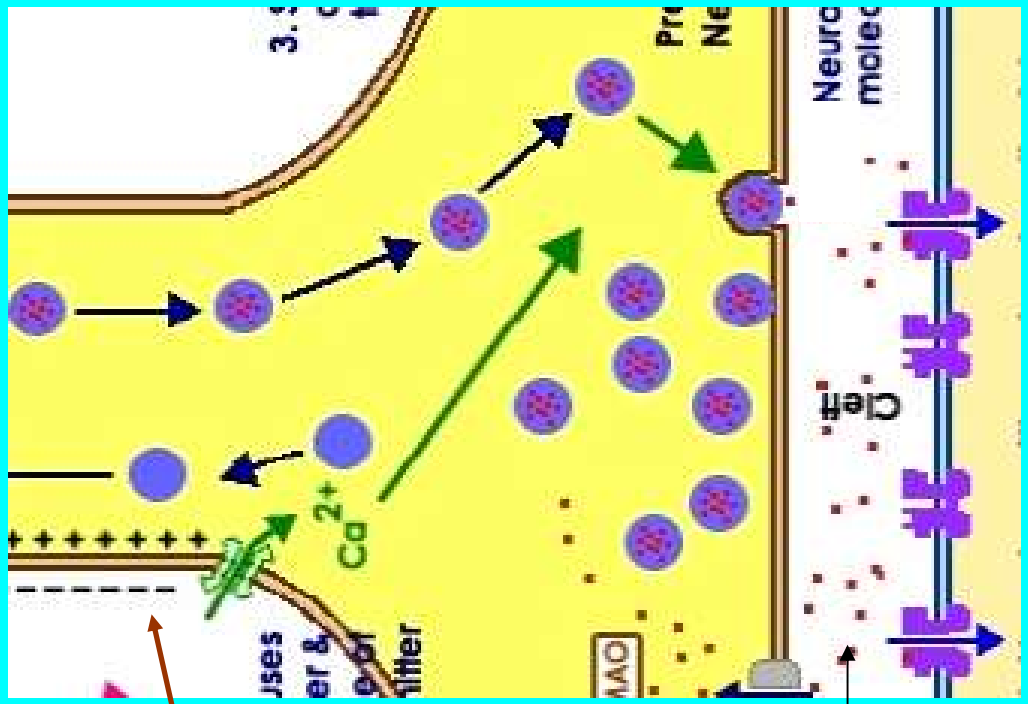
Fiber type	Average axon diameter (μm)	Conduction velocity ($m \cdot s^{-1}$)
Myelinated fibers		
Aα	18.5	42
Aβ	14.0	25
Aγ	11.0	17
B	Approximately 3.0	4.2
Unmyelinated fibers		
C	2.5	0.4–0.5

Effect of passive electric properties on signal transduction in synapses

Signal transmission in synapses

presynaptic terminal

postynaptic terminal

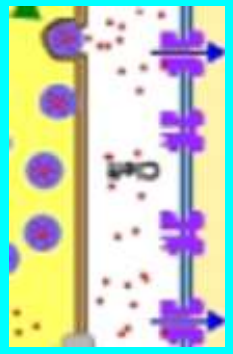


Action potential

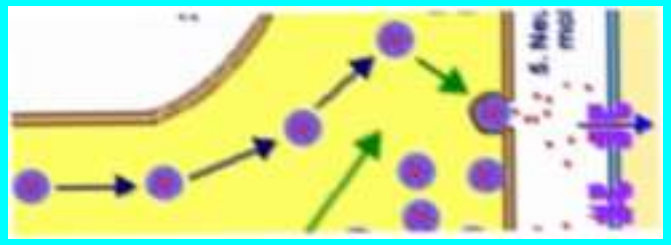
neurotransmitter

How can neurons transmit information from presynaptic to postsynaptic cells **if most synaptic effects are subthreshold**?

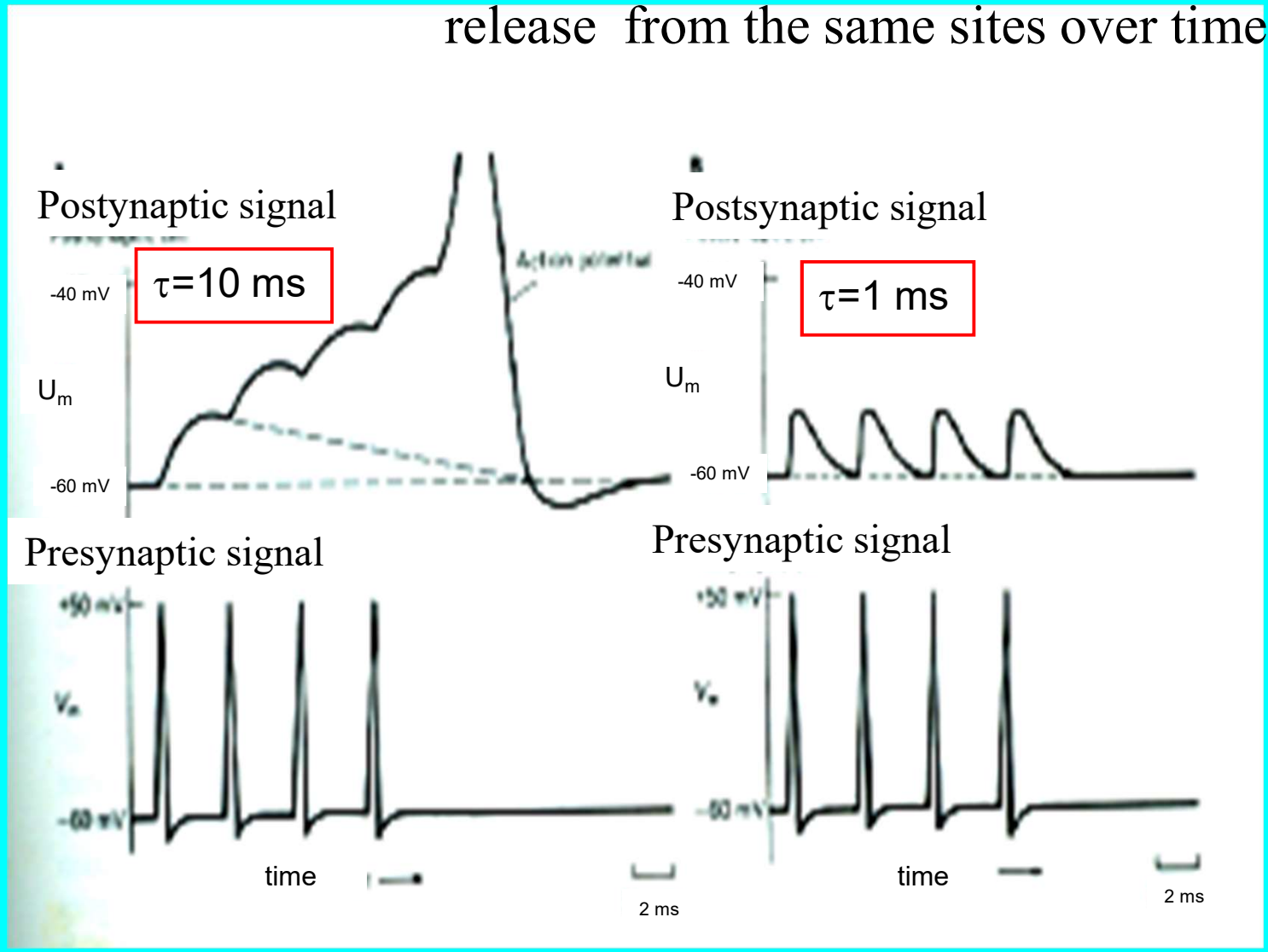
Spatial Summation : combined influences at the same cell at a particular moment in time



Temporal Summation : combined effects of neurotransmitter release from the same sites over time



Temporal Summation : combined effects of neurotransmitter release from the same sites over time



Temporal and spatial summation