

# Action potential

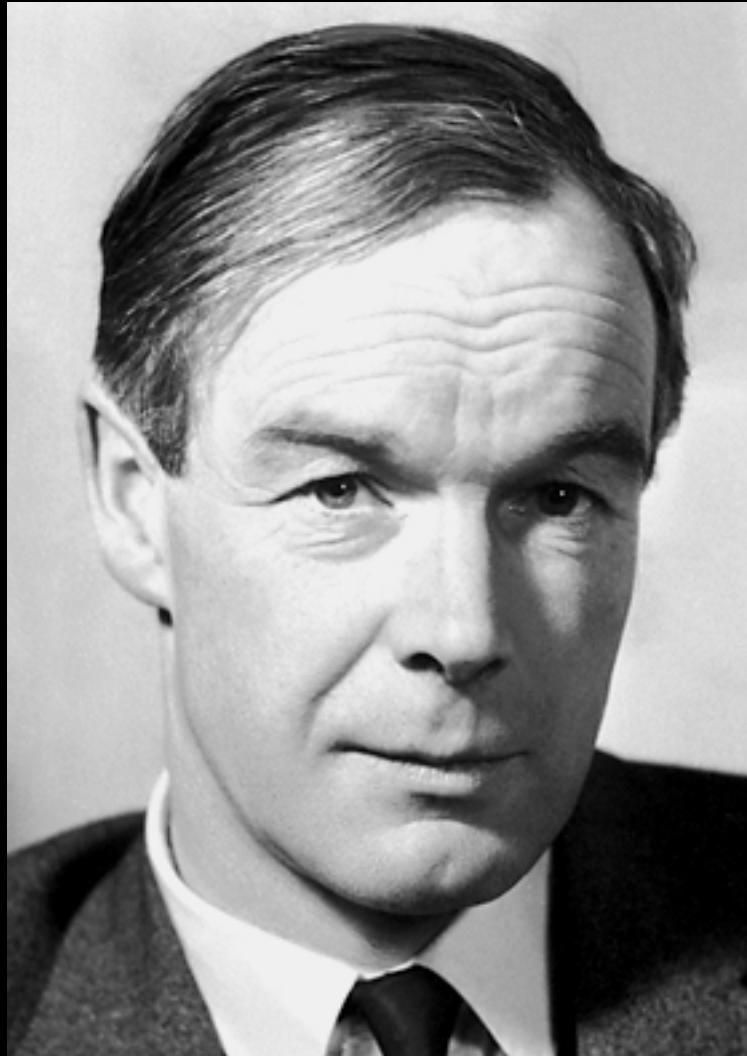
Valerio Mante

[valerio@ini.phys.ethz.ch](mailto:valerio@ini.phys.ethz.ch)

# The action potential



Sir Alan Hodgkin



Sir Andrew Huxley

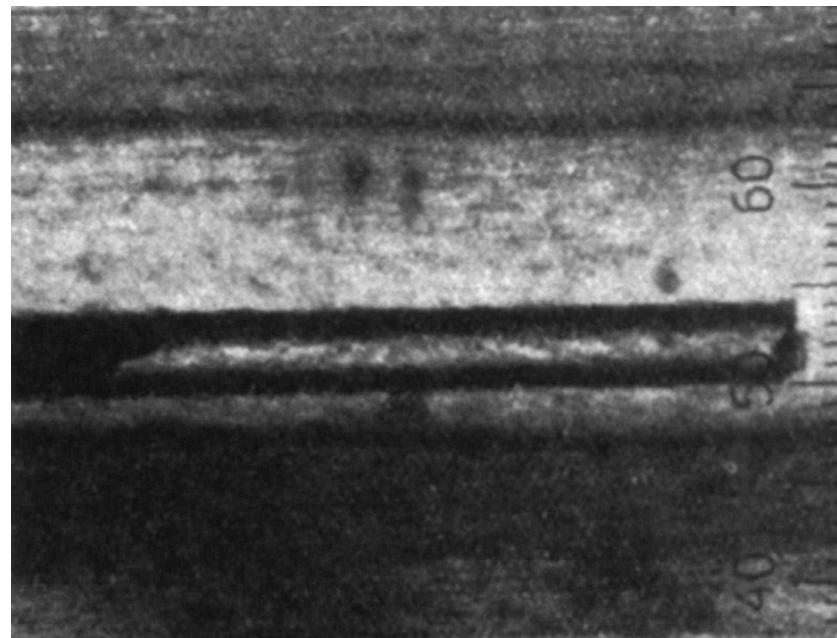
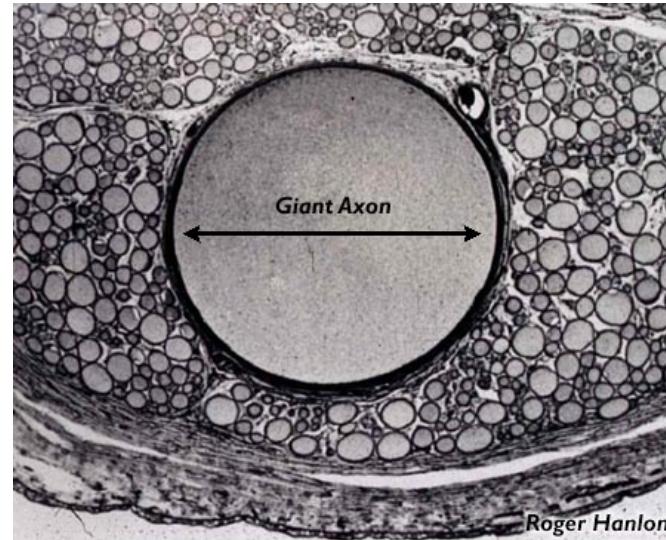
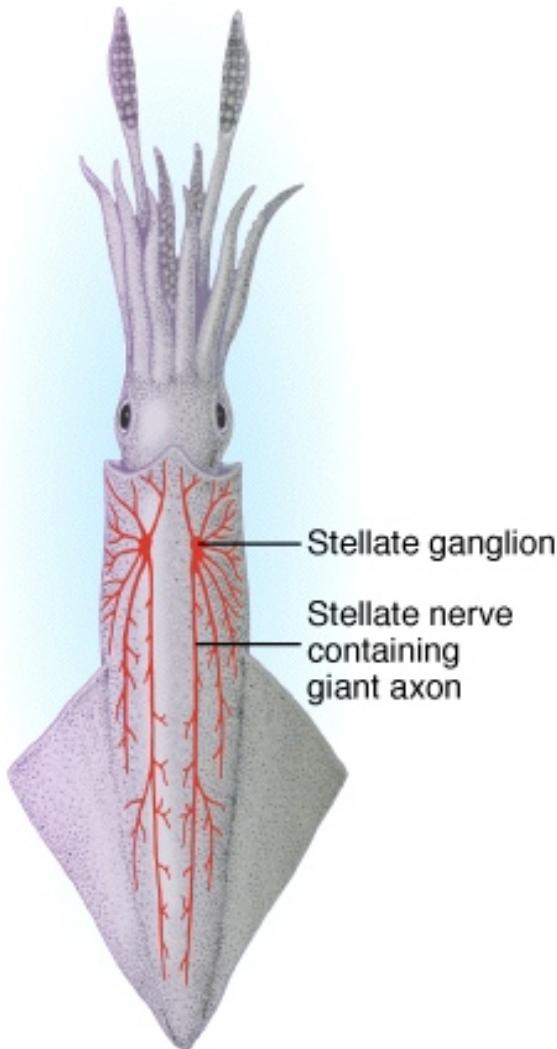


Nobel prize 1963

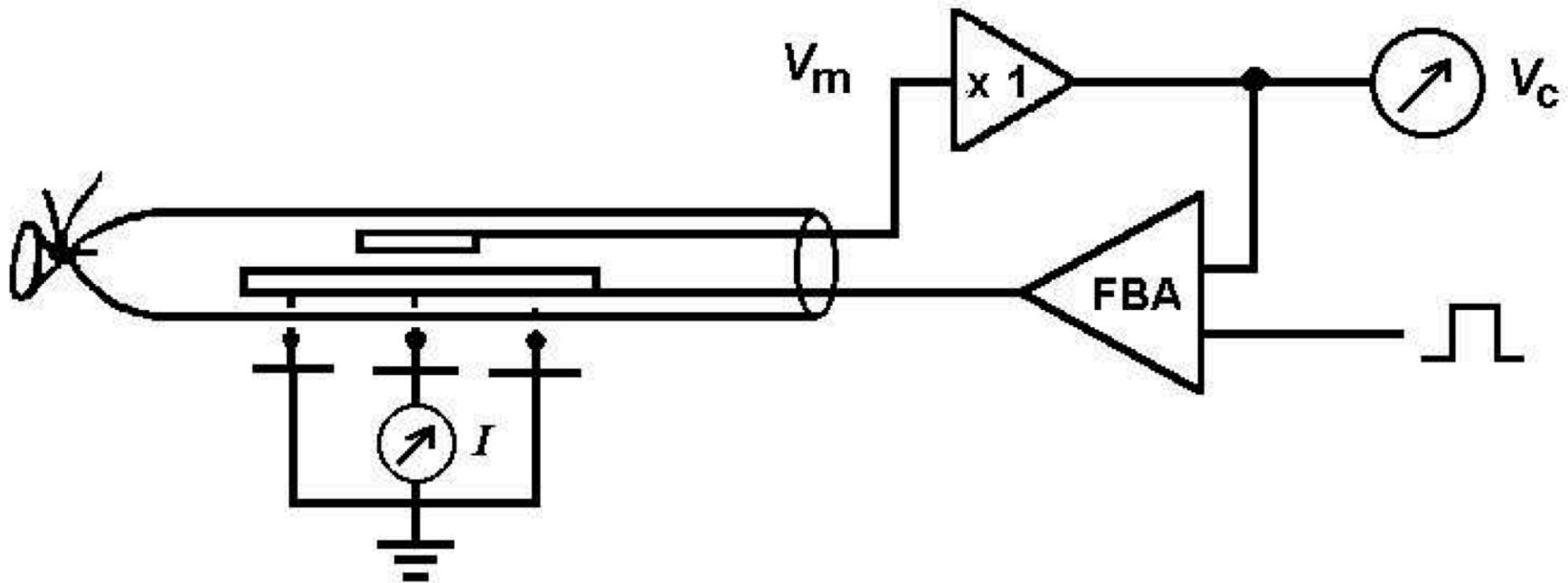


European Squid

# Squid giant axon



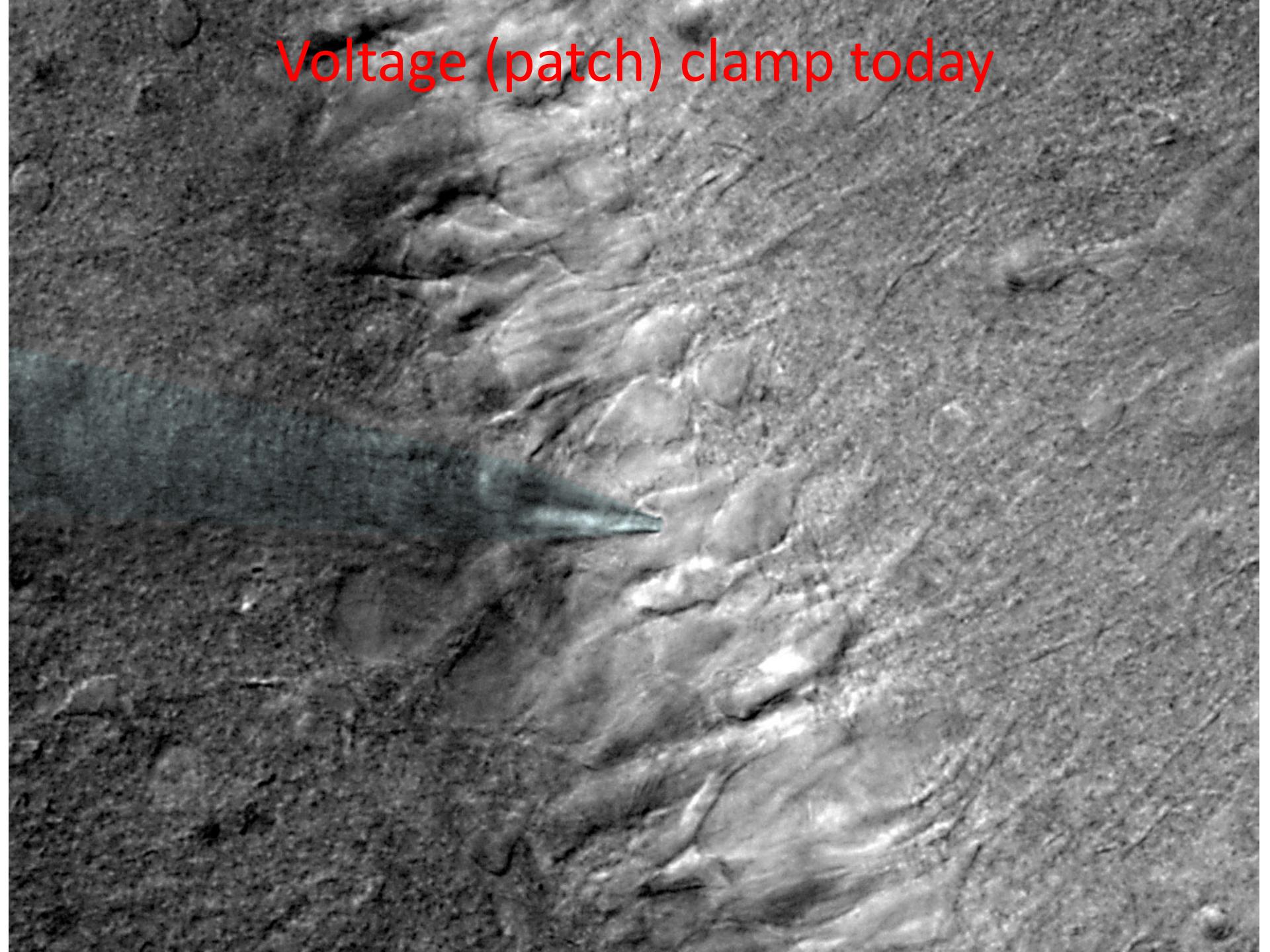
# Voltage clamp and Space clamp



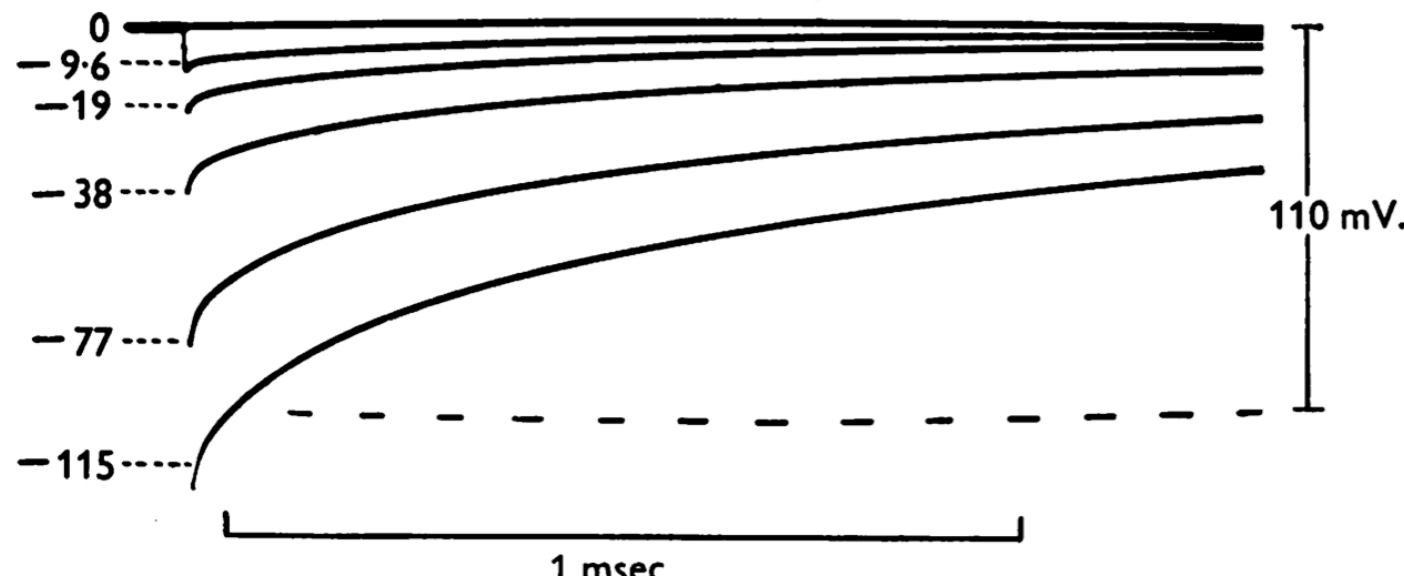
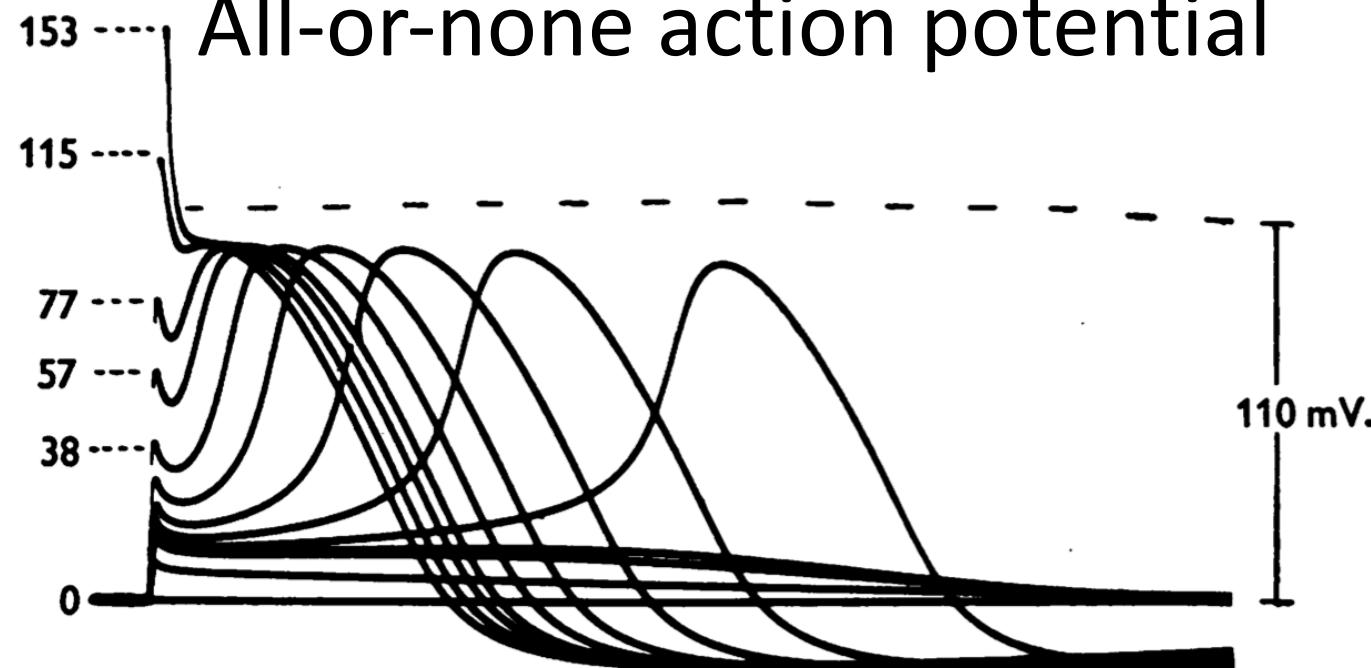
Here: Set **voltage V**, measure **current I**

Before: Set **current I**, measure **voltage V**

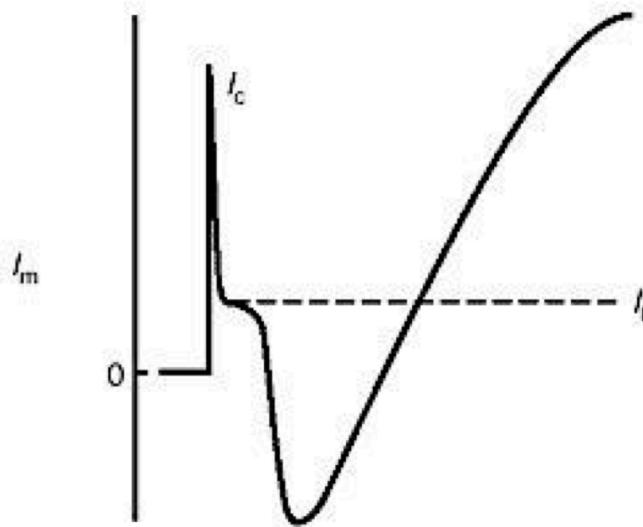
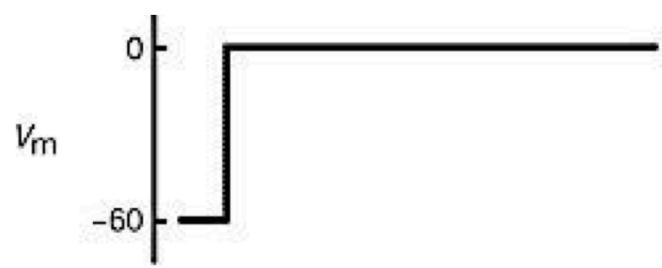
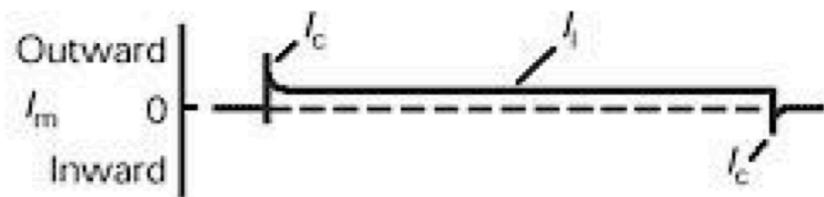
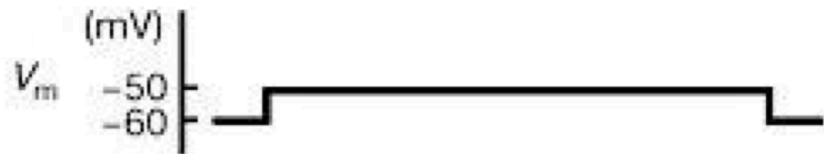
Voltage (patch) clamp today



# All-or-none action potential



# Voltage clamp experiment

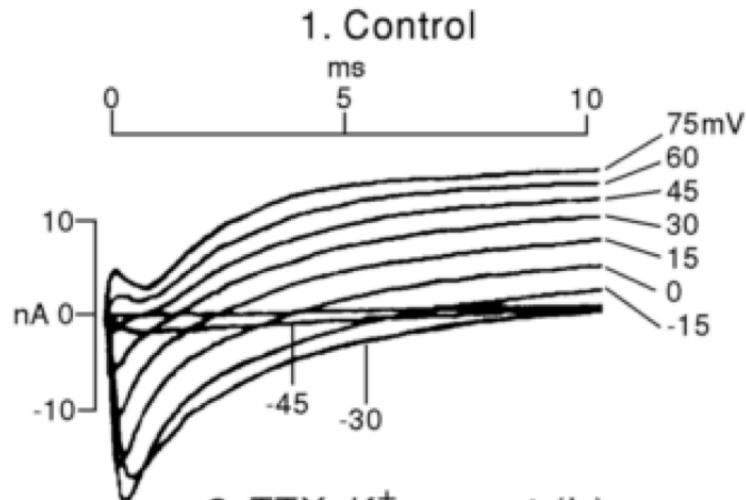


Conductances are:

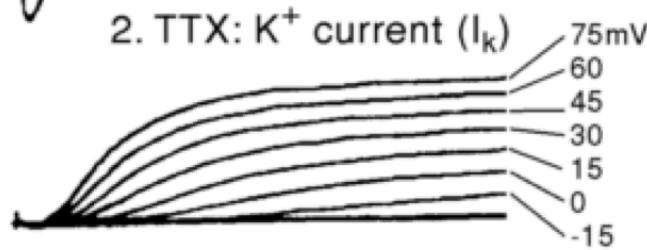
1. **Voltage** dependent
2. **Time** dependent

# Identifying the currents

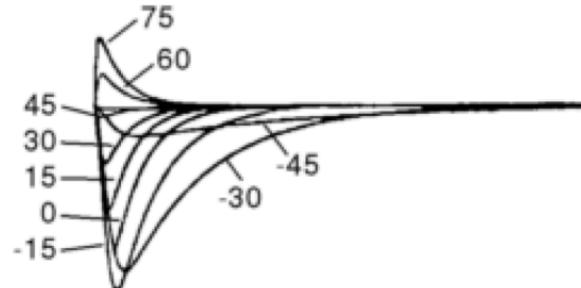
Pharmacological blockade



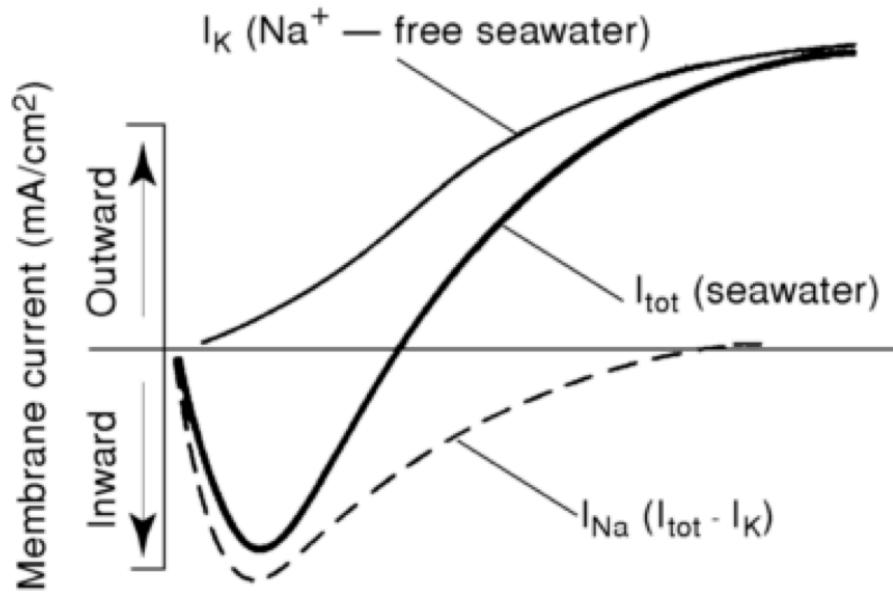
2. TTX:  $K^+$  current ( $I_K$ )



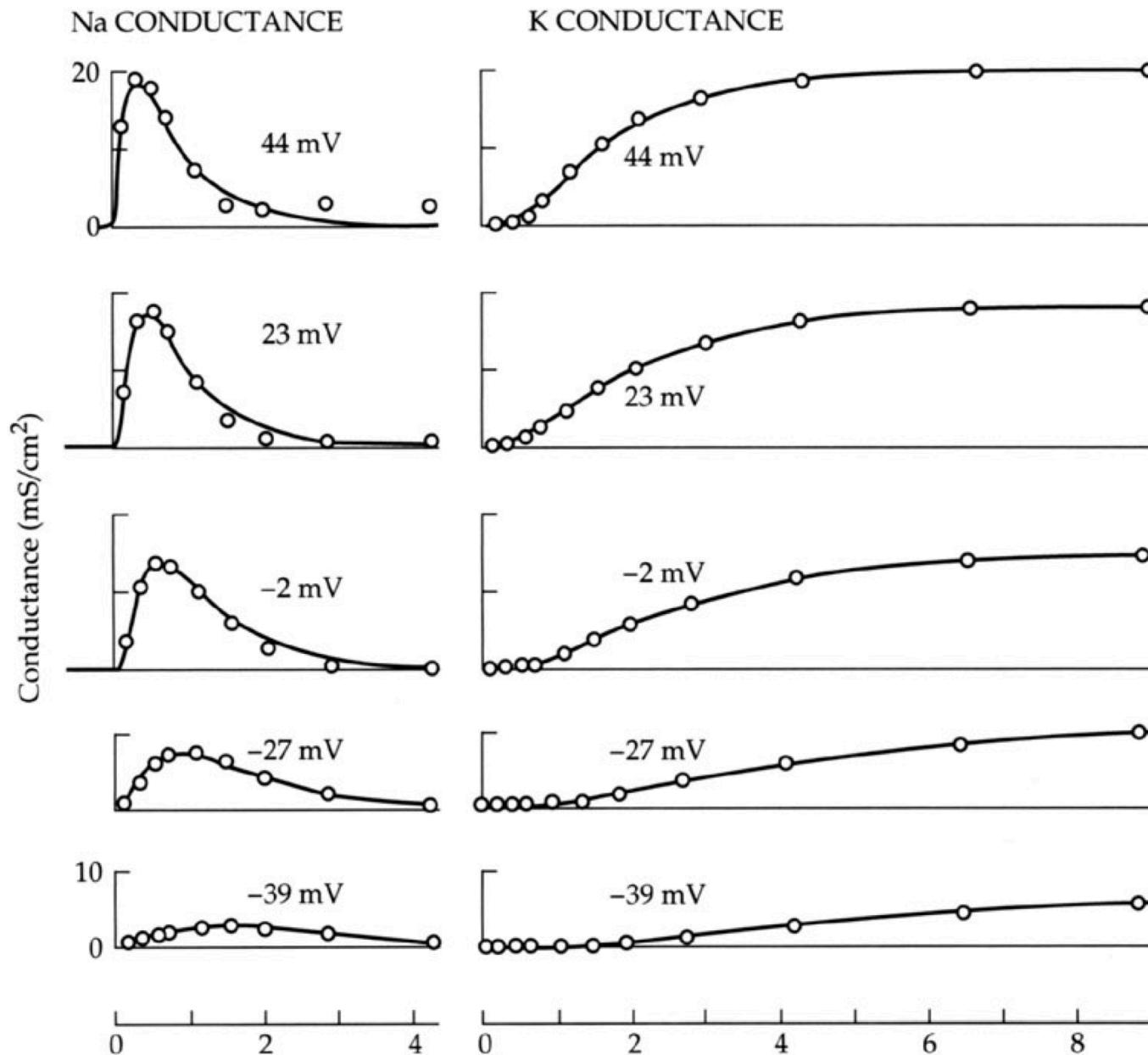
3. TEA:  $Na^+$  current ( $I_{Na}$ )



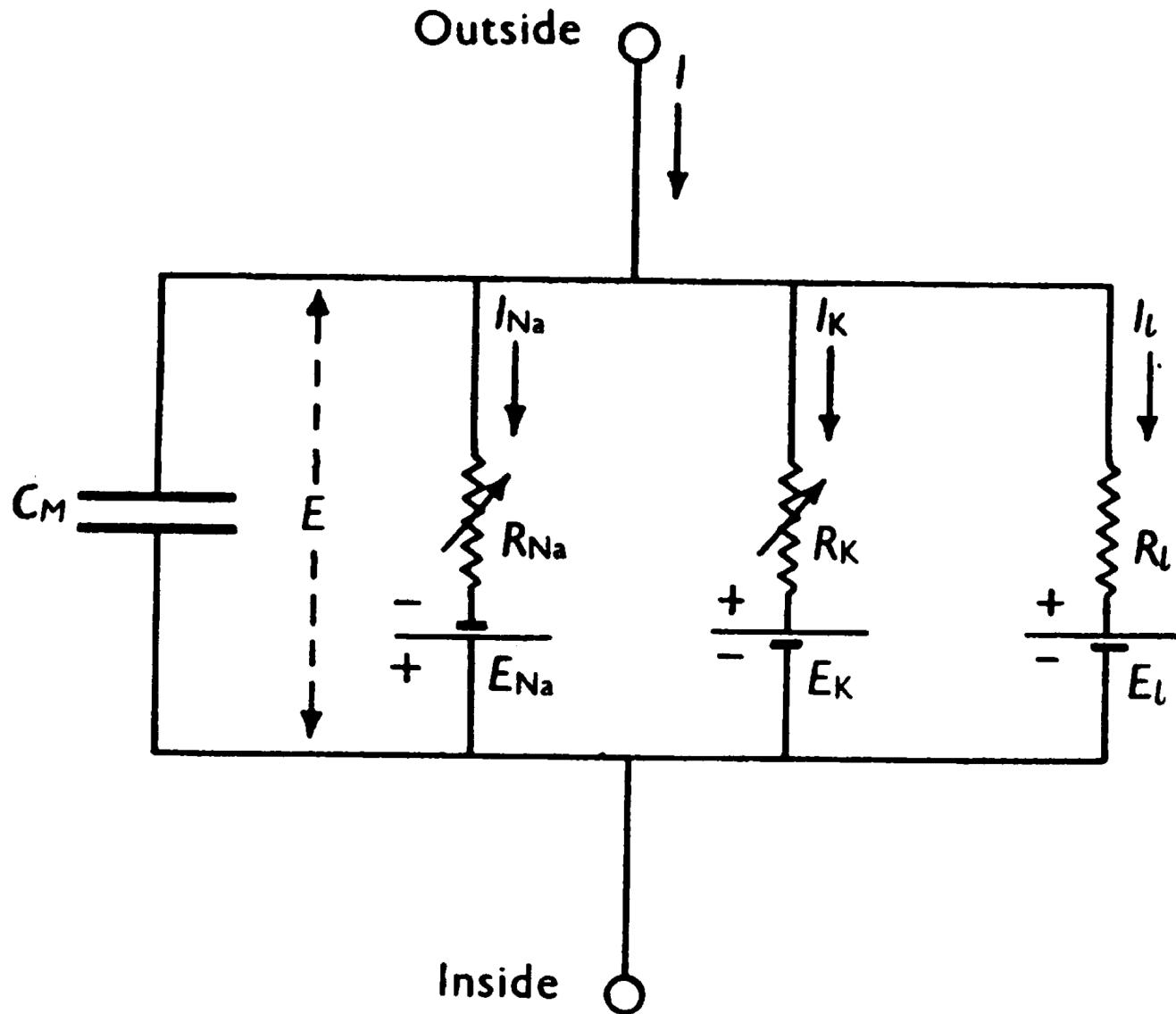
Ion replacement



# From current to conductance (via Ohm's law)

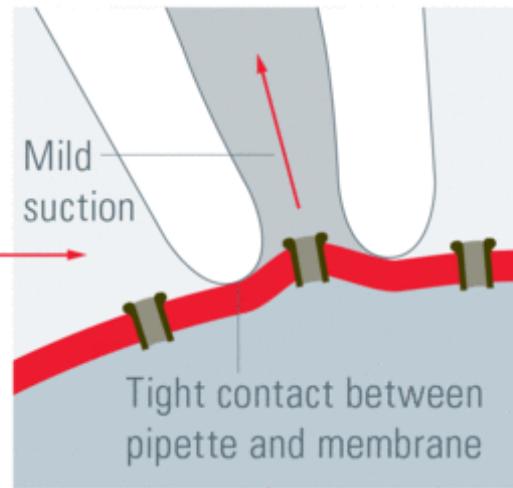
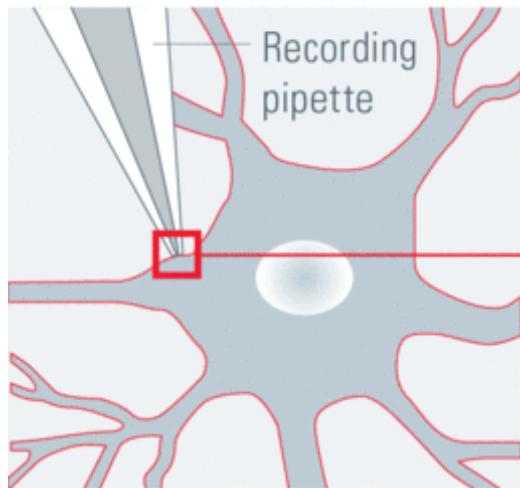


# The circuit for action potential generation

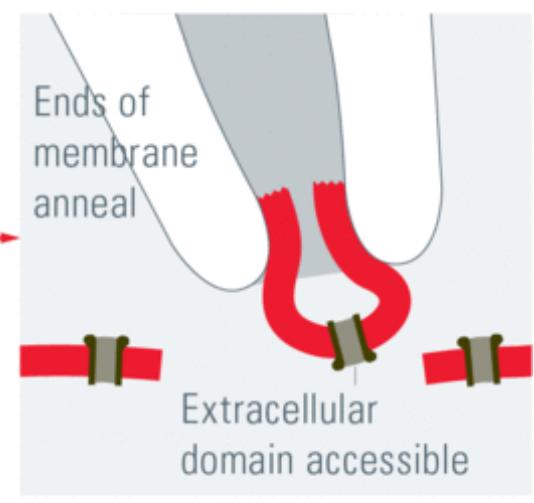
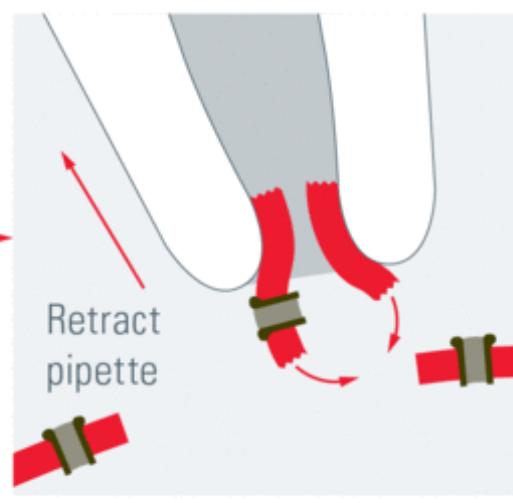
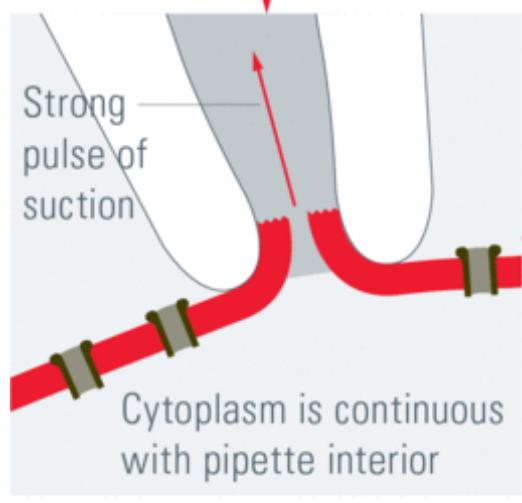
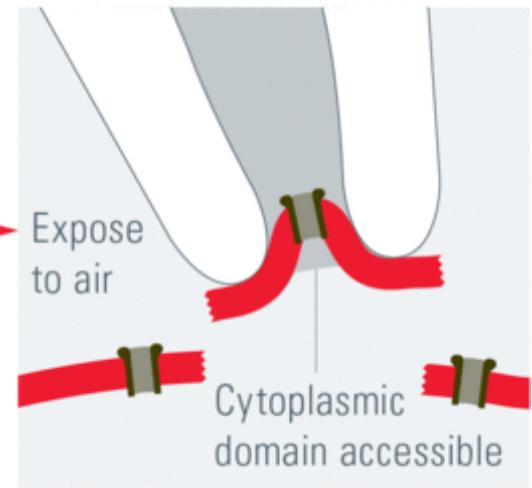


# Patch clamp

Cell-attached recording



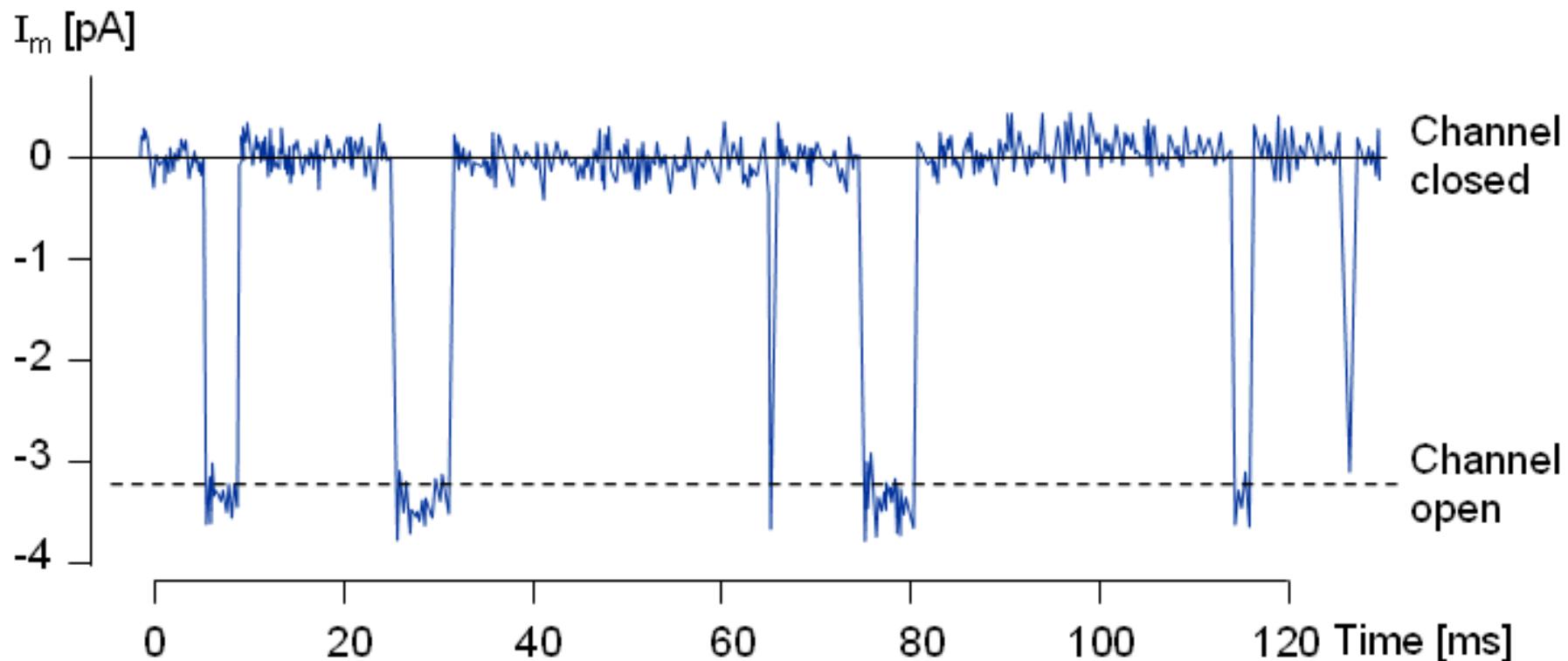
Inside-out recording



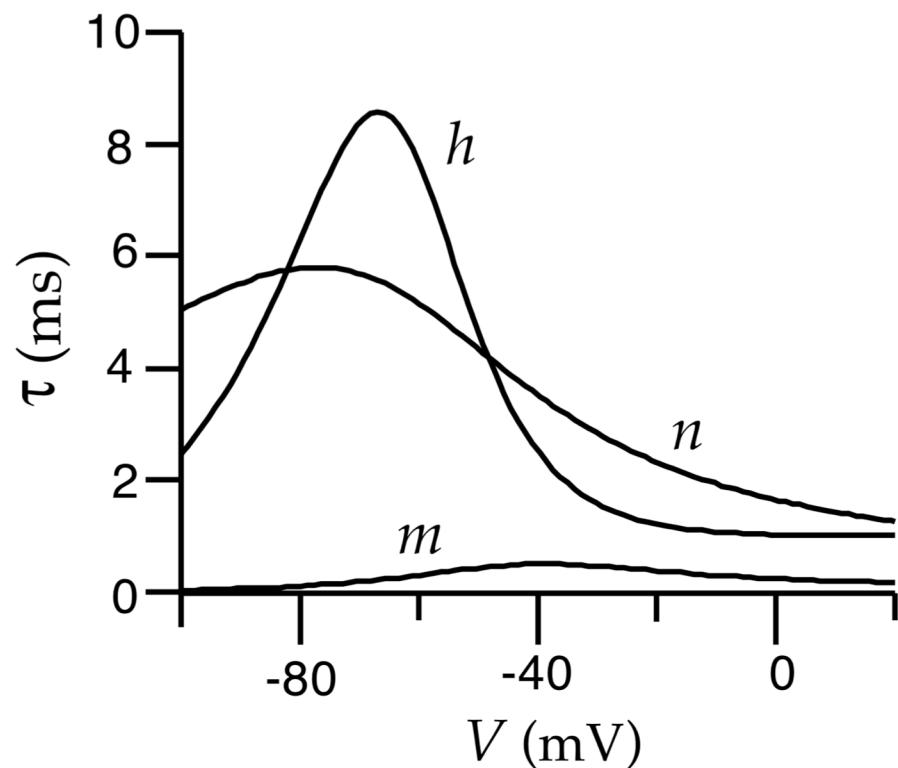
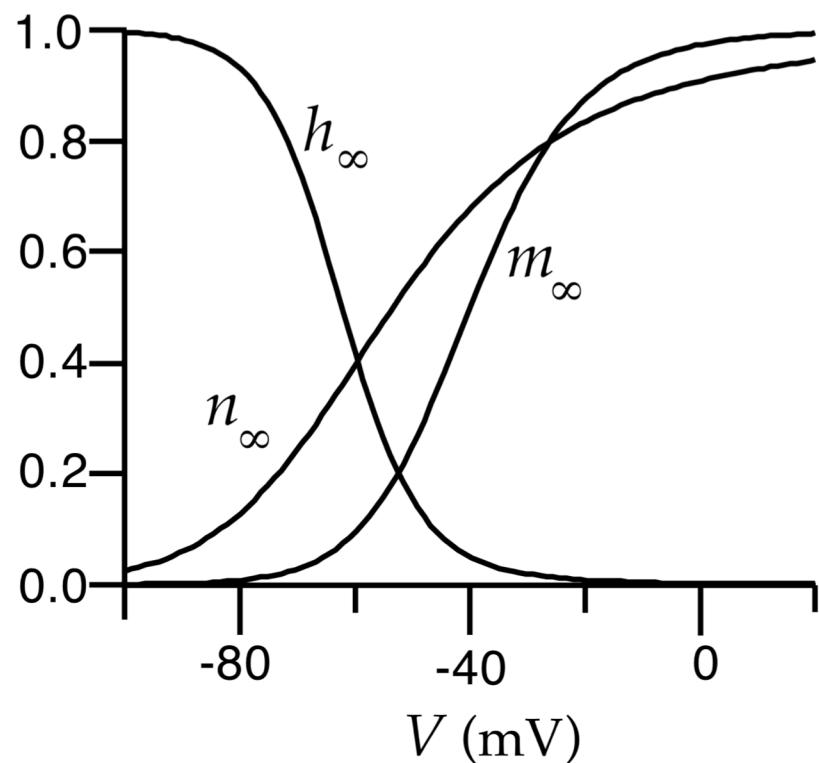
Whole-cell recording

Outside-out recording

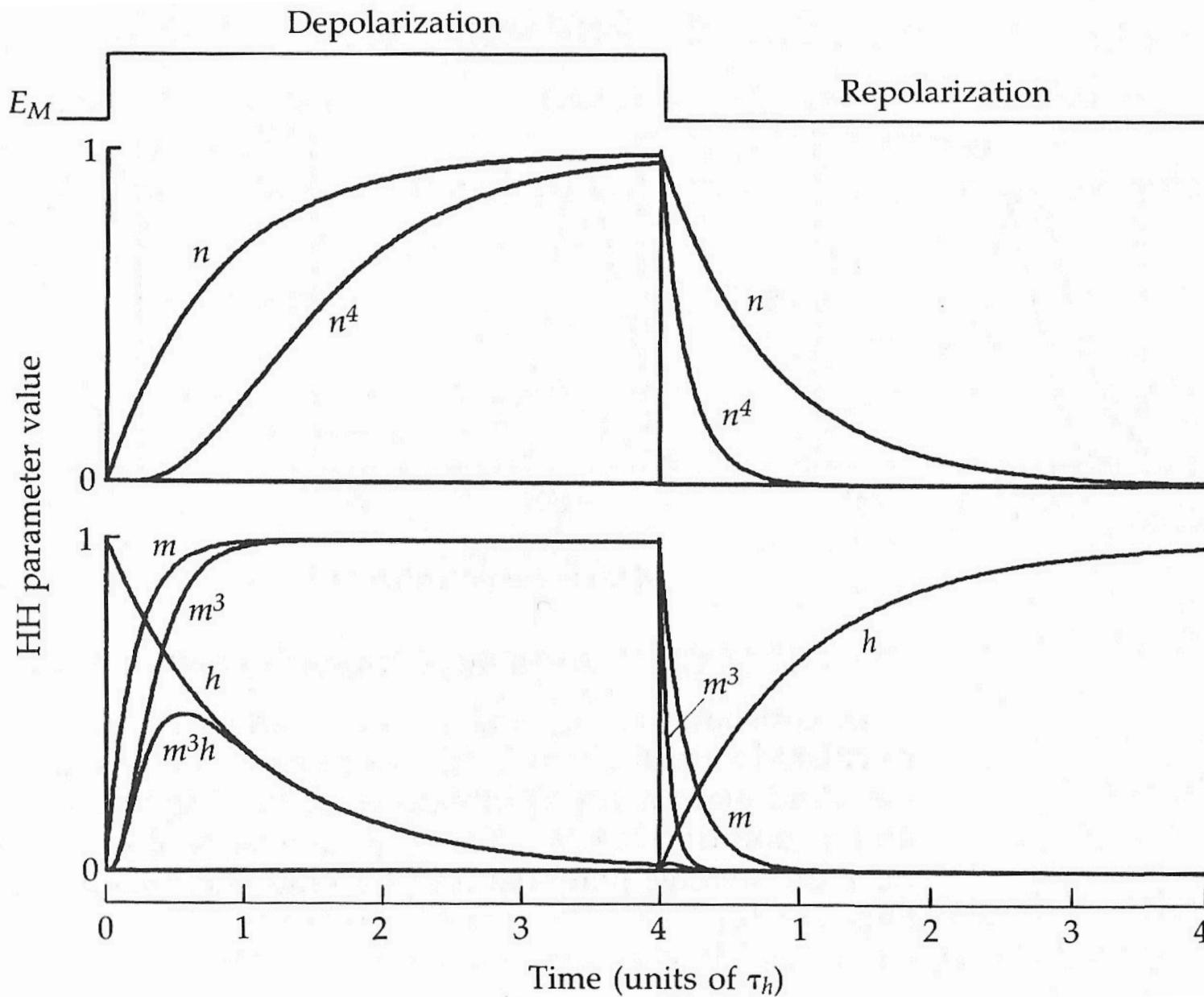
# Single channel current



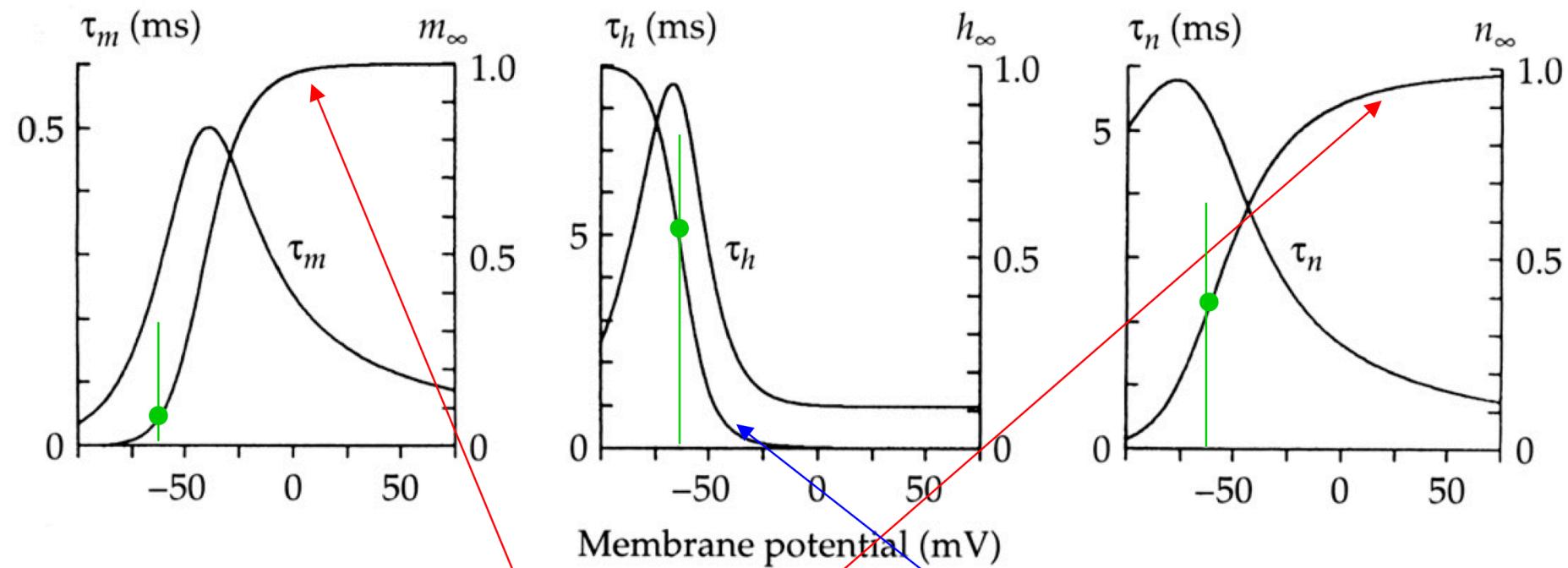
# Gating variables



# Gating variables: time-dependence



# Gating variables: voltage-dependence

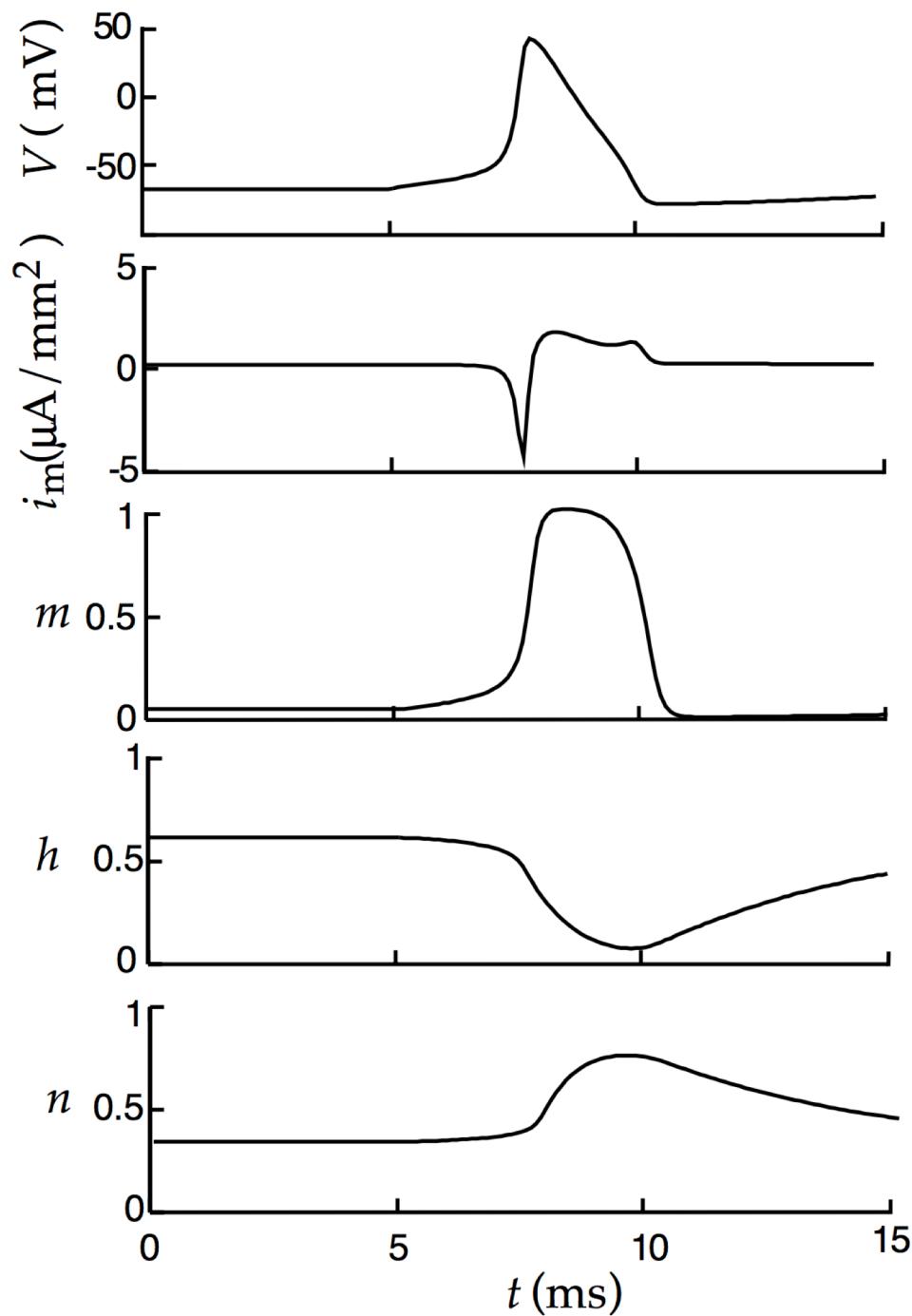


resting potential

the  $m$  and  $n$  gates open with depolarization

the  $h$  gate closes with depolarization

Gating variables during  
the action potential  
(predicted by HH-model)



# Predicted action potential

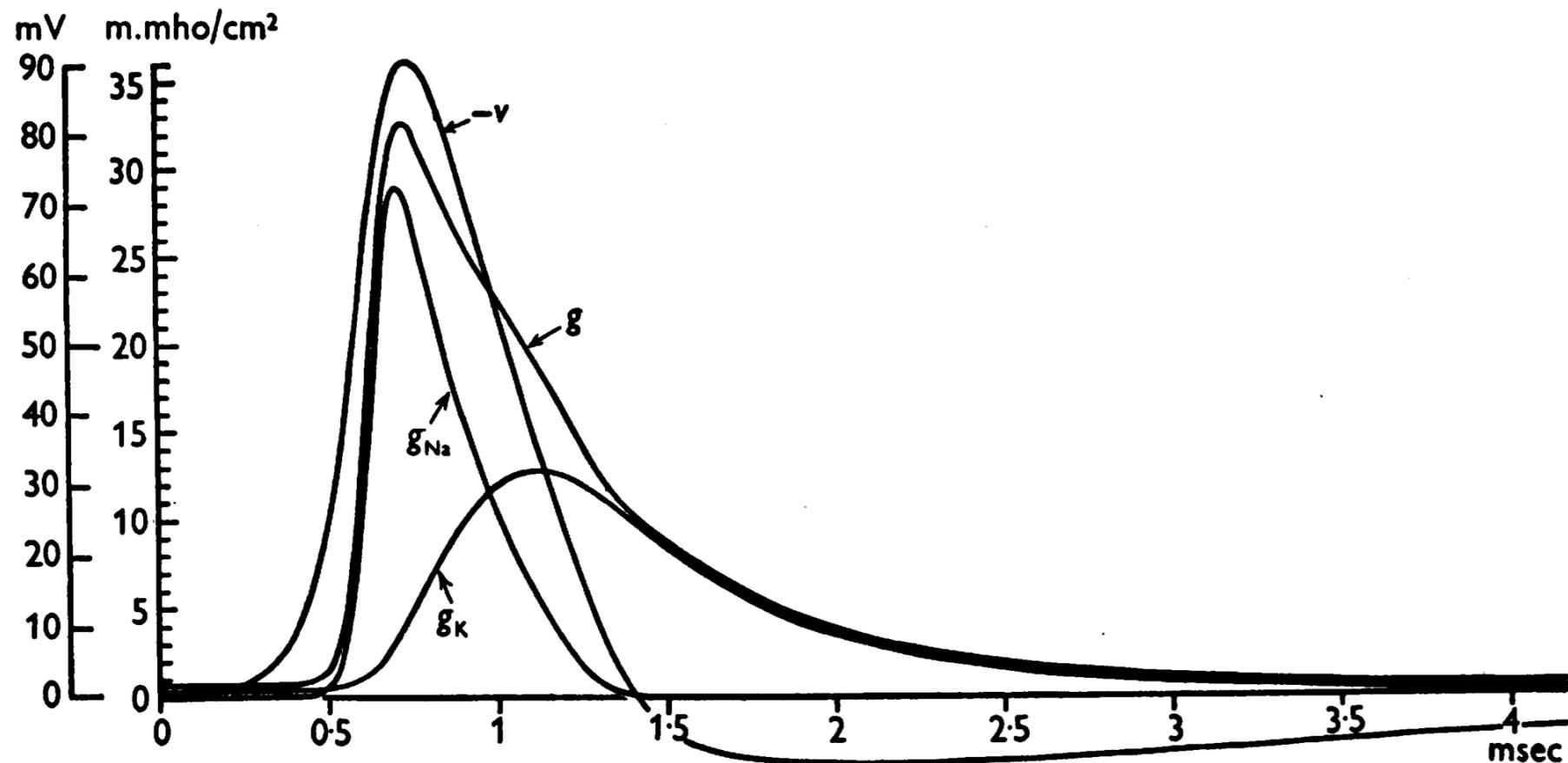
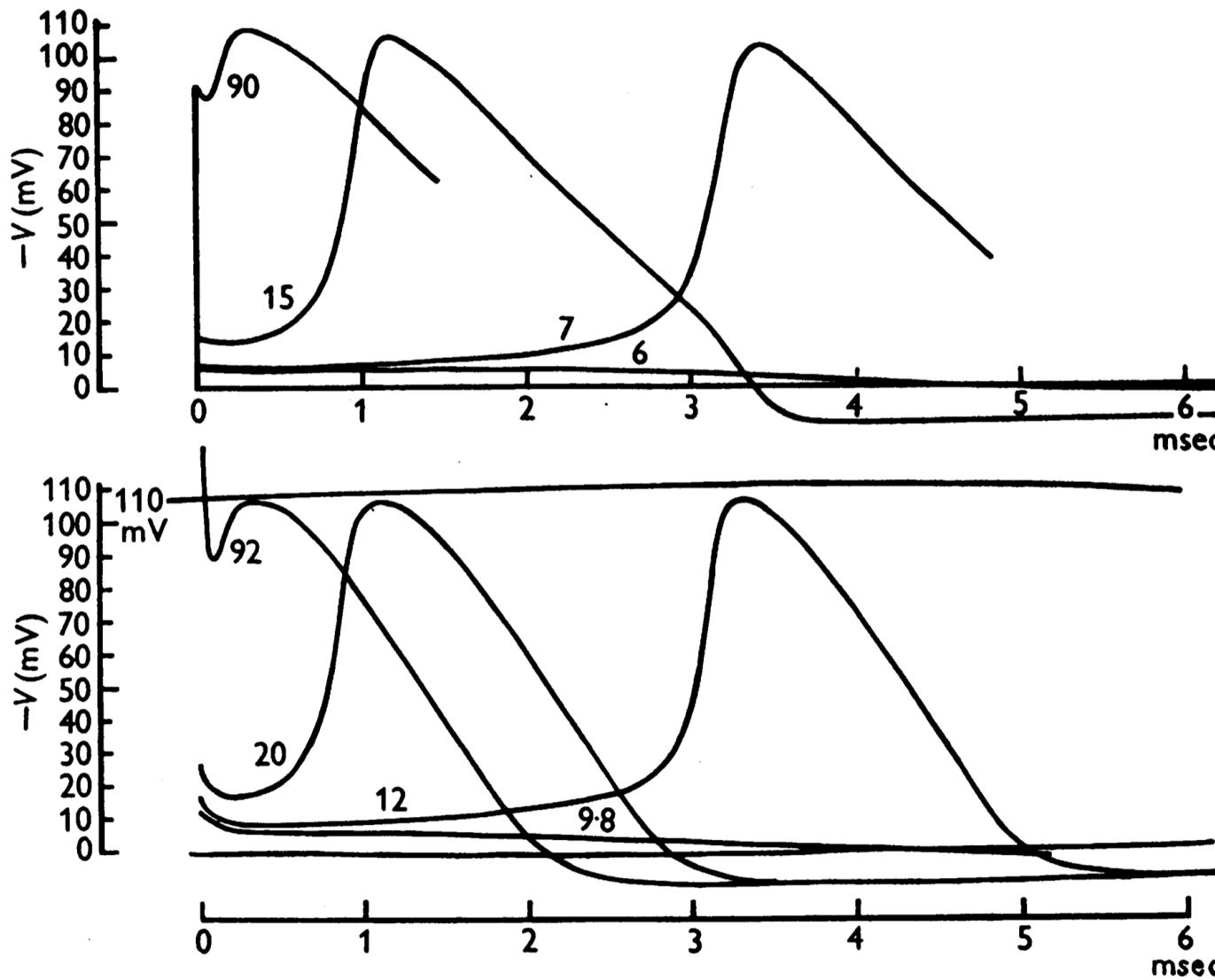
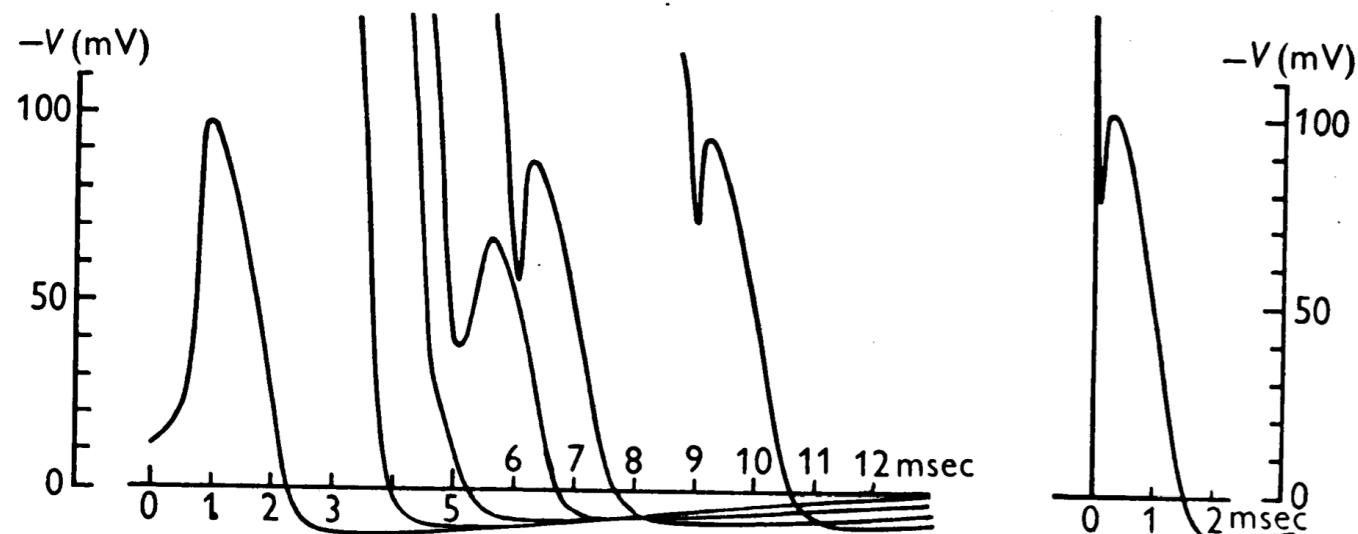
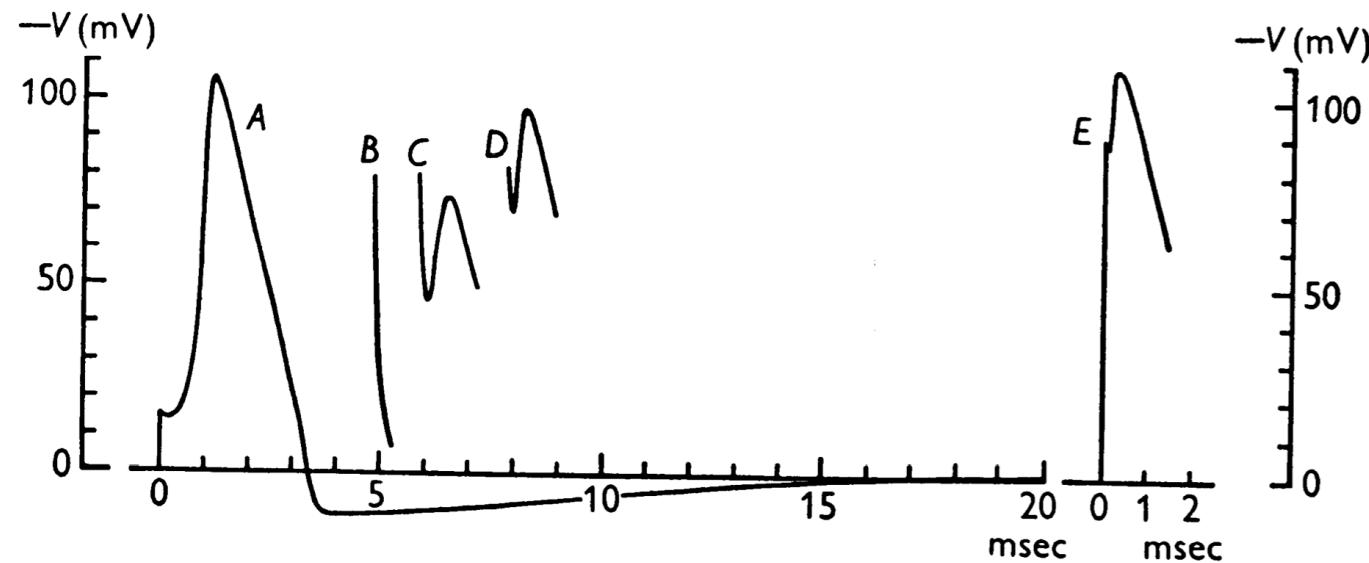


Fig. 17. Numerical solution of eqn. (31) showing components of membrane conductance ( $g$ ) during propagated action potential ( $-V$ ). Details of the analysis are as in Fig. 15.

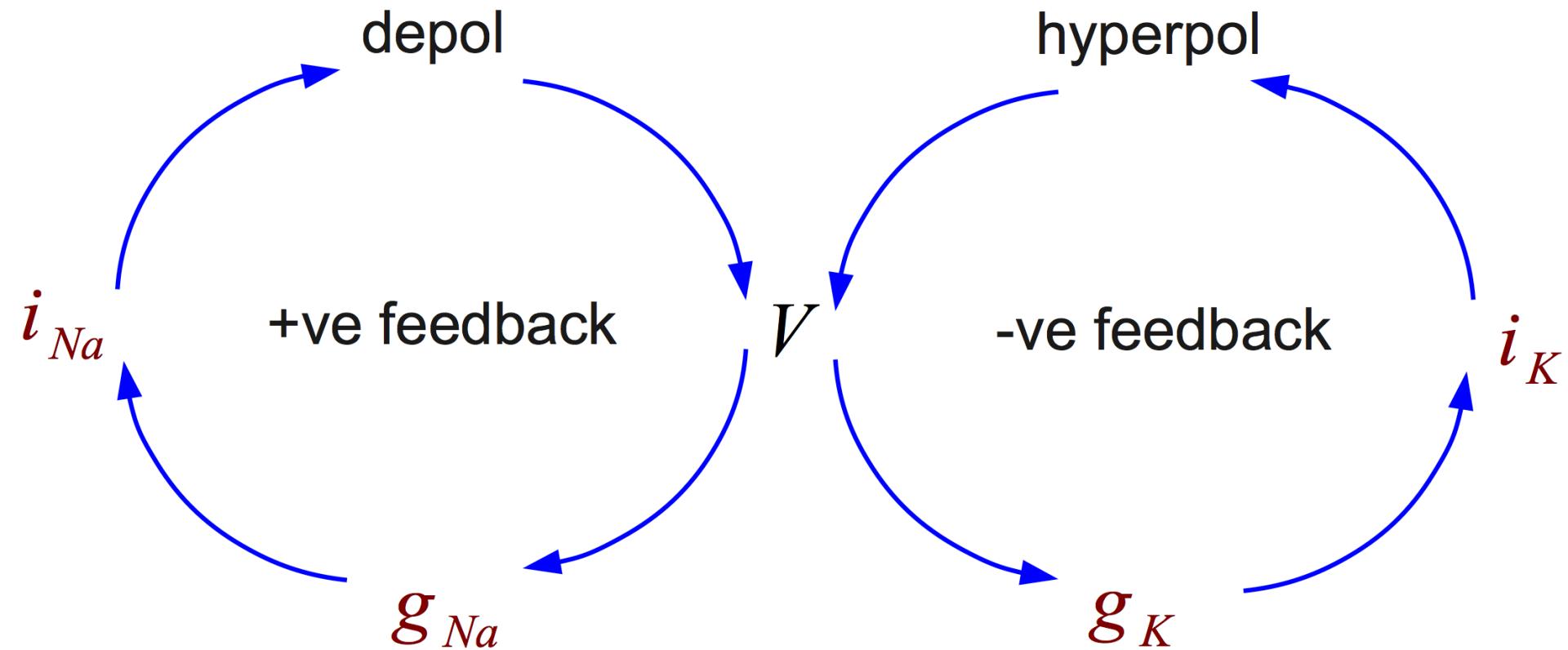
# Measured vs. predicted action potential



# Measured vs. predicted refractory period



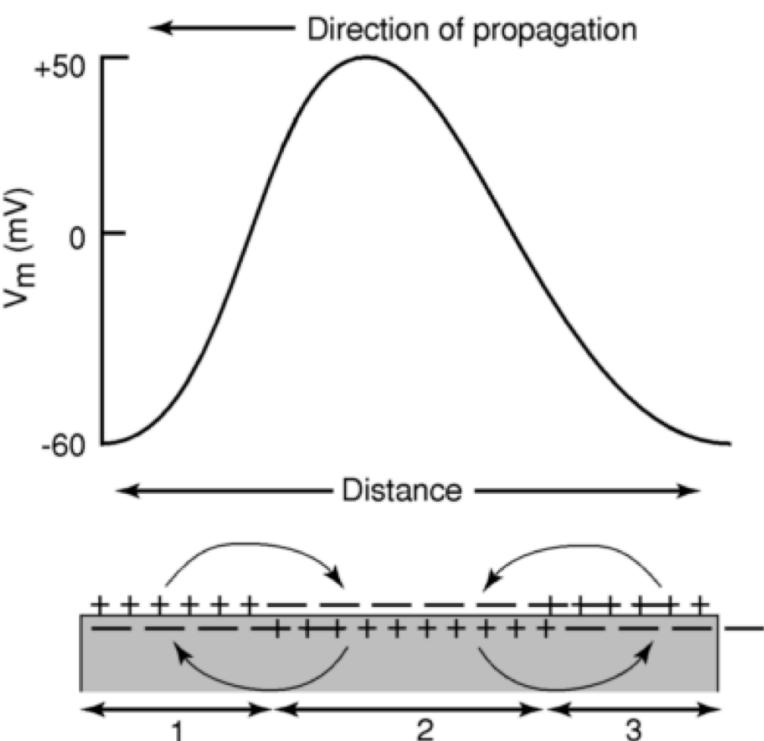
# Feedback mechanisms underlie the AP



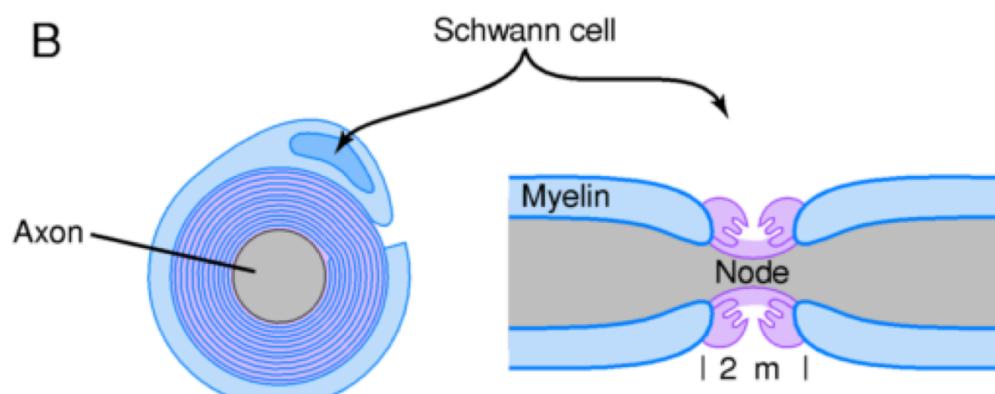
Why is there a threshold for action potential generation?

# Action potential propagation

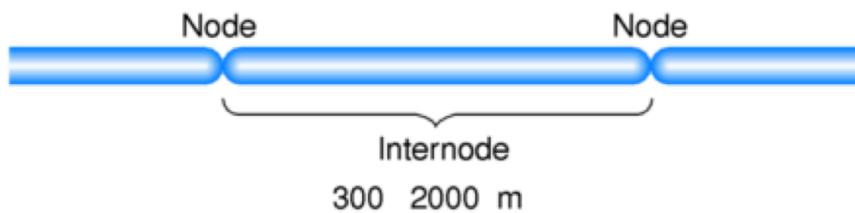
A



B

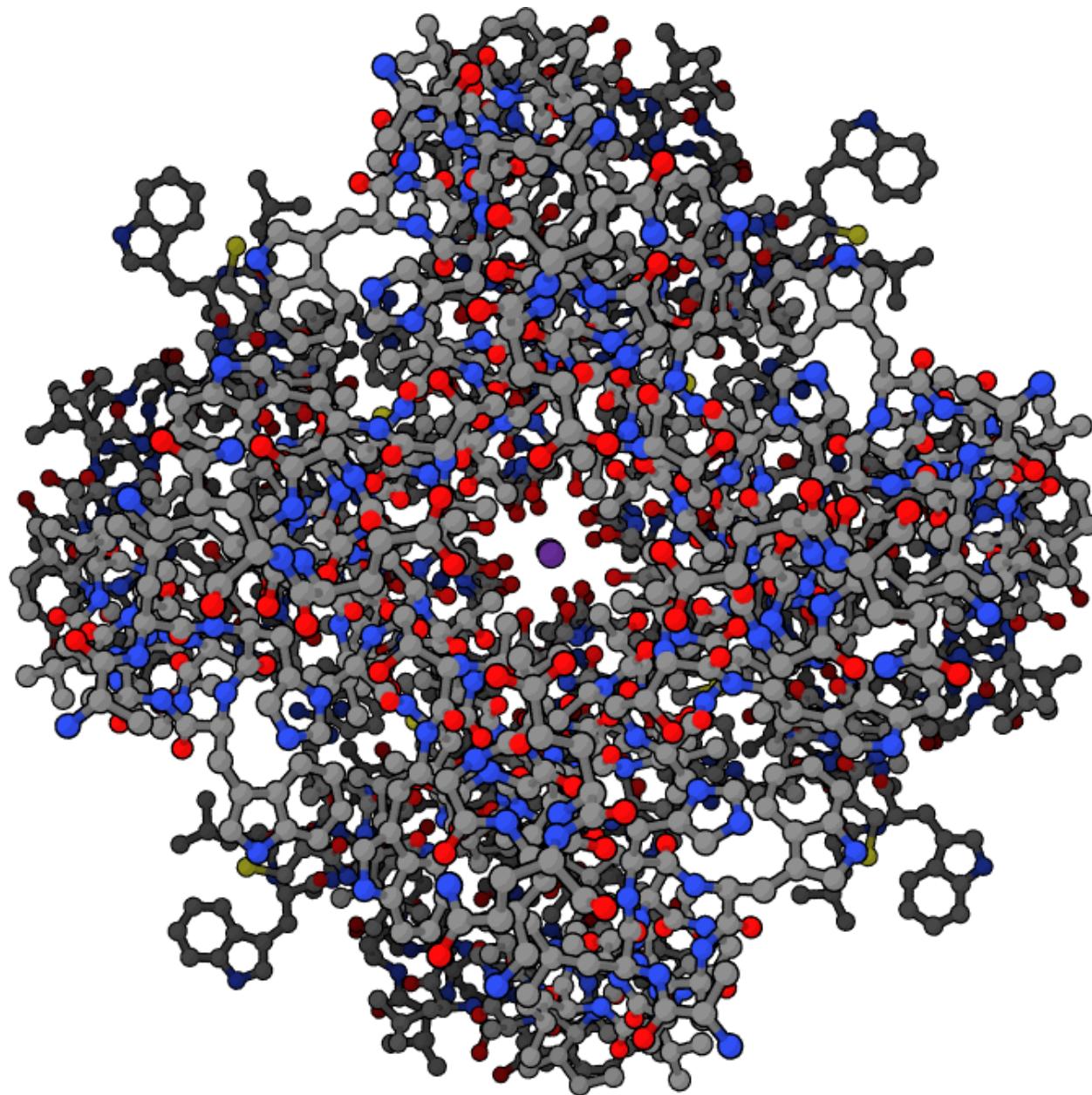


C

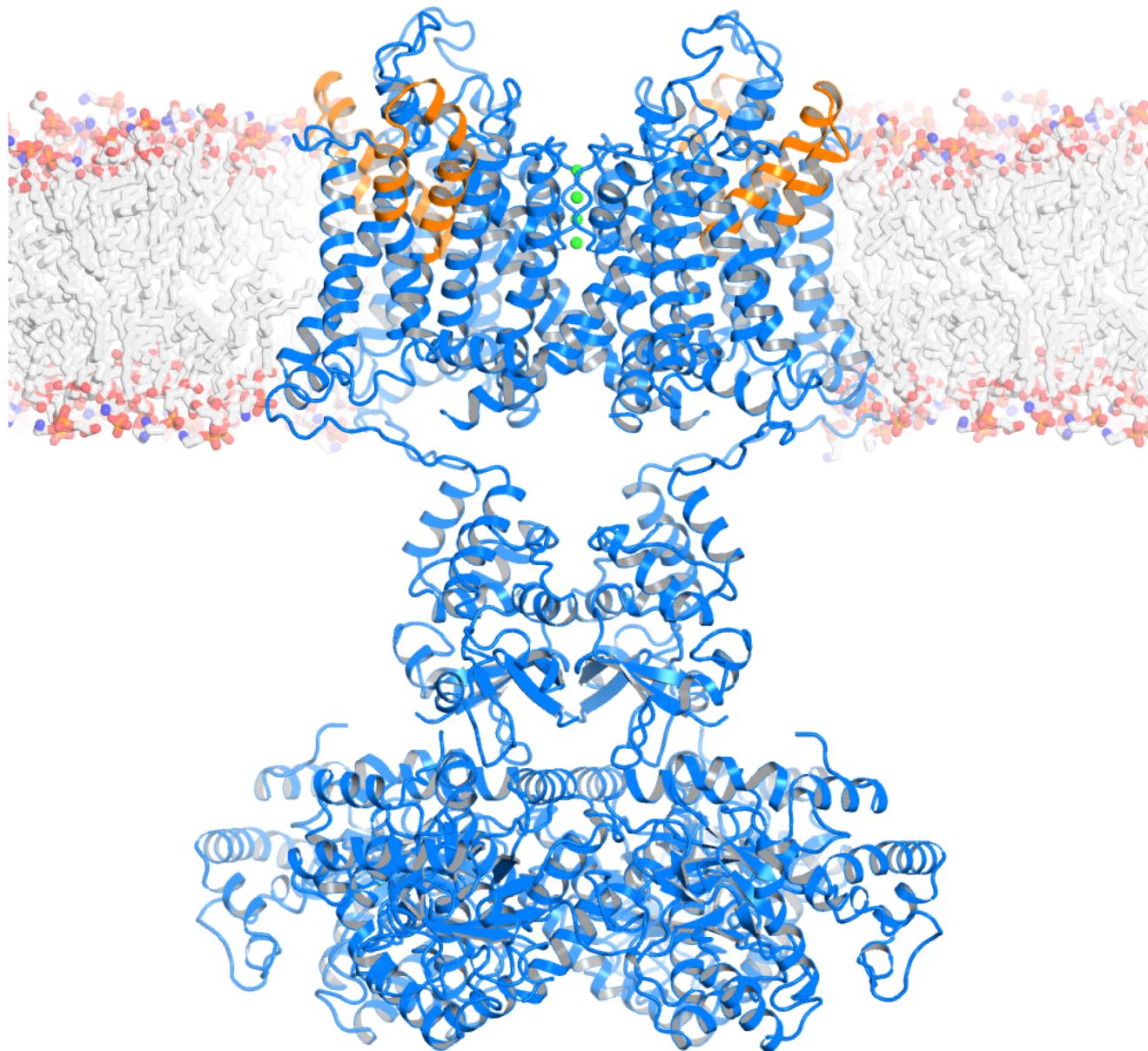


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# The potassium channel

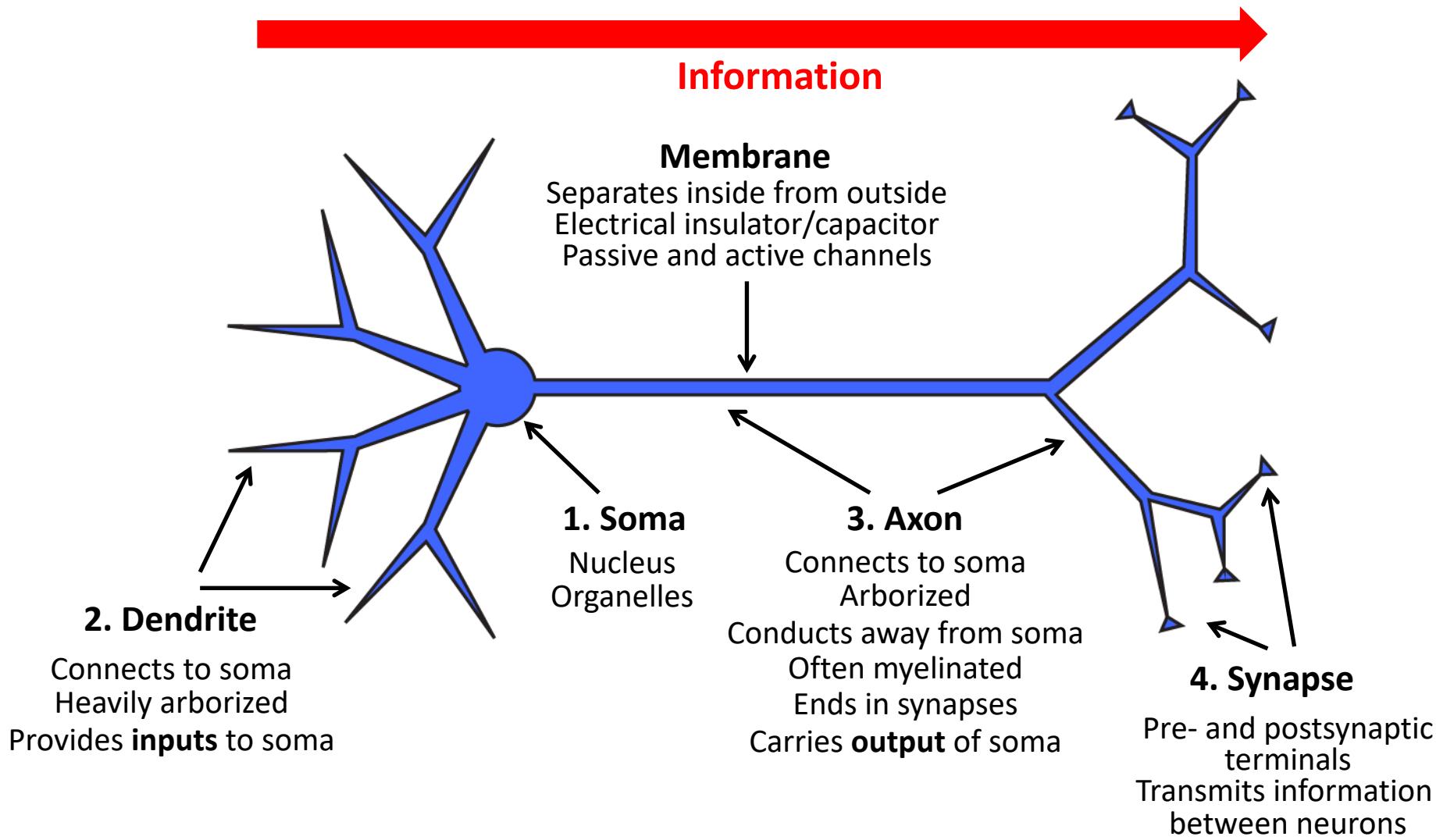


# The potassium channel

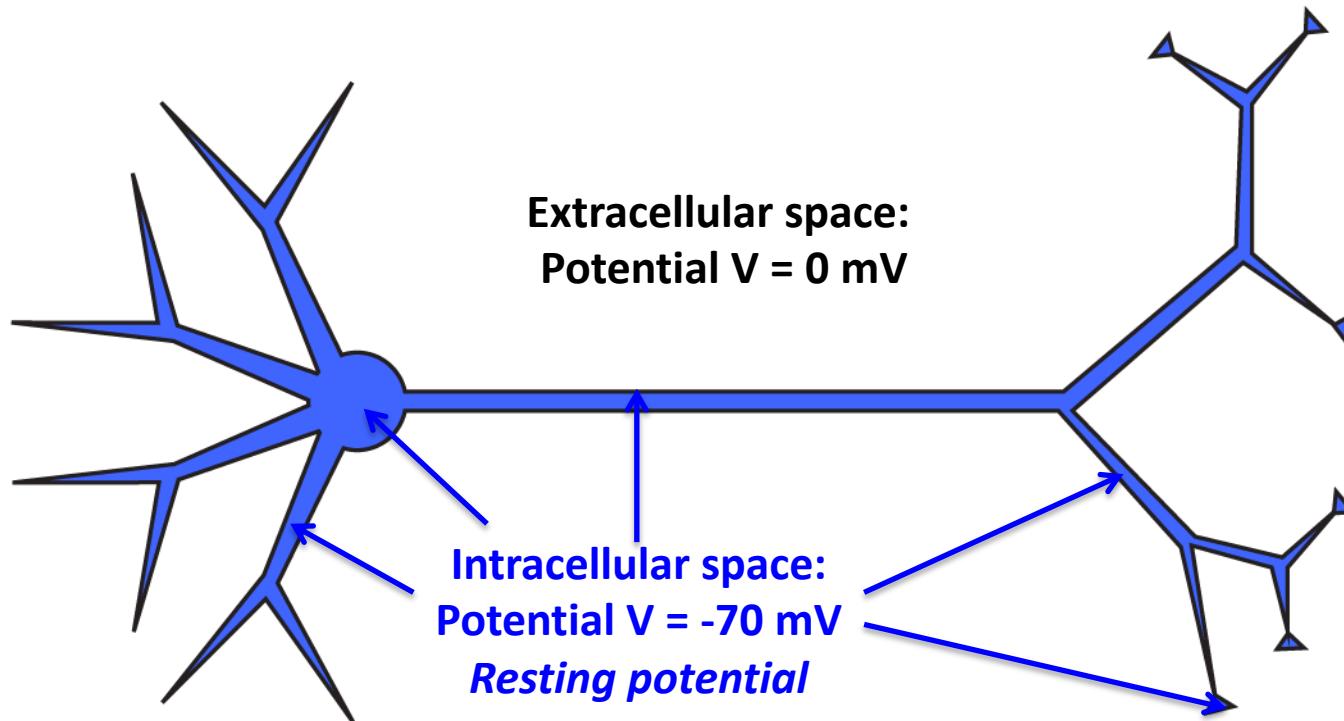




# Neurons

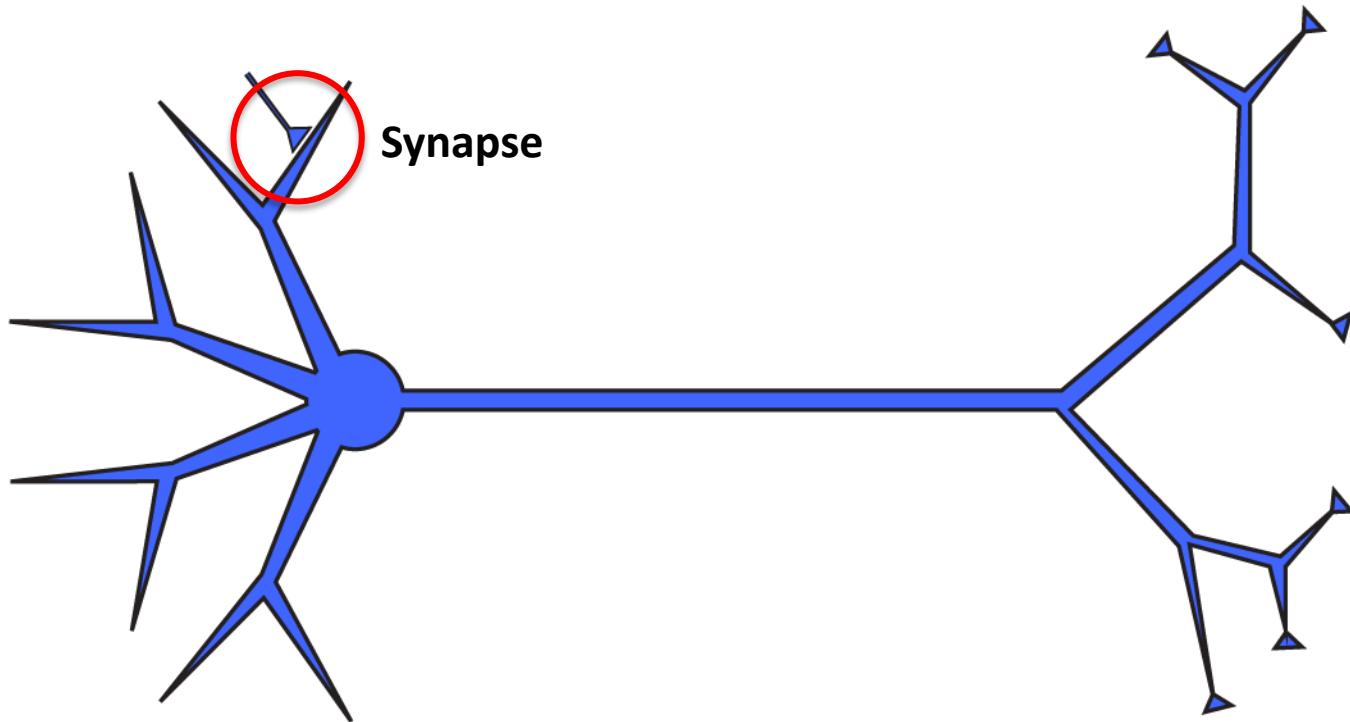


# Hyperpolarization

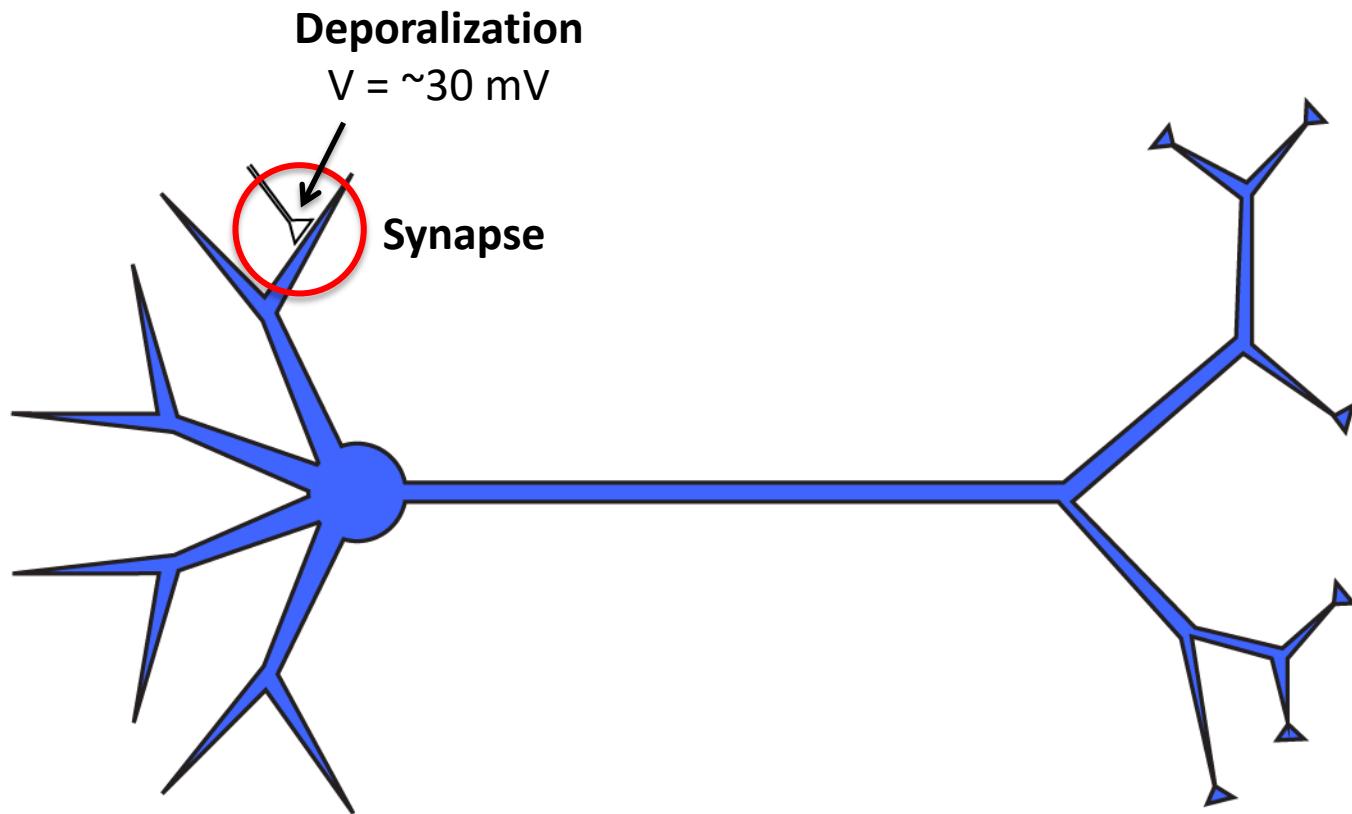


Like a **battery**  
(Nernst/GHK Equations)

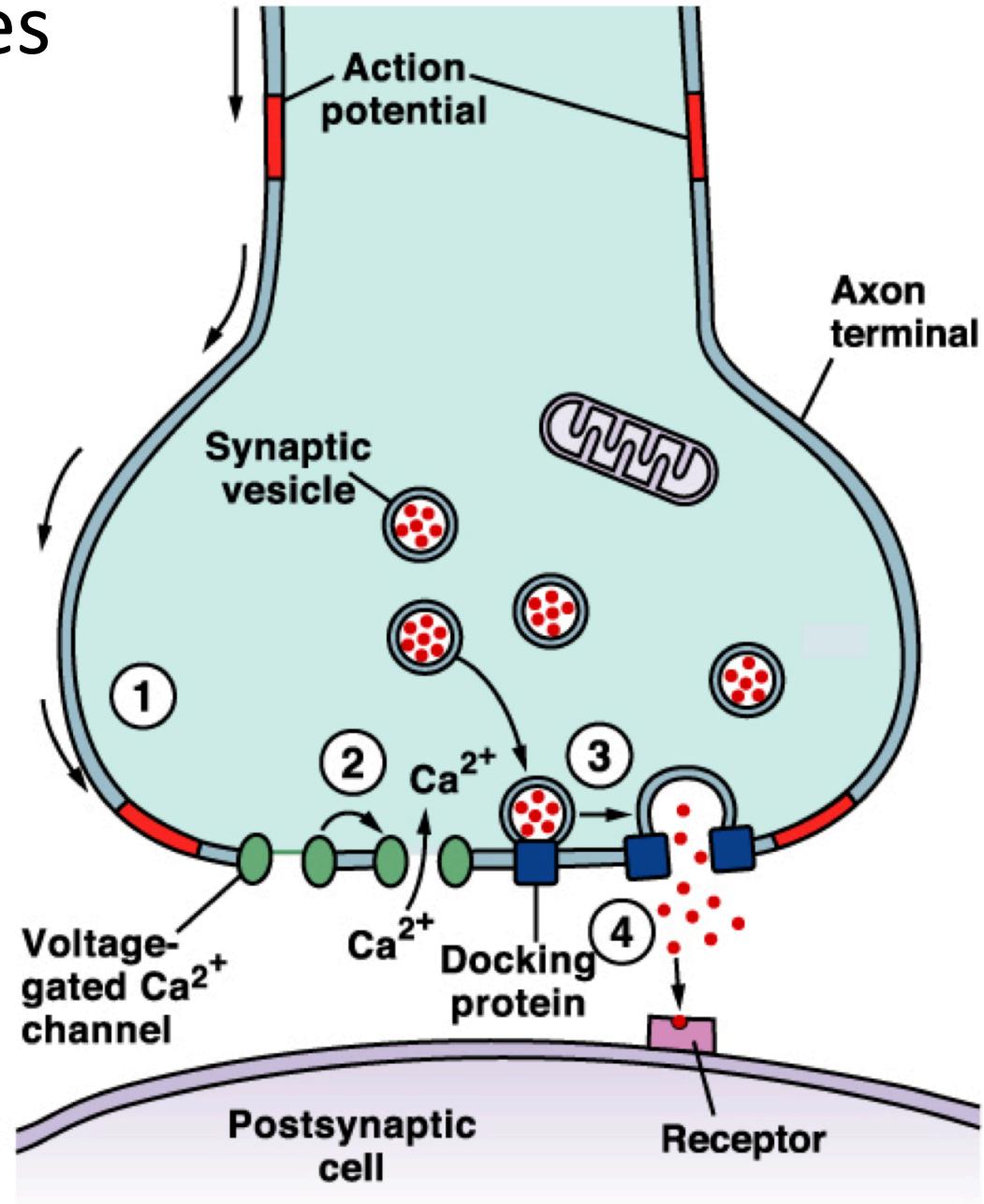
# Inputs into neurons



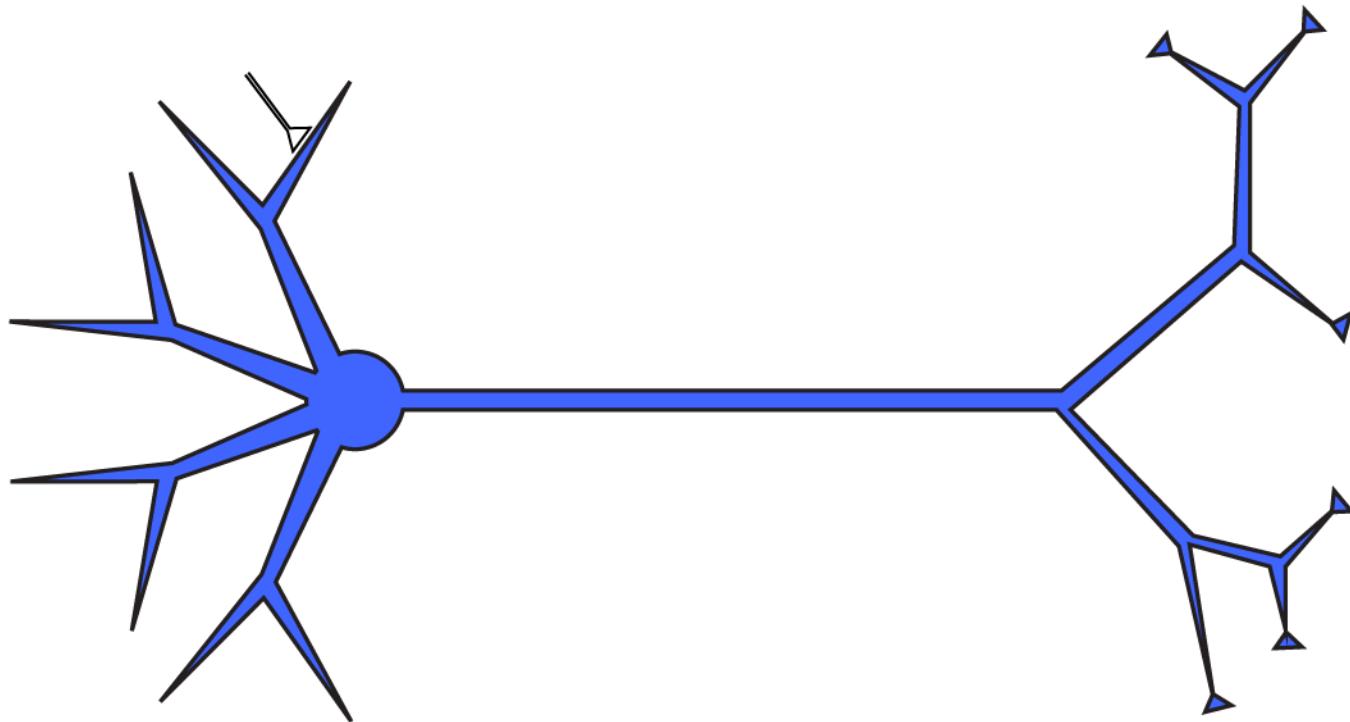
# Inputs into neurons



# Chemical synapses



# Synaptic currents

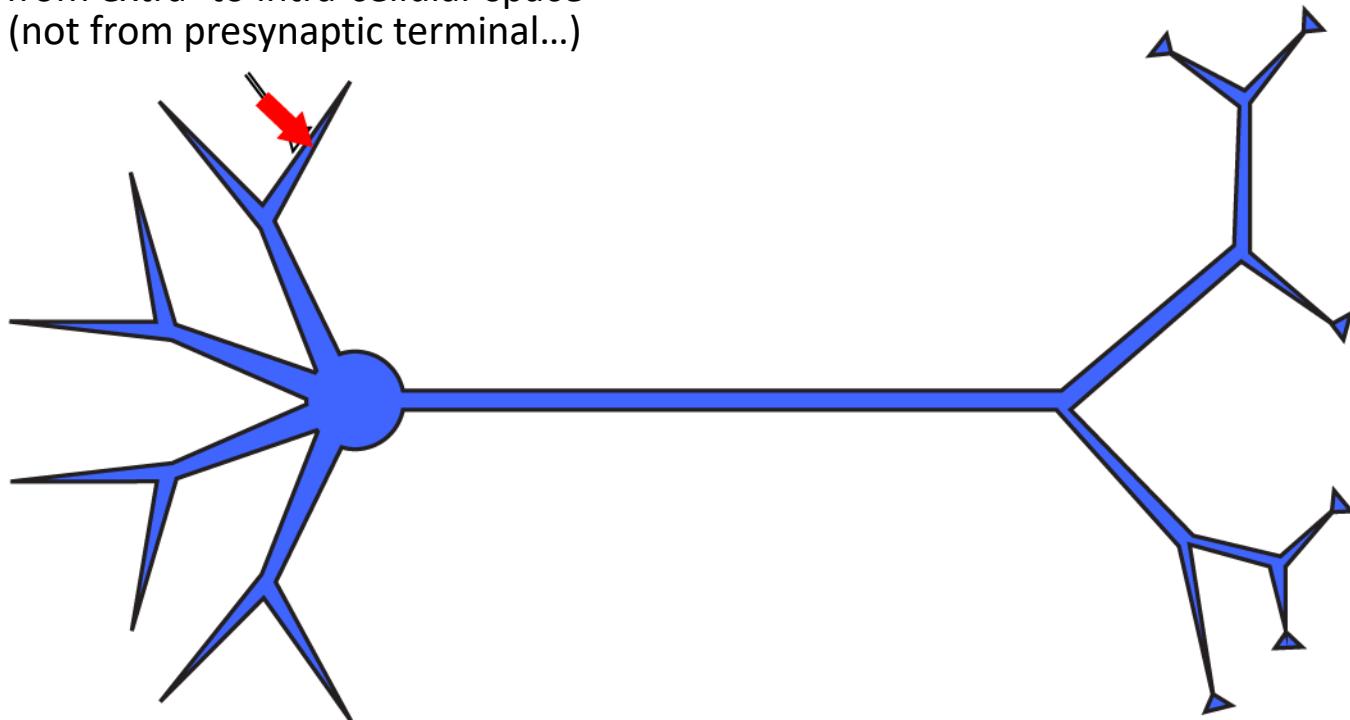


# Synaptic currents

## Excitatory current

positive charge

from extra- to intra-cellular space  
(not from presynaptic terminal...)

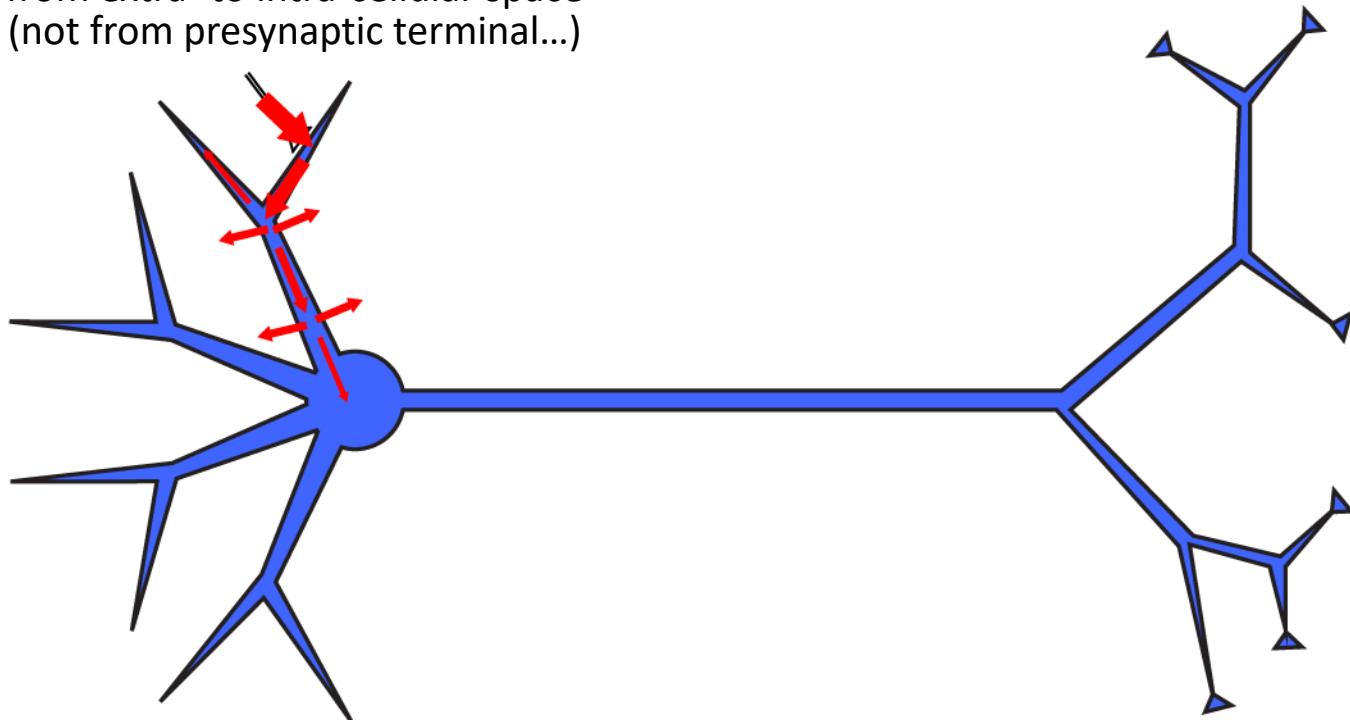


# Synaptic currents

## Excitatory current

positive charge

from extra- to intra-cellular space  
(not from presynaptic terminal...)

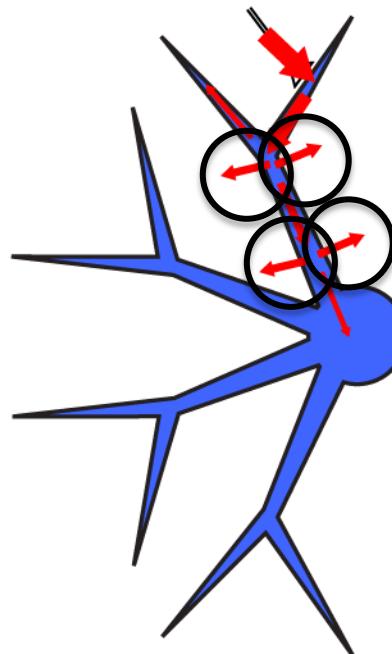


# Synaptic currents

## Excitatory current

positive charge

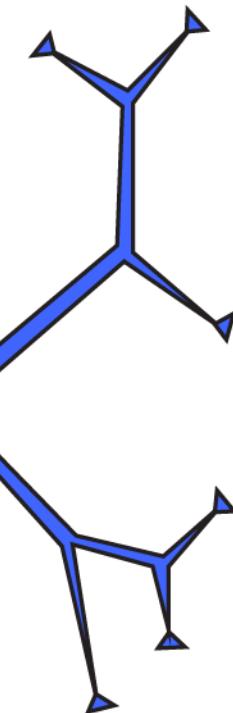
from extra- to intra-cellular space  
(not from presynaptic terminal...)



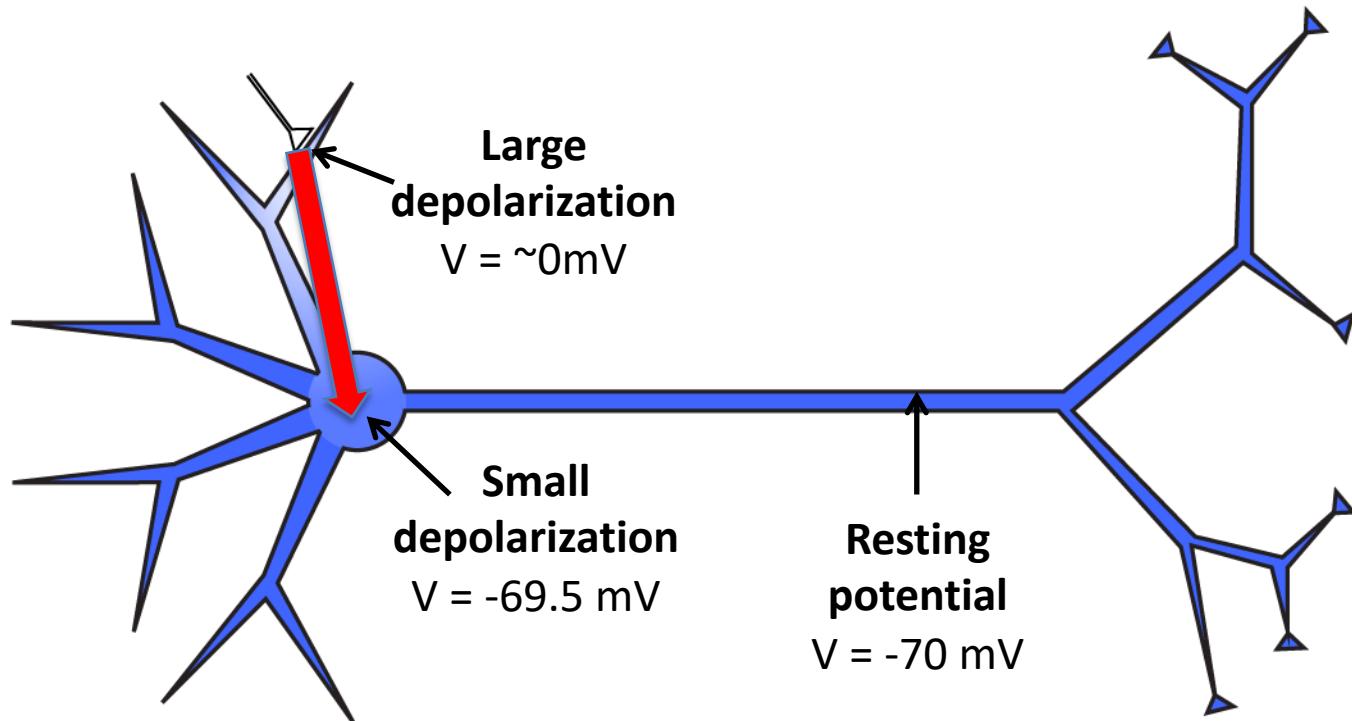
## Leak current

positive charge

leaves intra-cellular space  
reduces intra-cellular current

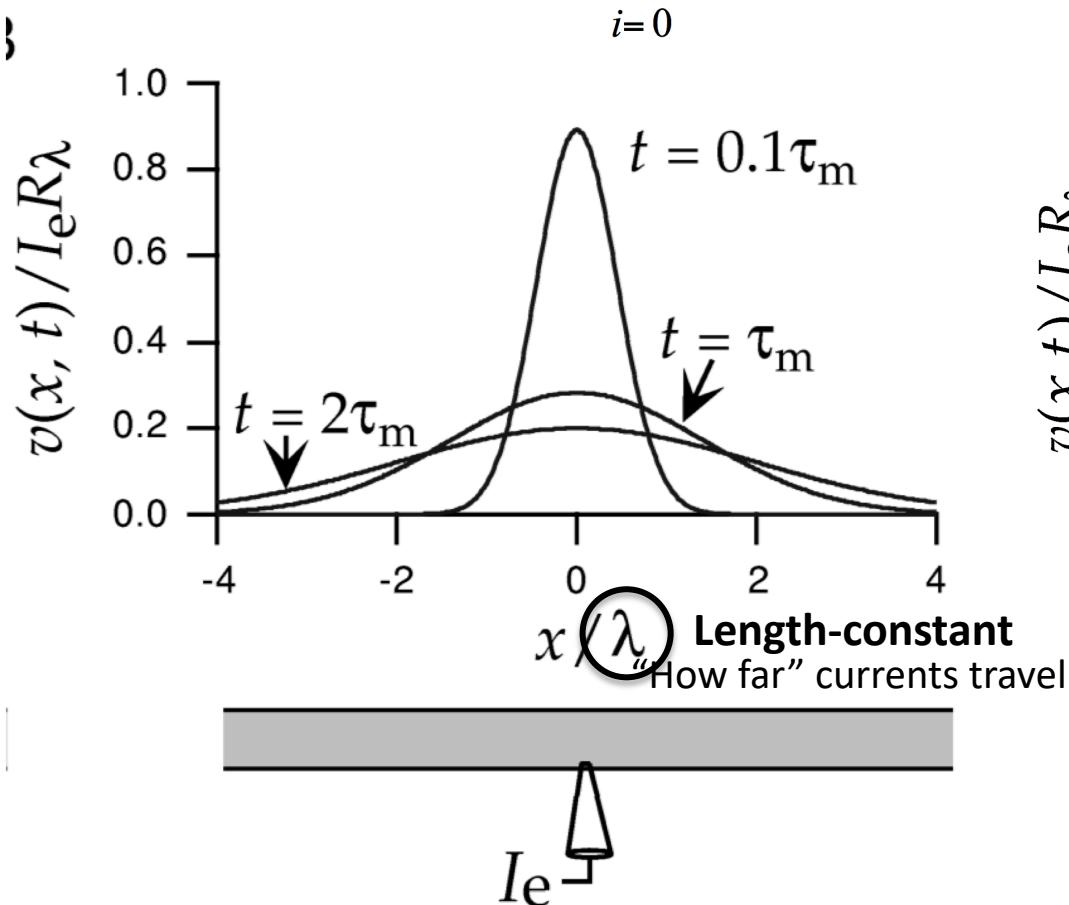


# Synaptic potential

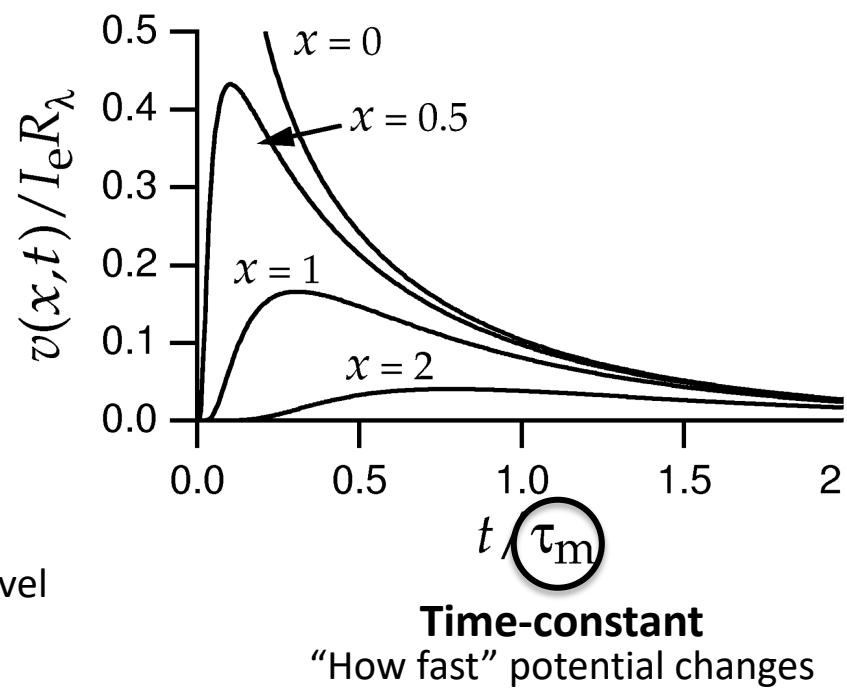


# Passive decay in an infinite cable

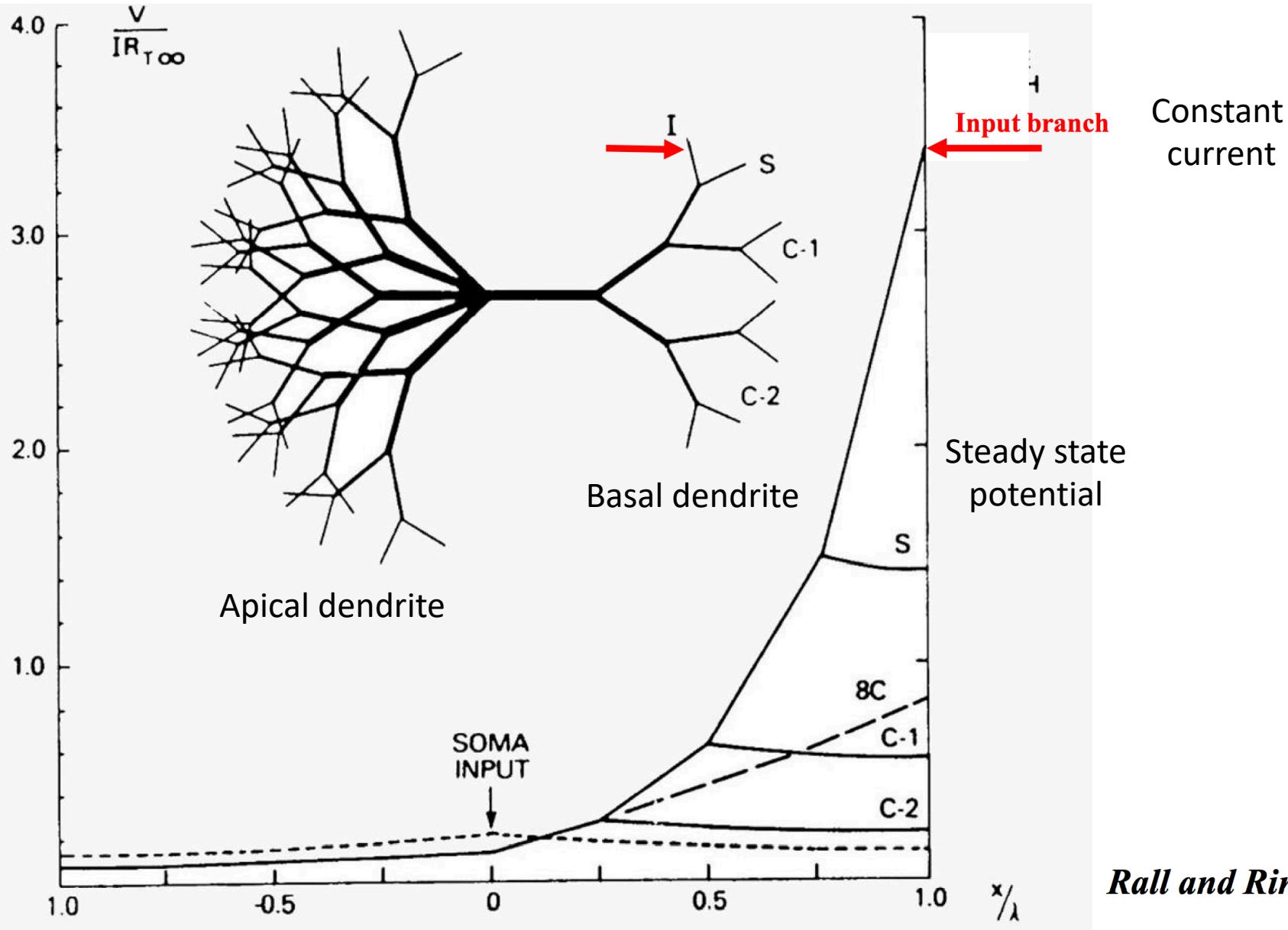
Spatial spread



Temporal spread

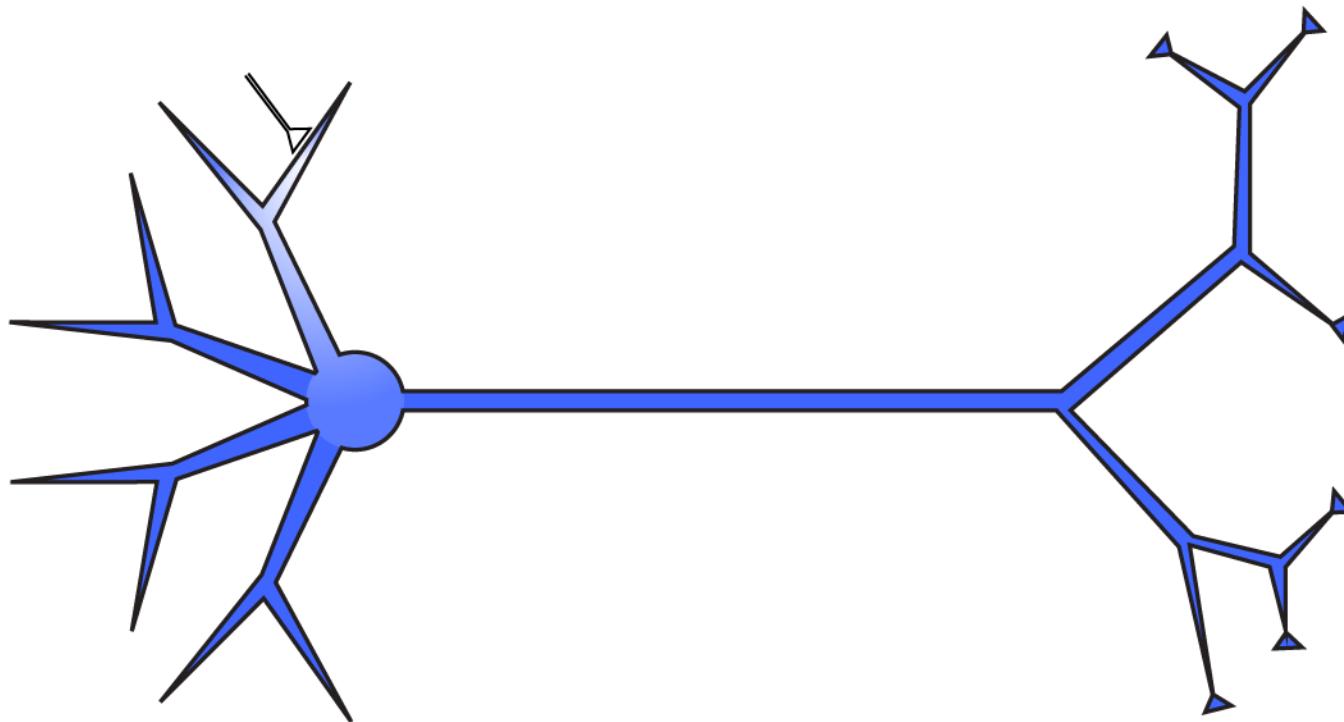


# Passive currents in a branching neuron

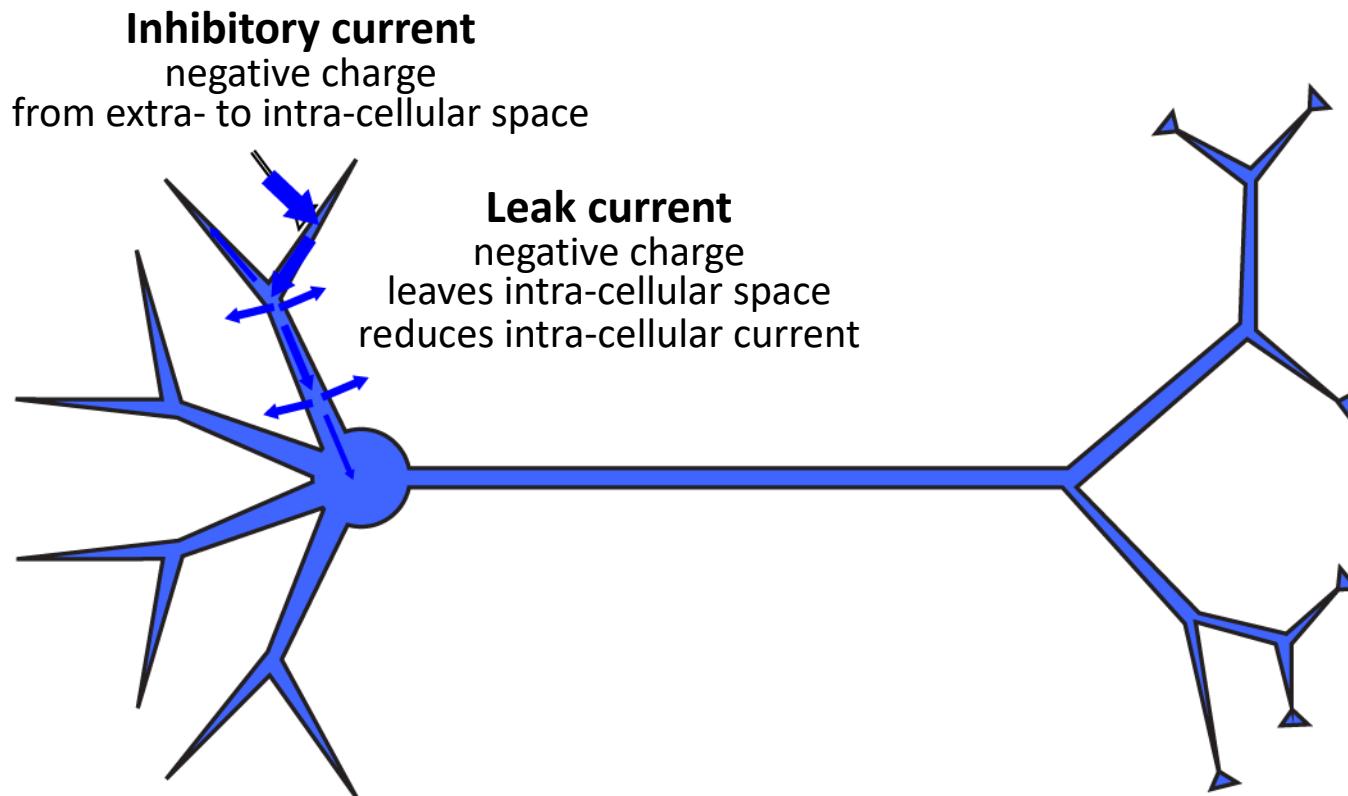


Rall and Rinzel, 1973

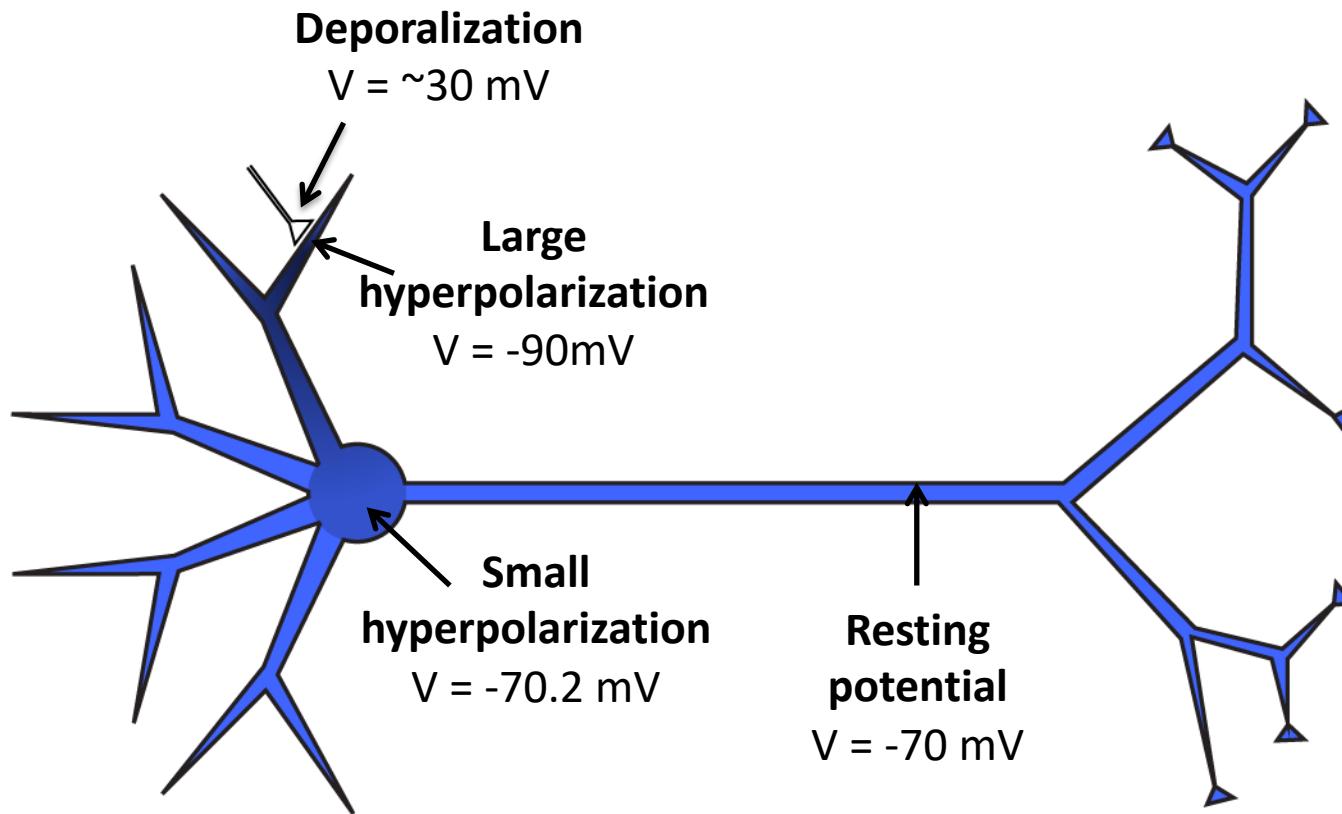
# Excitatory post-synaptic potential



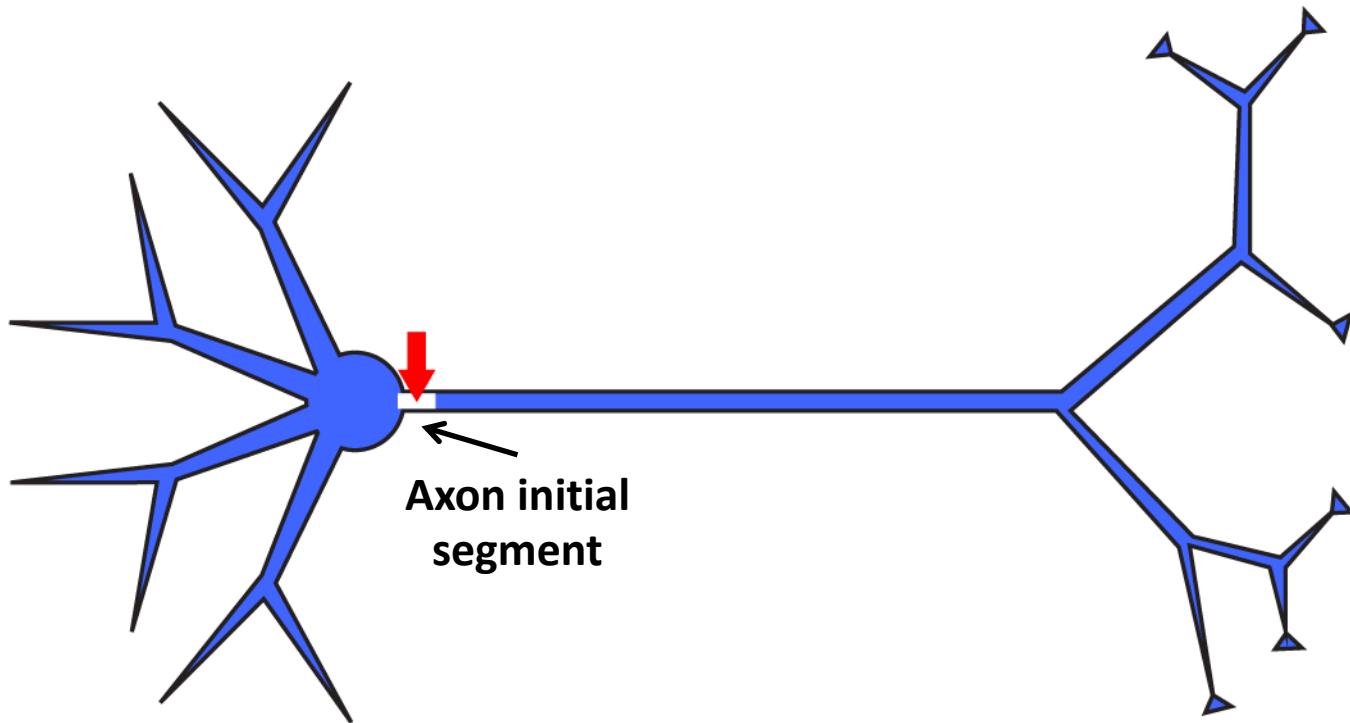
# Inhibitory post-synaptic current



# Inhibitory post-synaptic potential



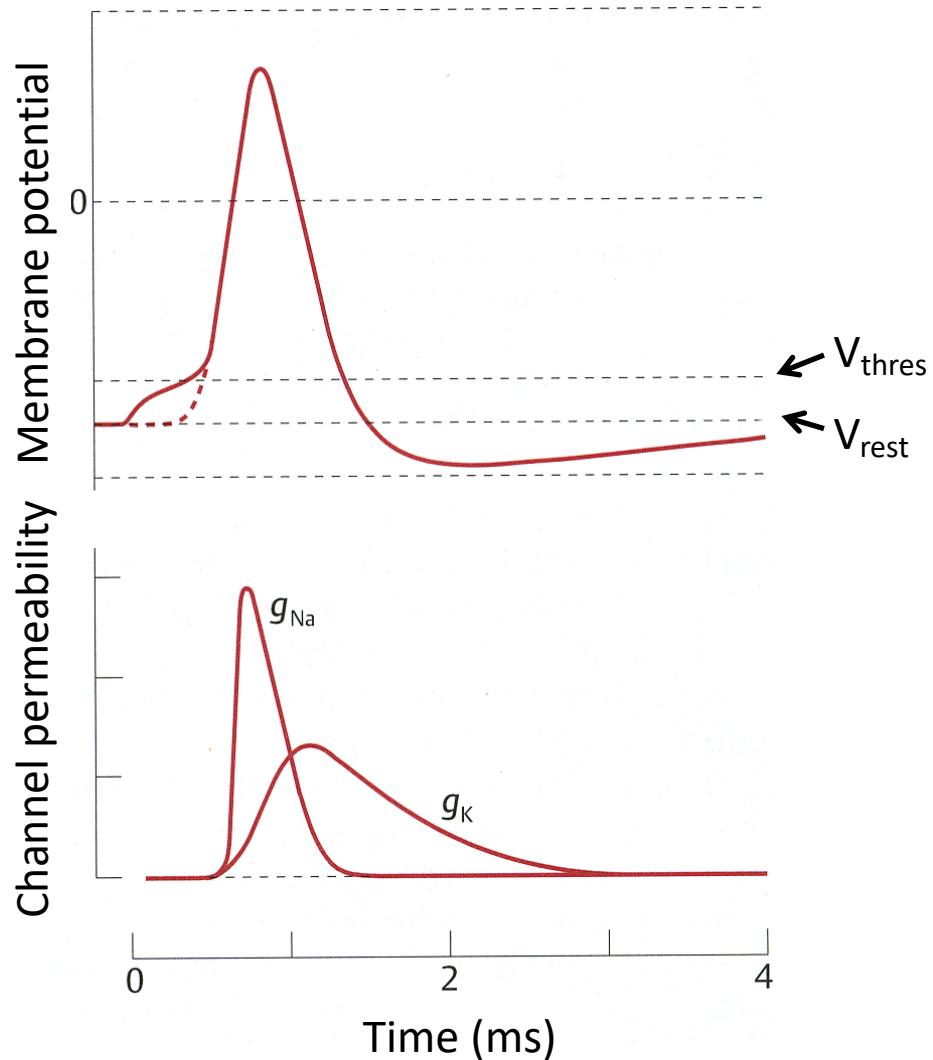
# Action potential



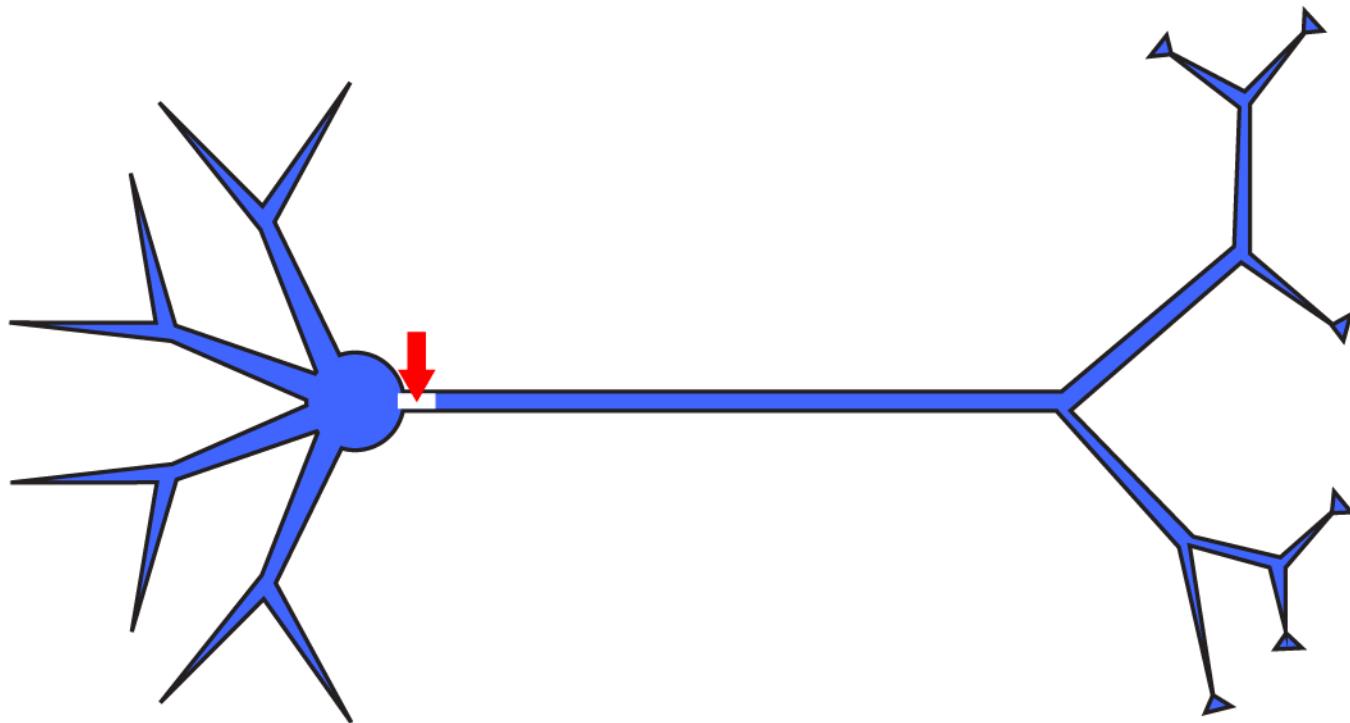
# Action potential

## Action potential

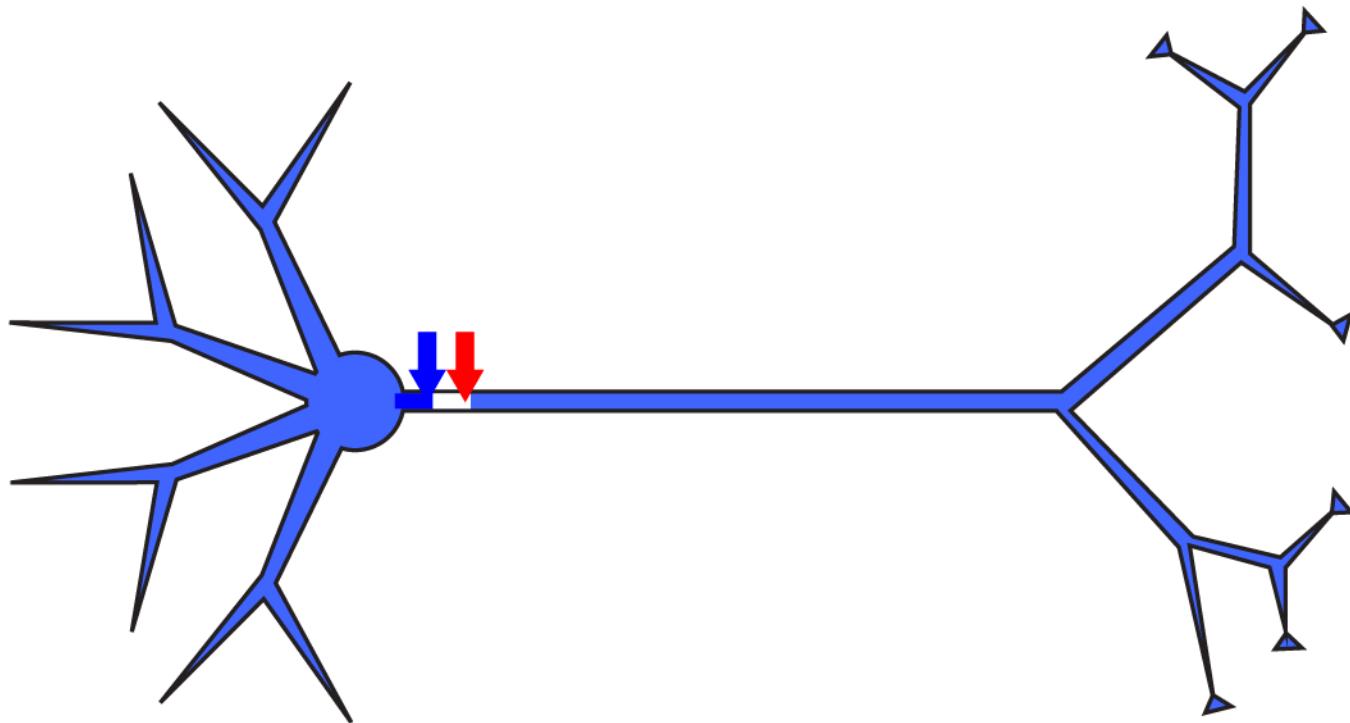
- Active regenerative process
- Duration: 1 – 2 ms
- All-or-none
- Amplitude to rate conversion.
- Components:
  - Depolarization
  - Overshoot (over 0 mV)
  - Repolarization/ Hyperpolarization
  - Refractory period



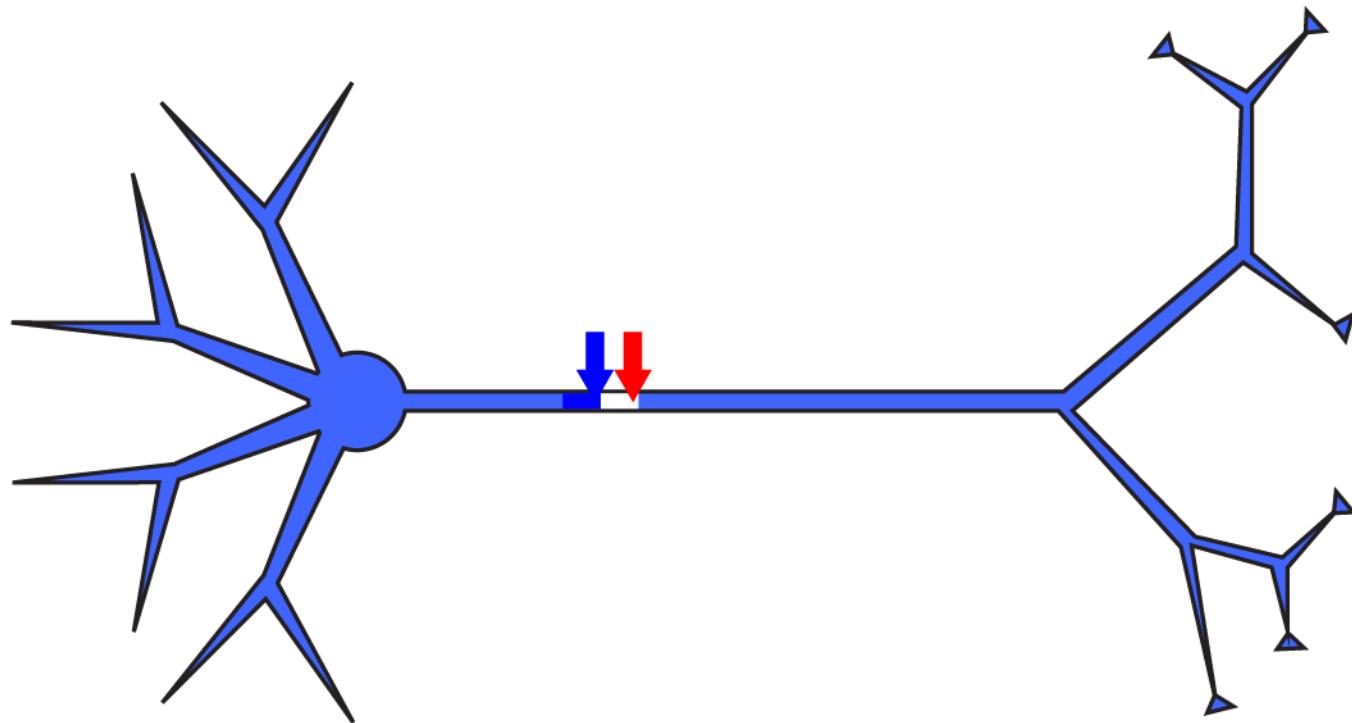
# Action potential propagation



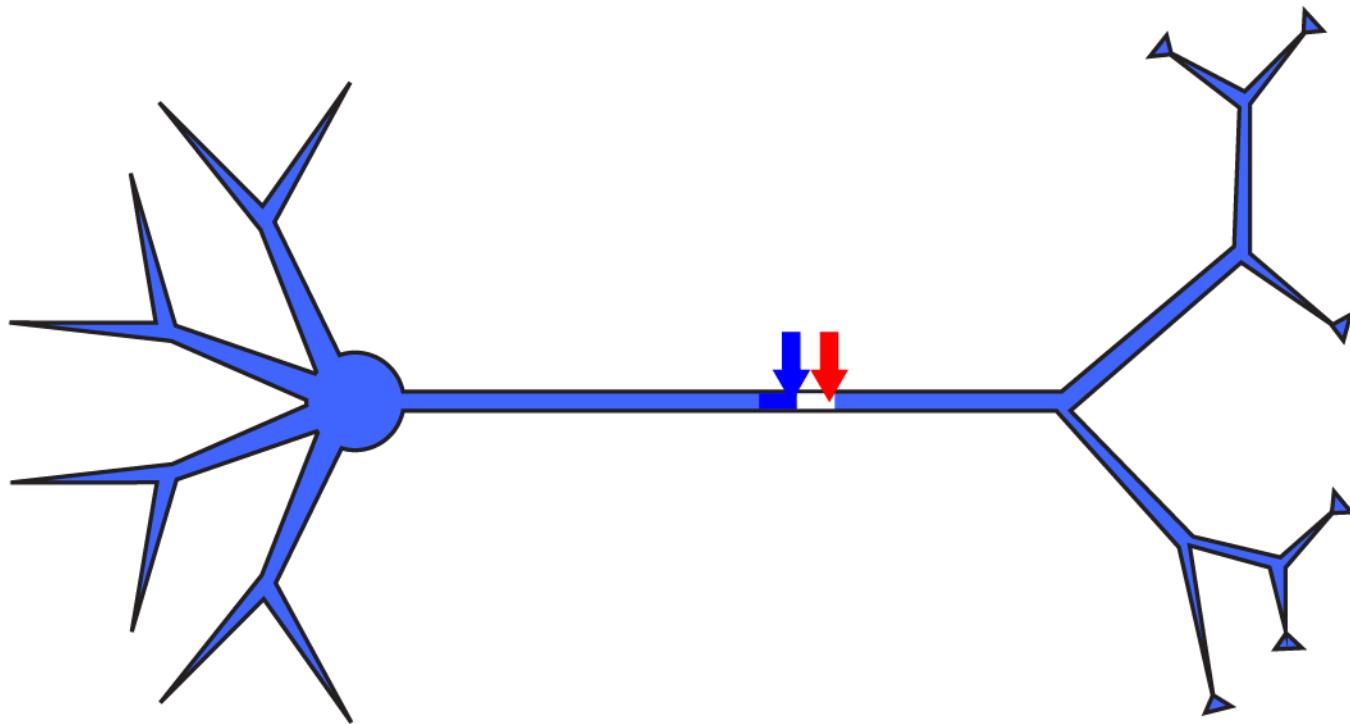
# Action potential propagation



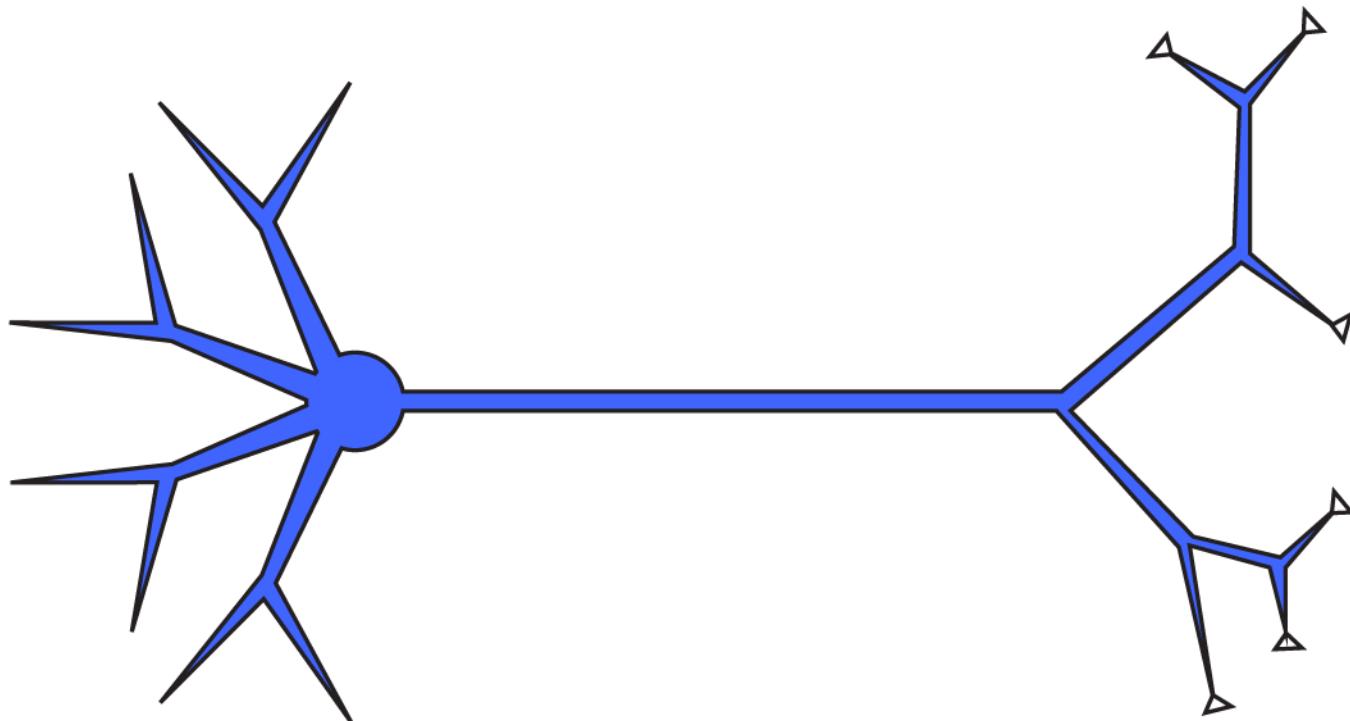
# Action potential propagation



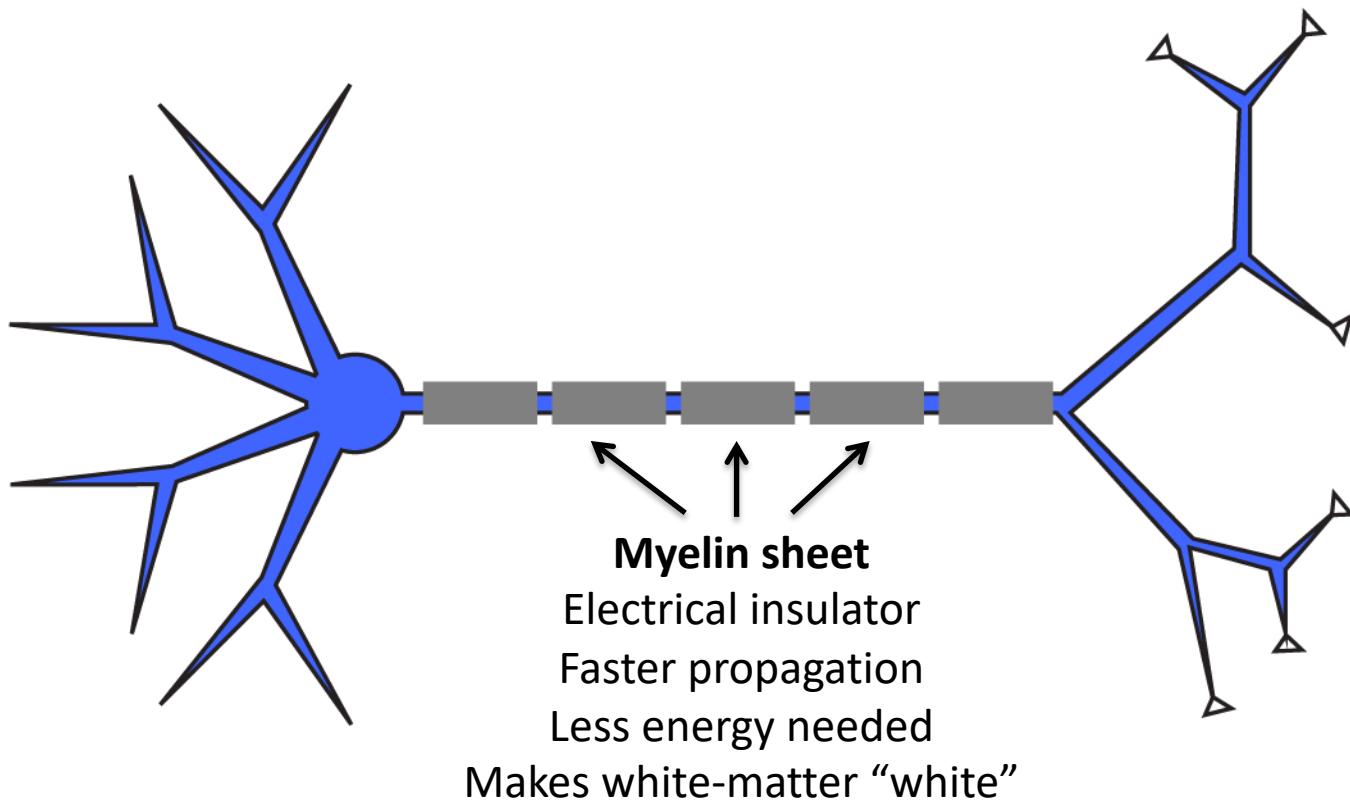
# Action potential propagation



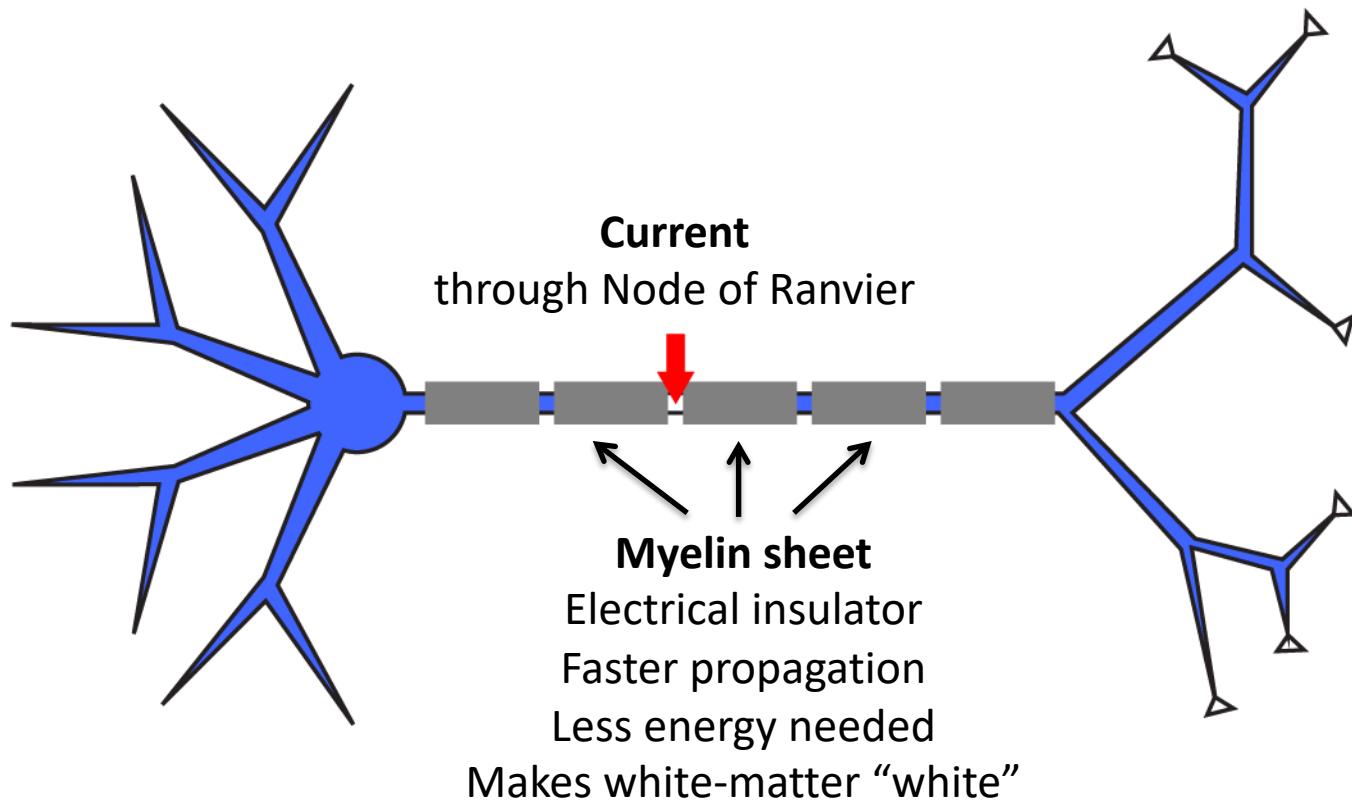
# Action potential propagation



# Myelinated axon

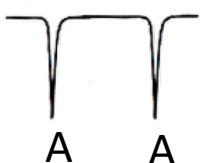
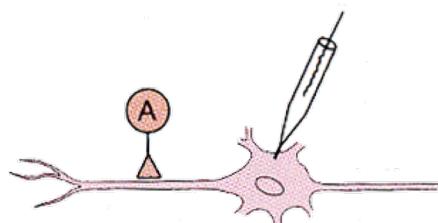


# Myelinated axon



# Summation of inputs

## Temporal summation



Postsynaptic current

Action potential

Long time-constant  
(100 ms)

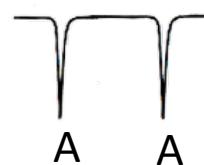
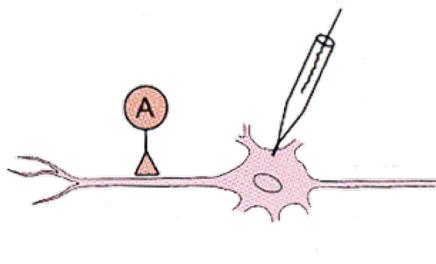
Threshold

Postsynaptic potential

Short time-constant  
(20 ms)

# Summation of inputs

## Temporal summation

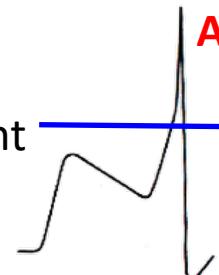


Postsynaptic current

Action potential

Long time-constant  
(100 ms)

Threshold

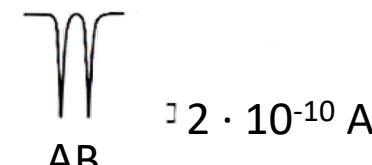
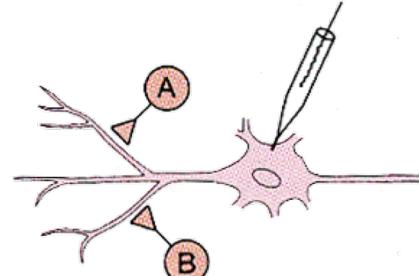


Postsynaptic potential

Short time-constant  
(20 ms)



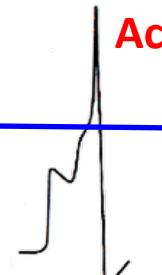
## Spatial summation



$2 \cdot 10^{-10} \text{ A}$

Action potential

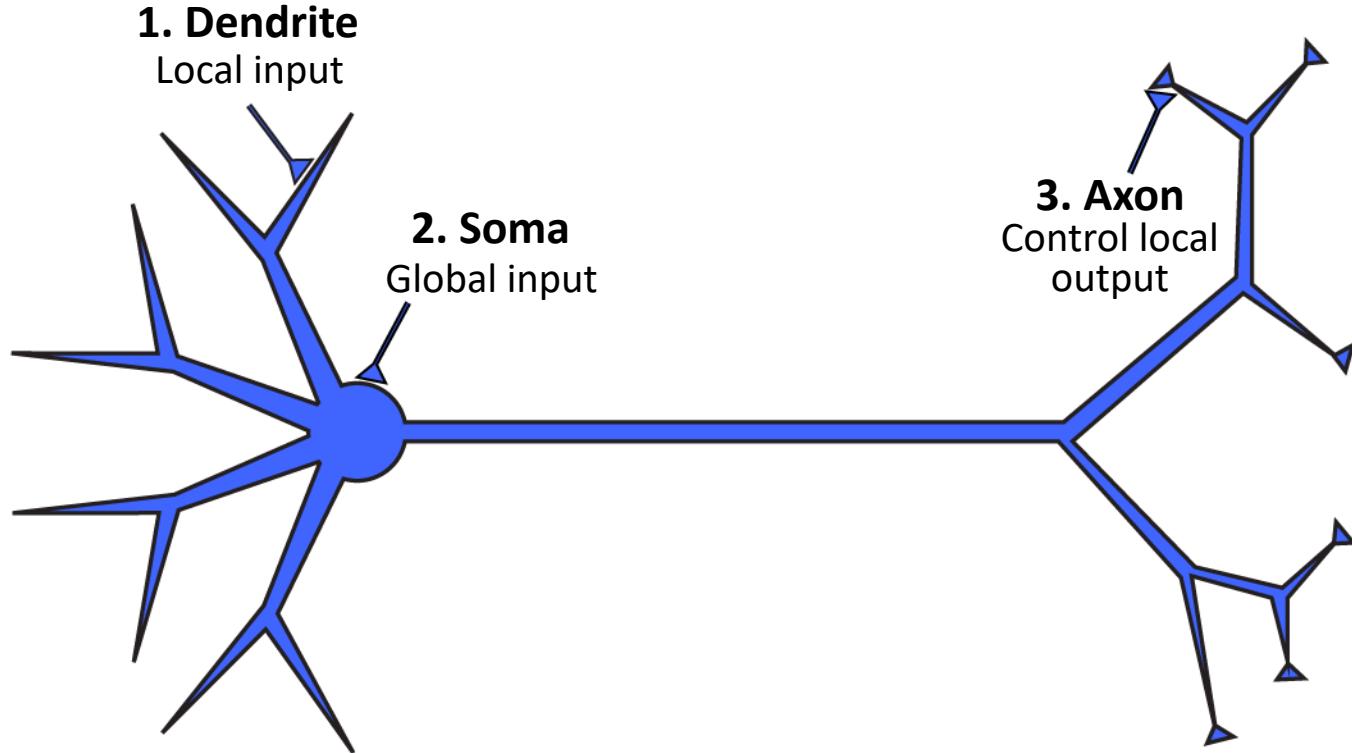
Long length-constant  
(1 mm)



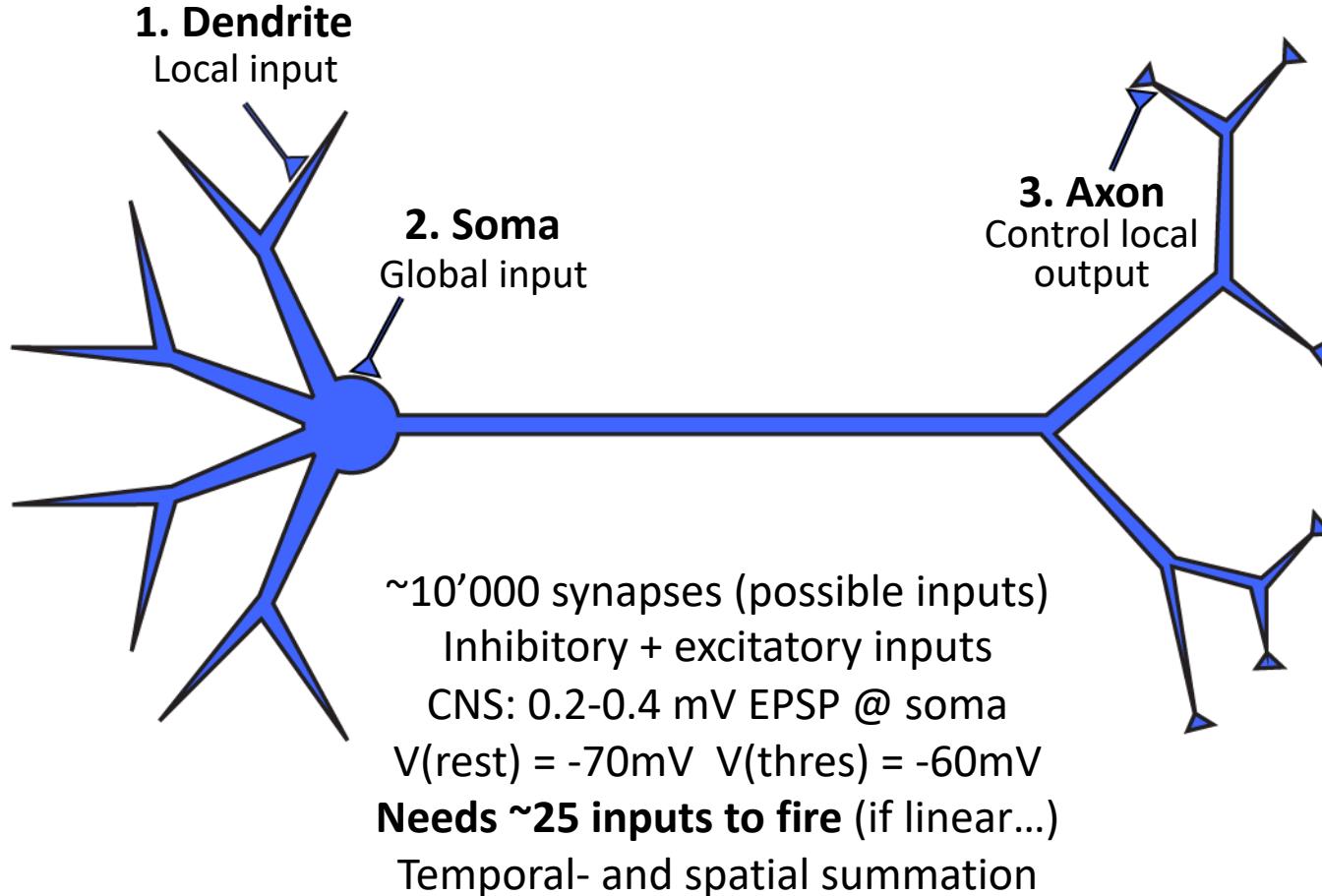
Short length-constant  
(0,33 mm)

$25 \text{ ms}$

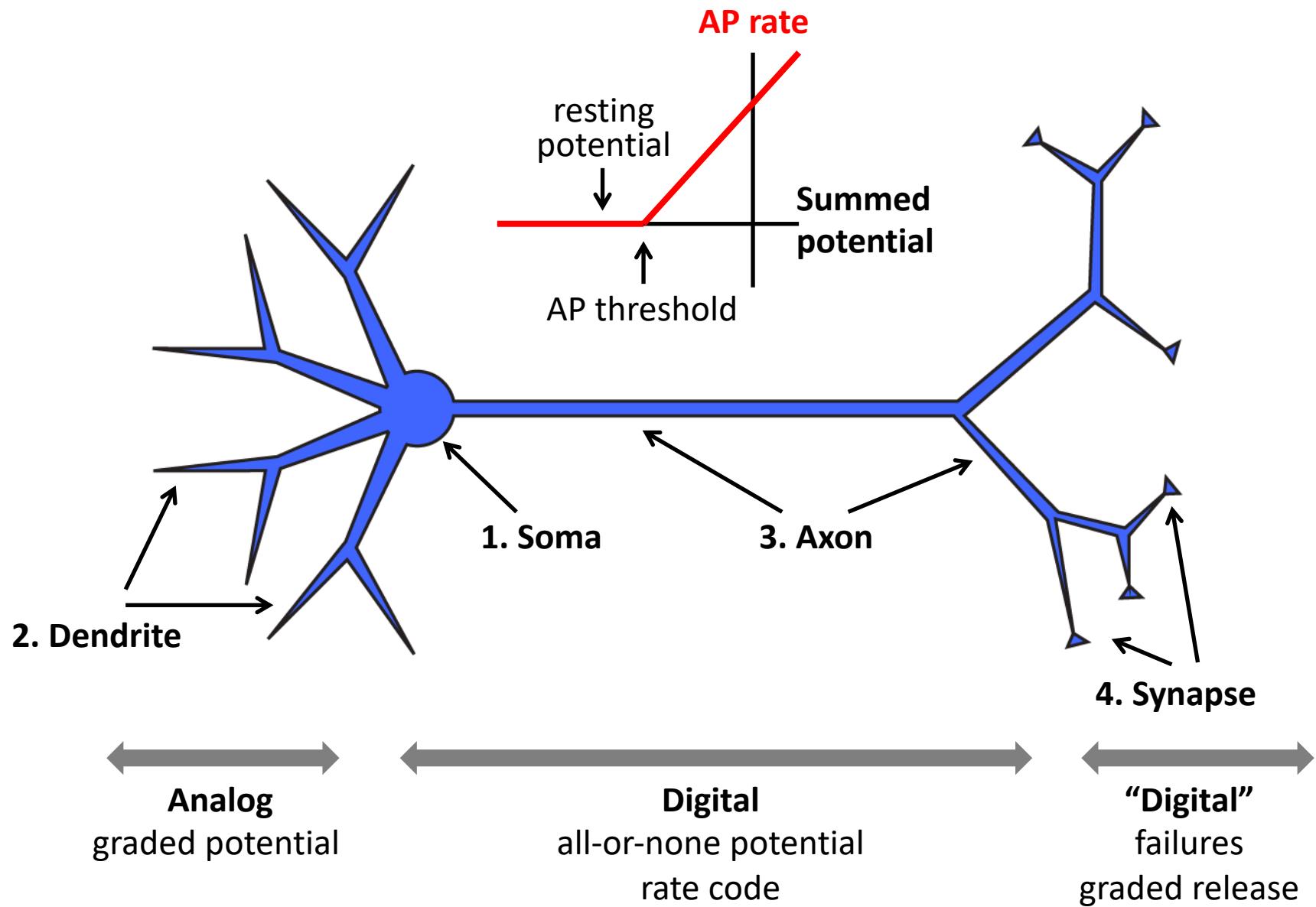
# Targets of synapses



# The big picture



# Single neuron computations



# Ionic currents depend on receptors

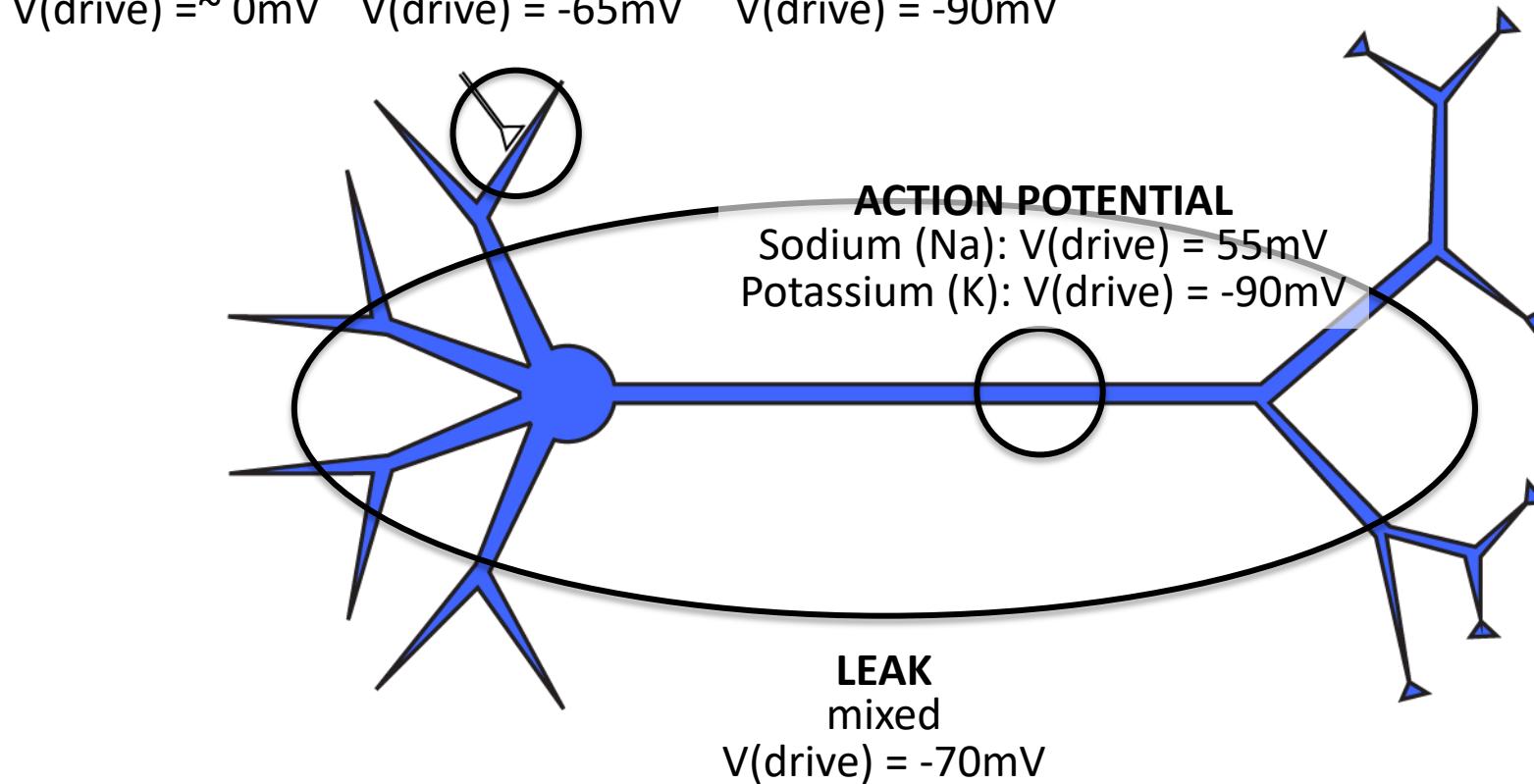
**EXCITATORY**

**AMPA/NMDA**  
mixed cation  
 $V(\text{drive}) = \sim 0\text{mV}$

**INHIBITORY**

**GABA A**  
Chloride ( $\text{Cl}^-$ )

**GABA B**  
Potassium (K)  
 $V(\text{drive}) = -90\text{mV}$



# Ionic currents depend on receptors

EXCITATORY	Valium (agonist)	INHIBITORY
<b>AMPA/NMDA</b> mixed cation	<b>GABA A</b> Chloride ( $\text{Cl}^-$ )	<b>GABA B</b> Potassium (K)
$V(\text{drive}) = \sim 0\text{mV}$	$V(\text{drive}) = -65\text{mV}$	$V(\text{drive}) = -90\text{mV}$
Ketamine (antagonist)		

