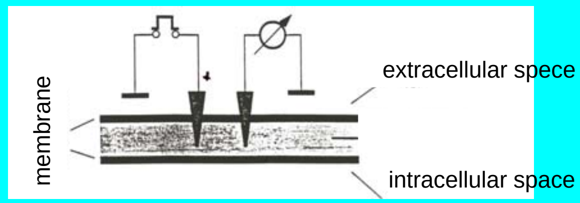
Alteration of resting membrane potential

1. "passive" electric properties of the membrane

Observation

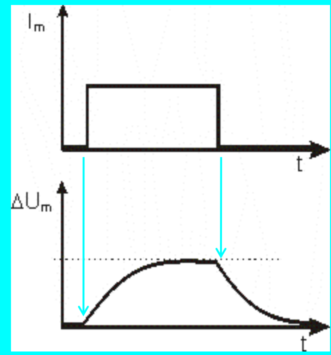
electric current

measuring electrodes



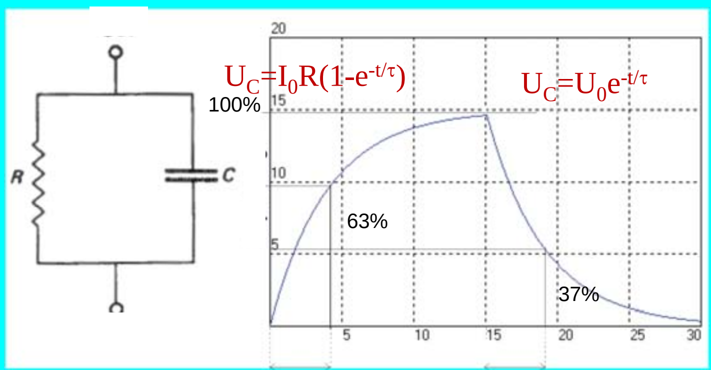
Inward current

Depolarization of the membrane



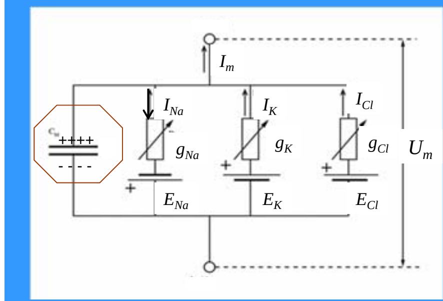
What is it like?

Charge and discharge of RC-circuit



$\tau = RC$

Interpretation with equivalent circuit model:



$$I_{ion} + I_c = I_m = 0$$

$g_{Na}\,(U_m - E_{Na}) = I_{Na}$

$g_{ion}\,(U_m - E) = I_{ion}$

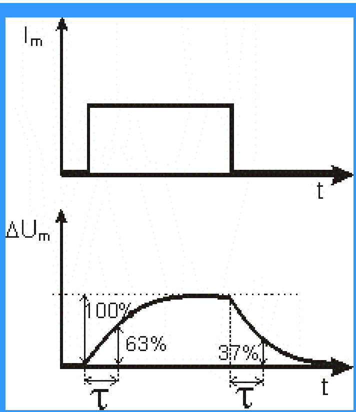
$$C_m \frac{\Delta U_m}{\Delta t} + \frac{\Delta U_m - E}{R_m} - I_{stimulus} = 0$$

Time from the beginning of stimulus

$$U_m(t) = U_t\left[1 - e^{-\frac{t}{R_m C_m}}\right]$$

Membrane potentiel after *t*

Saturation value of membrane potential



Capacitance of the membrane

Resistance of the membrane

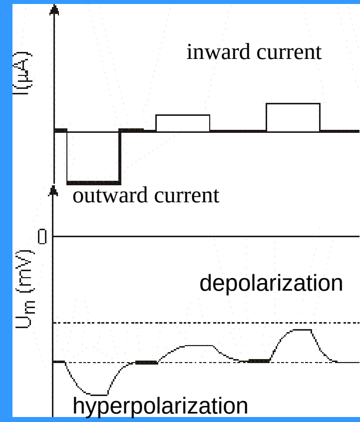
$$\tau = C_m R_m$$

***τ* : time constant of membrane**

-the time required for the membrane potential to reach 63% of its saturation value

-during which the membrane potential decreases to the e-th of its original value

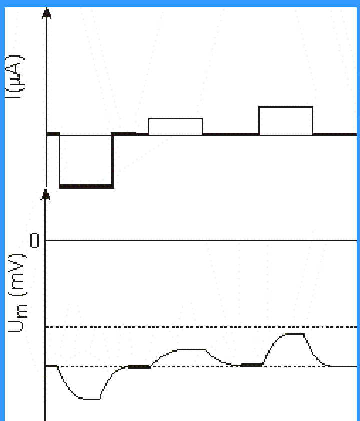
$$U_m(t) = U_t\left[1 - e^{-\frac{t}{R_m C_m}}\right]$$



U_t is proportional to the stimulating current

The rate of the change depends on U_t

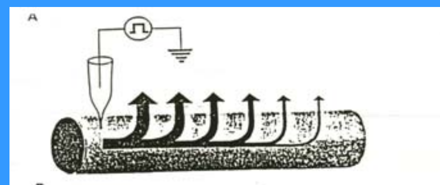
Local changes of membrane potential



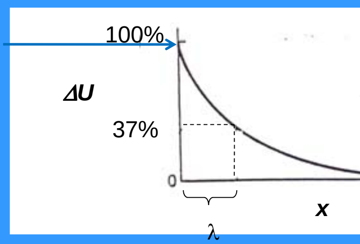
obligate
graded
magnitude varies directly
with the strength of the stimulus
direction varies
with the direction of the stimulus
„localized"

The local changes are not isolated from the neighborhood

Observation



Membrane potential change at the site of stimulation



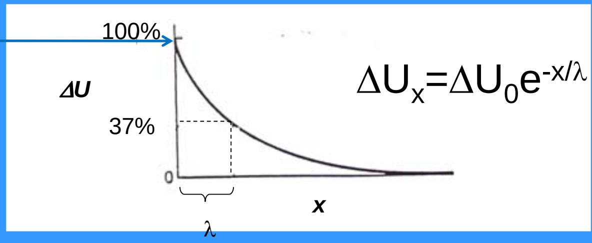
$$\Delta U_x = \Delta U_0 e^{-x/\lambda}$$

Decrease in amplitude with distance due to leaky membranes

λ: space constant of the membrane:

distance in which the maximal value of induced membrane potential change decreses to its e-th value

Membrane potential change at the site of stimulation



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

Resistance of intracellular space

Local changes of resting membrane potential can be induced

- by electric current pulses
- by adequate stimulus at receptor cells
- by neurotransmitters at postsynaptic membrane
  - -excitatory inhibitory postsynaptic potential - depolarization
  - - inhibitory postsynaptic potential - hyperpolarization

Significance of the local changes of resting membrane potential

Sensory function

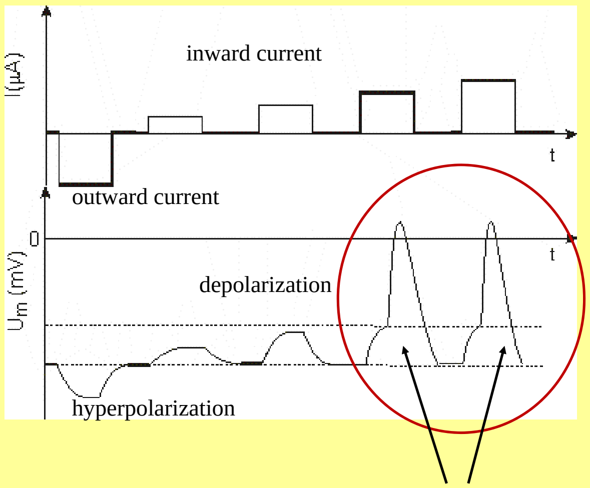
Impulse conduction

Signal transduction

Alteration of resting membrane potential

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

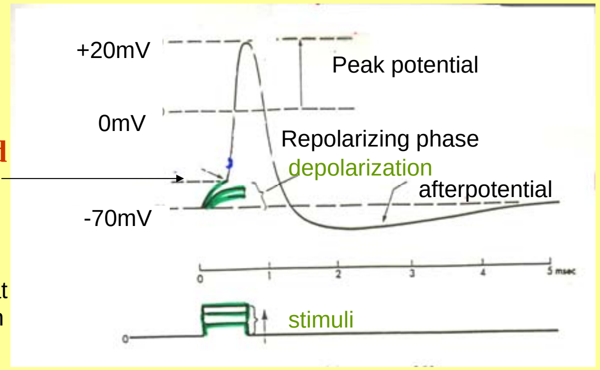
Observation



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

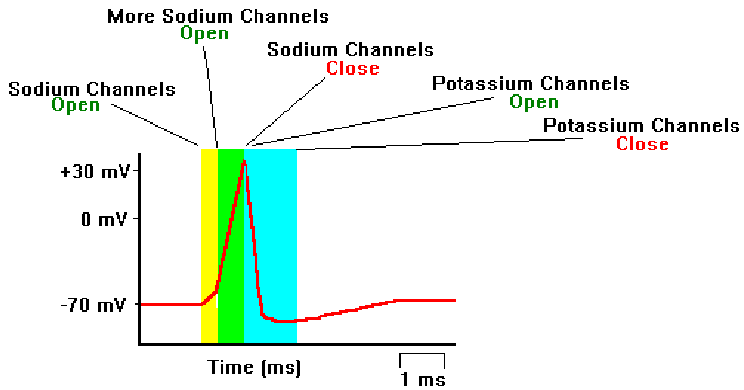
$$\varphi_e - \varphi_i = -\frac{RT}{F}\ln\frac{\Sigma p_k^+ c_{ke}^+ + \Sigma p_k^- c_{ki}^-}{\Sigma p_k^+ c_{ki}^+ + \Sigma p_k^- c_{ke}^-}$$

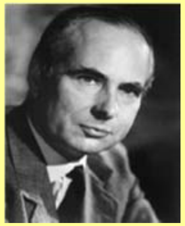
depolarization

inward Na^+ current

p_{Na} (g_{Na}) increases

Hodgkin-Katz hypothesis of action potential sequence





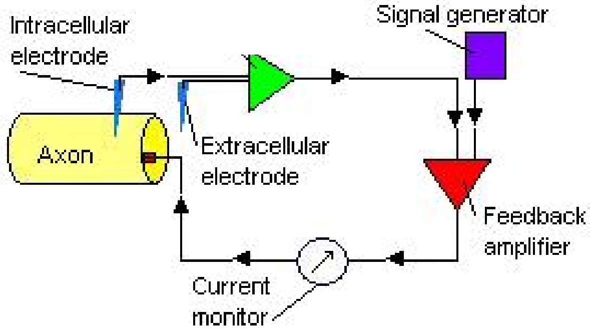
Andrew Fielding Huxley (1917-)

Alan Loyd Hodgkin (1914-1998)

The Nobel Prize in Physiology or Medicine
1963

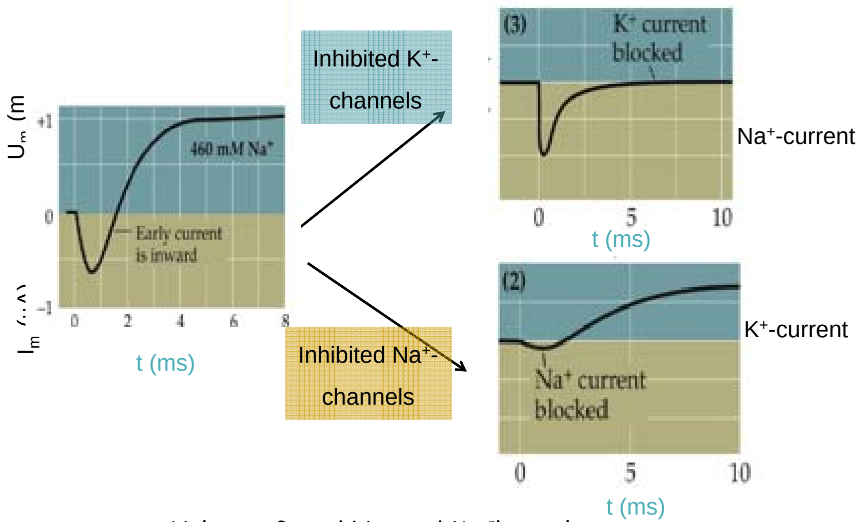
“for their discoveries concerning the ionic mechanisms involved in excitation and inhibition in the peripheral and central portions of the nerve cell membrane"

Voltage Clamp



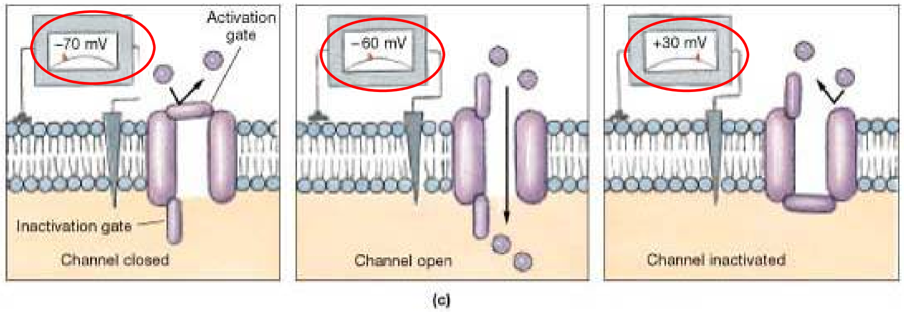
- Membrane potential is stabilized
- Ionic current is measured

Measurement of separated ionic currents



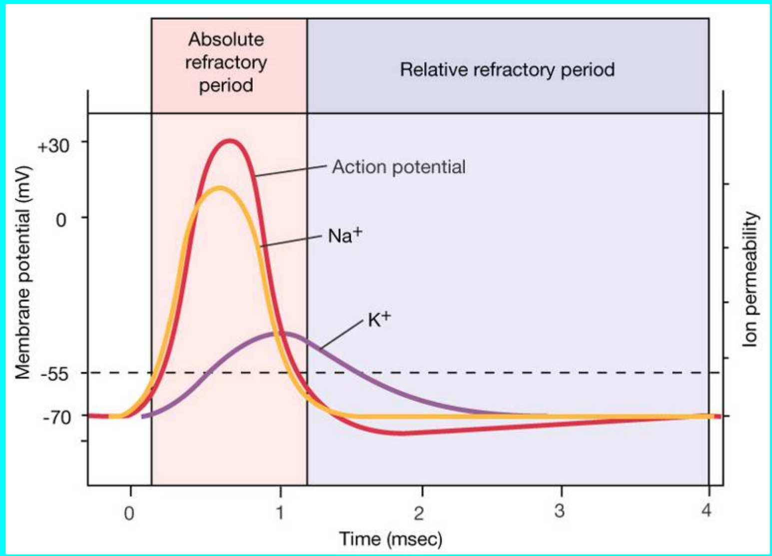
Voltage-Gated Na^+ and K^+ Channels

States of voltage-gated sodium channels



at depolarization threshold

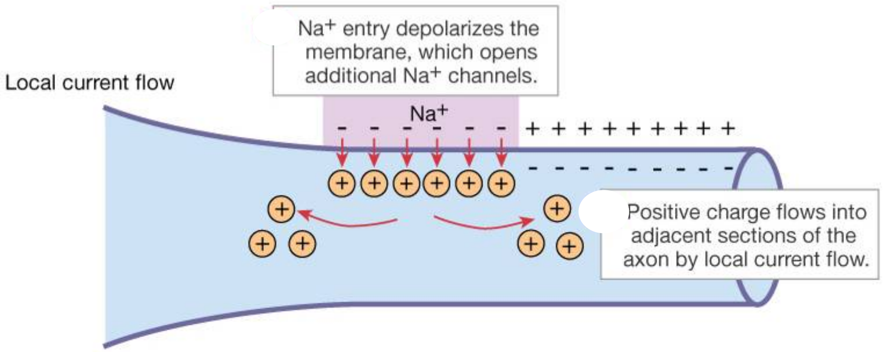
Conductivities during action potential



Factors Influencing Conduction Direction and Velocity

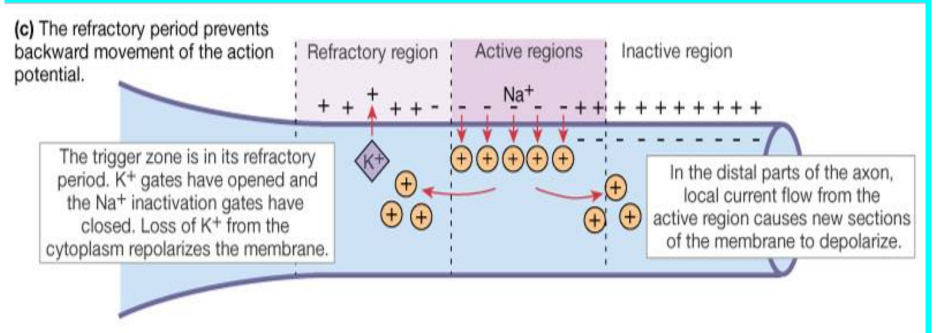
The evolutionary need for the fast and efficient transduction of electrical signals

Propagation of action potential (1)



based on local current flow and depolarization of adjacent membrane area

Propagation of action potential (2)

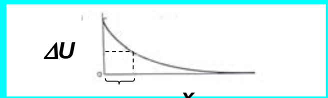


Speed and distance of propagation?

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

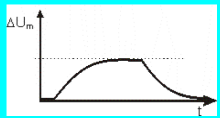
Generation of the next peak potential

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

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Effect of axon diameter:

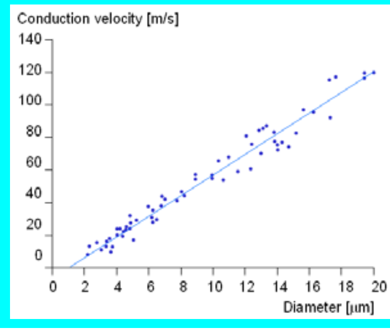
$$\tau = C_m R_m$$

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

r↑ → R_i↓ (~1/r²), R_m↓ (~1/r) → τ↓, λ↑

Squid giant axon r=250µm v=25m/s

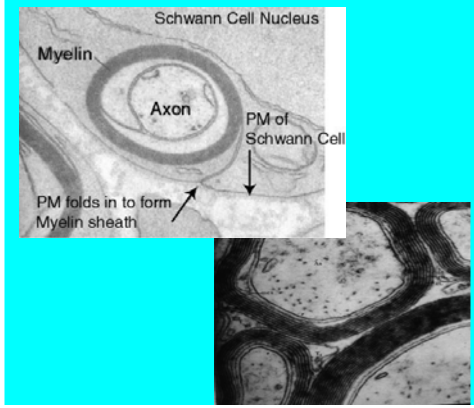
human nerve cell r= 10 µm v≠0.5m/s ?



Myelination!

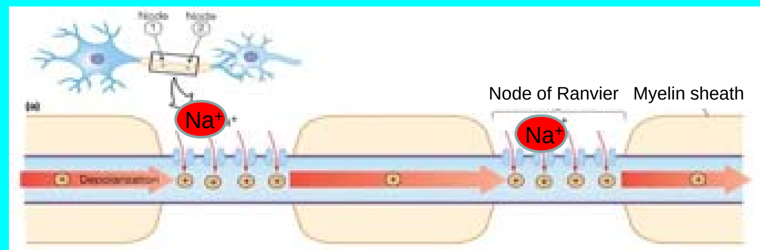
R_m – very high → big space constant

C_m – very small → small time constant

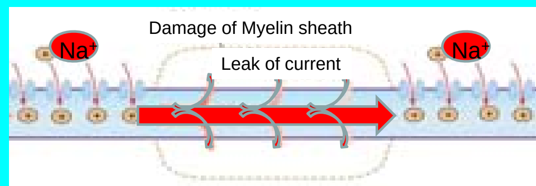


human nerve cell r= 10 µm v~ 100 m/s

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.

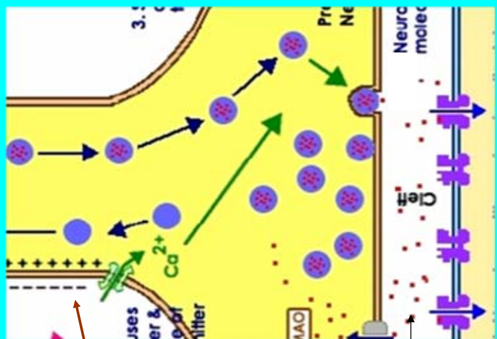
Fiber type	Average axon diameter (μm)	Conduction velocity ($m \cdot s^{-1}$)
Myelinated fibers		
Aα	18.5	42
Aβ	14.0	25
Aγ	11.0	17
B	Approximately 3.0	4.2
Unmyelinated fibers		
C	2.5	0.4–0.5

Effect of passive electric properties on signal transduction in synapses

Signal transmission in synapses

presynaptic terminal

postynaptic terminal

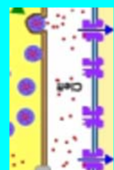


Action potential

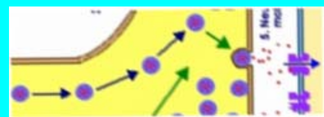
neurotransmitter

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

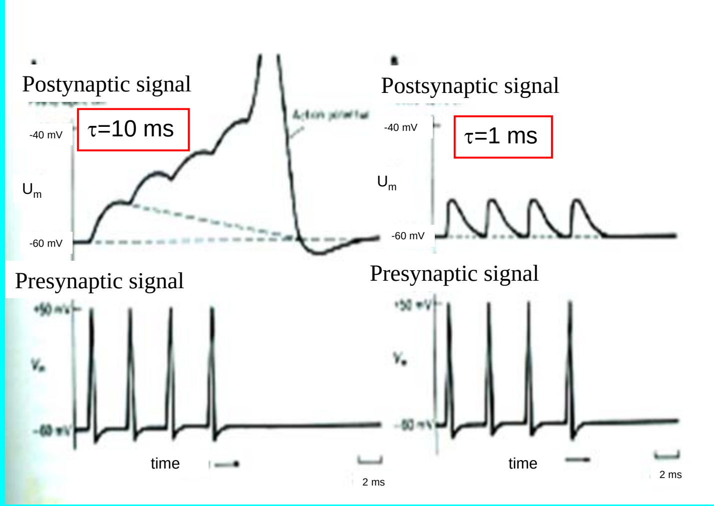
Spatial Summation : combined influences at the same cell at a particular moment in time



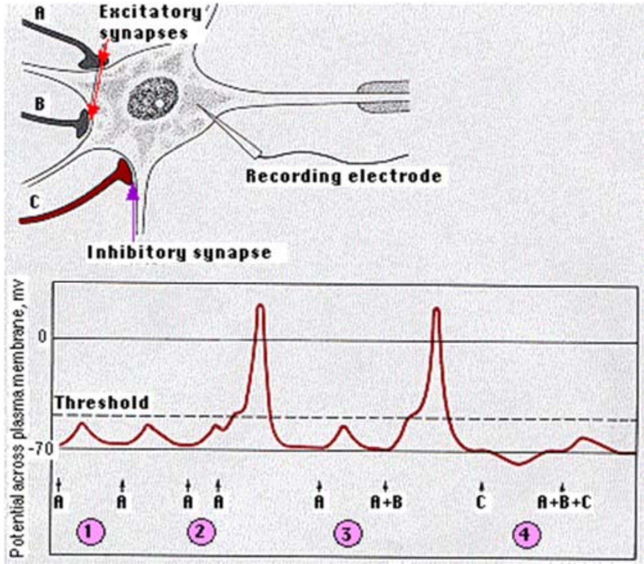
Temporal Summation : combined effects of neurotransmitter release from the same sites over time



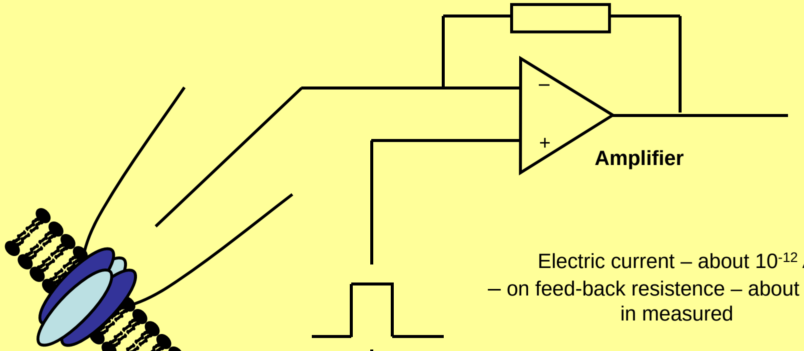
Temporal Summation : combined effects of neurotransmitter release from the same sites over time



Temporal and spatial summation

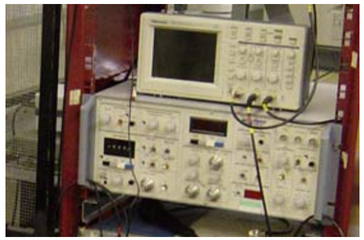


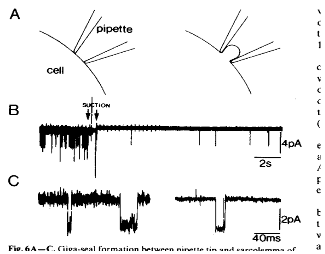
Patch-Clamp circuit



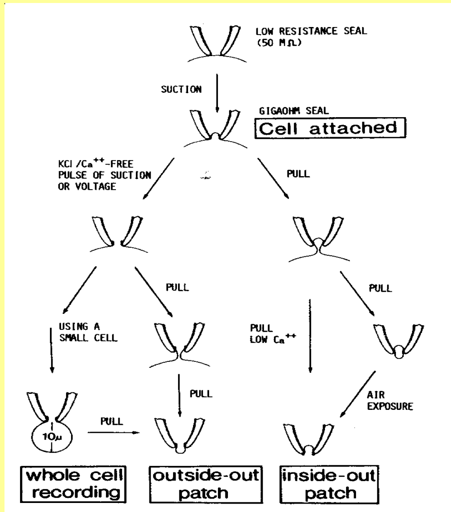
Electric current – about 10^{-12} A
– on feed-back resistence – about 50 GΩ
in measured

Patch-Clamp technique



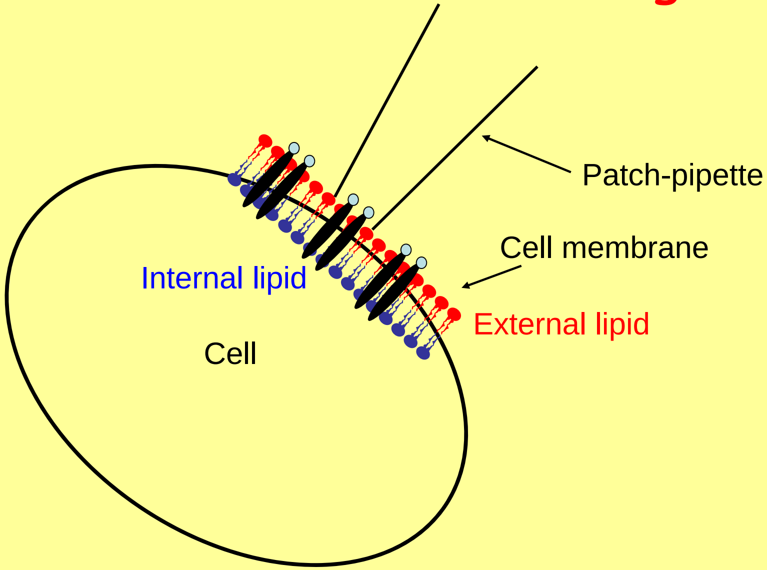


Patch-Clamp variations

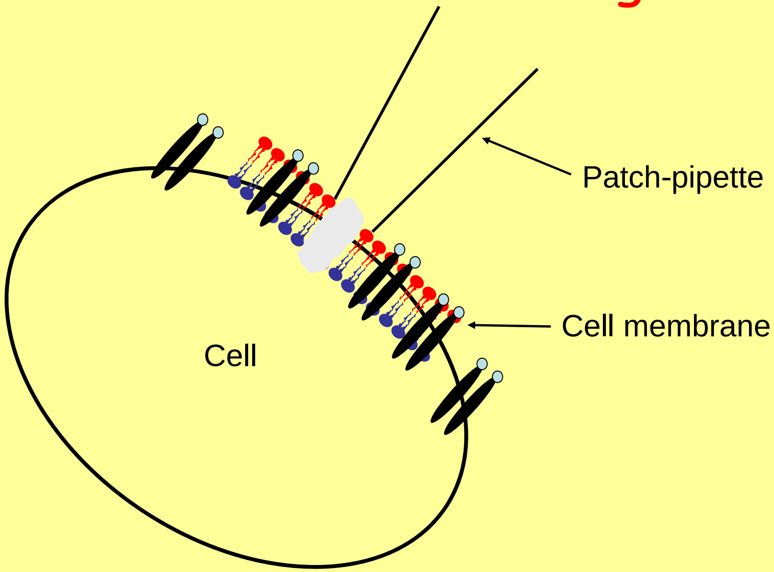


From Hamill *et al* 1981

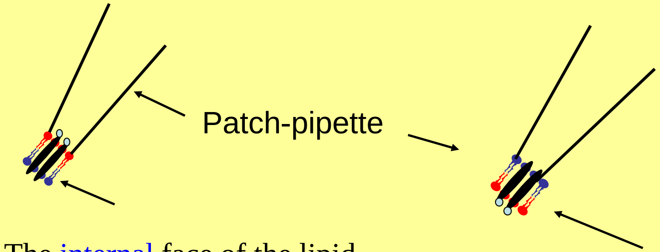
Cell-attached recording



Whole-cell recording



Inside-out recording

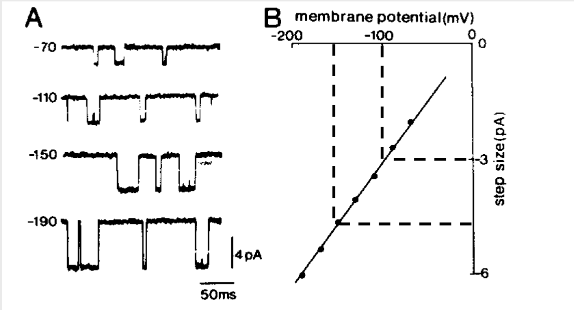


The internal face of the lipid bi-layer faces the bath solution

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

Outside-out recording

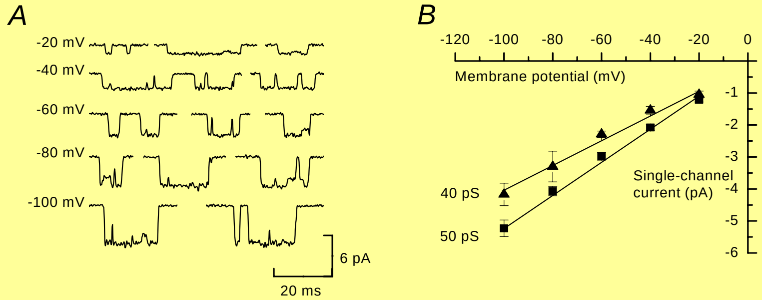
Single-channel I/V plots are used to determine the conductance of an ion channel



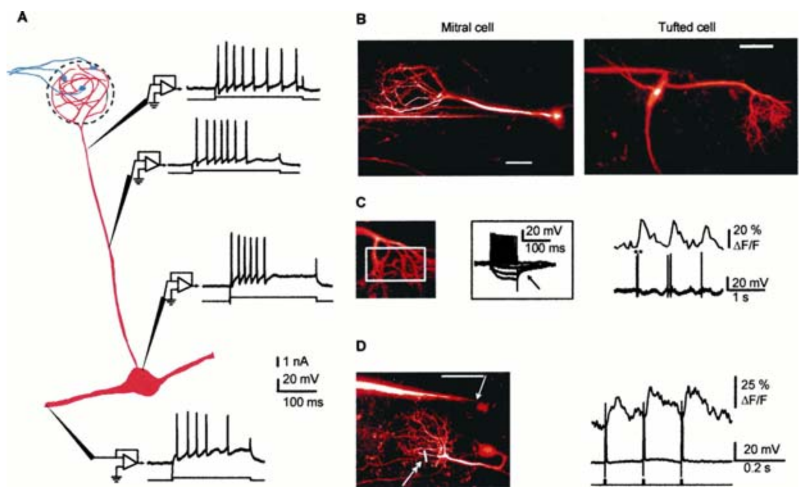
$$
\begin{aligned}
g_{channel} &= \Delta I \div \Delta V \\
&= 1.6 \times 10^{-12}\,A \div 50 \times 10^{-3}\,V \\
&= 32 \times 10^{-12}\,S \\
&= 32\ pS
\end{aligned}
$$

From Hamill *et al* 1981

Single channel with multiple states



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