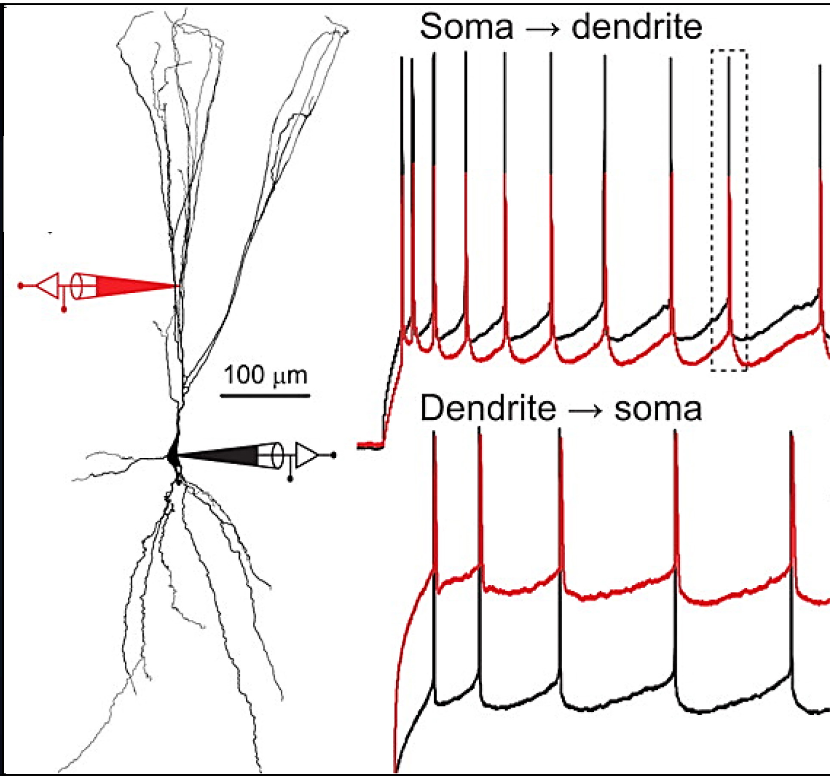
Chapter 10: Propagated Signaling – The Action Potential



Passive vs. Active Currents

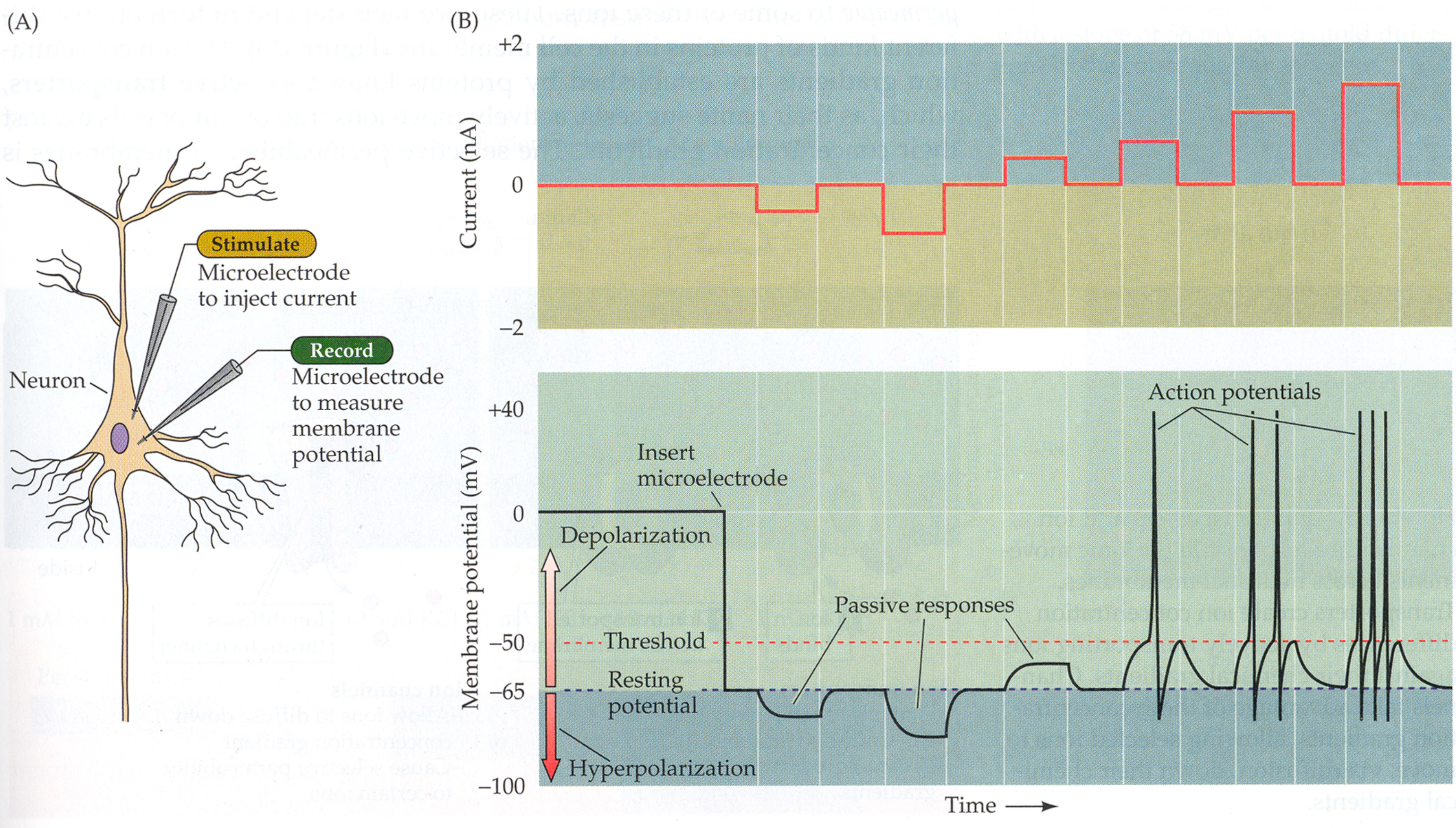
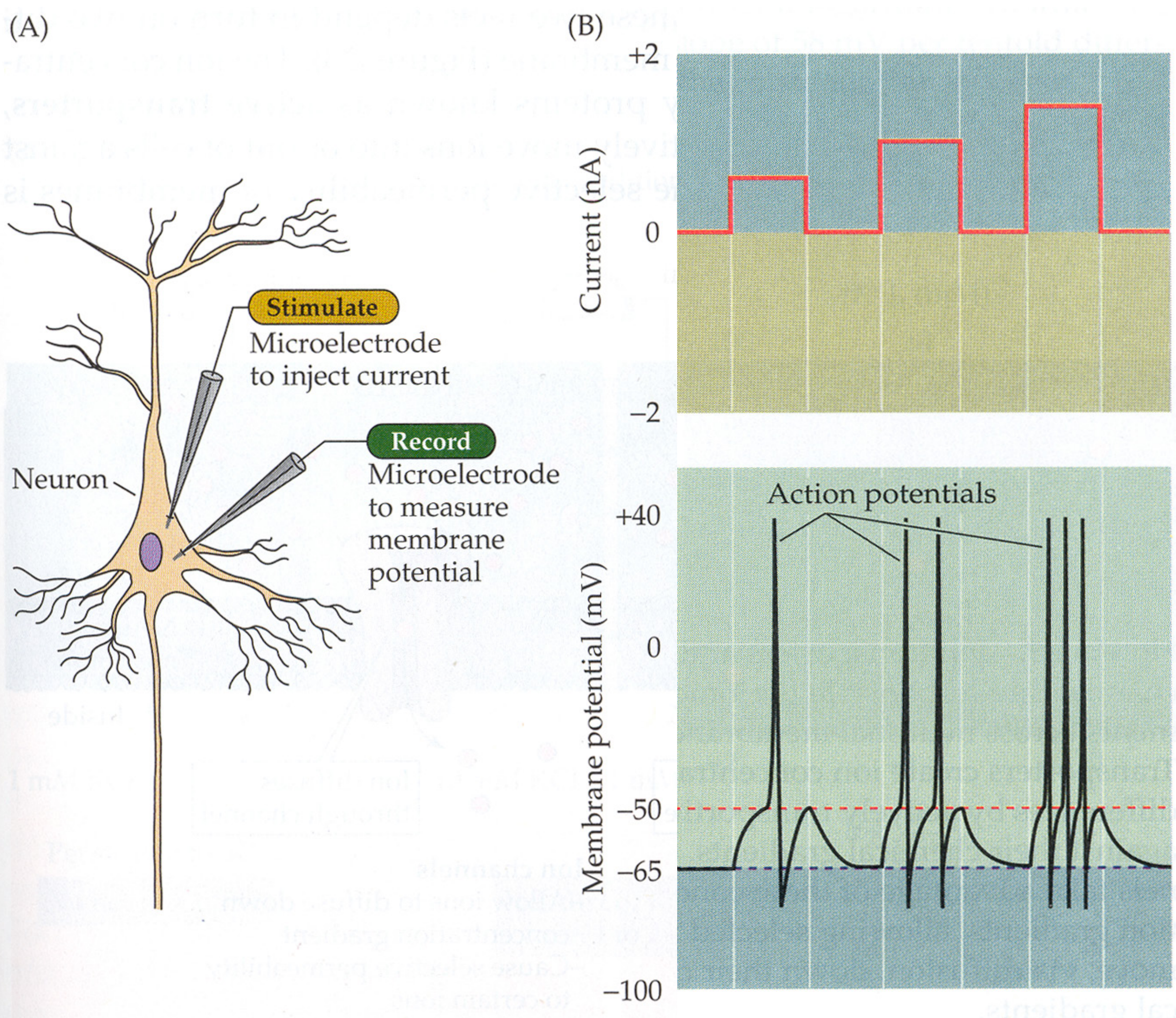


Figure 2.2, Purves

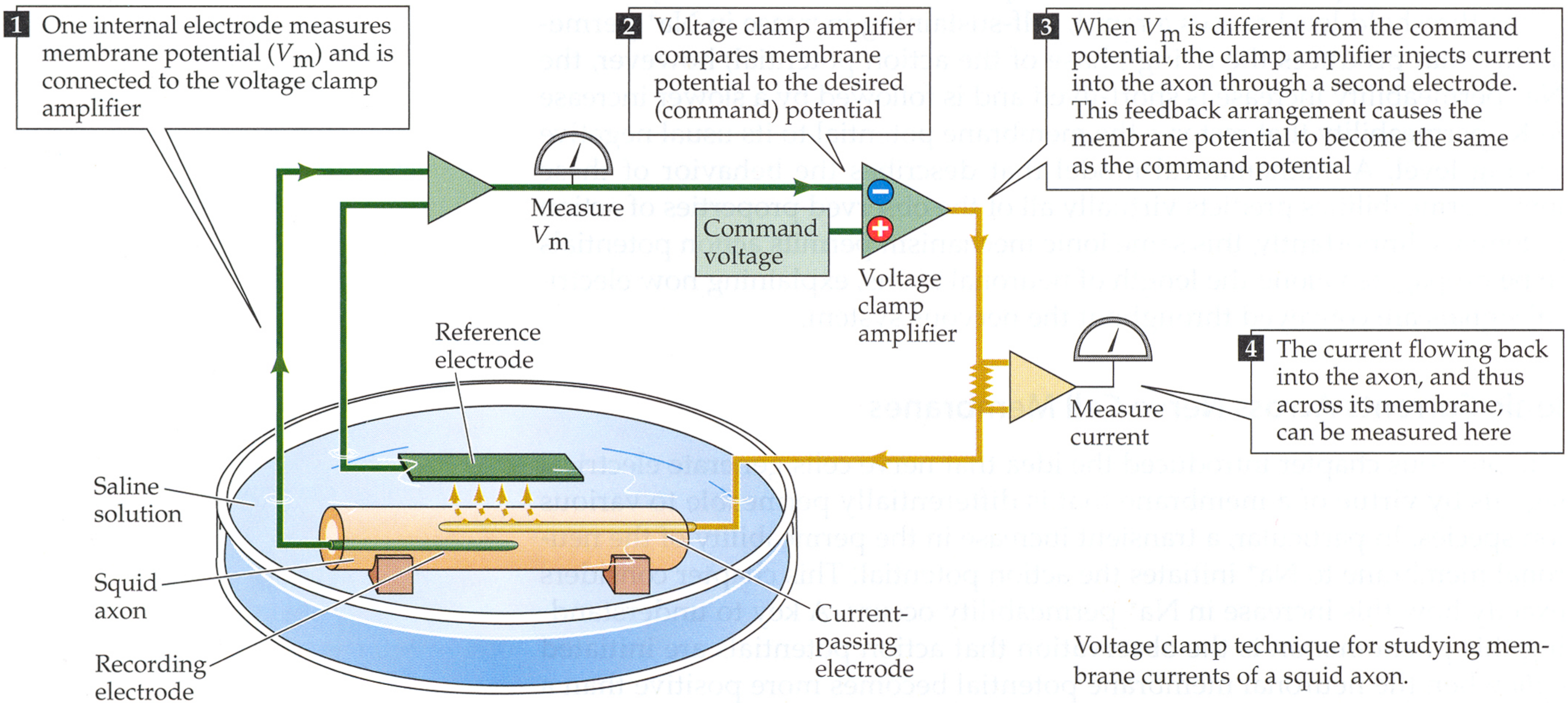
Properties of Action Potentials



- Initiated when V_m reaches threshold
- All-or-none amplitude
- Conducted down the axon without decrement (regenerative)
- Refractory period

Figure 2.2, Purves

Voltage Clamp



Voltage clamp technique for studying membrane currents of a squid axon.

Early Voltage Clamp Data – Hodgkin & Huxley

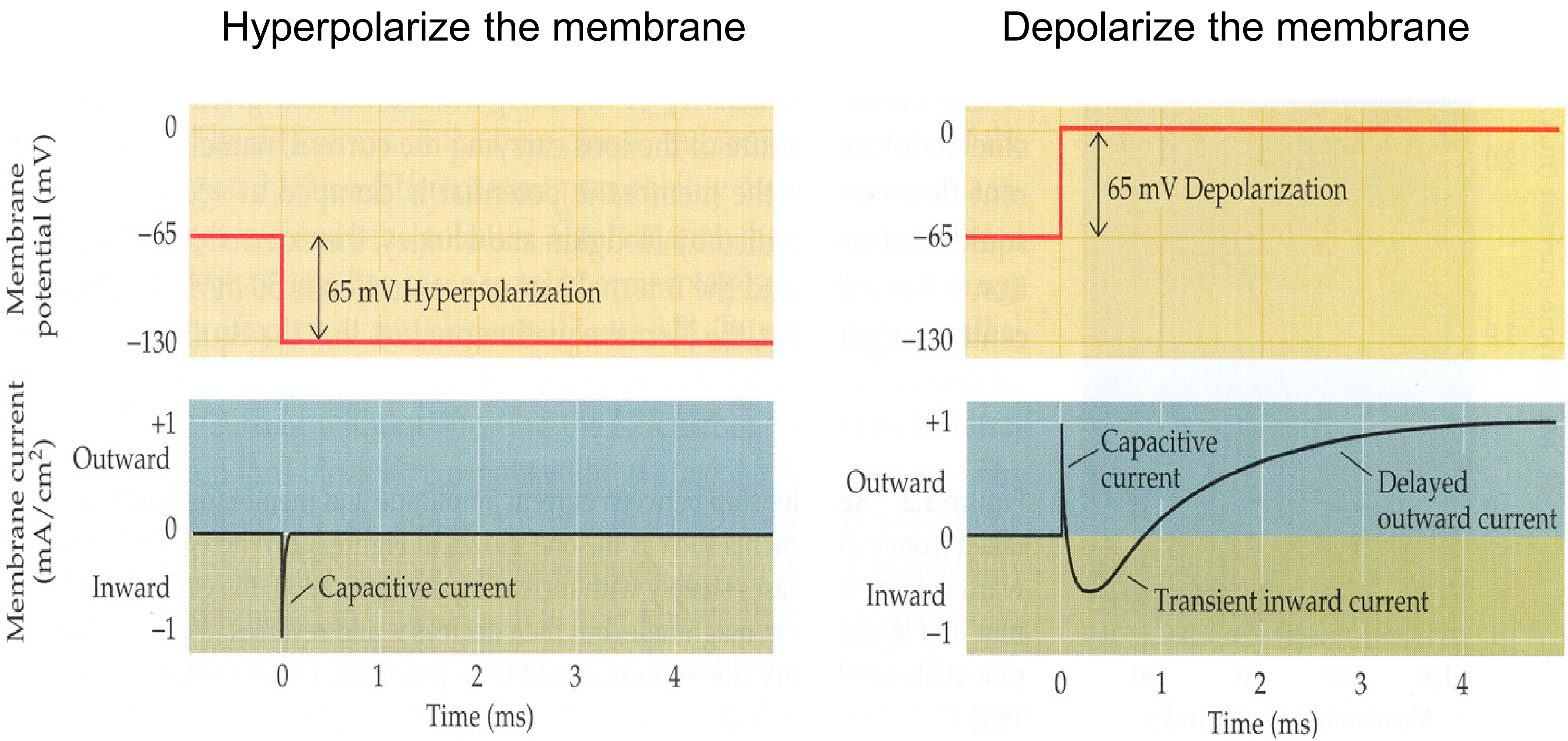
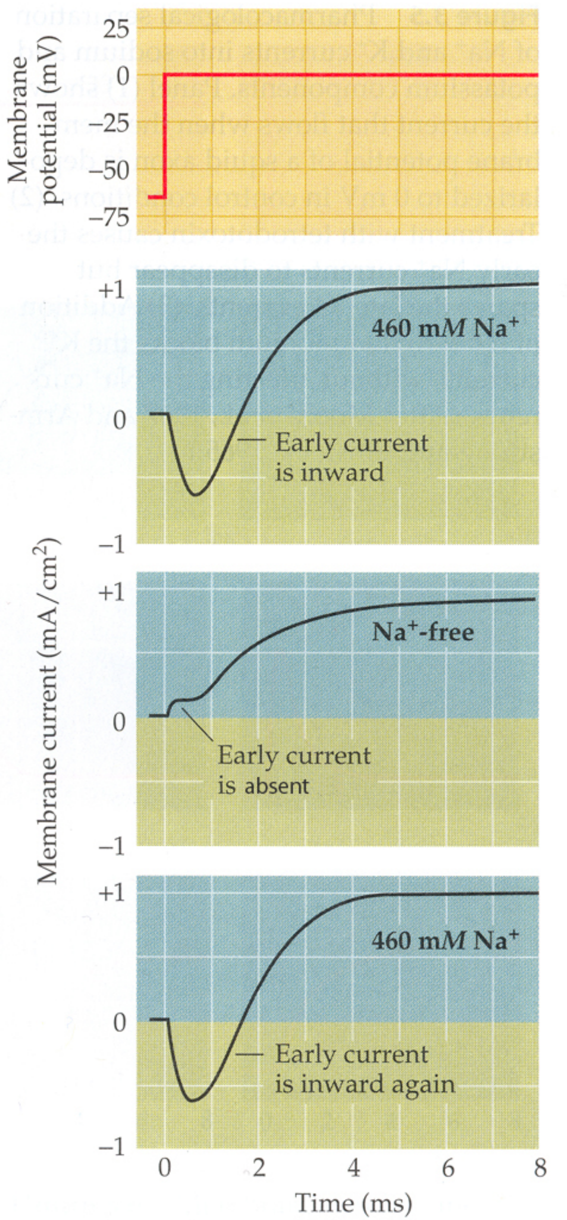


Figure 3.1, Purves

Early Voltage Clamp Data – Hodgkin & Huxley



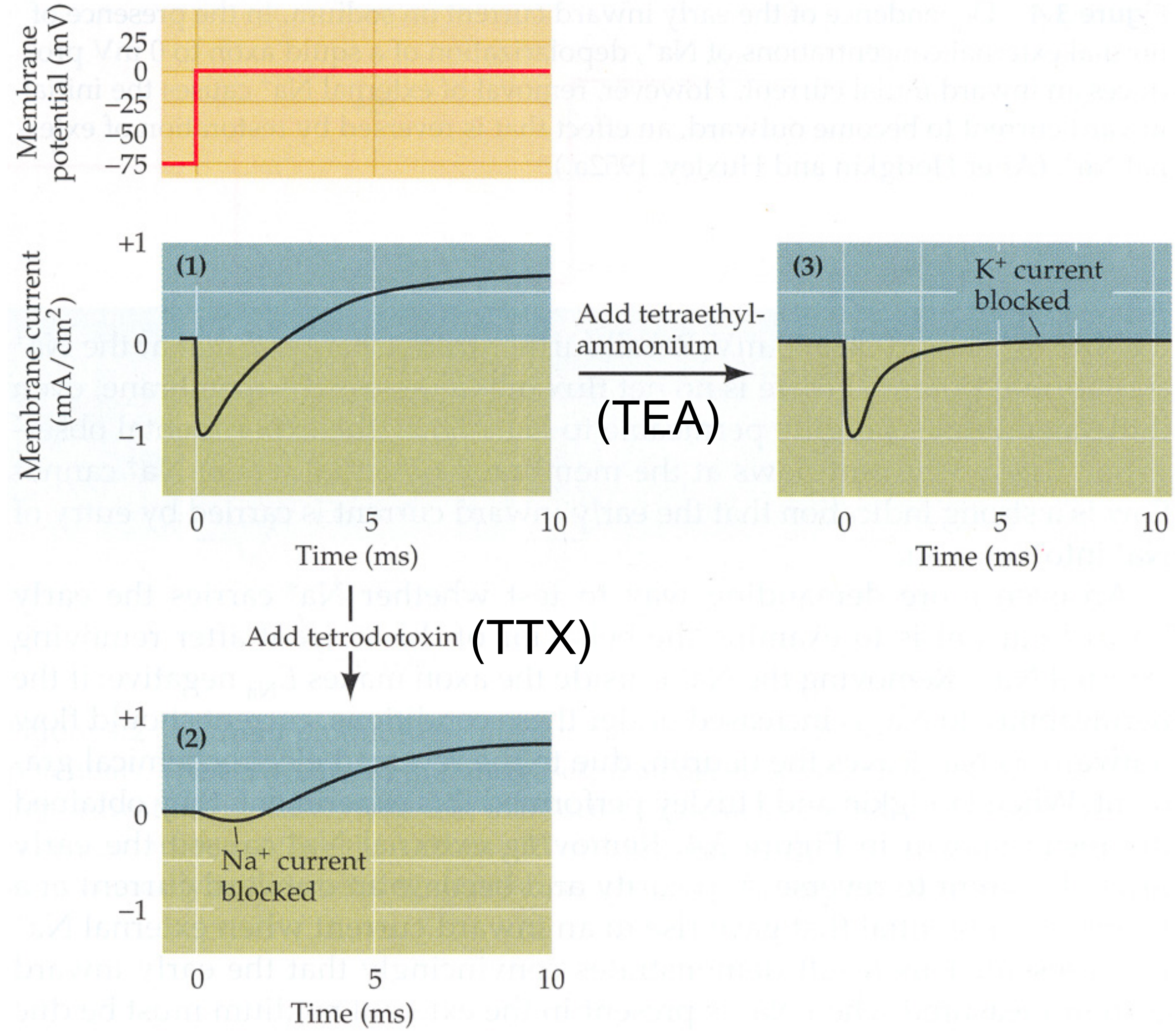


Figure 23.4 and 3.5, Purves

Hodgkin & Huxley's Conclusions

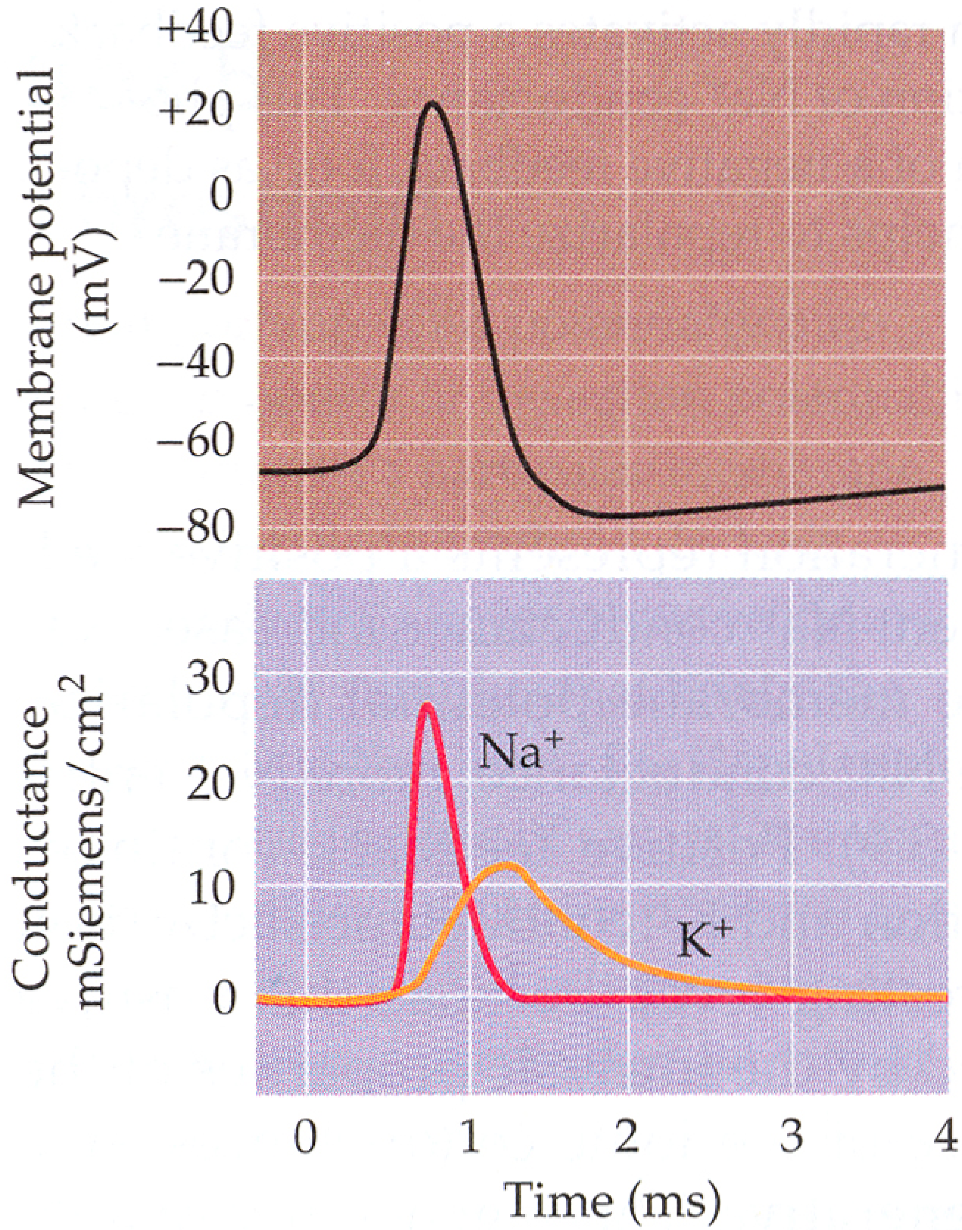
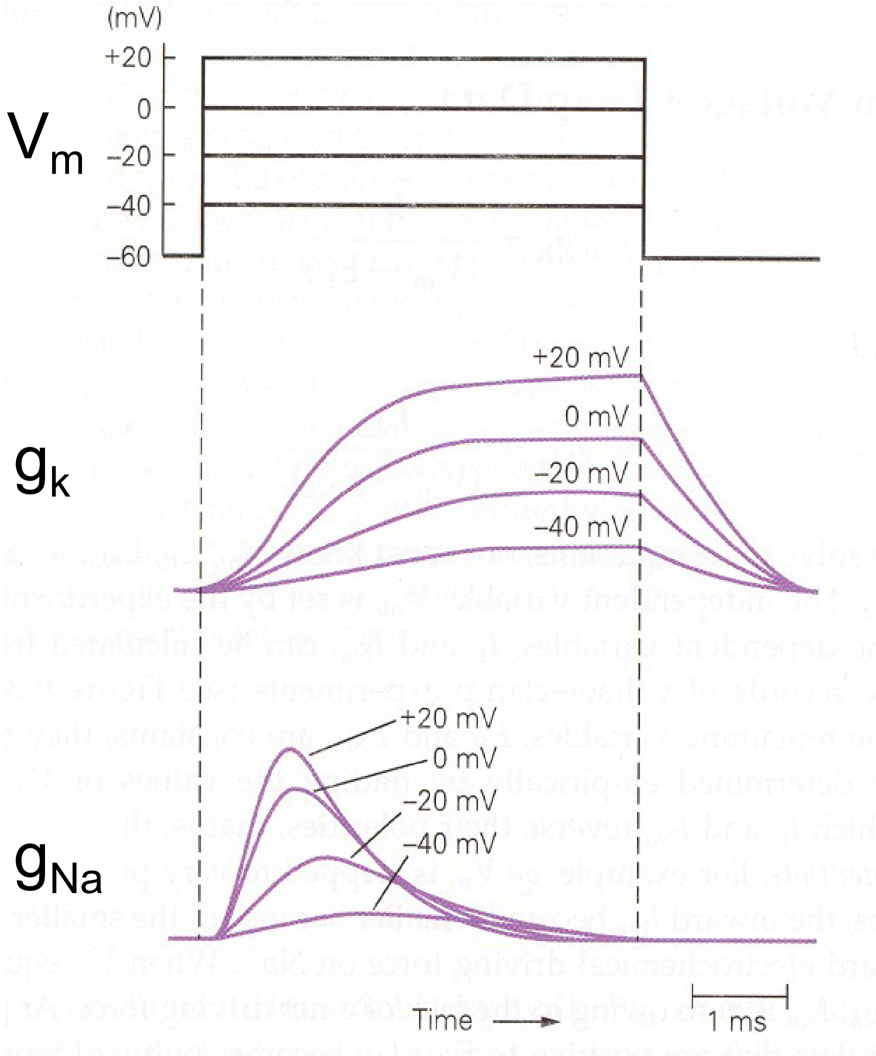
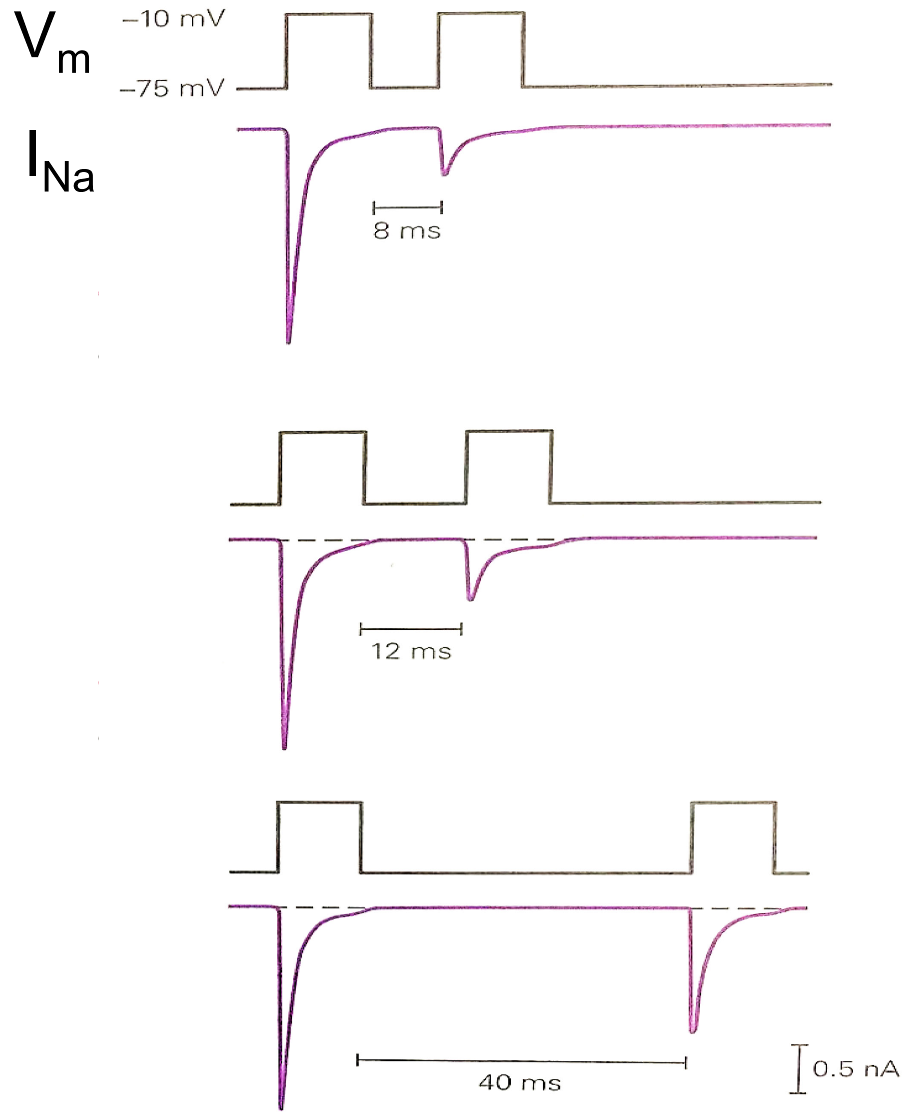


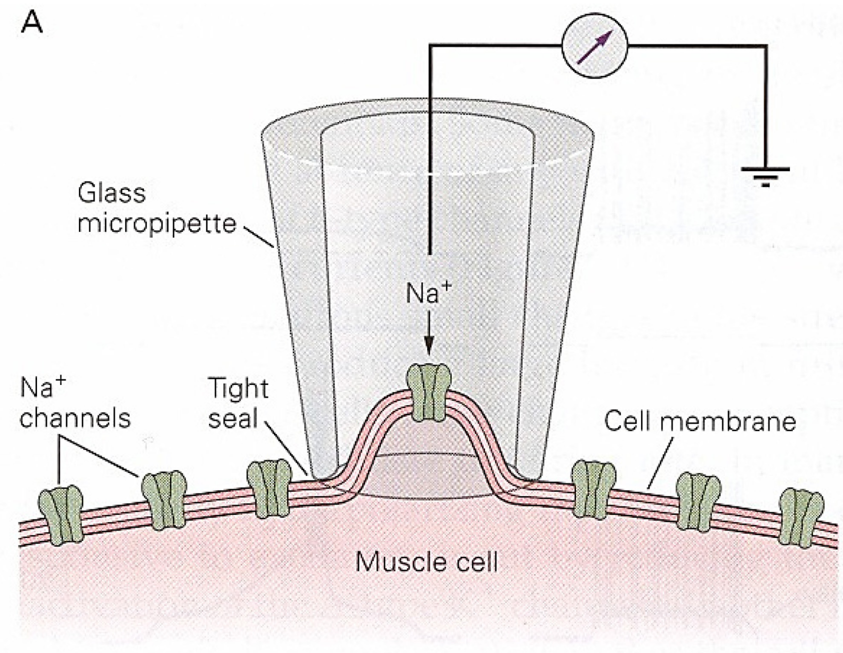
Figure 3.8, Purves

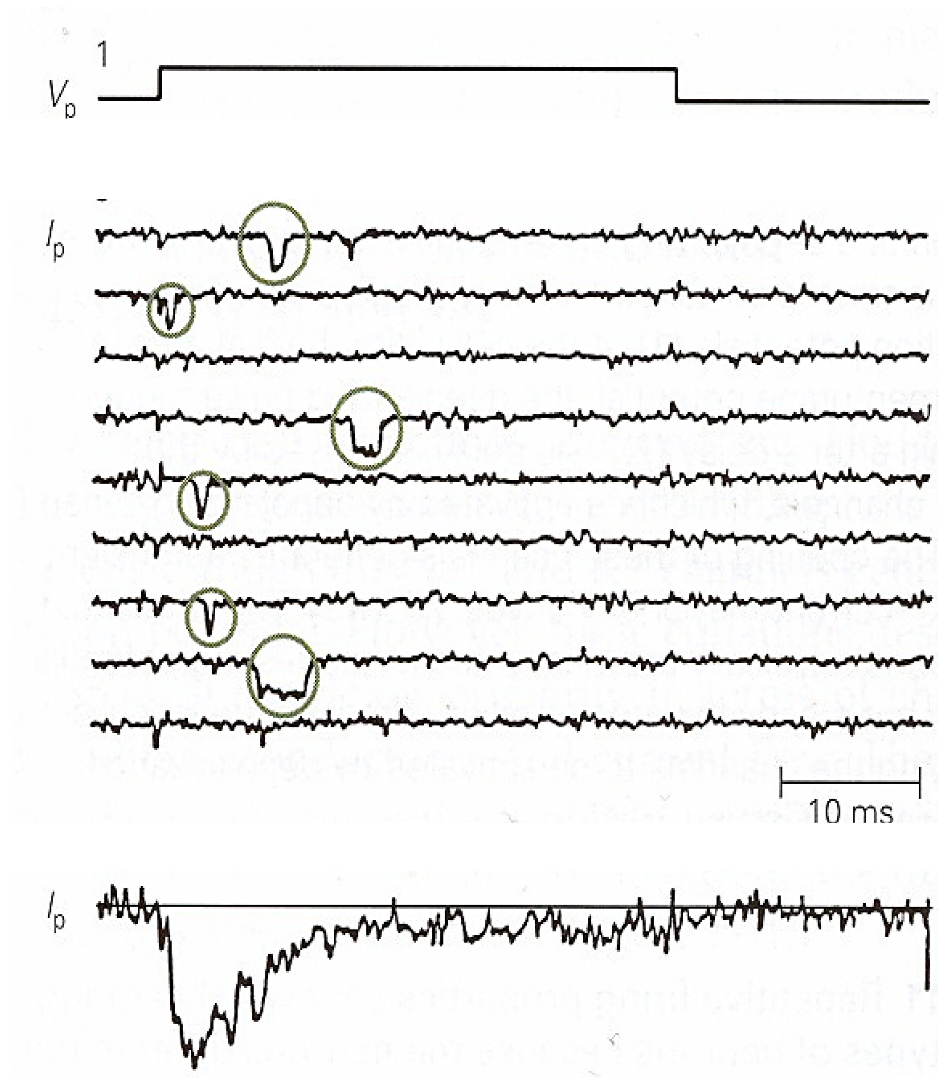
Exploring the Na^+ and K^+ Currents



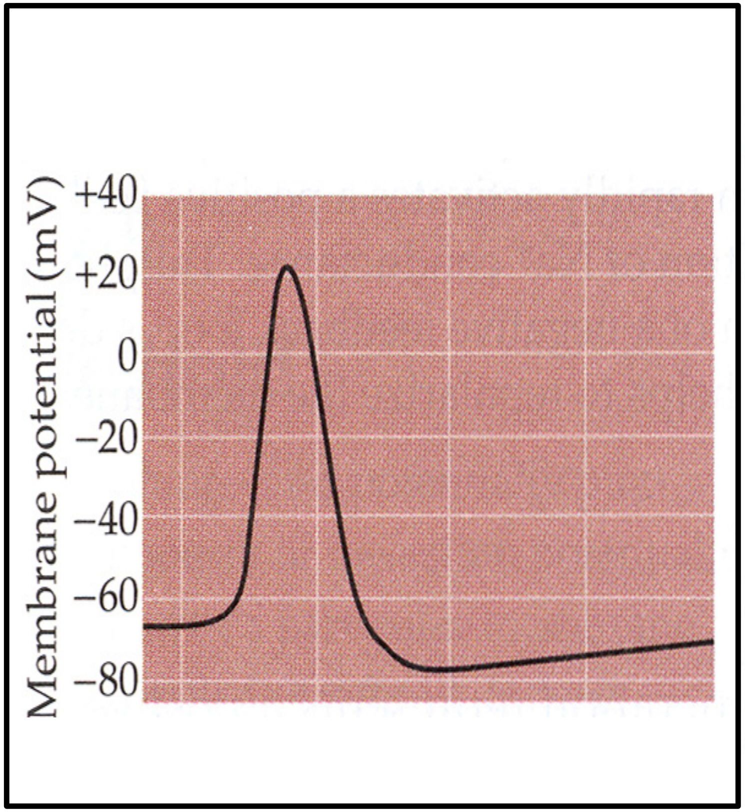


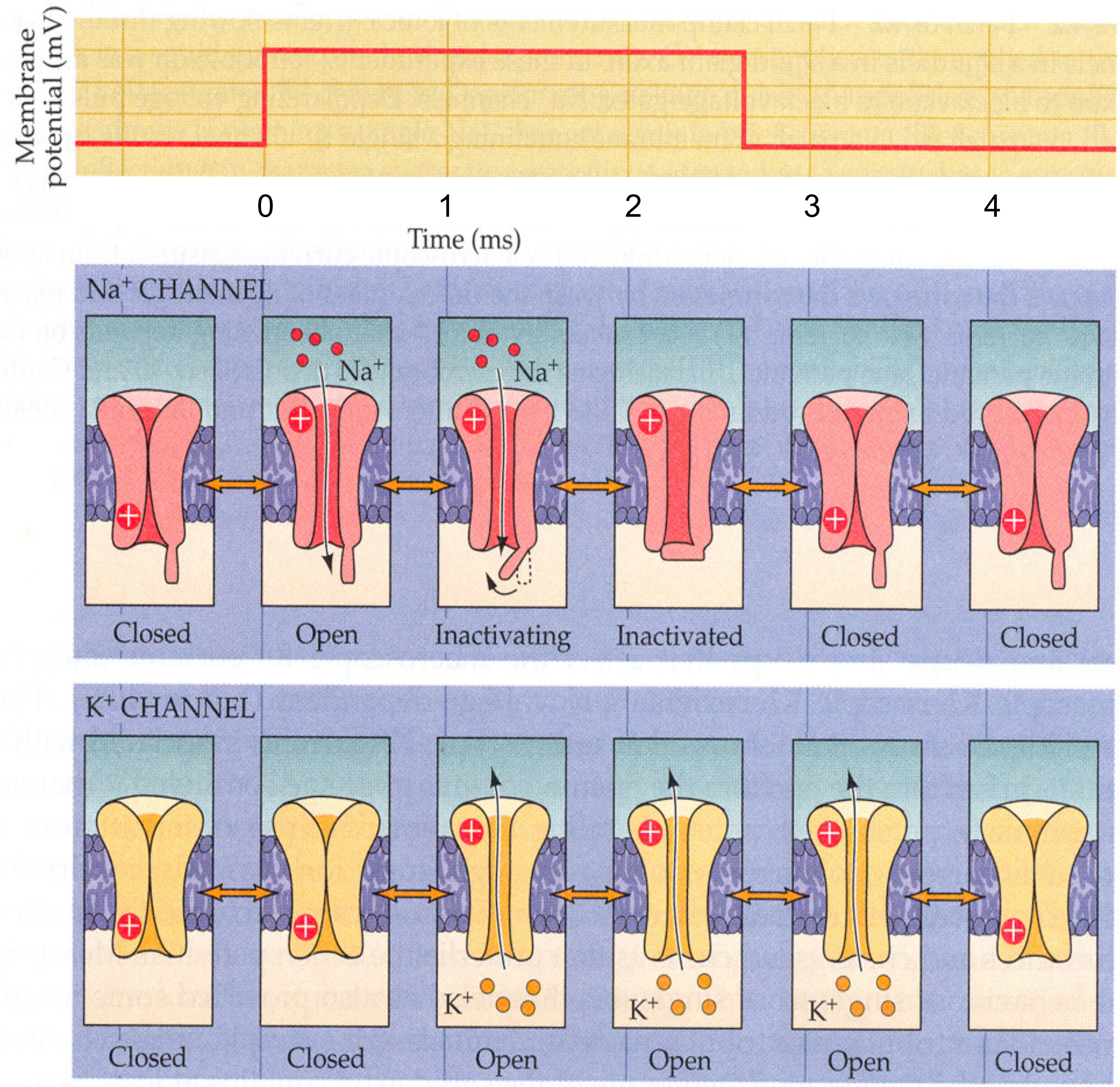
Exploring the Na^+ Current



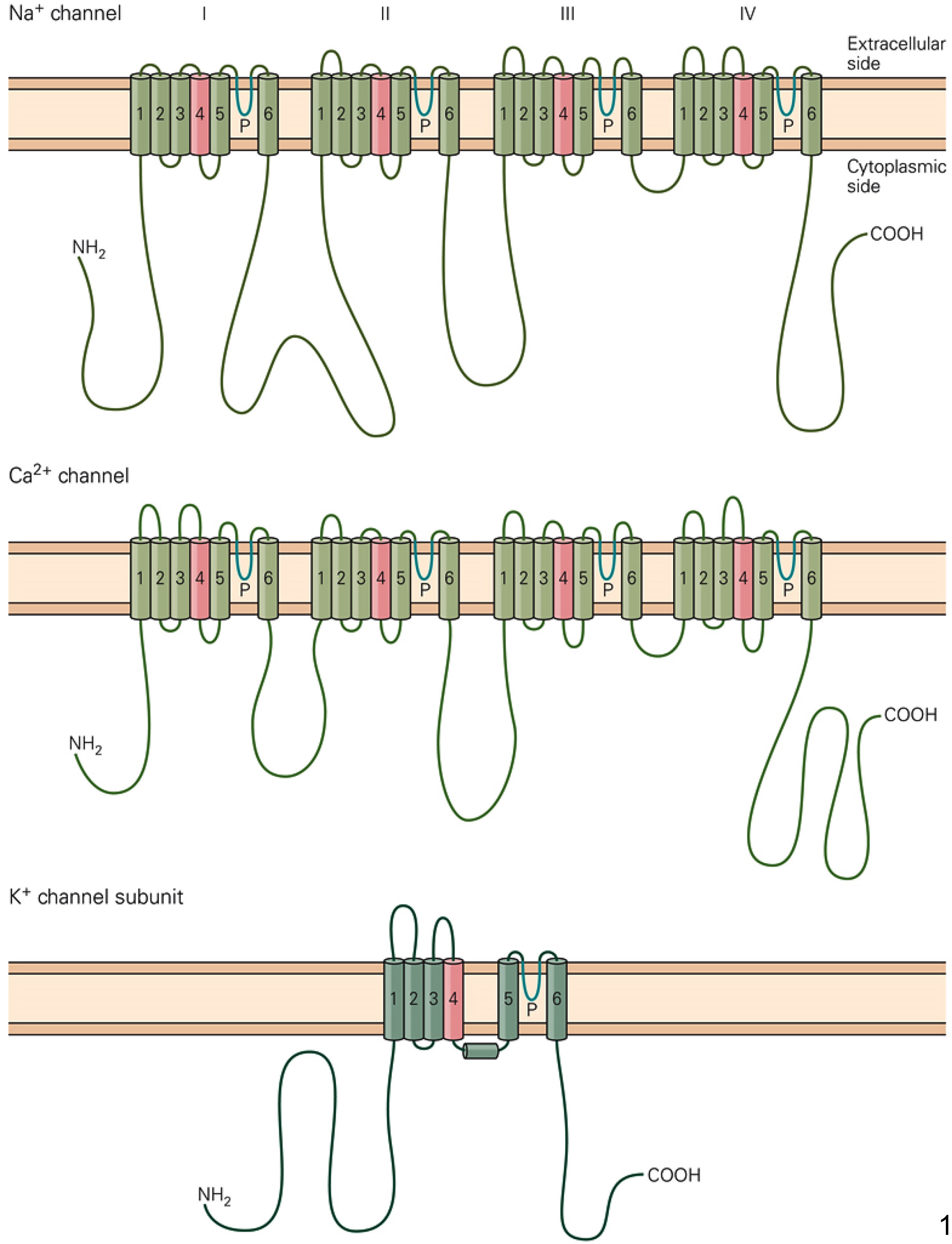


Molecular Events of the Action Potential





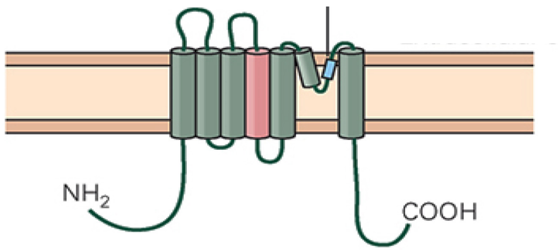
Families of Voltage-Gated Channels



Modification of the basic ion channel design leads to novel channels

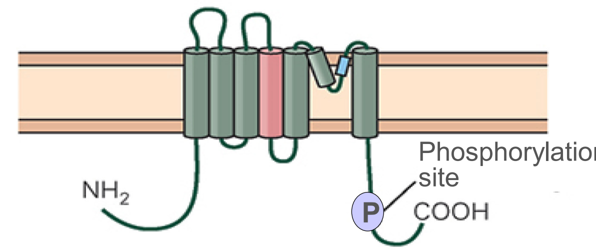
I_K

Depolarization-activated, non-inactivating K^+ channel



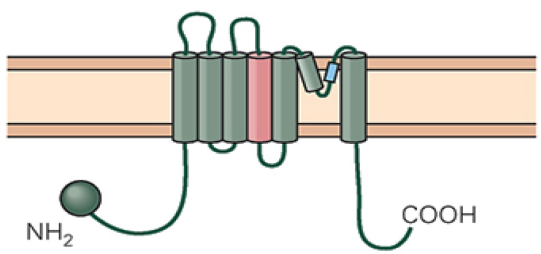
I_M

Depolarization-activated, phosphorylation-deactivated K^+ channel



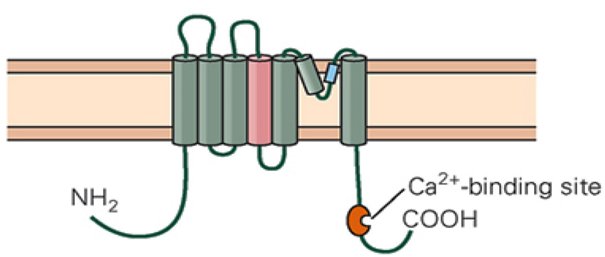
I_A

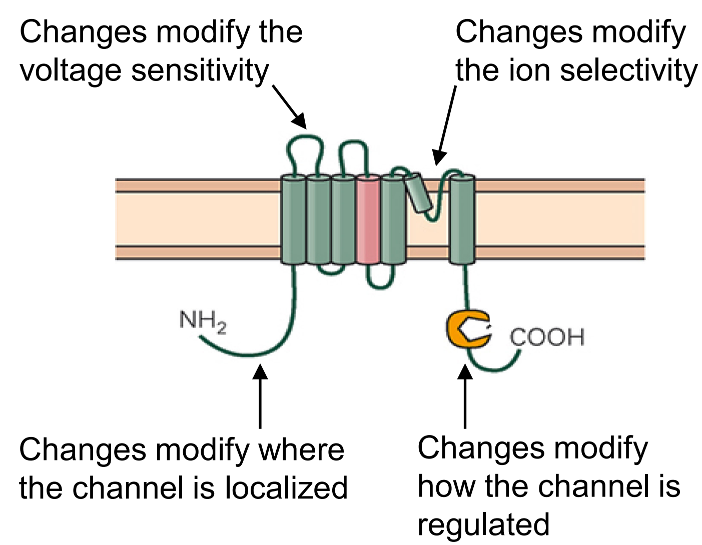
Depolarization-activated, inactivating K^+ channel



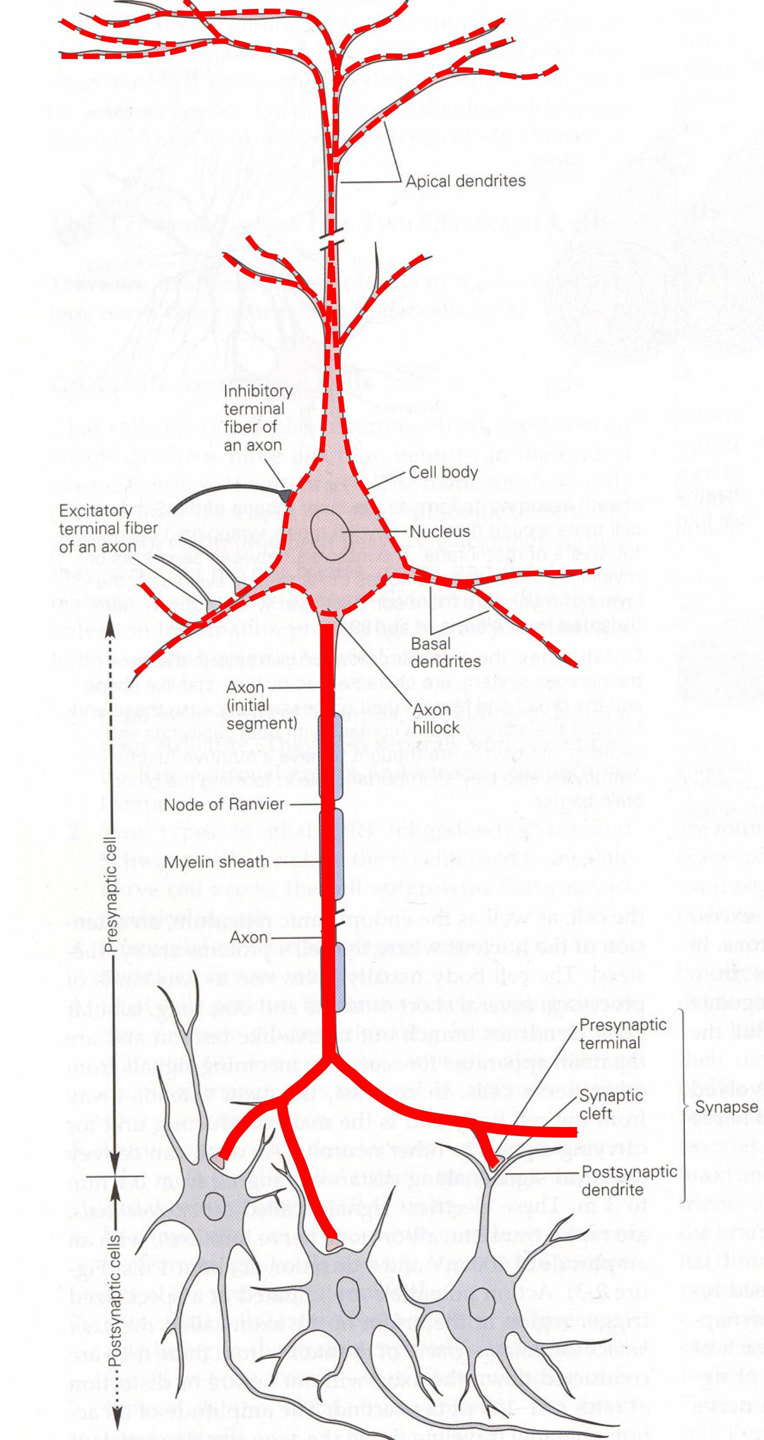
I_C

Depolarization- and Ca^{2+}-activated K^+ channel





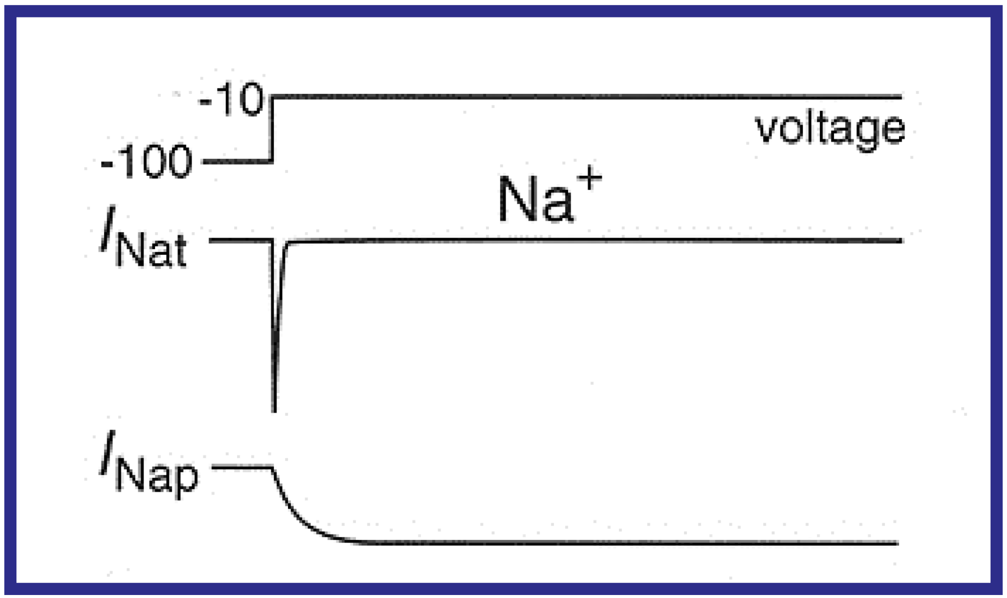
Location of Voltage-Gated Channels



Inward Na^+ Currents

Activated by Depolarization

Current	Description	Location	Function
I_{Nat}	• *Transient* • Fast activation • Fast inactivation	Axon	• Upswing of action potentials
I_{Nap}	• *Persistent* • Slow activation • Non-inactivating	Soma and dendrites	• Enhances depolarization of neuron • Contributes to steady-state firing

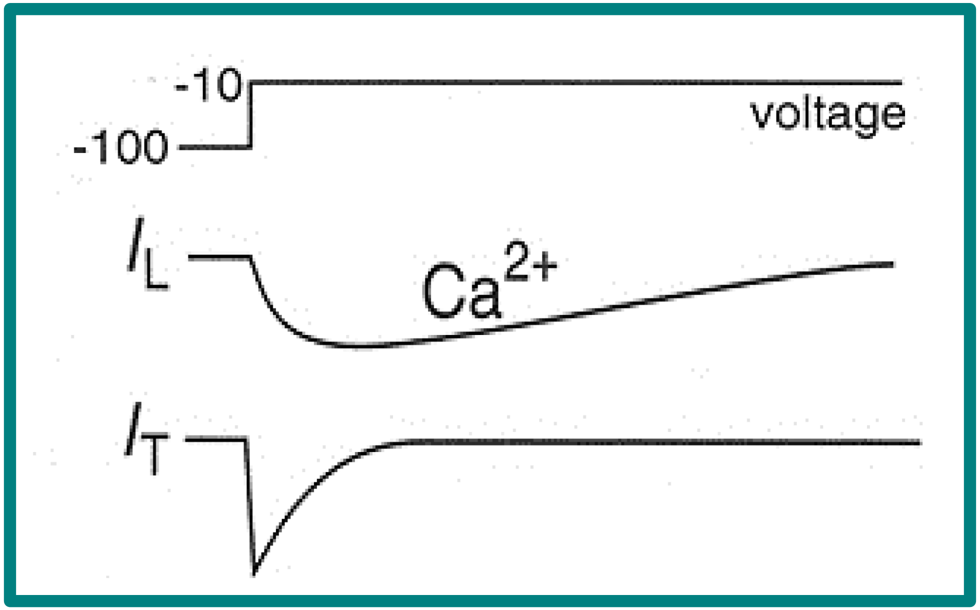


Byrne and Roberts,
From Molecules to Networks

Inward Ca^{2+} Currents

Activated by Depolarization

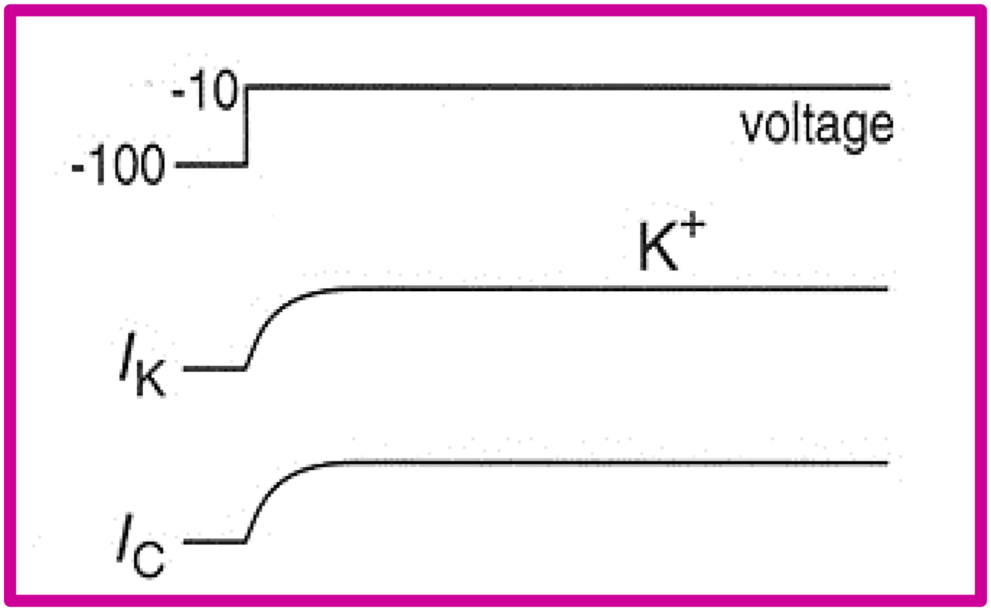
Current	Description	Location	Function
I_L	• *Long-lasting* • High threshold (-20 mV) • Slow activation • Slow inactivation	Dendrites	• Dendritic excitation • Ca^{2+}-mediated events in dendrites
		Axon terminal	• Synaptic transmission
I_T	• *Transient* • Low threshold (-70 mV) • Fast activation • Fast inactivation	Dendrites	• Quick depolarization of dendrites • Causes burst firing • Ca^{2+}-mediated events in dendrites



Byrne and Roberts,
From Molecules to Networks

Outward K$^+$ Currents
Activated by Depolarization

Current	Description	Location	Function
I_K	• Slowly activated by depolarization • Non-inactivating	Axon	• Repolarization of action potentials
I_C	• Slowly activated by depolarization • Non-inactivating • Requires increase in $[Ca^{2+}]_{inside}$	Soma and dendrites	• Increases interval between action potentials

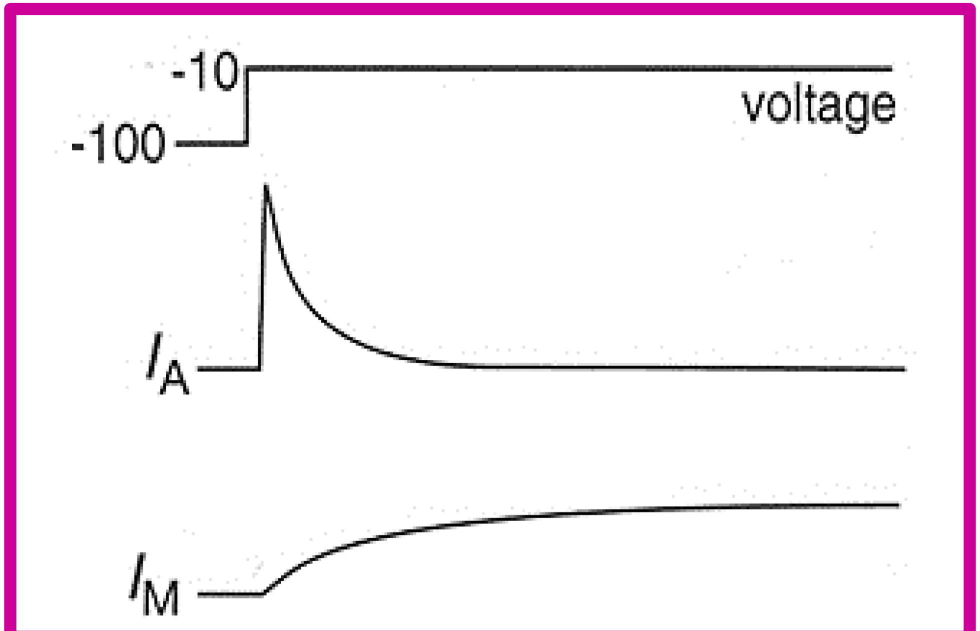


Byrne and Roberts,
From Molecules to Networks

Outward K^+ Currents

Activated by Depolarization

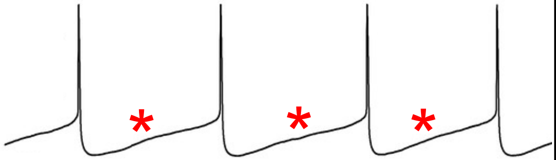
Current	Description	Location	Function
I_A	• Transient • Fast activation by depolarization • Fast inactivation	Soma and dendrites	• Delays onset of action potential firing
I_M	• Slowly activated by depolarization • Non-inactivating • Blocked by activation of muscarinic ACh receptors	Soma and dendrites	• Contributes to spike frequency adaptation • Blocking this current enhances cell excitability

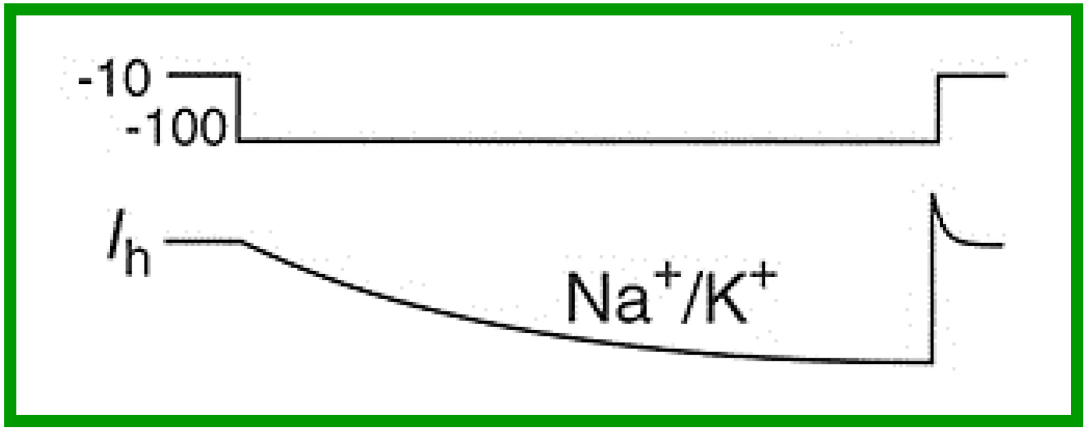


Byrne and Roberts, From Molecules to Networks

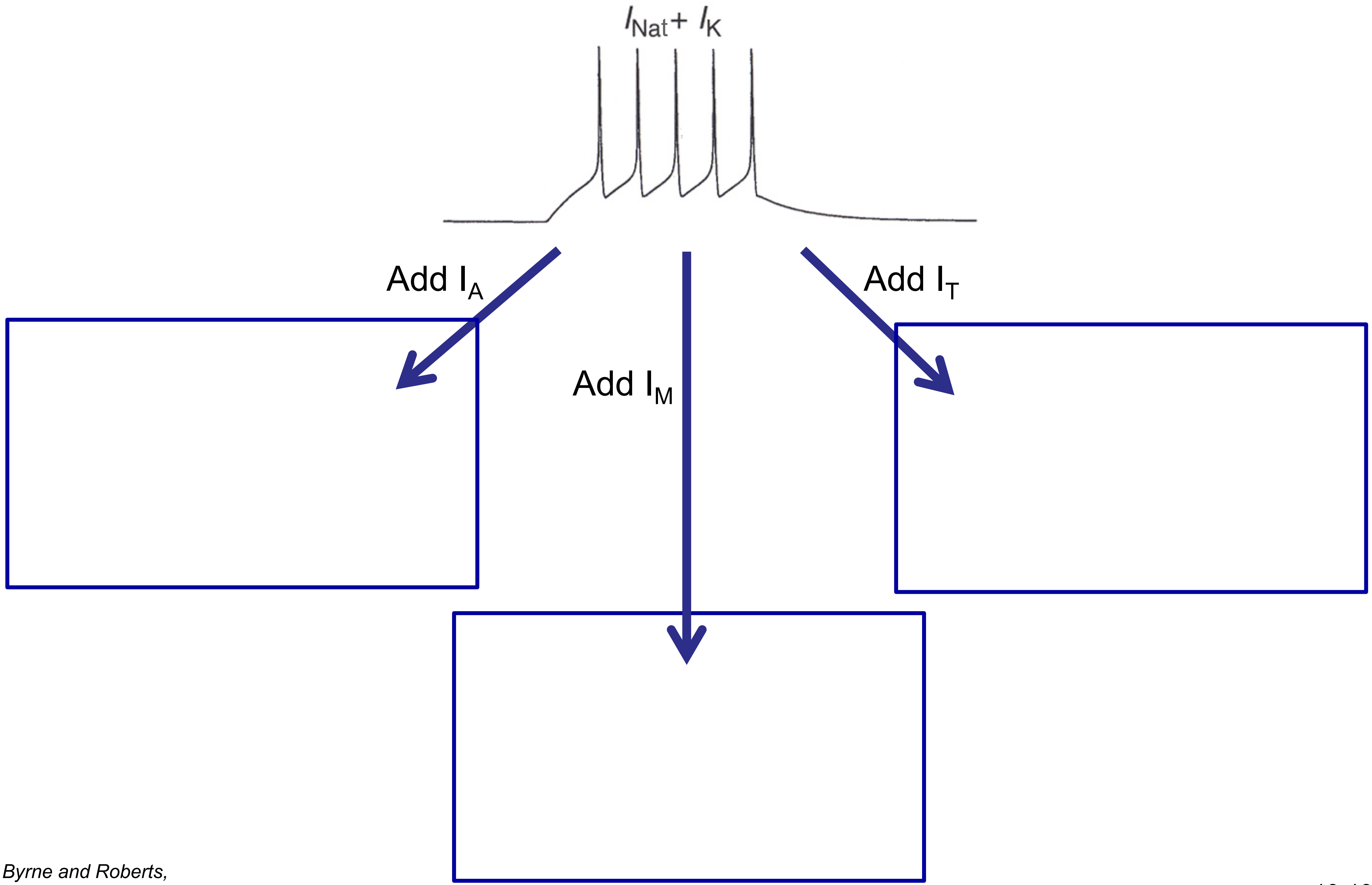
Inward Cation Current

Activated by Hyperpolarization

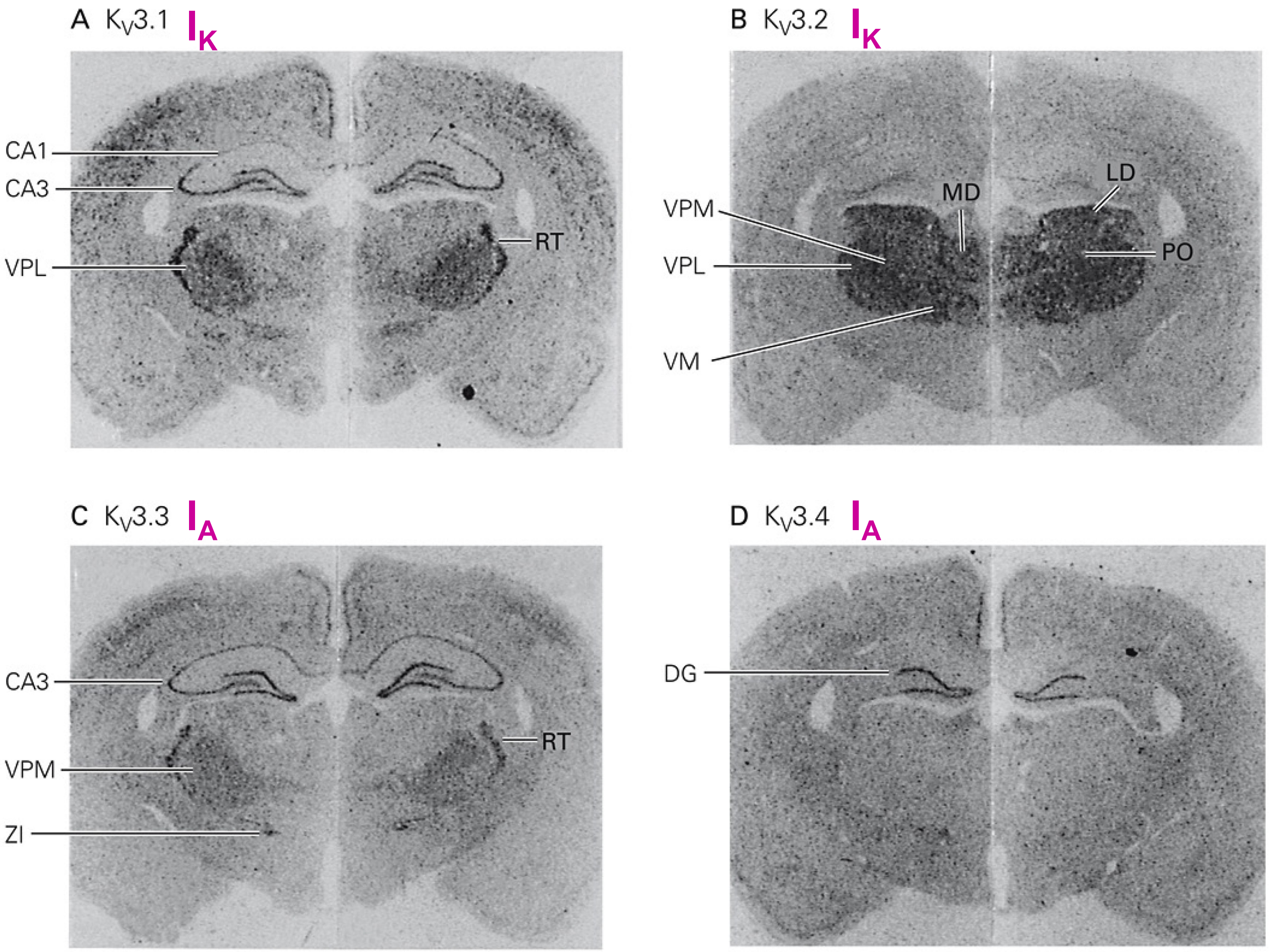
Current	Description	Location	Function
I_h	• Activated by hyperpolarization (-70 mV) • Depolarizing mixed cation current • Slow activation • Non-inactivating, but stops once hyperpolarization ends	Soma and Dendrites	Causes a depolarizing pacemaker potential 



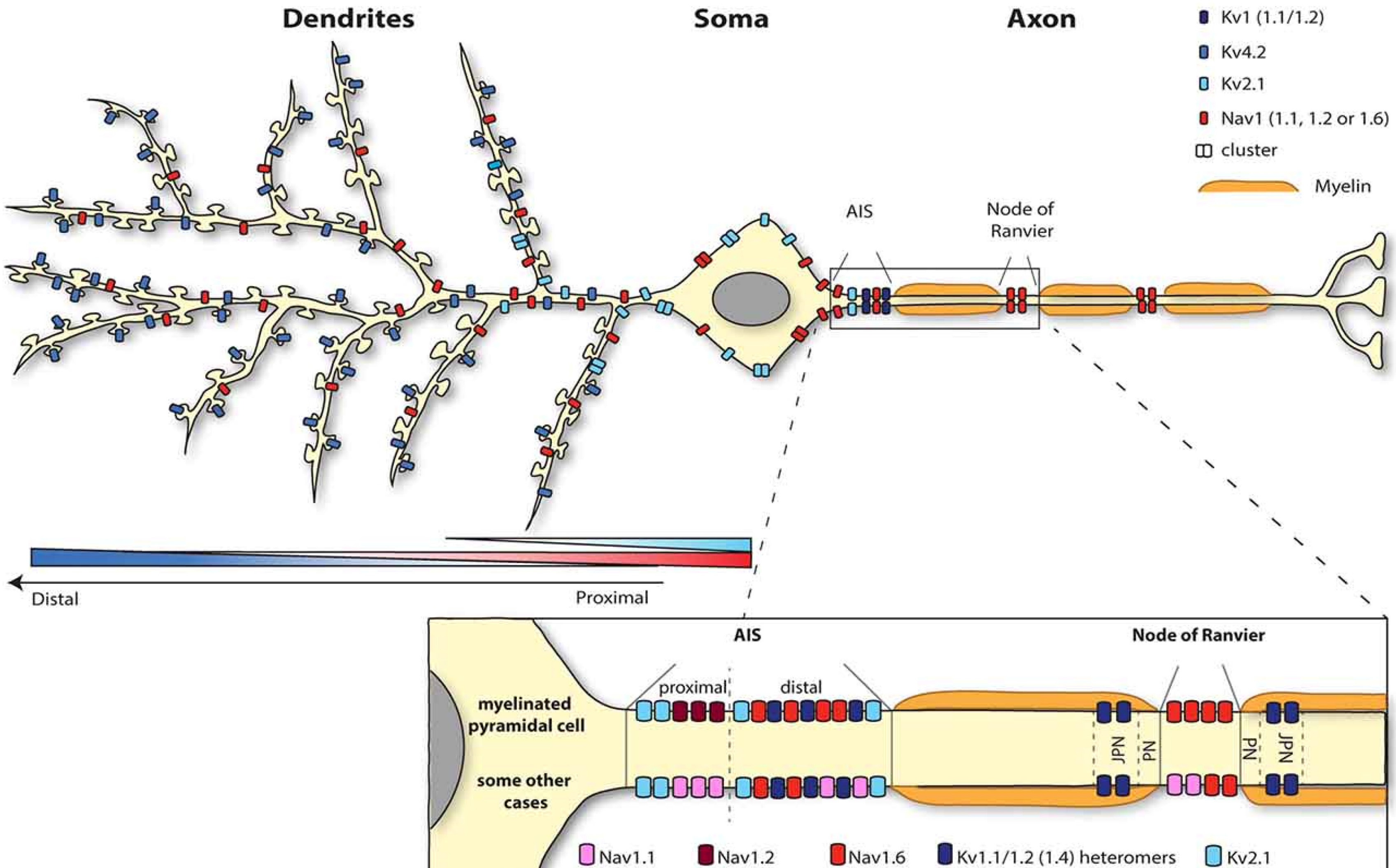
Channel Types Influence Neuronal Excitability



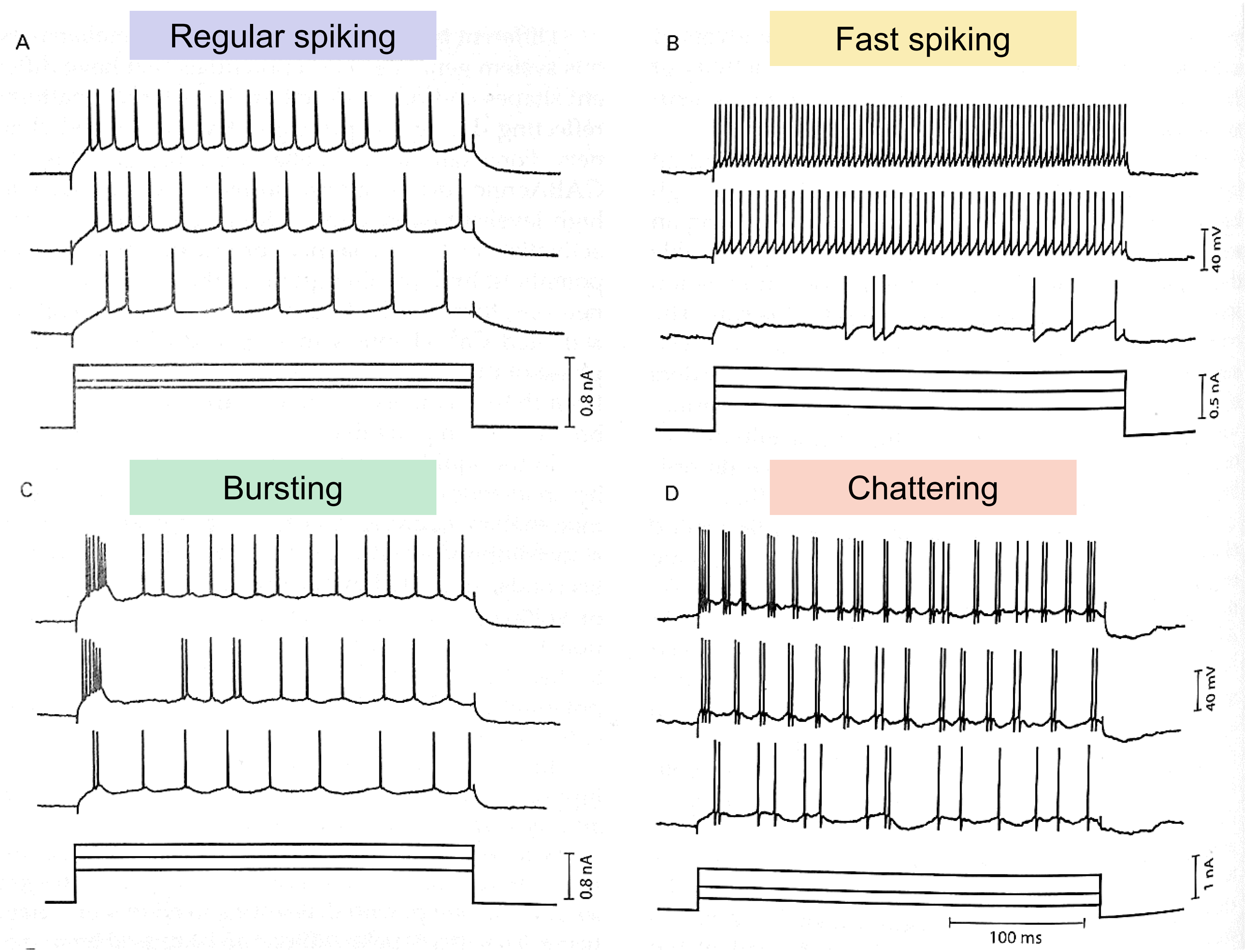
Expression Patterns of Channels Vary between Brain Regions



Expression Patterns of Channels Vary between Cell Type and Subcellular Region

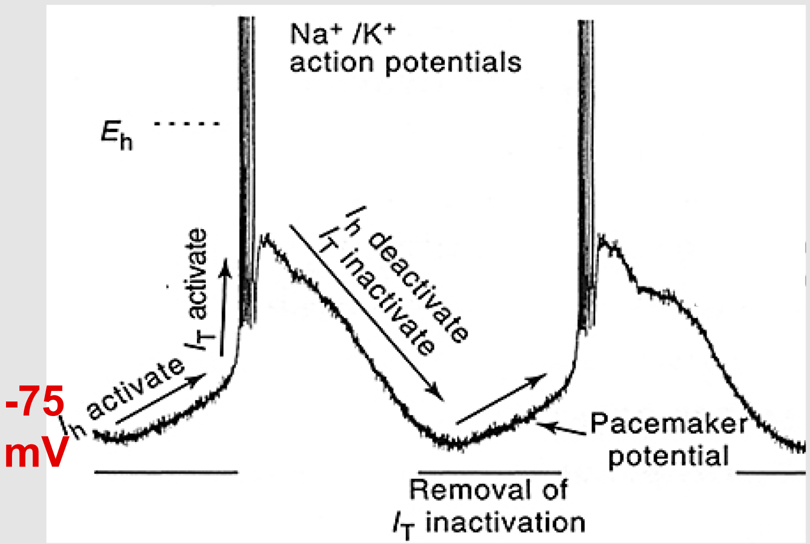


Channel Types Cause Different Firing Patterns



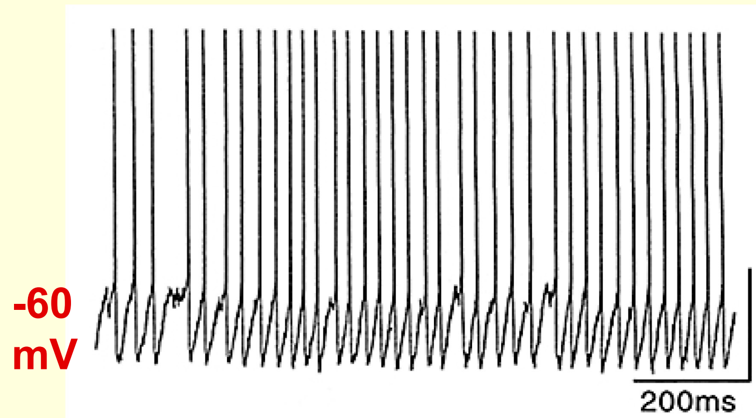
Firing Patterns of Cells Can Change

Thalamic neurons when asleep–
Spontaneous bursting without input



I_h	Depolarizing pacemaker potential leads to spontaneous activity
I_T	Low threshold Ca^{2+} current, causes bursting
I_{Nat} I_K	Action potentials in axon when threshold is reached (spontaneously)

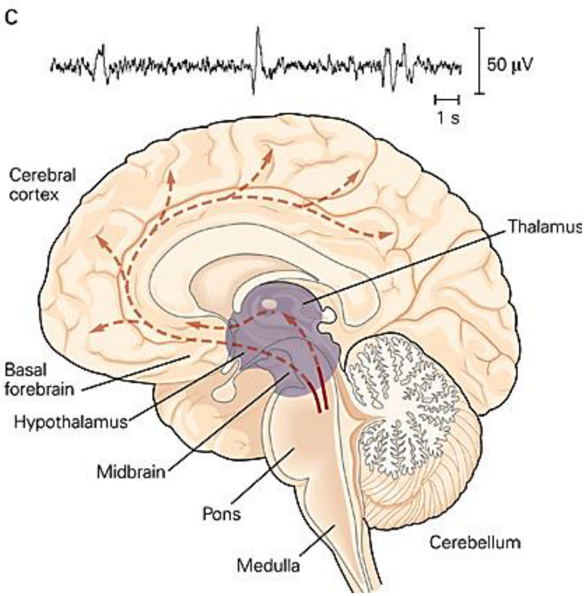
Thalamic neurons when awake–
Single APs only when stimulated



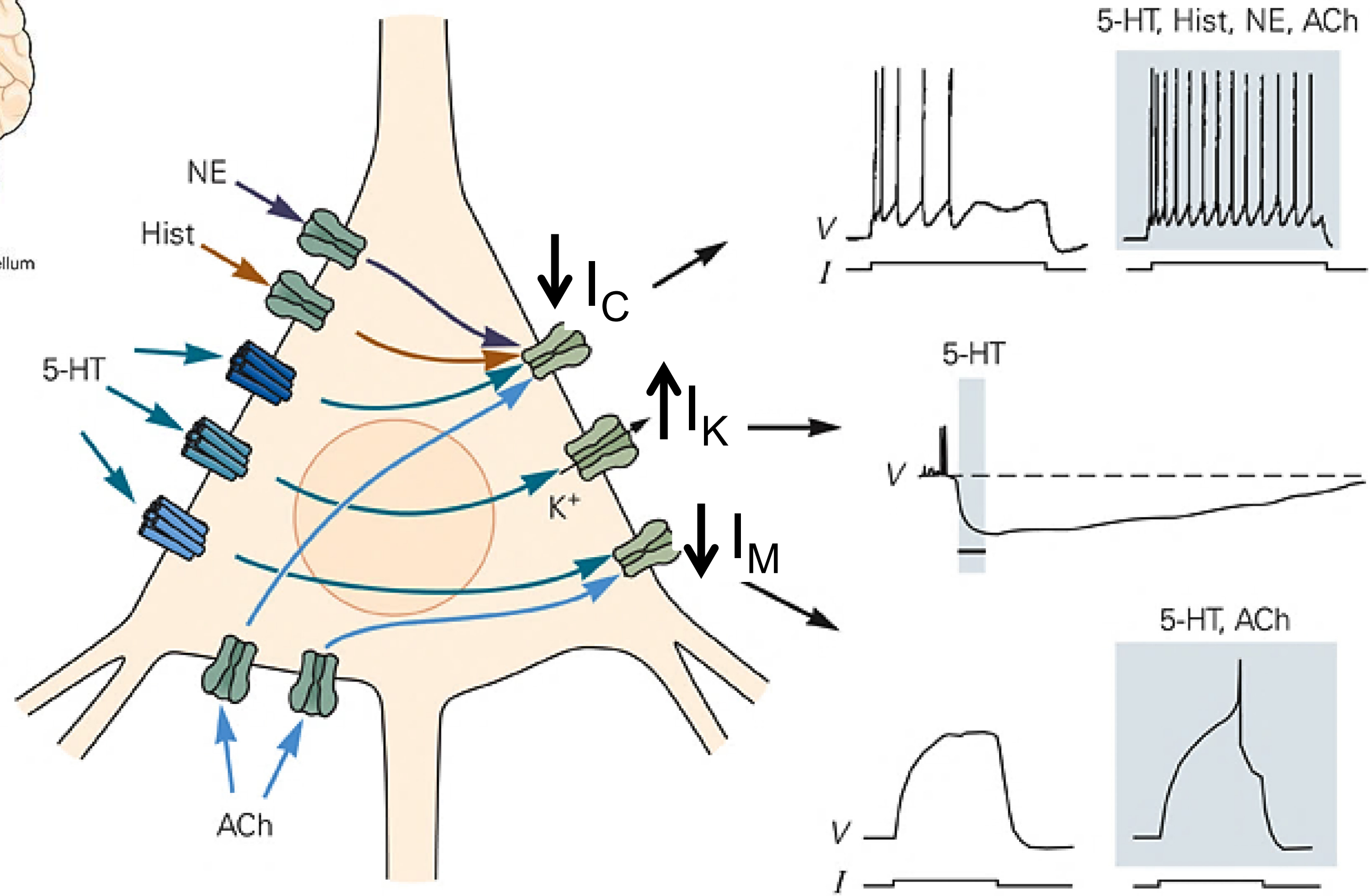
I_h	Never opens, no pacemaker potential
I_T	Always inactivated, no bursting
I_{Nat} I_K	Action potentials in axon when threshold is reached (from input)

Byrne and Roberts., From Molecules to Networks

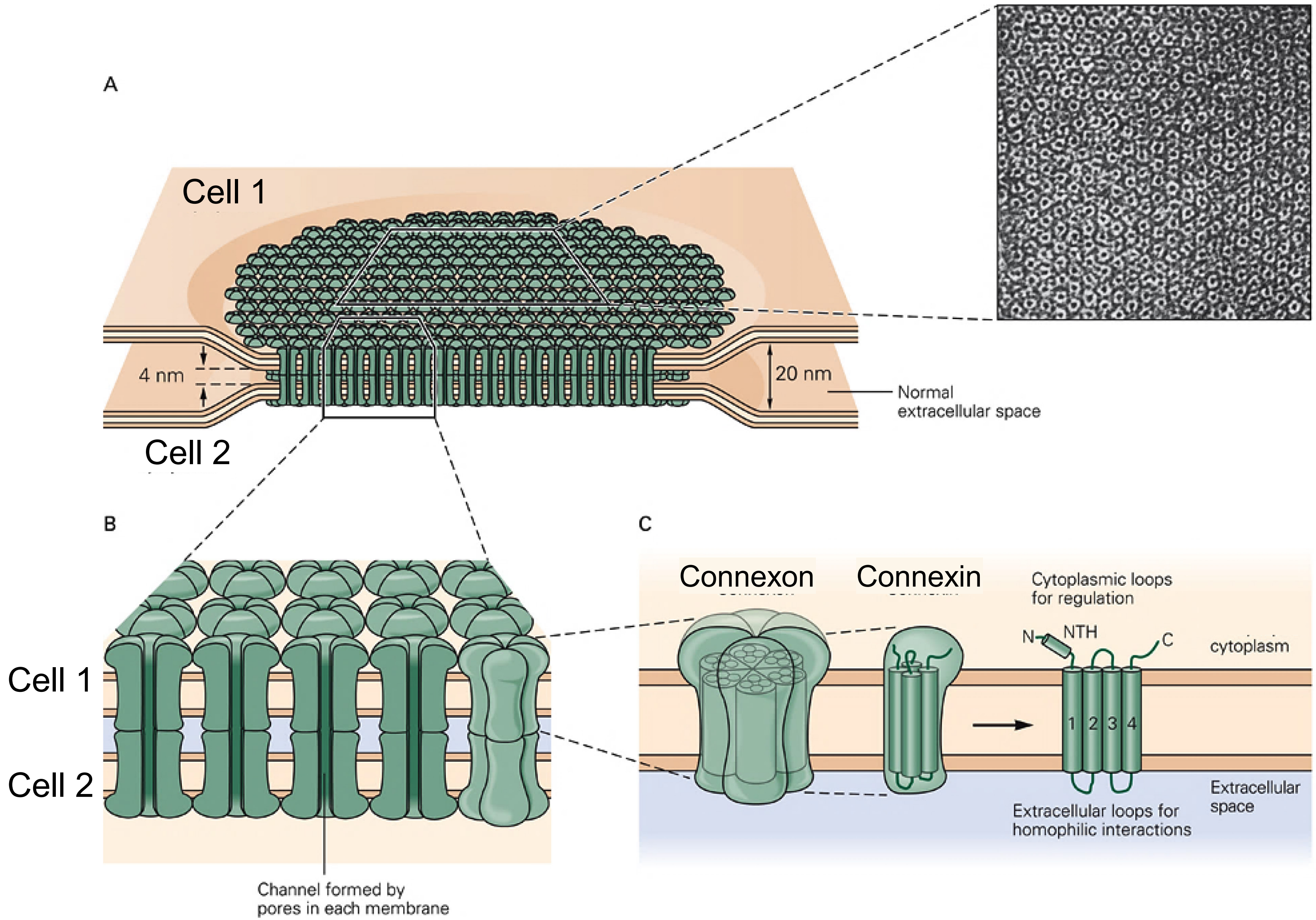
Firing Patterns of Cells Can Change



Cortical pyramidal neuron activity is regulated by ascending modulatory systems

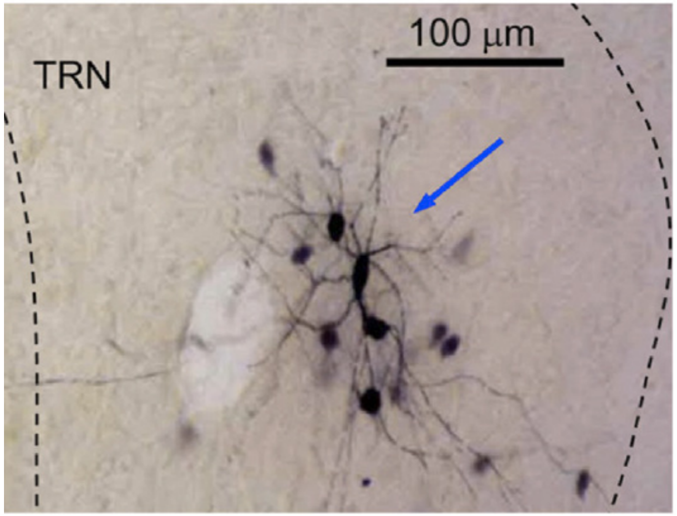


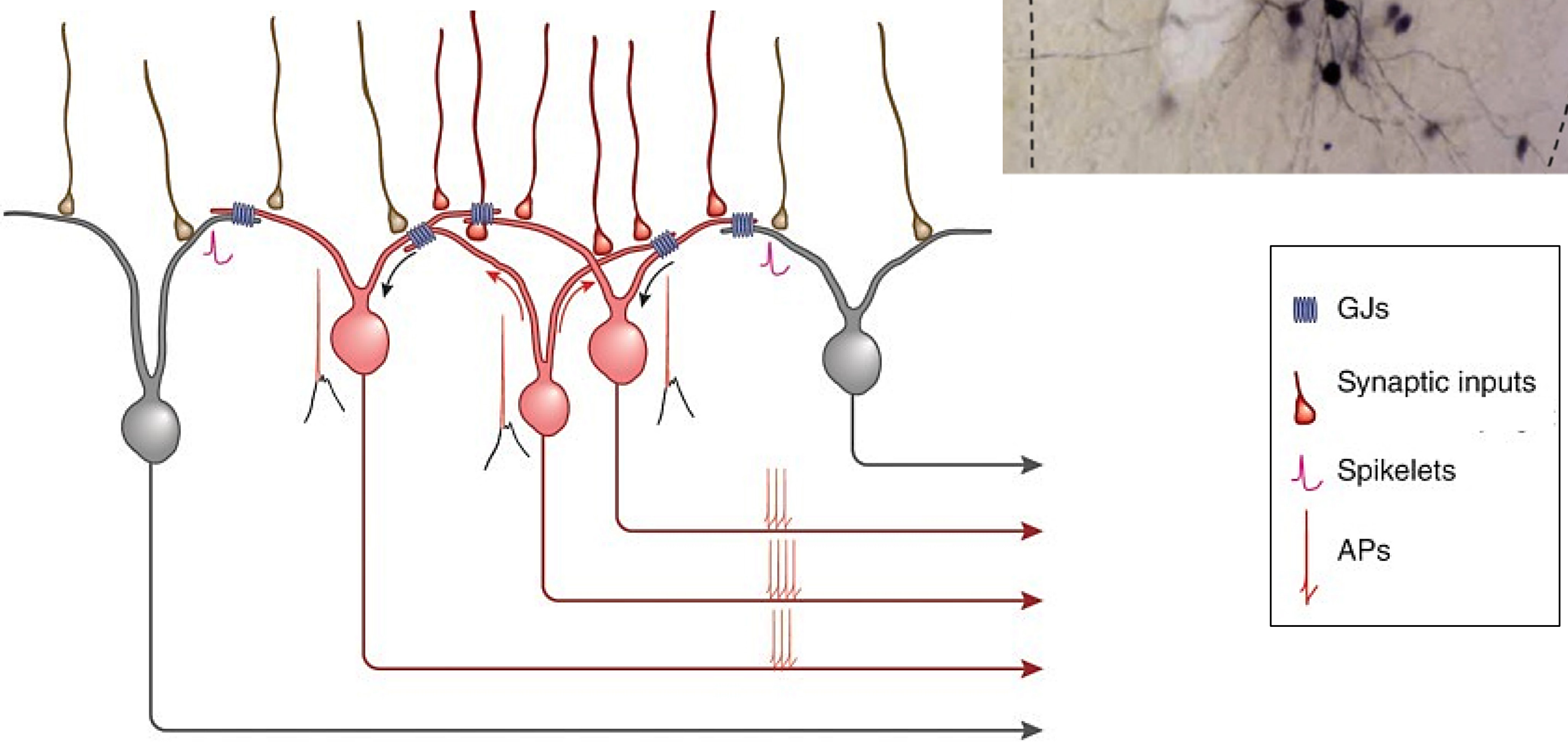
Gap Junctions Synchronize Neural Activity



Gap Junctions Synchronize Neural Activity

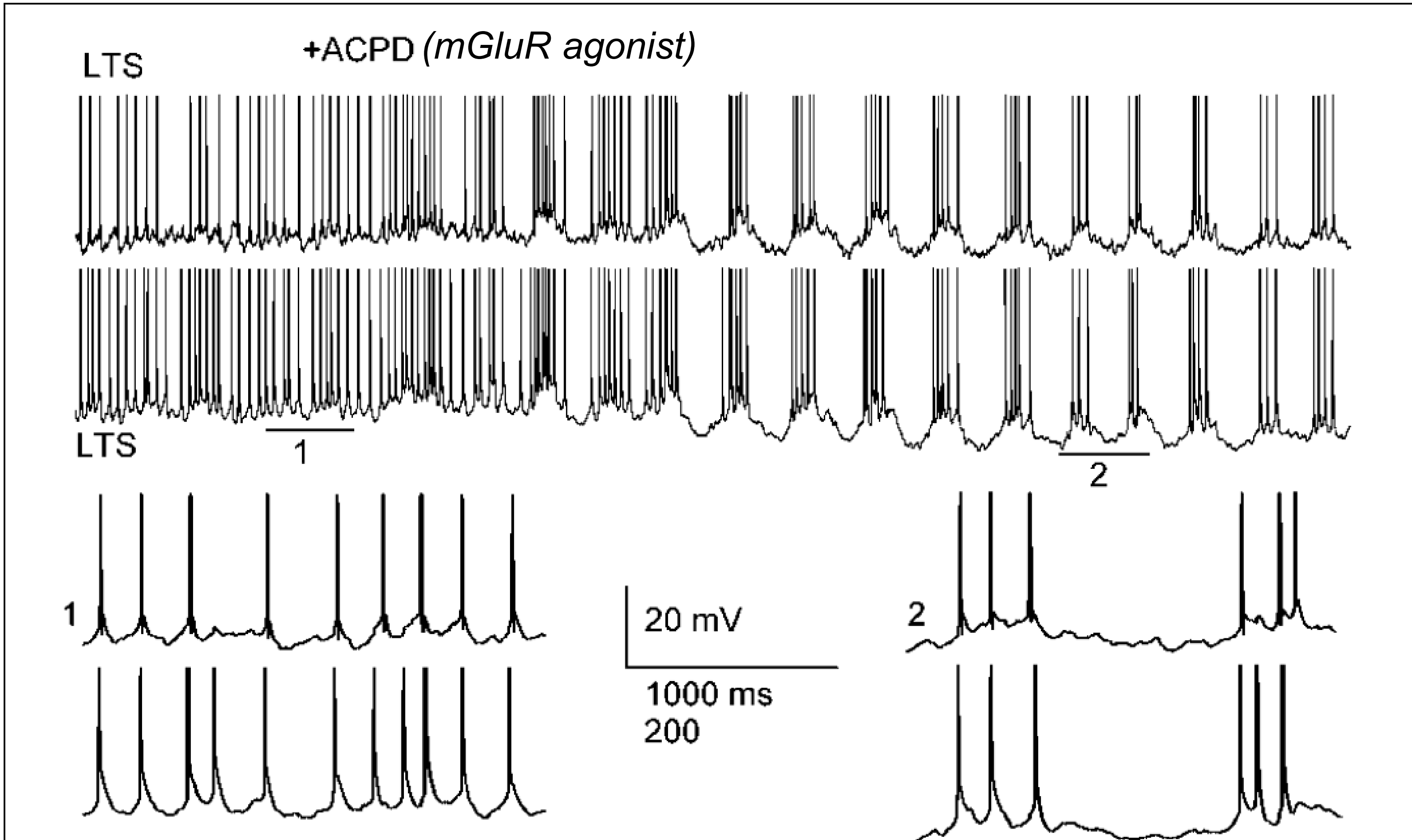
In mammals, gap junctions occur most often between the dendrites of multiple neurons of the same class (typically GABAergic interneurons)





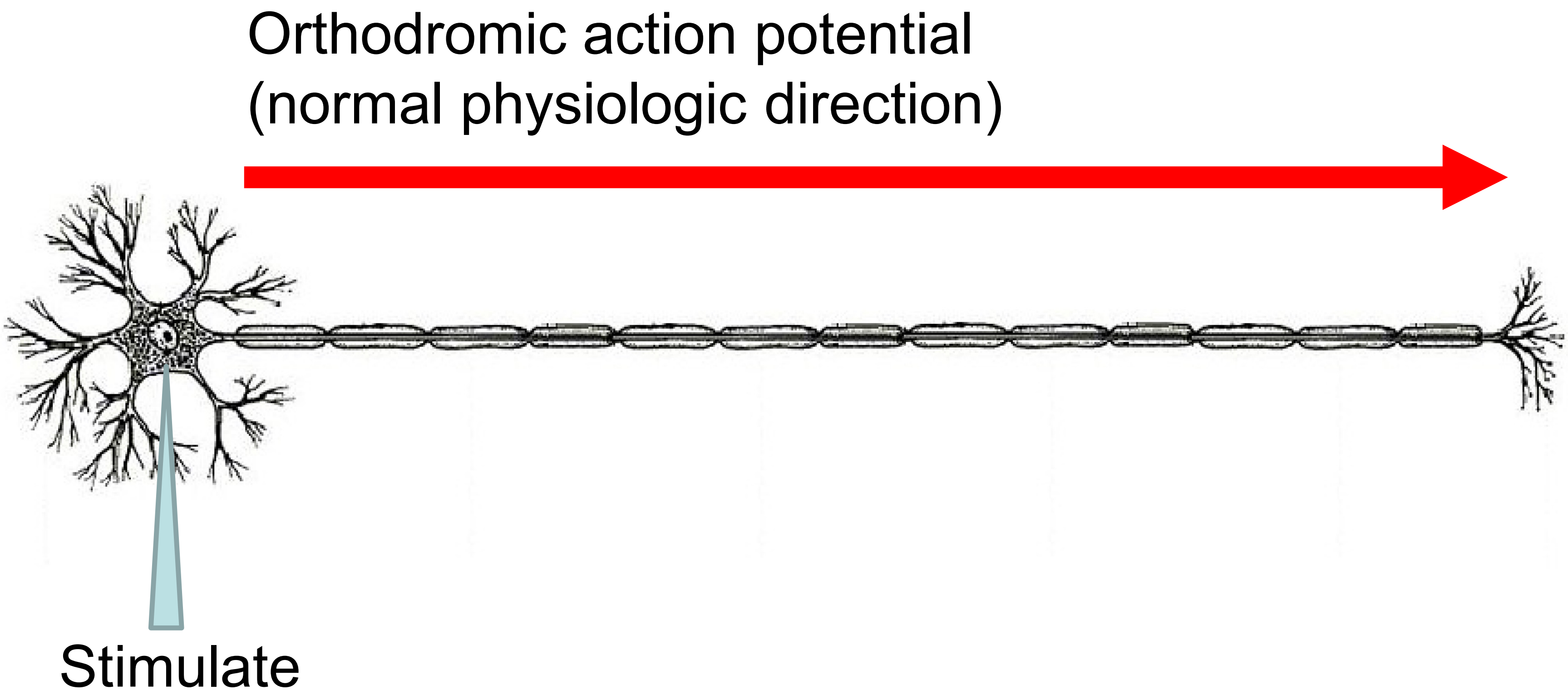
Gap Junctions Synchronize Neural Activity

Electrically coupled interneurons in the hippocampus fire synchronously



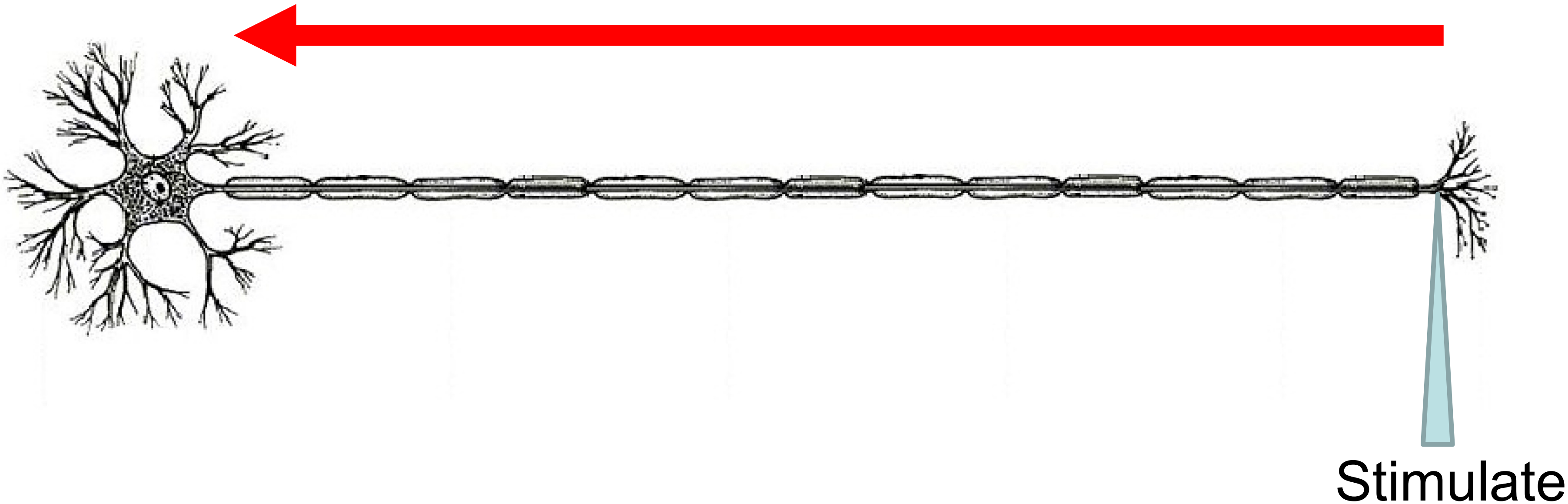
Beierlein et al, 2000

Action Potential Conduction in Axons

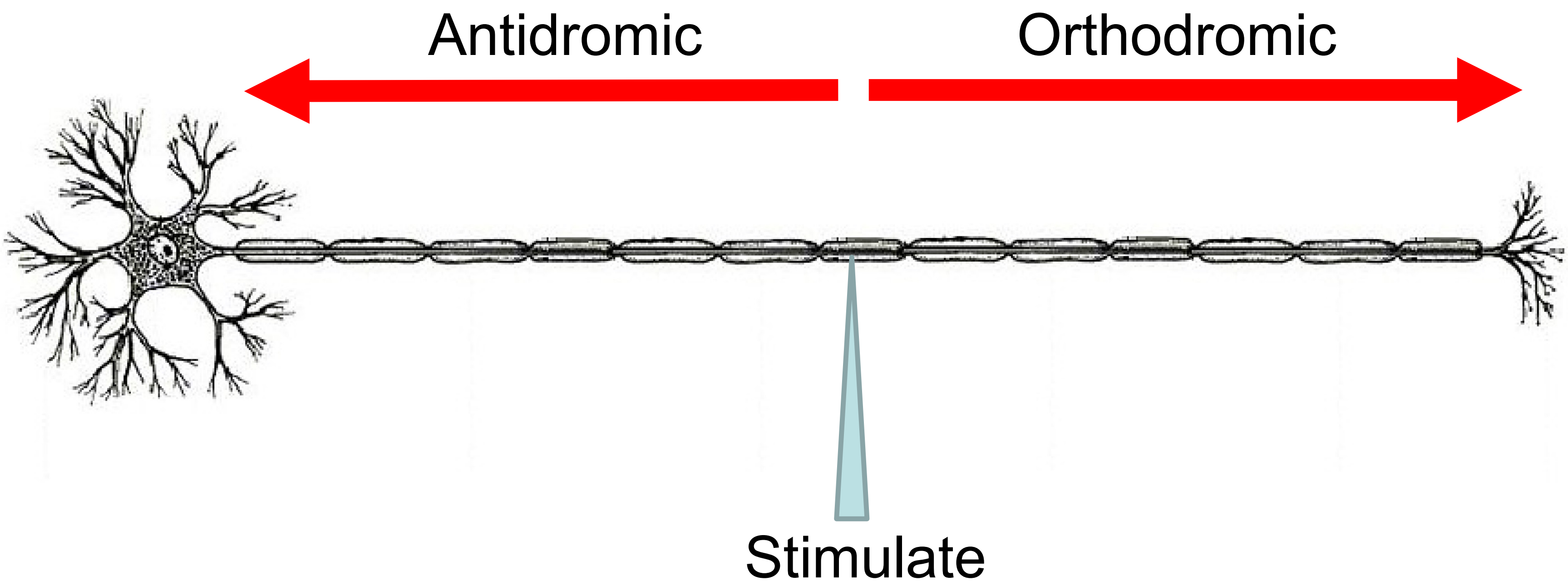


Action Potential Conduction in Axons

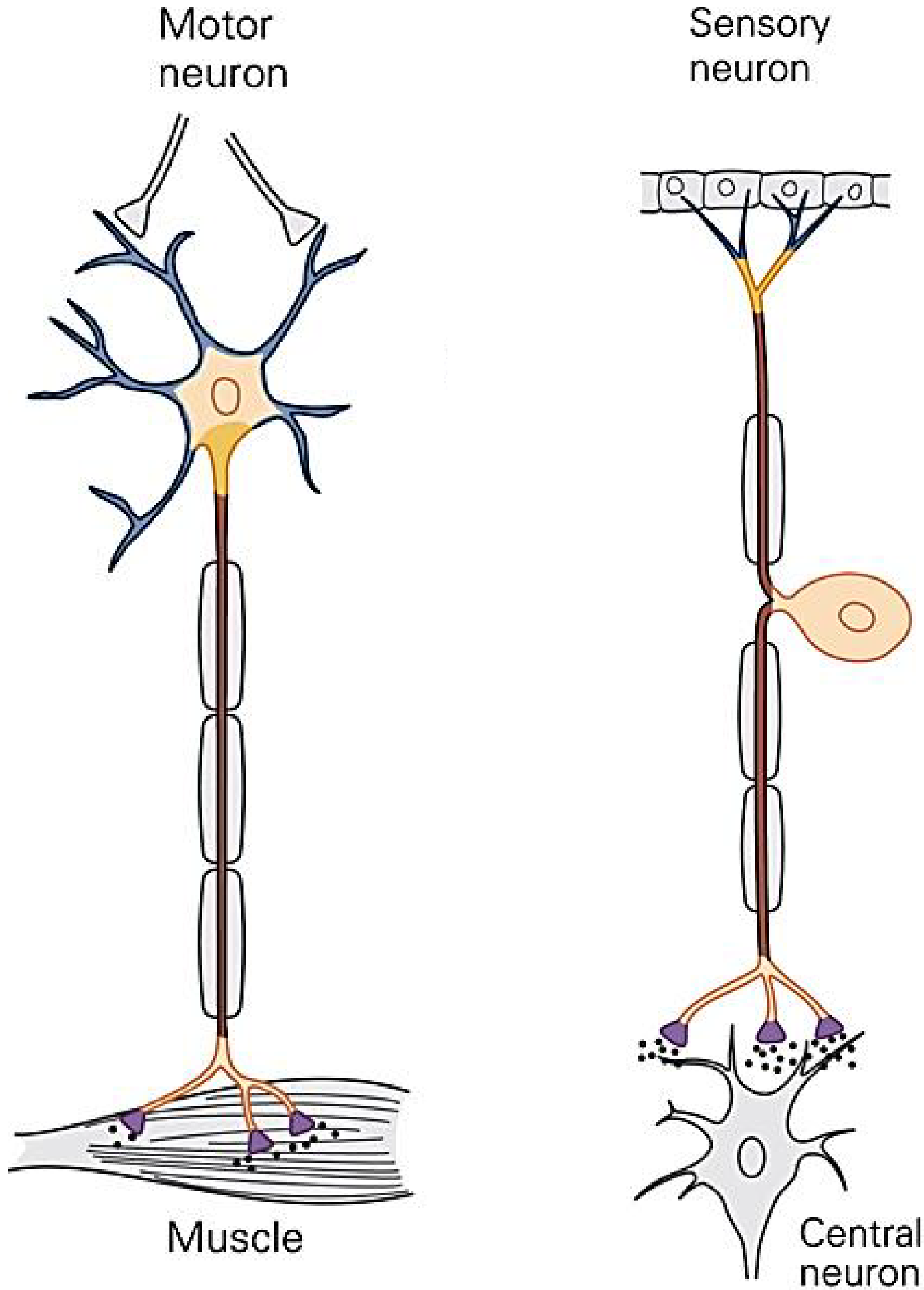
Antidromic action potential
(against normal physiologic direction)



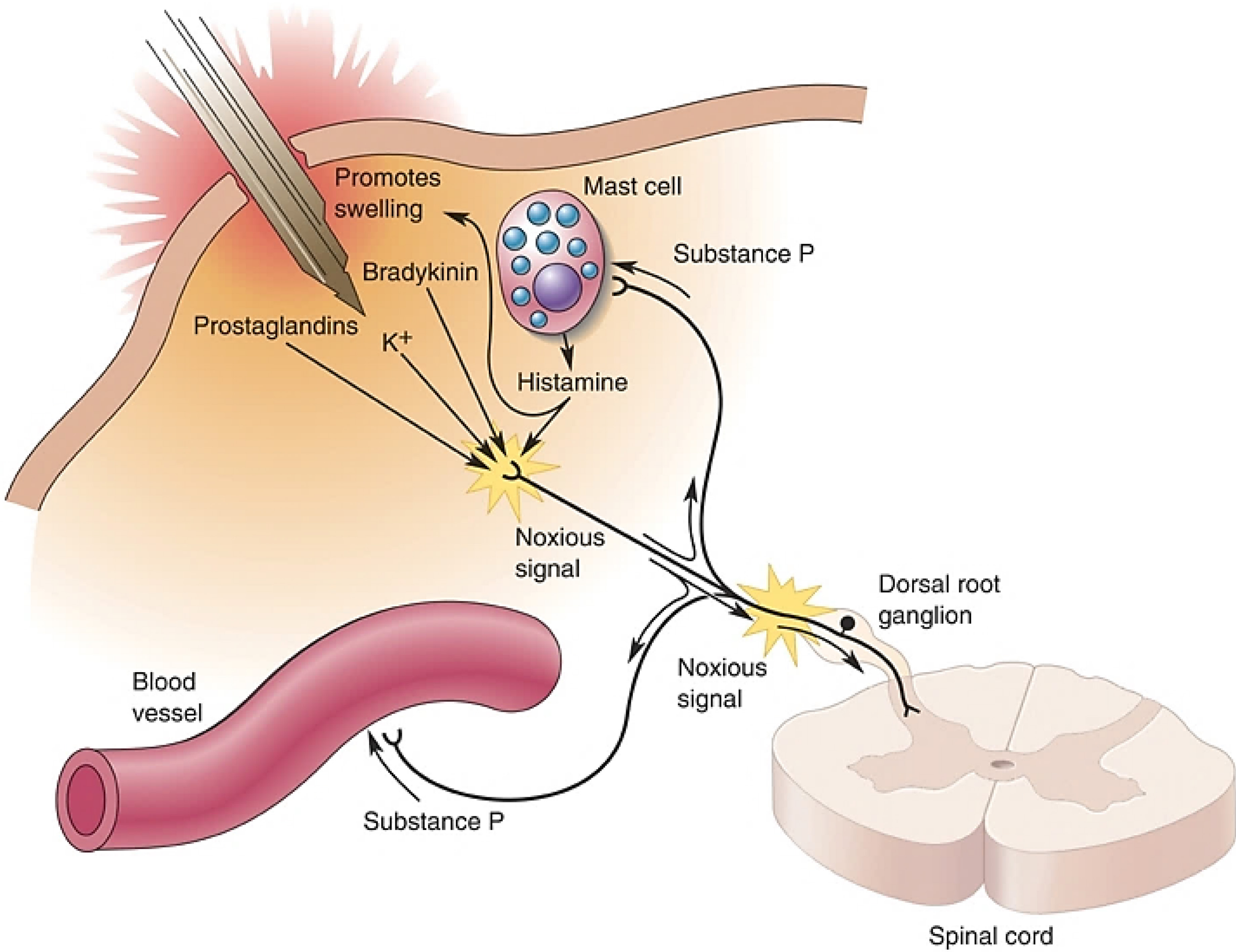
Action Potential Conduction in Axons



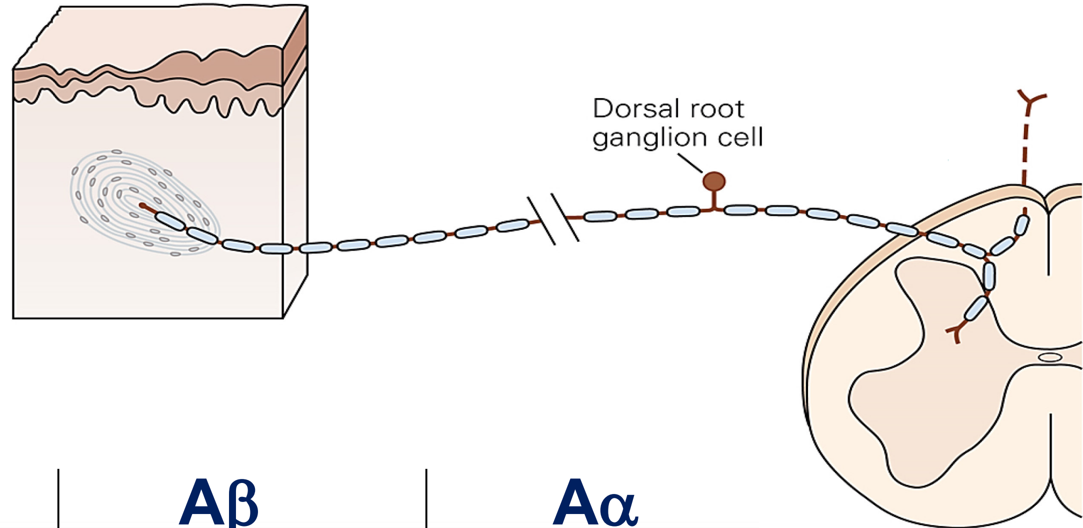
Orthodromic and Antidromic Action Potentials



Action Potentials in Nociceptive Neurons

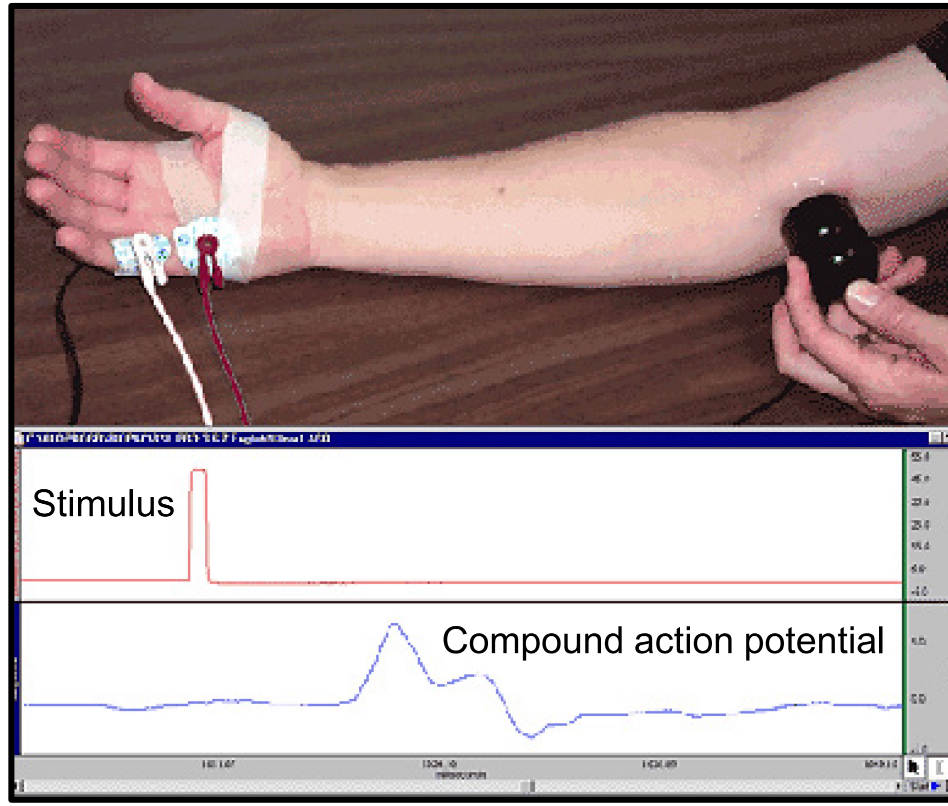


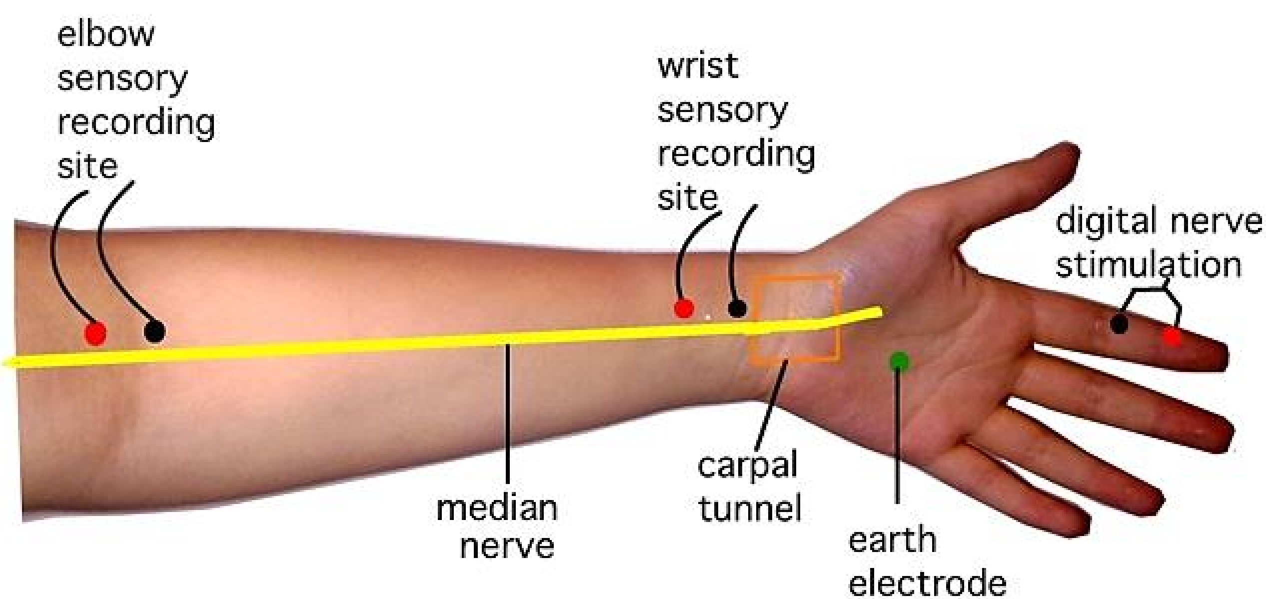
Variations of Sensory Axons

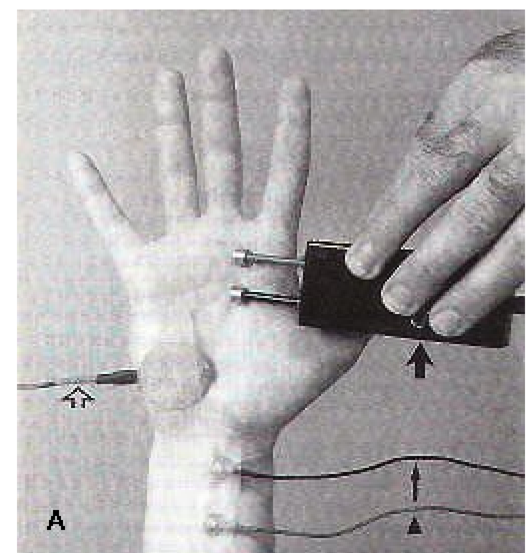


	C	Aδ	Aβ	Aα
Axon diameter (µm)	1	5	12	20
Conduction velocity (m/s)	1	30	72	120
Sensory axons from muscles	Slow pain	Fast pain	Proprioception	Proprioception
Sensory axons from skin	Slow pain, temp	Fast pain, temp	Touch	Touch

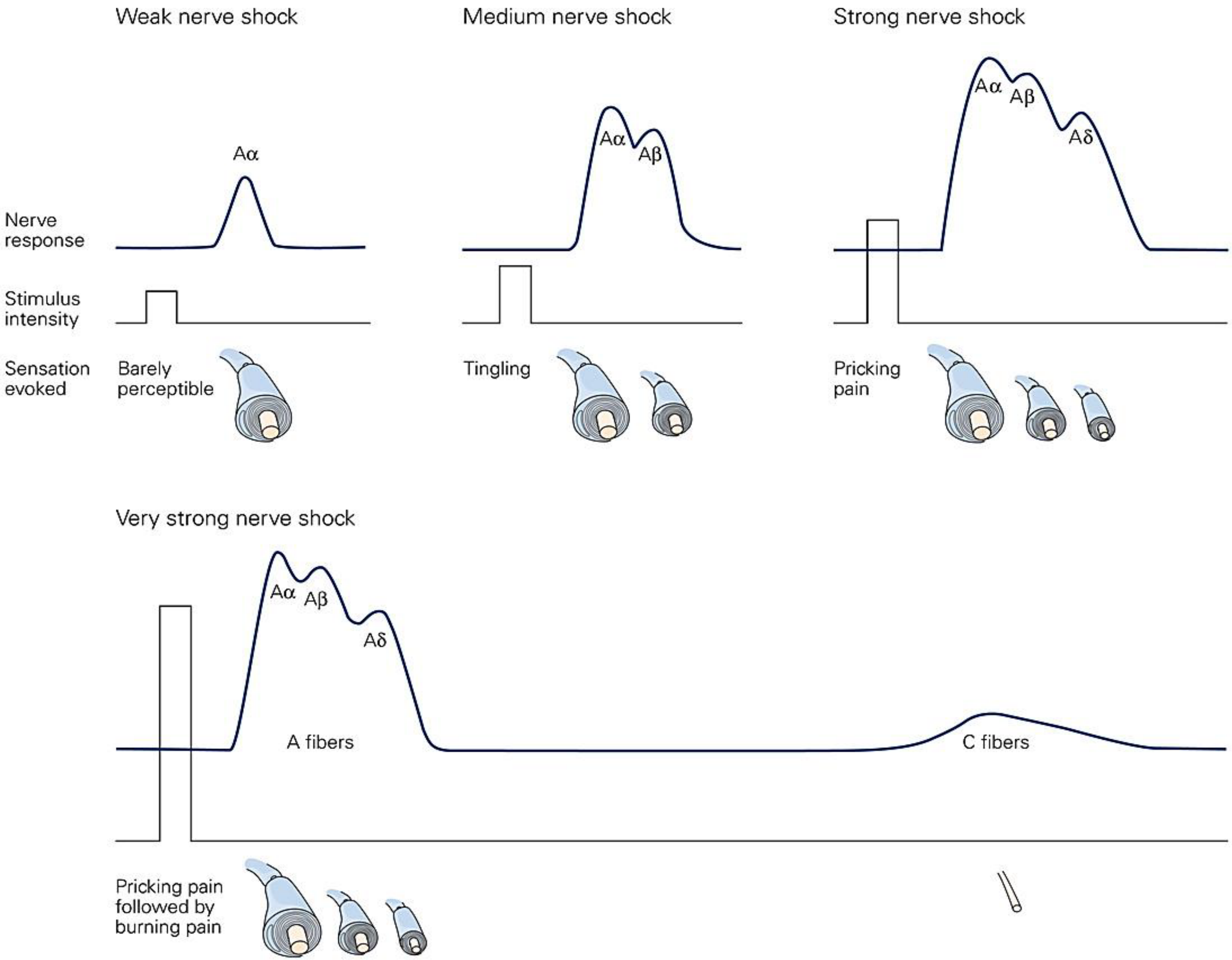
Nerve Conduction Studies



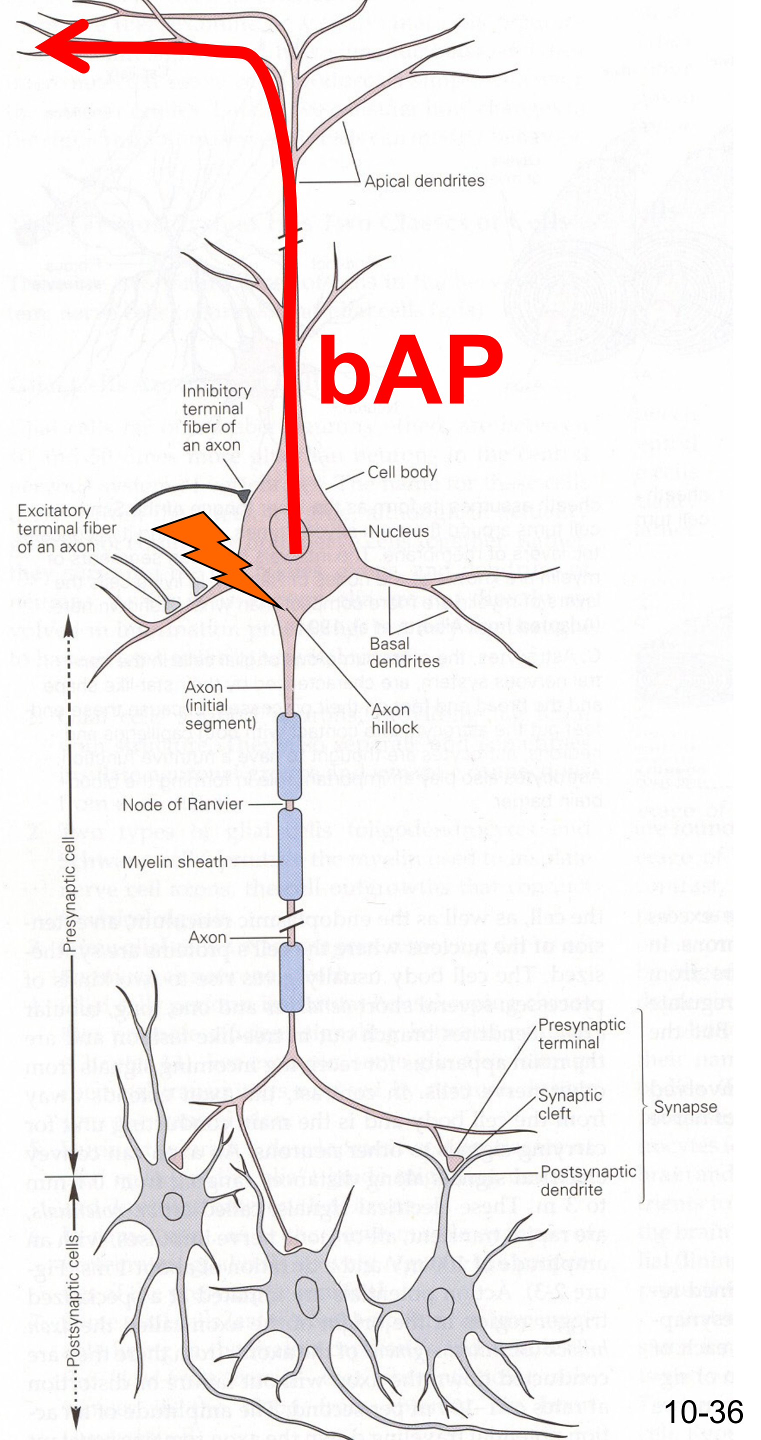




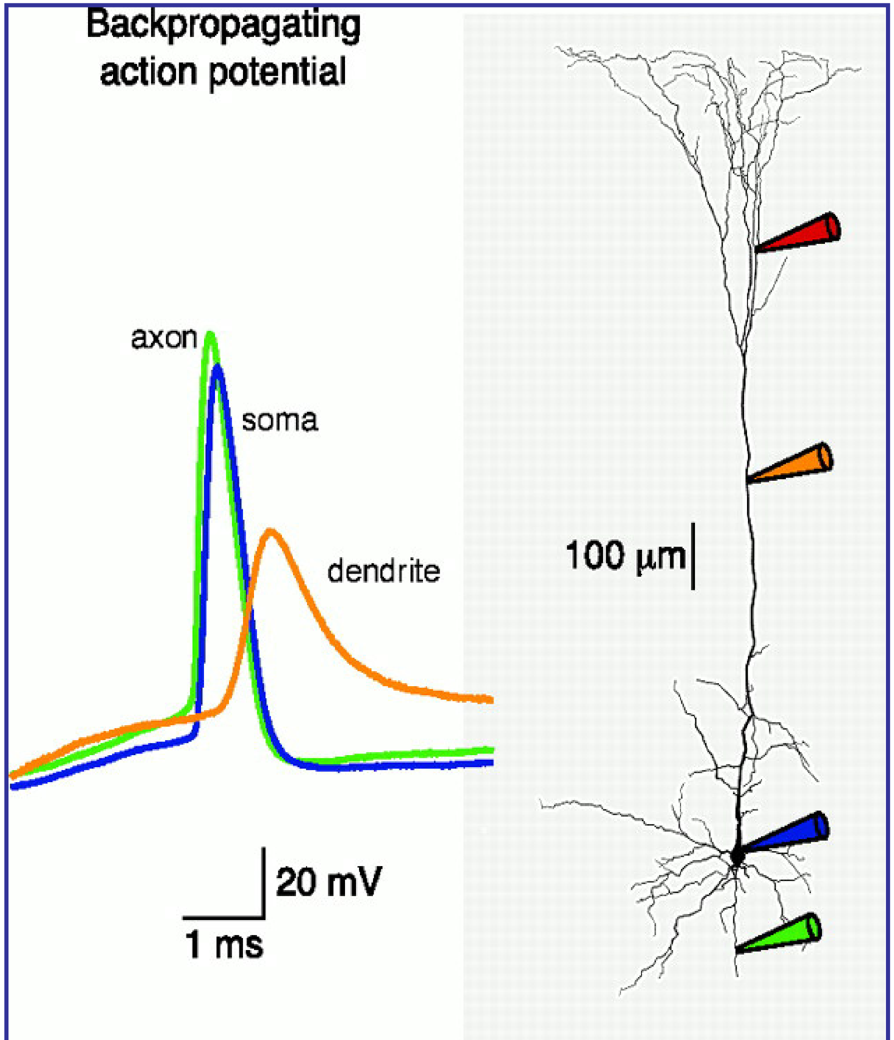
Compound Action Potentials



Back-Propagating Action Potentials



Back-Propagating Action Potentials



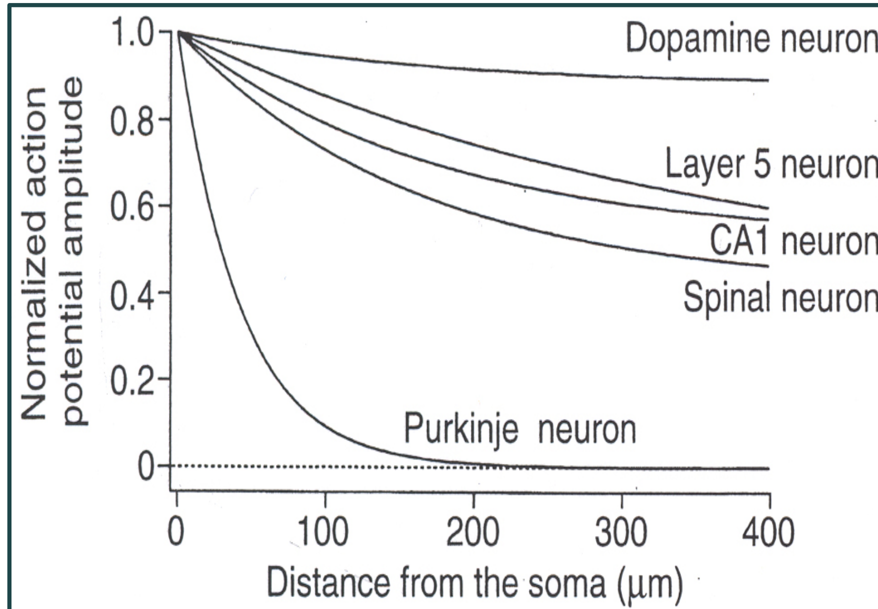
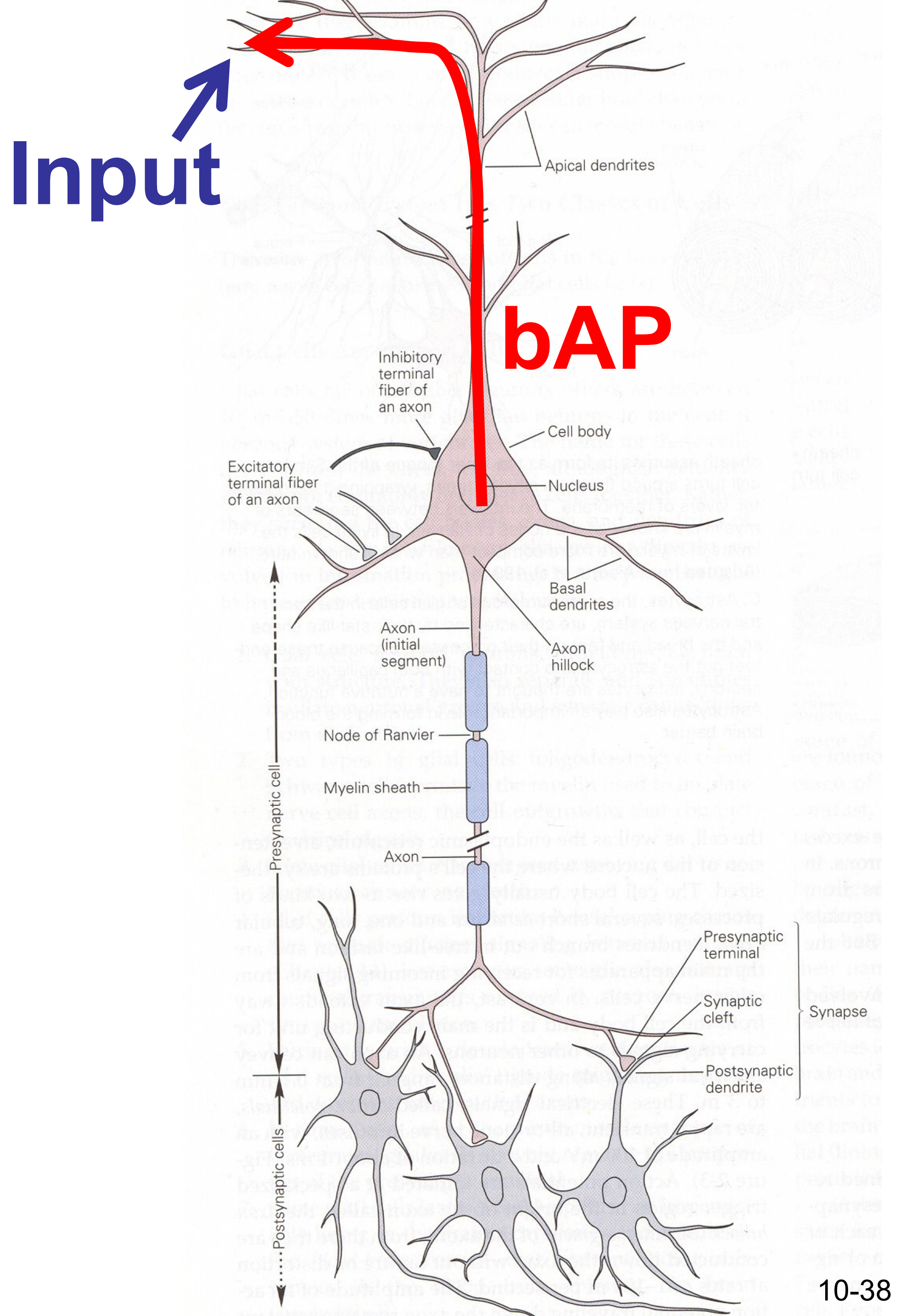


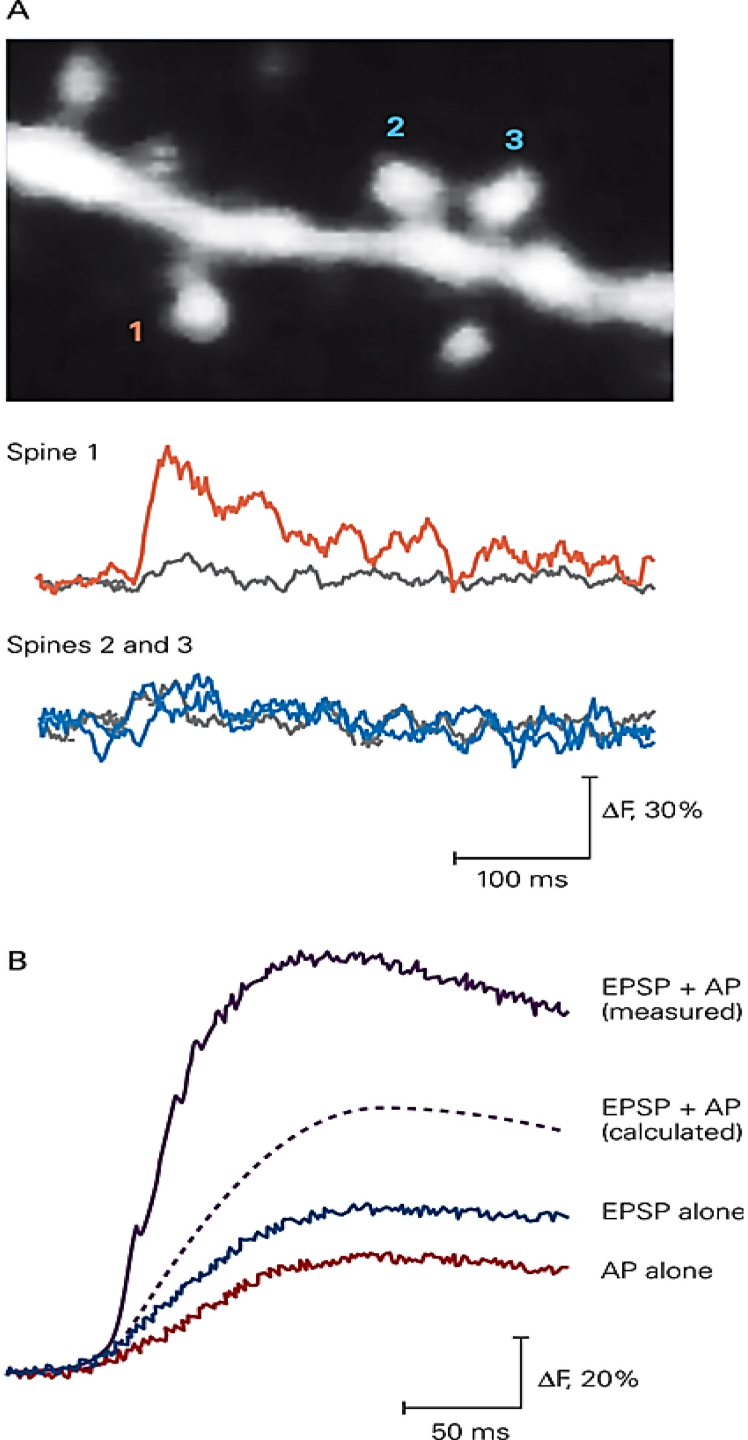
Fig. 4. ***Comparison of dendritic action potential amplitude at different distances from the soma.*** *Dendritic action potential amplitude, normalized to the amplitude of action potentials at the soma, is plotted against the distance from the soma the dendritic recording was made for neocortical layer-5 and hippocampal CA1-pyramidal, spinal cord, cerebellar Purkinje and substantia nigra dopamine neurons. The best single exponential fit to the experimental data in the different neuronal types is shown.* Adapted from Refs 36–40.

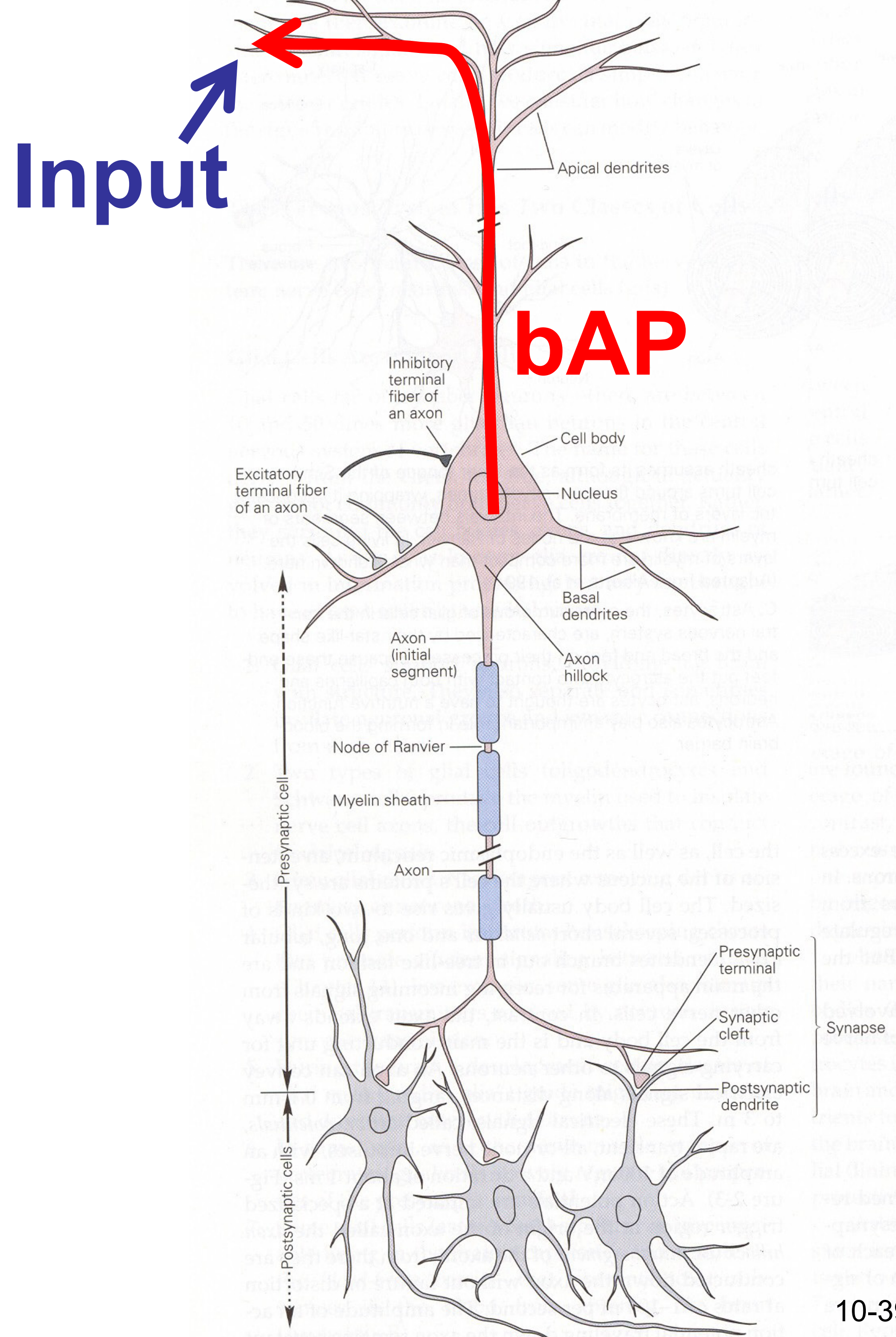
Hausser et al., Science 290:739-744

Stuart et al., TINS 20:125-131

Convergence of forward-propagating and back-propagating signals often induces synaptic plasticity




A
2
3
1
Spine 1
Spines 2 and 3
ΔF, 30%
100 ms
B
EPSP + AP
(measured)
EPSP + AP
(calculated)
EPSP alone
AP alone
ΔF, 20%
50 ms


Input
bAP
Apical dendrites
Inhibitory
terminal
fiber of
an axon
Cell body
Excitatory
terminal fiber
of an axon
Nucleus
Basal
dendrites
Axon
(initial
segment)
Axon
hillock
Node of Ranvier
Myelin sheath
Axon
Presynaptic cell
Presynaptic
terminal
Synaptic
cleft
Synapse
Postsynaptic
dendrite
Postsynaptic cells