Tutorial on basic concepts in Neuroscience

Martin Wojtowicz, PhD
Physiology
University of Toronto

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Discovery of bioelectricity

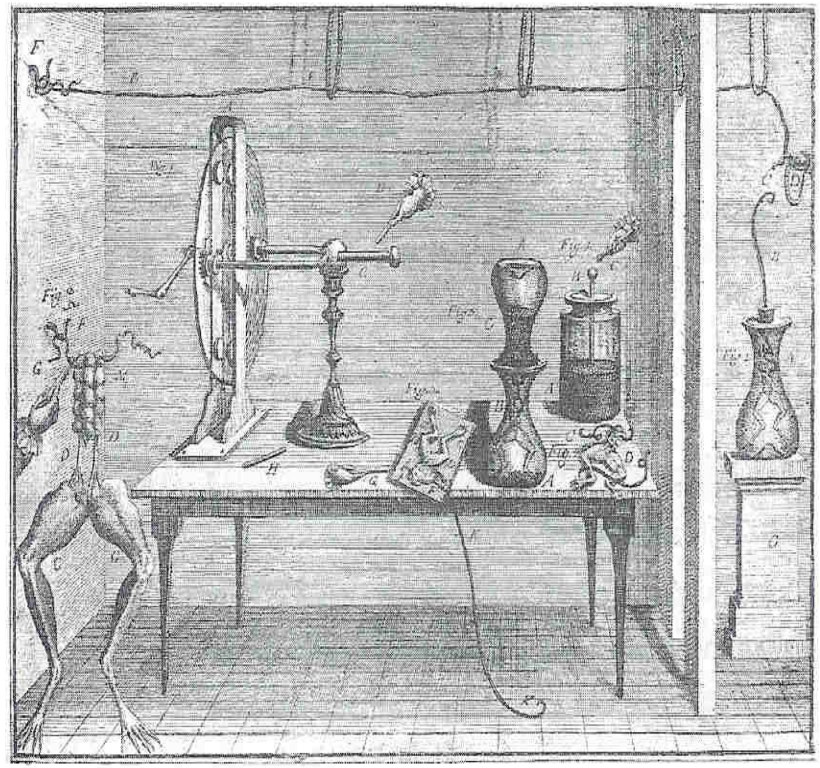


Fig. 1. *Plate I of the* **Commentarius.** *The prepared frog and the electric machine on the left allude to the spark experiment.*

Luigi Galvani 1791

- Resting membrane potential
- Action potential
- The synapse
- The neuron
- Neuronal circuit

Credit to Prof. Bill MacKay, UofT

Na^+/K^+ Pump

- **Na^+,K^+-dependent ATPase** is enzyme that moves Na^+ out of cell, and K^+ into cell
- for each ATP molecule broken down, 3 Na^+ ions are pumped out and 2 K^+ pumped in
- consumes 1/3 of energy needs of body
- Na/K inequality $\rightarrow$ p.d. of -10 mV

Resting Potential

Efflux of K until electrochemical equilibrium reached.

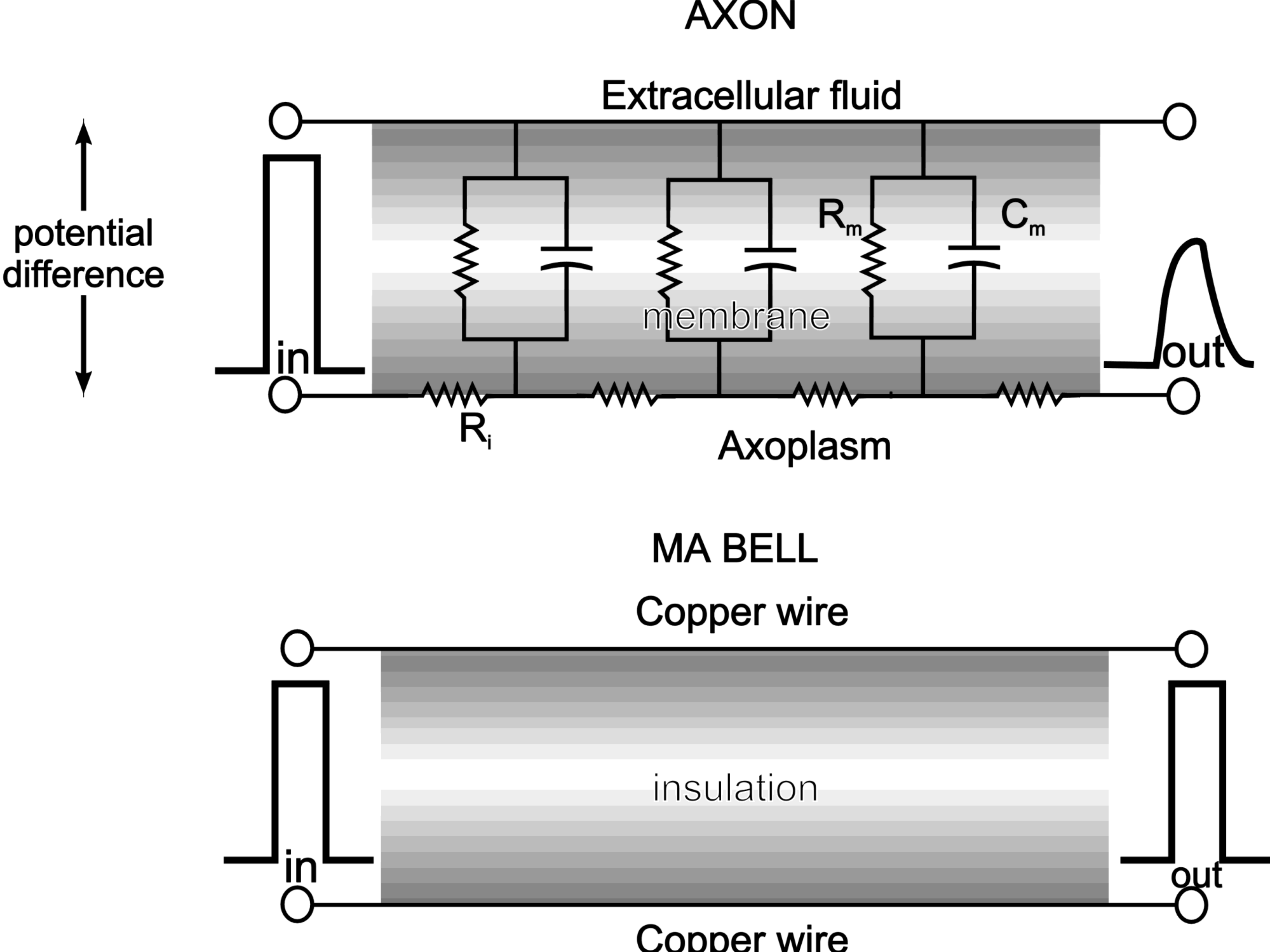
Nernst Equation

- $E_{K+} = (RT/F) \ln([K^+]_o / [K^+]_i) = -90$ mV
- the equation gives the potential difference across the membrane, inside with respect to outside, at equilibrium

Which membrane potential is greater,
-90mV or -40mV?

Goldman Equation

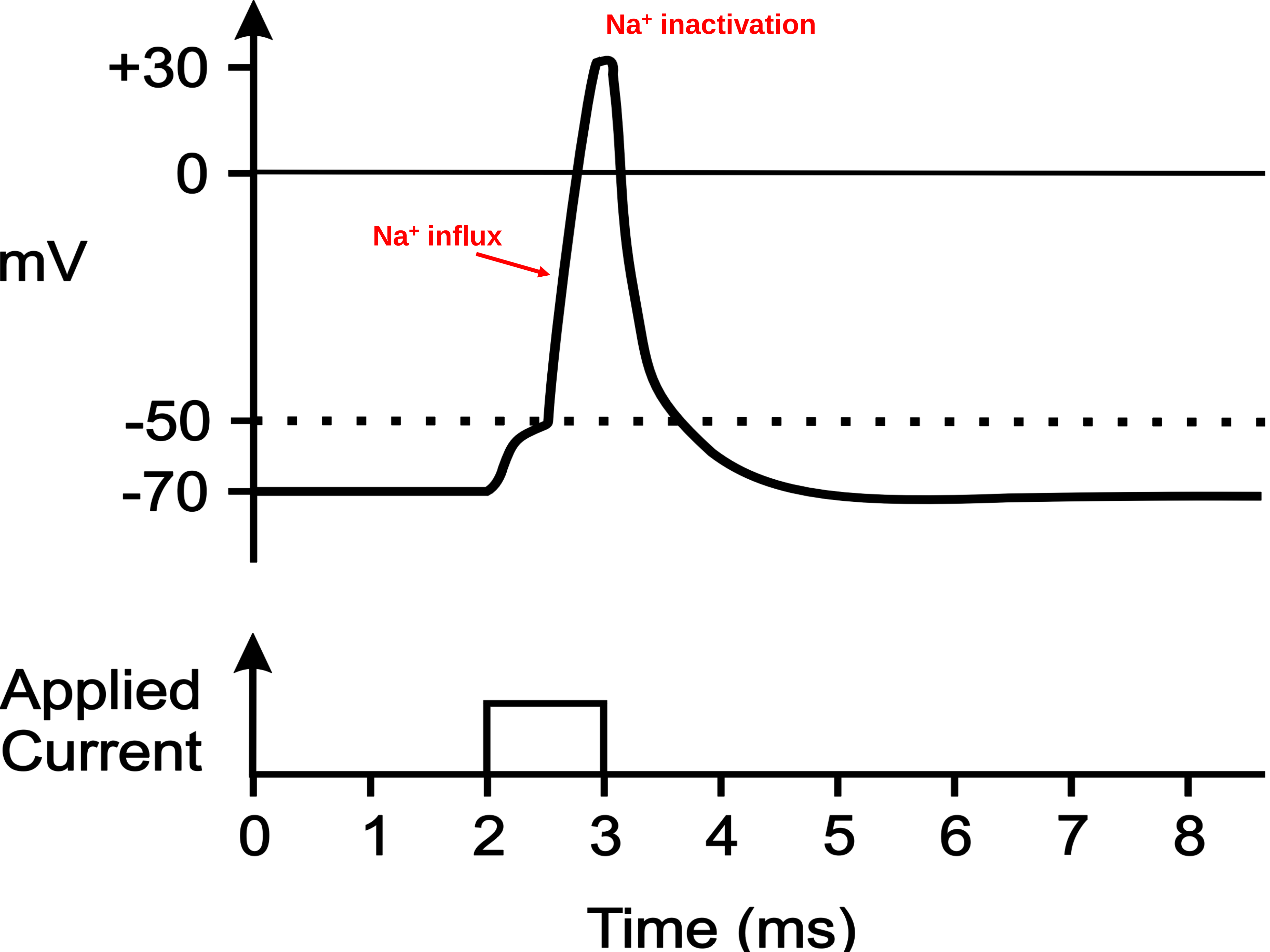
$$E_m = \left(\frac{RT}{F}\right) \ln\left(\frac{P_K[K^+]_o + P_{Na}[Na^+]_o + P_{Cl}[Cl^-]_i}{P_K[K^+]_i + P_{Na}[Na^+]_i + P_{Cl}[Cl^-]_o}\right)$$

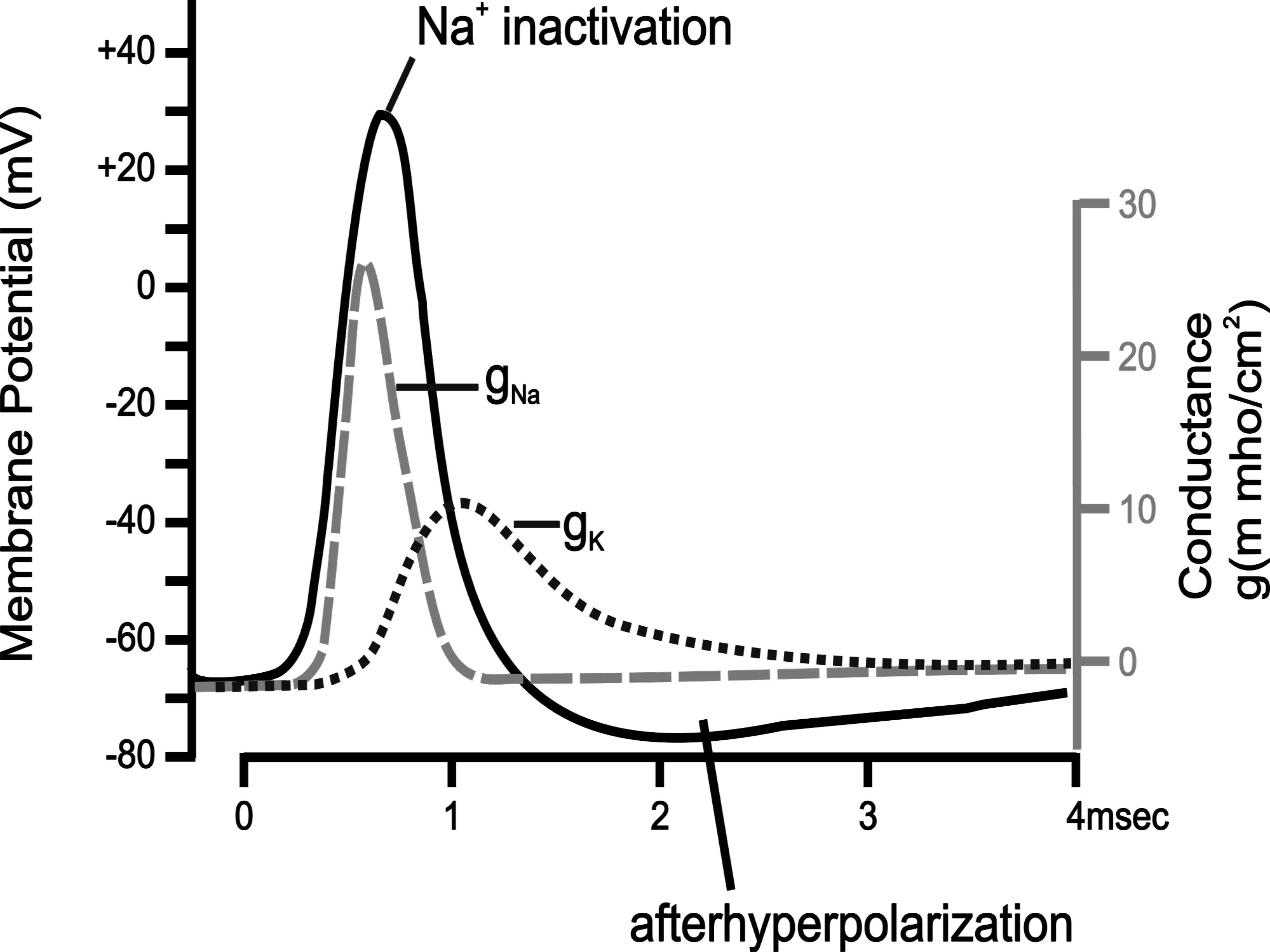

AXON
Extracellular fluid
potential difference
in
Rm
Cm
membrane
out
Ri
Axoplasm
MA BELL
Copper wire
insulation
in
out
Copper wire

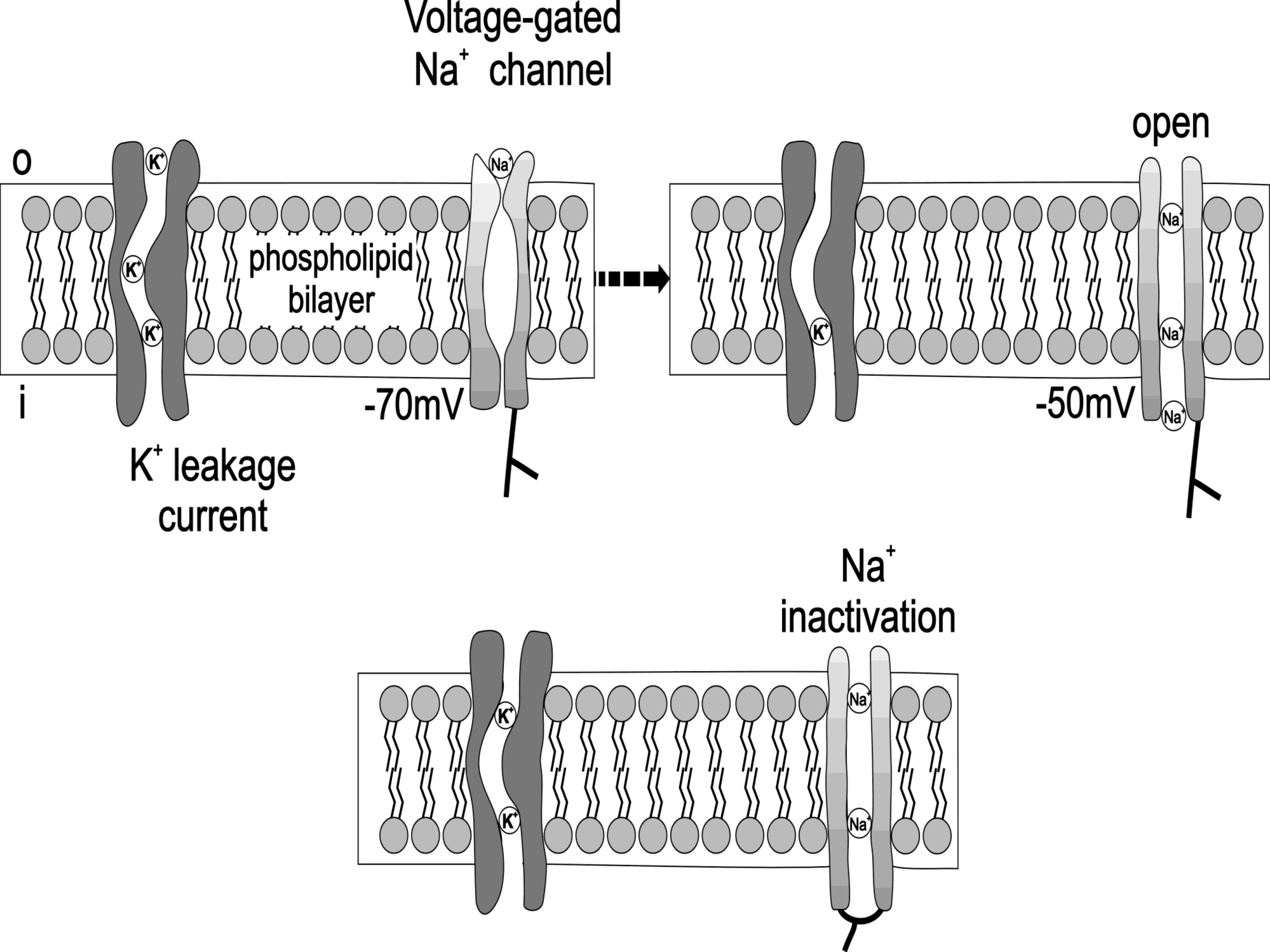
Passive potential simulation

Action Potential

- Na^+ channels occur in high density within ‘excitable’ membranes
- when channels are open, membrane potential surges towards $E_{Na+} = 60$ mV
- but channels rapidly inactivate
- **Na^+ inactivation** leaves K^+ leakage as main current, and resting potential is restored

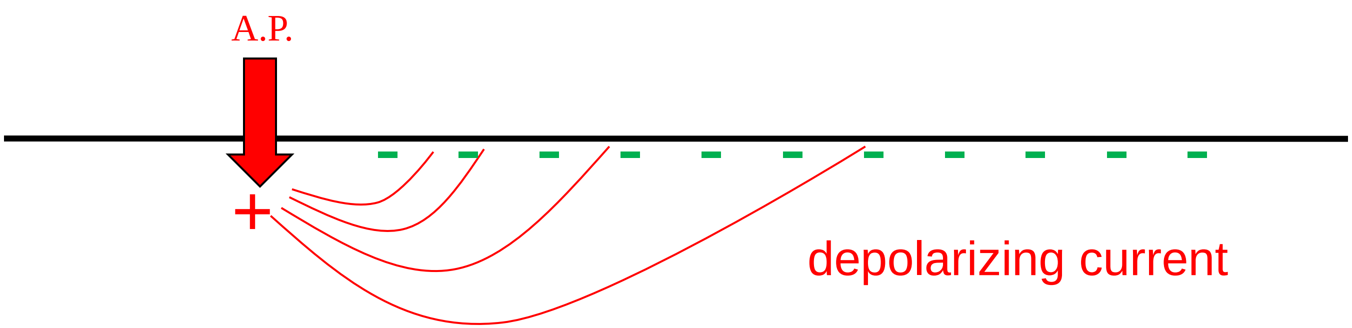

Na+ inactivation
+30
0
mV
Na+ influx
-50
-70
Applied
Current
0
1
2
3
4
5
6
7
8
Time (ms)


Na+ inactivation
Membrane Potential (mV)
+40
+20
0
-20
-40
-60
-80
gNa
gK
Conductance
g(m mho/cm2)
30
20
10
0
0
1
2
3
4msec
afterhyperpolarization


Voltage-gated
Na+ channel
o
i
K+
K+
K+
Na+
phospholipid
bilayer
-70mV
K+ leakage
current
open
Na+
Na+
Na+
K+
-50mV
Na+
inactivation
K+
K+
Na+
Na+

Impulse conduction

- When a patch of excitable membrane generates an action potential, zone of reversed polarity serves as source of depolarizing current for adjacent membrane
- Na^+ channels opened in adjacent membrane
- therefore, once started, an a.p. will propagate from its origin across the rest of the cell



Action potential simulation

Rate Code

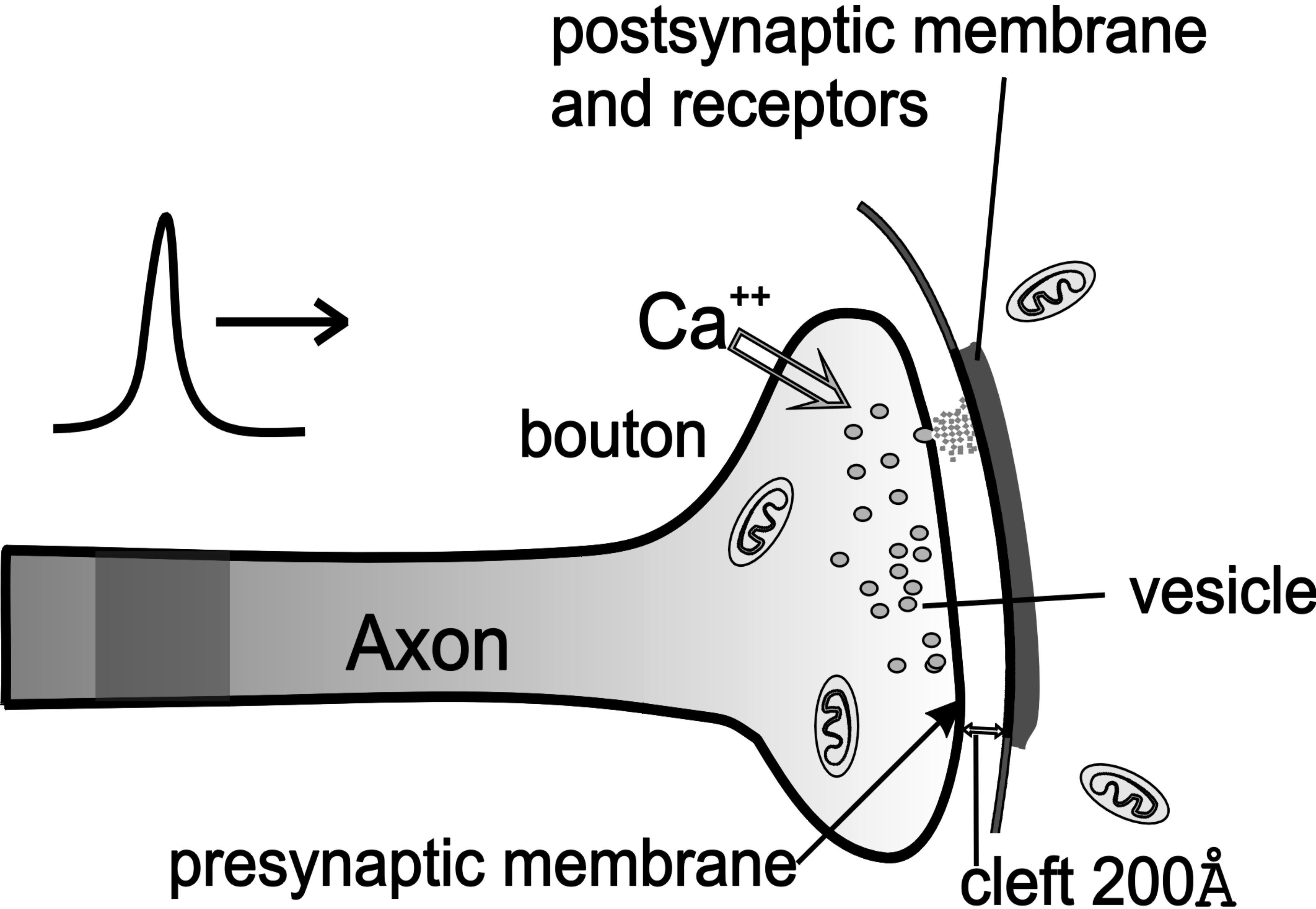
- Mean frequency of action potential train conveys information
- Commonly used to code <u>stimulus intensity</u>
- Ceiling imposed on individual axons by refractory period (roughly 200 imp/s)
- Requires integration over a specific time window

Bursting

- Bursts encode more info than individual spikes; common in layer 5 pyramidal cells
- Prefered input for induction of LTP
- NMDA spikes in basal dendrites: suited for burst detection, and provide prolonged somatic depolarization that generates output burst
- Similar role for Ca_V channels in apical dendrites [*J.Neurosci. 29(38):11891*]

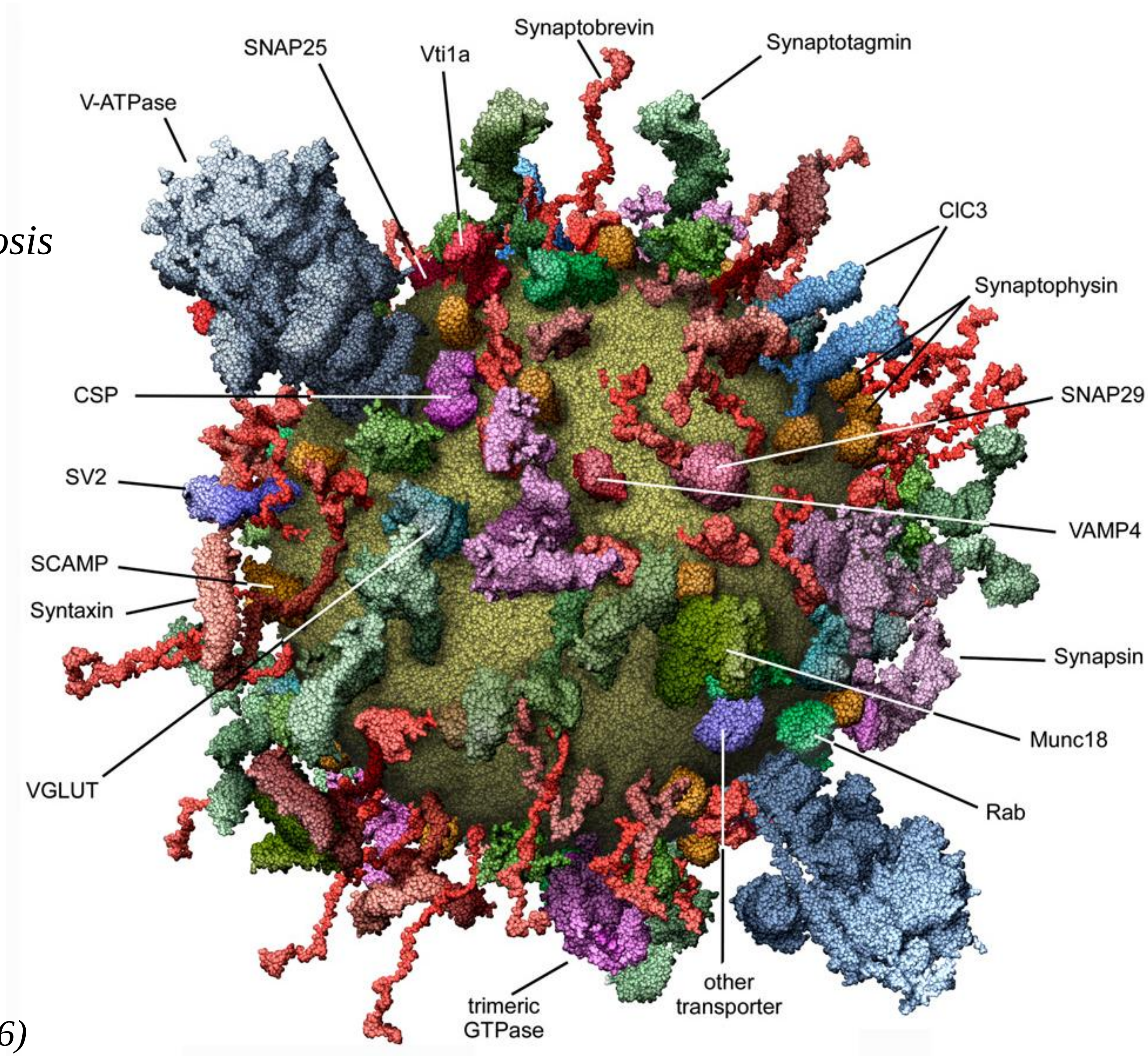
Synaptic Transmission

substrate for neuronal processing


postsynaptic membrane
and receptors
Ca++
bouton
vesicle
Axon
presynaptic membrane
cleft 200Å

Synaptic Vesicle

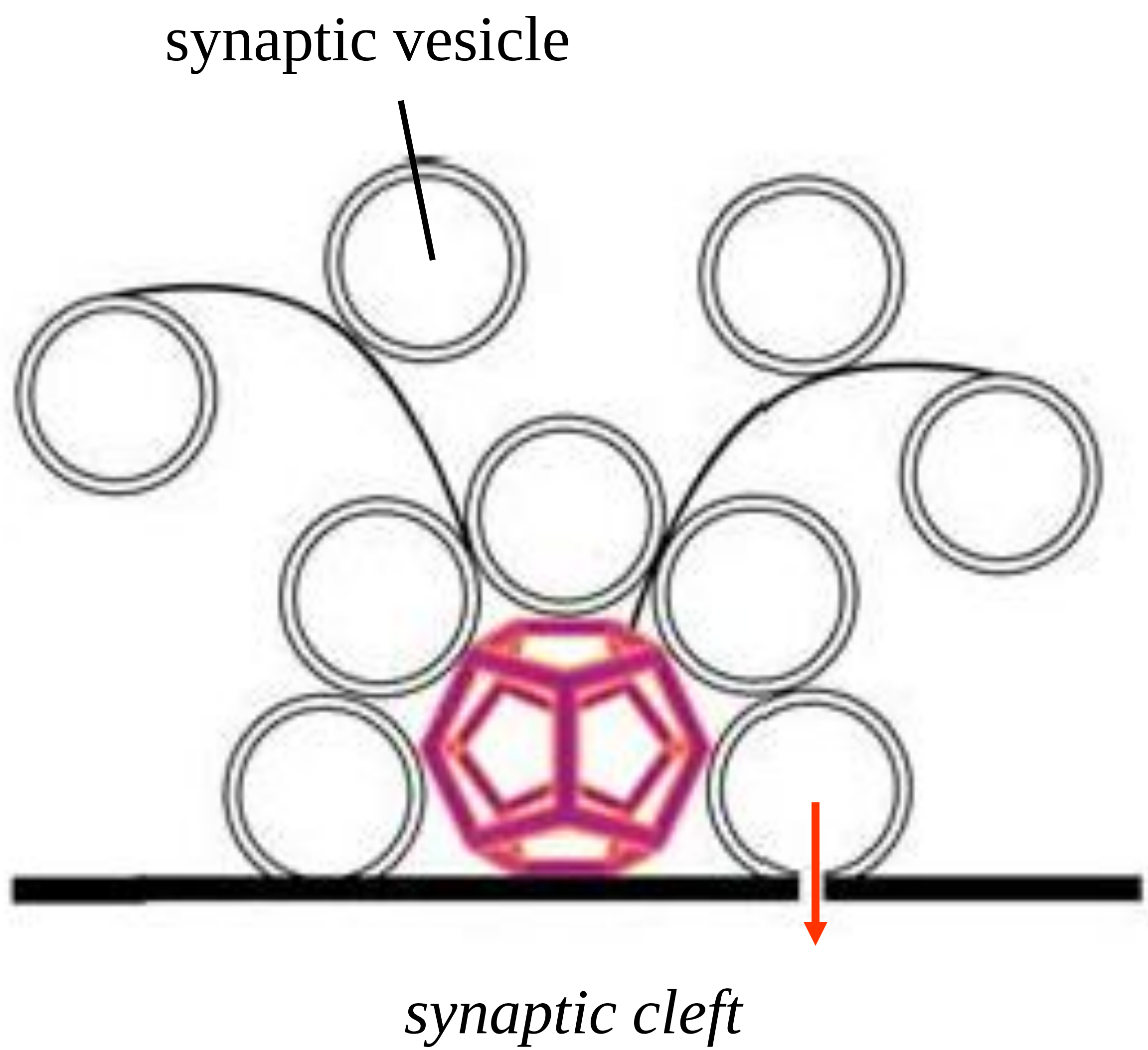
SNARE proteins are necessary for exocytosis

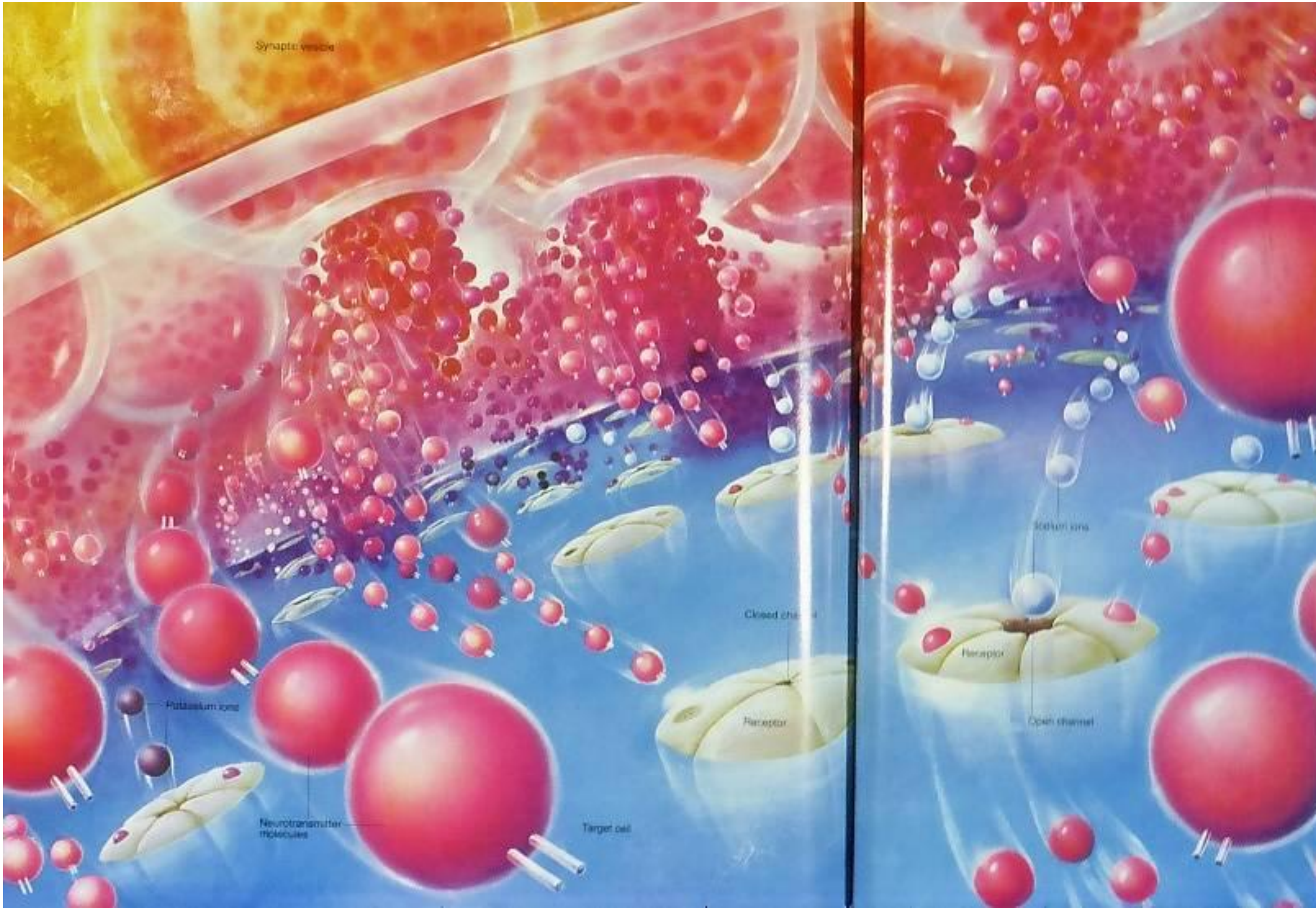


Cell 127: 831-846 (2006)

Vesicle Docking

Vesicles are assembled for release around a polyhedral scaffold: ‘readily releasable pool’



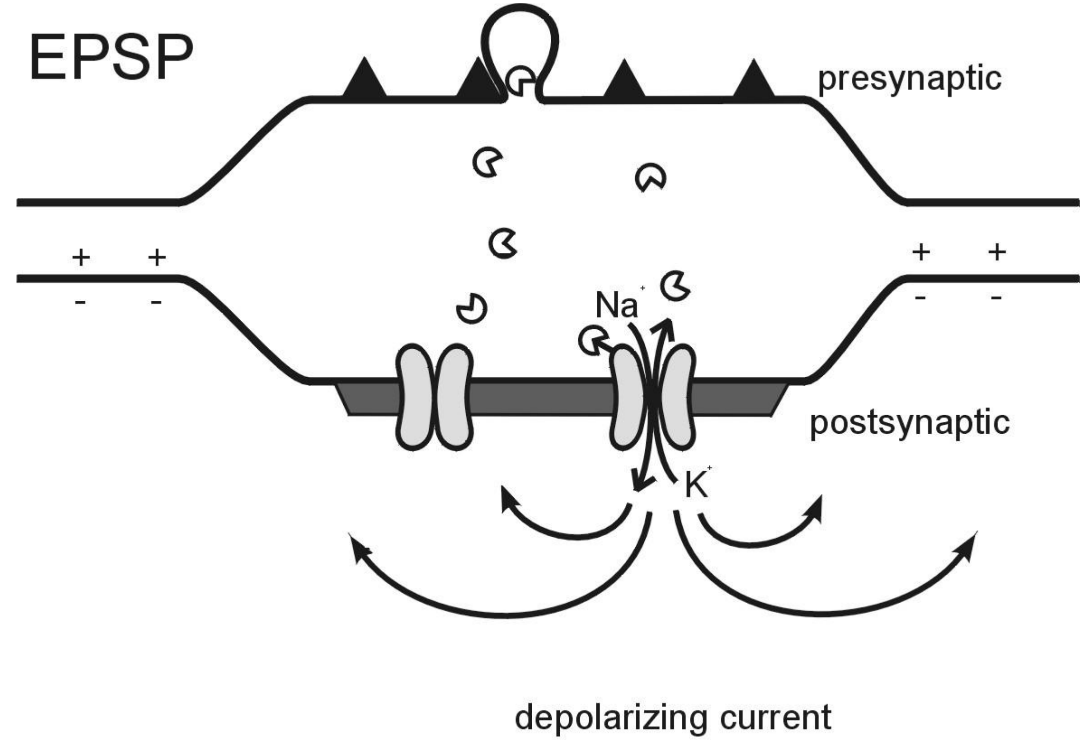


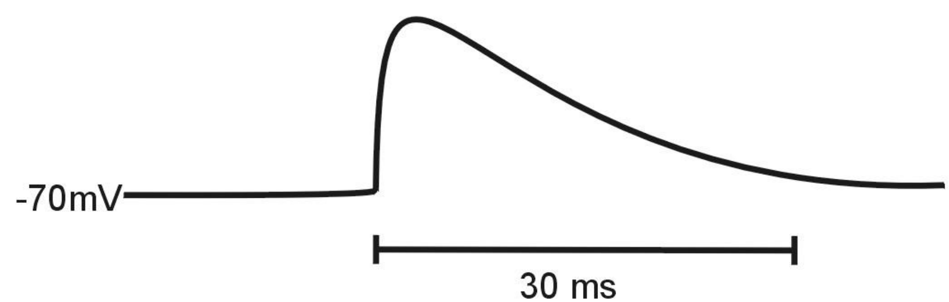
The incredible machine, National Geographic

Excitatory Post Synaptic Potential

Ligand-gated ion channel opens to allow diffusion of small cations (mainly Na^+ and K^+)

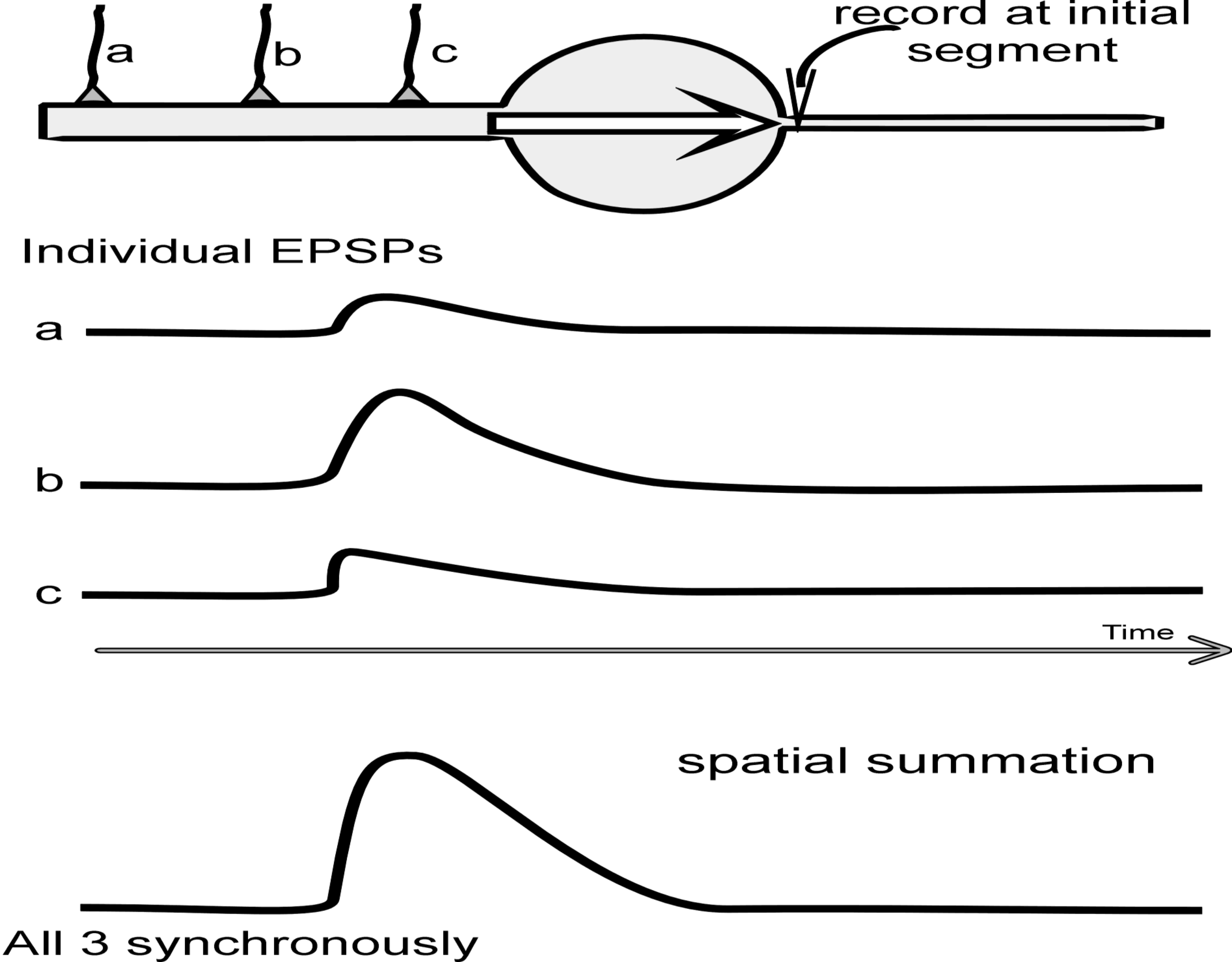
Individual ion channels open and close sporadically for varying amounts of time. Total current from all the post-synaptic receptor channels generates the EPSP (V=IR)

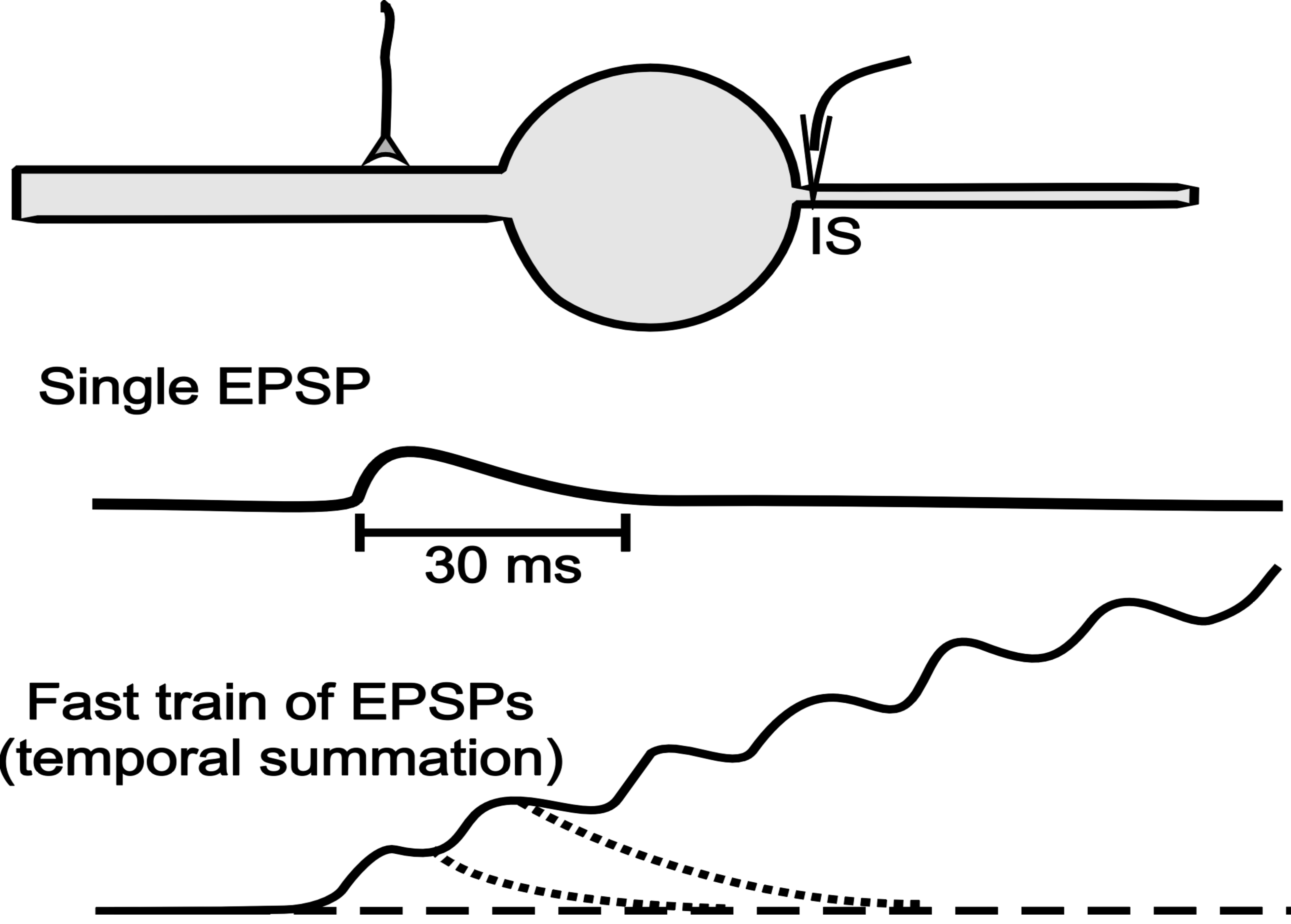




Types of PSP summation

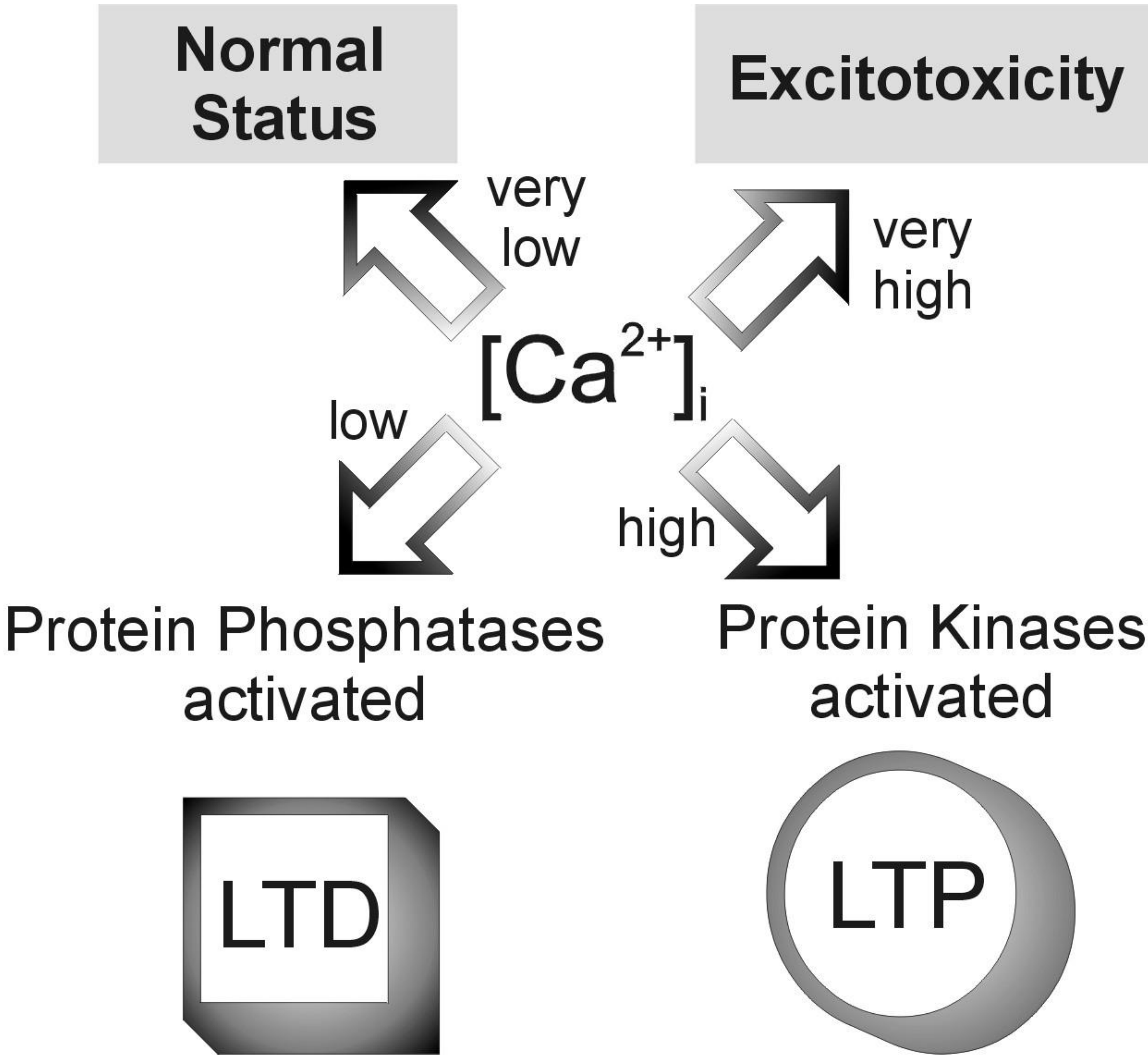
- 1) **Spatial summation**: minimum of 10-30 synchronous EPSPs in dendritic tree, each generated at a different synapse
- 2) **Temporal summation**: only a few active synapses, but each generating EPSPs at high frequency; summated potentials reach threshold over a period of time


record at initial segment
a
b
c
Individual EPSPs
a
b
c
Time
spatial summation
All 3 synchronously

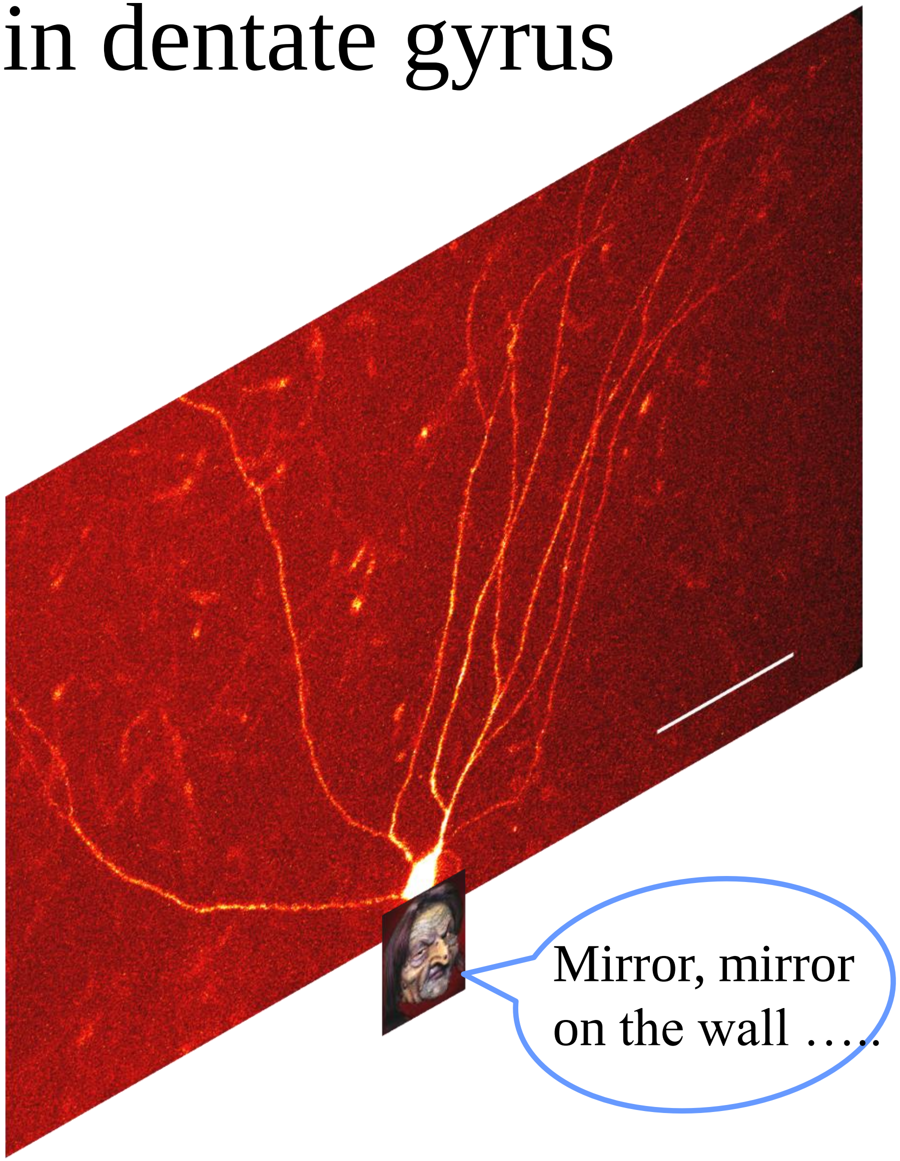

IS
Single EPSP
30 ms
Fast train of EPSPs
(temporal summation)

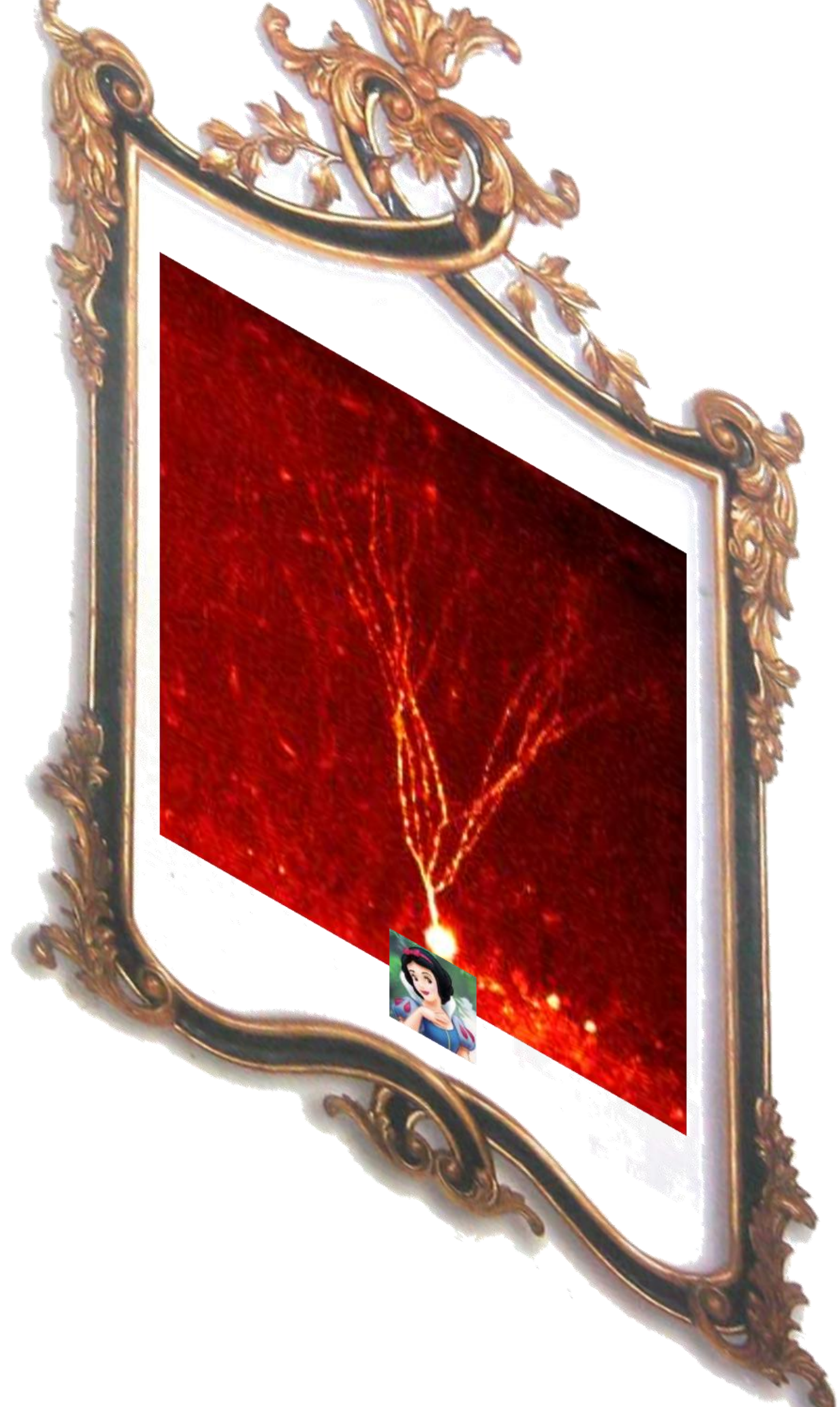
Metabotropic effects

- Ligand-receptor binding activates an enzyme (usually via G-protein coupling)
- $\rightarrow$ [2nd messenger] $\uparrow$ or $\downarrow$
- 2nd messenger is cAMP, cGMP, or InP_3
- 2nd messenger activates other enzymes, e.g. phosphokinases which phosphorylate iono-tropic receptors $\rightarrow$ modulate ion currents

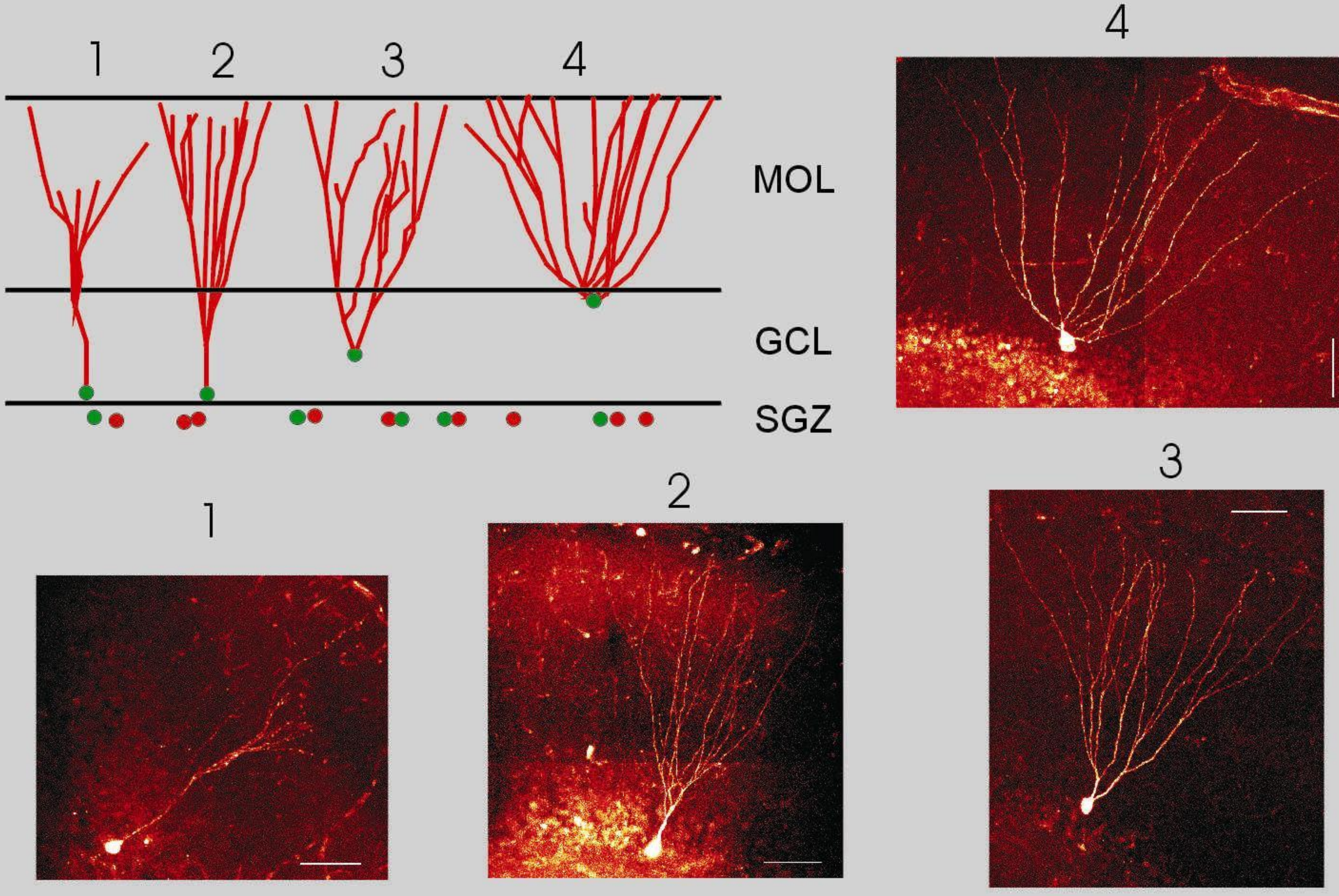

Normal Status
Excitotoxicity
very low
very high
[Ca2+]i
low
high
Protein Phosphatases activated
Protein Kinases activated
LTD
LTP

Young and old neurons in dentate gyrus



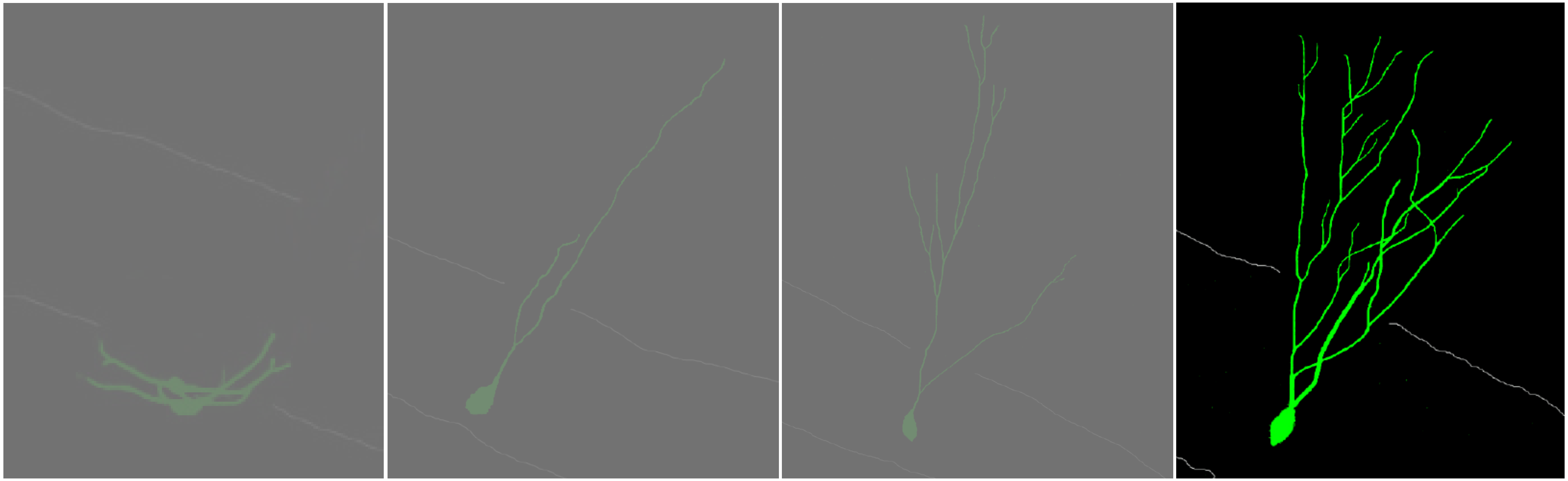


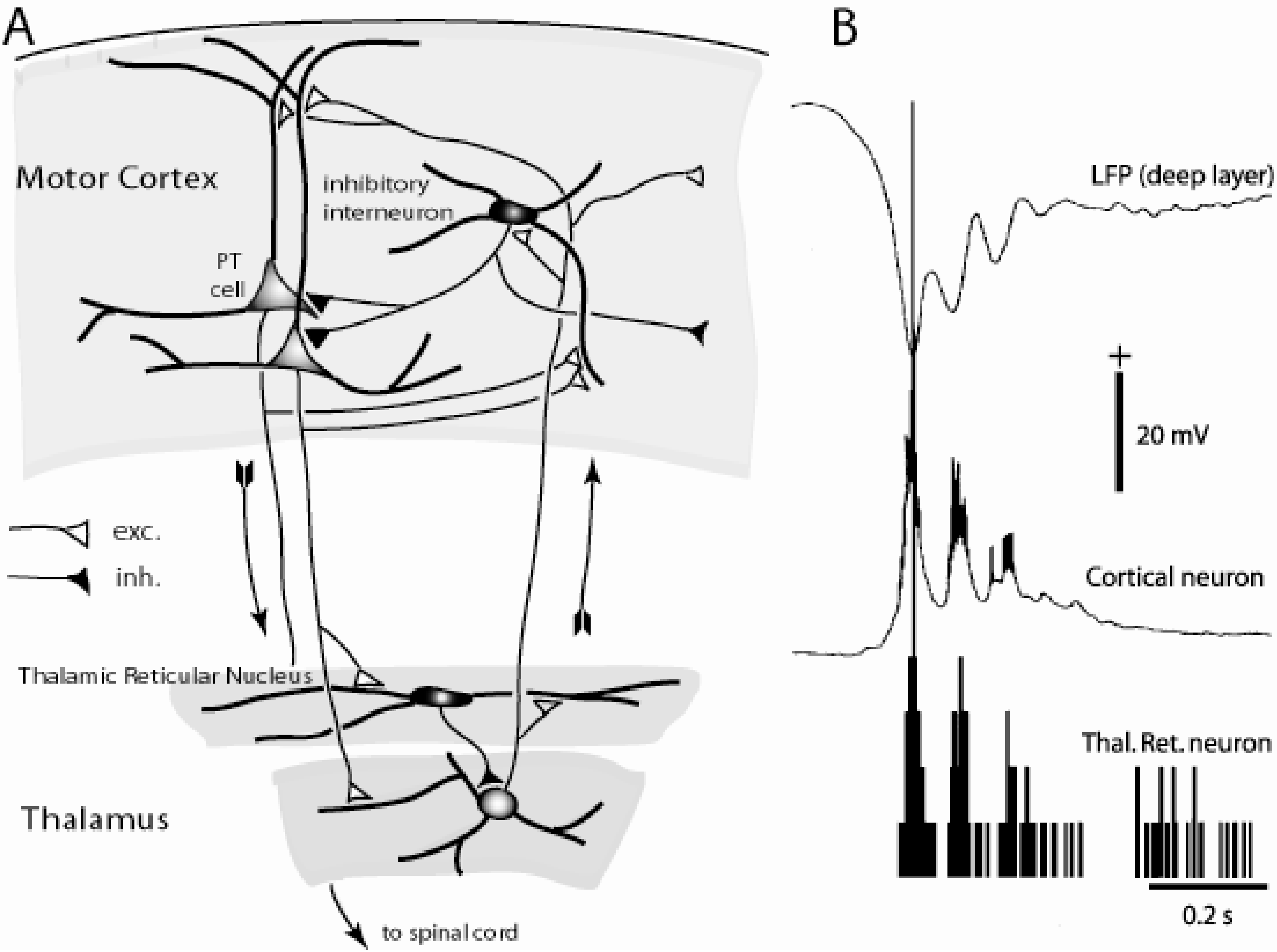
GRANULE CELL DEVELOPMENT IN ADULT RAT



Wang, Scott, Wojtowicz, 2000

Neuronal growth in adult brain





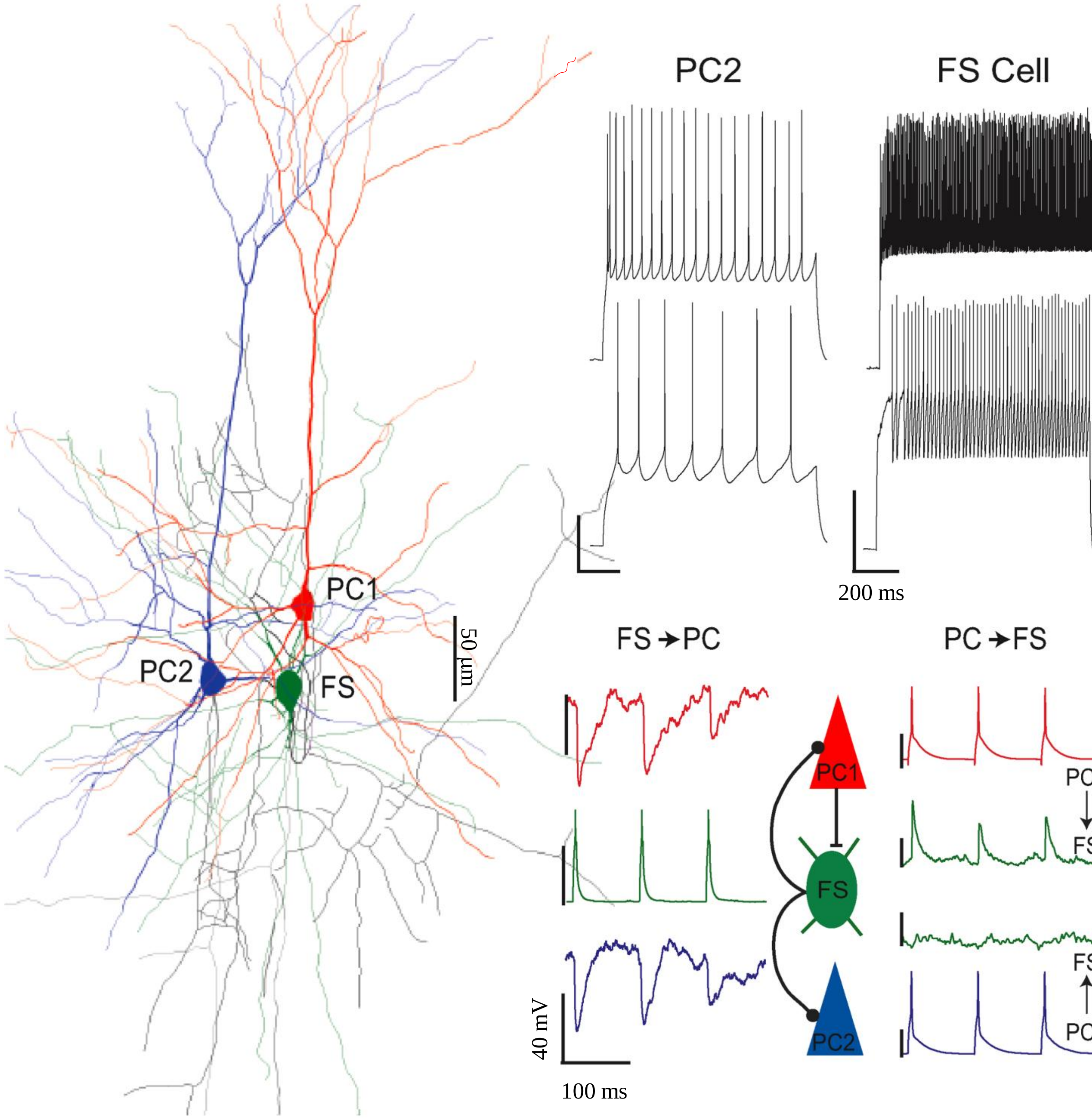
A
Motor Cortex
inhibitory
interneuron
PT
cell
exc.
inh.
Thalamic Reticular Nucleus
Thalamus
to spinal cord
B
LFP (deep layer)
+
20 mV
Cortical neuron
Thal. Ret. neuron
0.2 s

Module of gamma rhythm network

Fast Spiking interneurons (FS), or basket cells, inhibit neighboring pyramidal cells (PC). Within an intersomatic distance of 50 μm, most inhibitory connections occur in reciprocal pairs (i.e. PC excites FS that inhibits PC)

Auditory cortex.

High frequency rhythms are generated by smaller networks than low frequency rhythms



J.Neurosci. 29(33): 10321-10334 (2009)

Brain Rhythm ‘Octaves’

0.01 – 0.1 Hz	Infra Slow
0.2-0.4, 0.5–1	Slow
1 – 2, 2 – 4	Delta rhythms
4 – 8	Theta
8 – 14	Alpha (Mu)
14 – 30	Beta
30 – 50	Low Gamma
50 – 80	High Gamma
>80	High Frequency

Break !