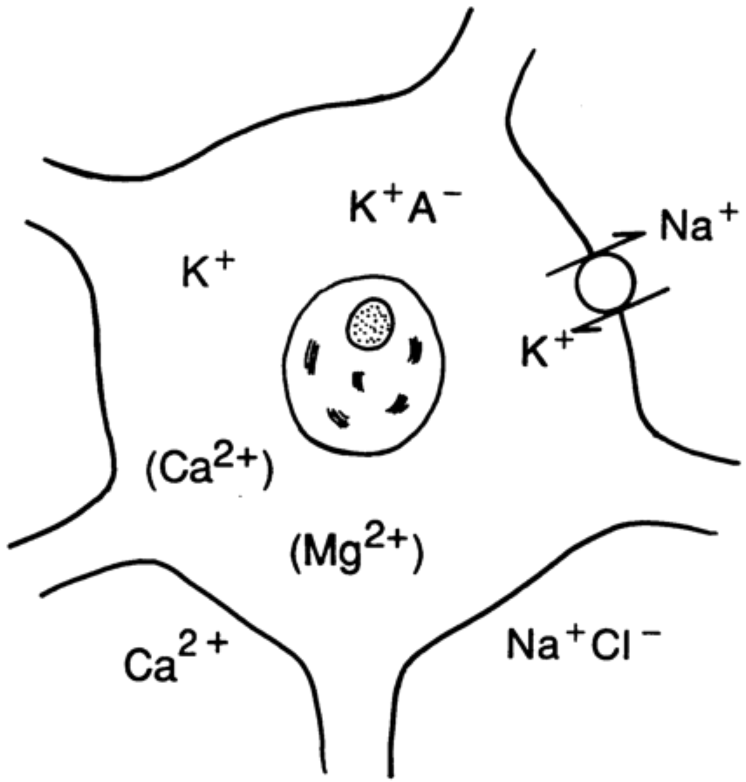
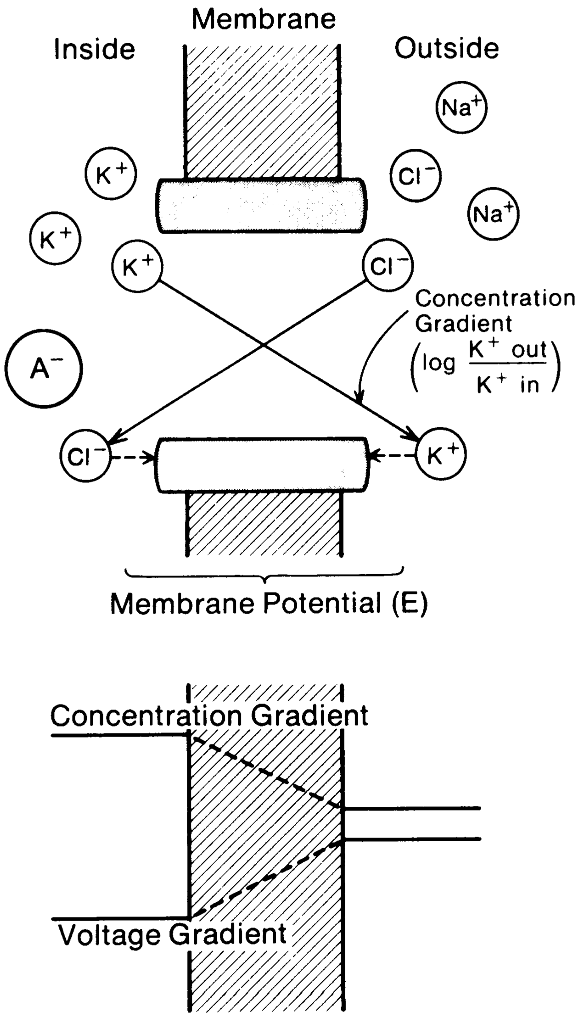


Fig. 4.1 A nerve cell and its ions. A, organic anions; Cl, chloride; K, potassium; Na, sodium; Ca, calcium; Mg, magnesium.

Ionic balance



Relations between electrical and chemical gradients across the membrane. (Modified from Woodbury, 1965)

Electrical and chemical (concentration) gradient via membrane

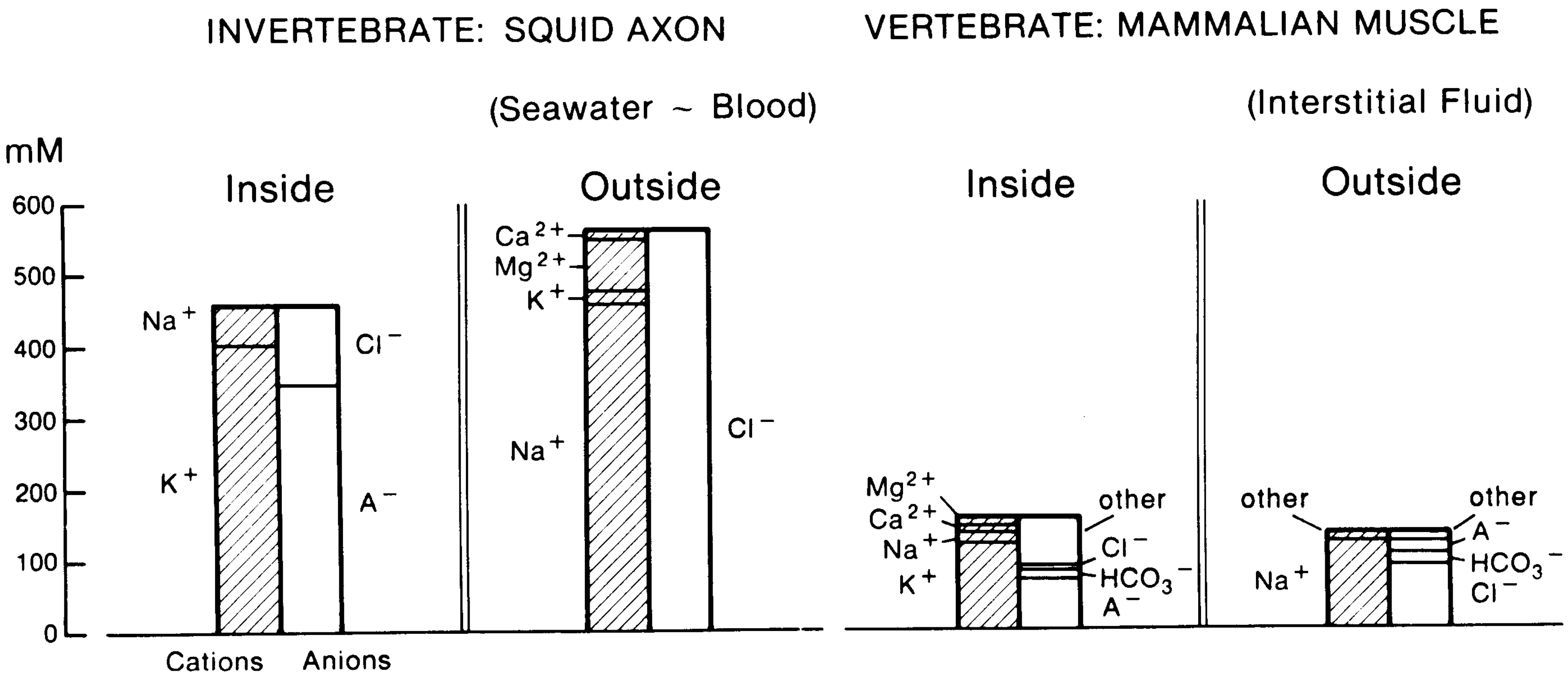
Table 4.1 Ionic concentrations for squid axon and mammalian muscle fiber

Ions	Invertebrate squid axon (seawater≈blood) Internal	External	Vertebrate muscle (neurons) (interstitial fluid) Internal	External
Cations				
K^+	400	(10)	124	2
Na^+	50	460	10	(125)
Ca^{2+}	(.4)	10	5	2
Mg^{2+}	10	54	14	1
other	—	—	—	—
Total	460	534	153	130
Anions				
Cl^-	40–150	560	2	77
HCO_3^-	—	—	12	27
$(A)^-$	345	—	74	13
other	—	—	(65)	(13)
Total	460	560	153	130

Concentrations in mM. The values for the mammalian muscle fiber are believed to be representative of neurons. ( ) indicates estimates, to give electroneutrality between cations and anions. Note lack of osmotic equilibrium across the membrane (between internal and external medium).

After Aidley (1989)

Fig. 4.2 Ionic concentrations for an invertebrate neuron (squid axon) and a mammalian fiber. (Based on Aidley, 1989)



Electrochemical potential is defined as:

$$\mu = \mu_0 + RTlnC + zFE$$

where:

μ_0 = elektrochemical potential of ions in a defined state
(e.g. concentration 1 M, temperature 0 ºC, electrical potential equals 0),
R = general gas constant,
T = absolute temperature,
InC = natural logarithm of concentration,
z = number of charges (+2 for Ca^{++}, -1 for Cl^-, etc.),
F = Faraday's number,
E = electrical potential.

Nernst equation

Walther Nernst, 1888

$$W_E = W_C$$

$$FE = RT \ln \frac{[K^+]_{OUT}}{[K^+]_{IN}}$$

$$E = 2.3 \frac{RT}{F} \log \frac{[K^+]_{OUT}}{[K^+]_{IN}}$$

Nernst potential for K^+

$$E_K = 58 \log \frac{[K^+]_{OUT}}{[K^+]_{IN}} \text{ mV}$$

$$= 58 \log \frac{20}{400} \text{ mV}$$

$$= -75 \text{ mV}$$

Nernst potential for Na⁺

$$E_{Na} = 58 \log \frac{[Na^+]_{OUT}}{[Na^+]_{IN}}$$

$$= 58 \log \frac{460}{50}$$

$$= +55 \text{ mV}$$

Resting membrane potential

$$I_K = g_K(E_m - E_K)$$

$$I_{Na} = g_{Na}(E_m - E_{Na})$$

$$I_{Cl} = g_{Cl}(E_m - E_{Cl})$$

$$I_K + I_{Na} + I_{Cl} = 0$$

$$g_K\,(E_m - E_K) + g_{Na}\,(E_m - E_{Na}) = 0$$

$$E_m = \frac{g_K}{g_K + g_{Na}} E_K + \frac{g_{Na}}{g_K + g_{Na}} E_{Na}$$

$$E_m = \frac{g_K}{g_T} E_K + \frac{g_{Na}}{g_T} E_{Na} + \frac{g_{Cl}}{g_T} E_{Cl} + \frac{g_{Ca}}{g_T} E_{Ca}$$

where

$$g_T = g_K + g_{Na} + g_{Cl} + g_{Ca}$$

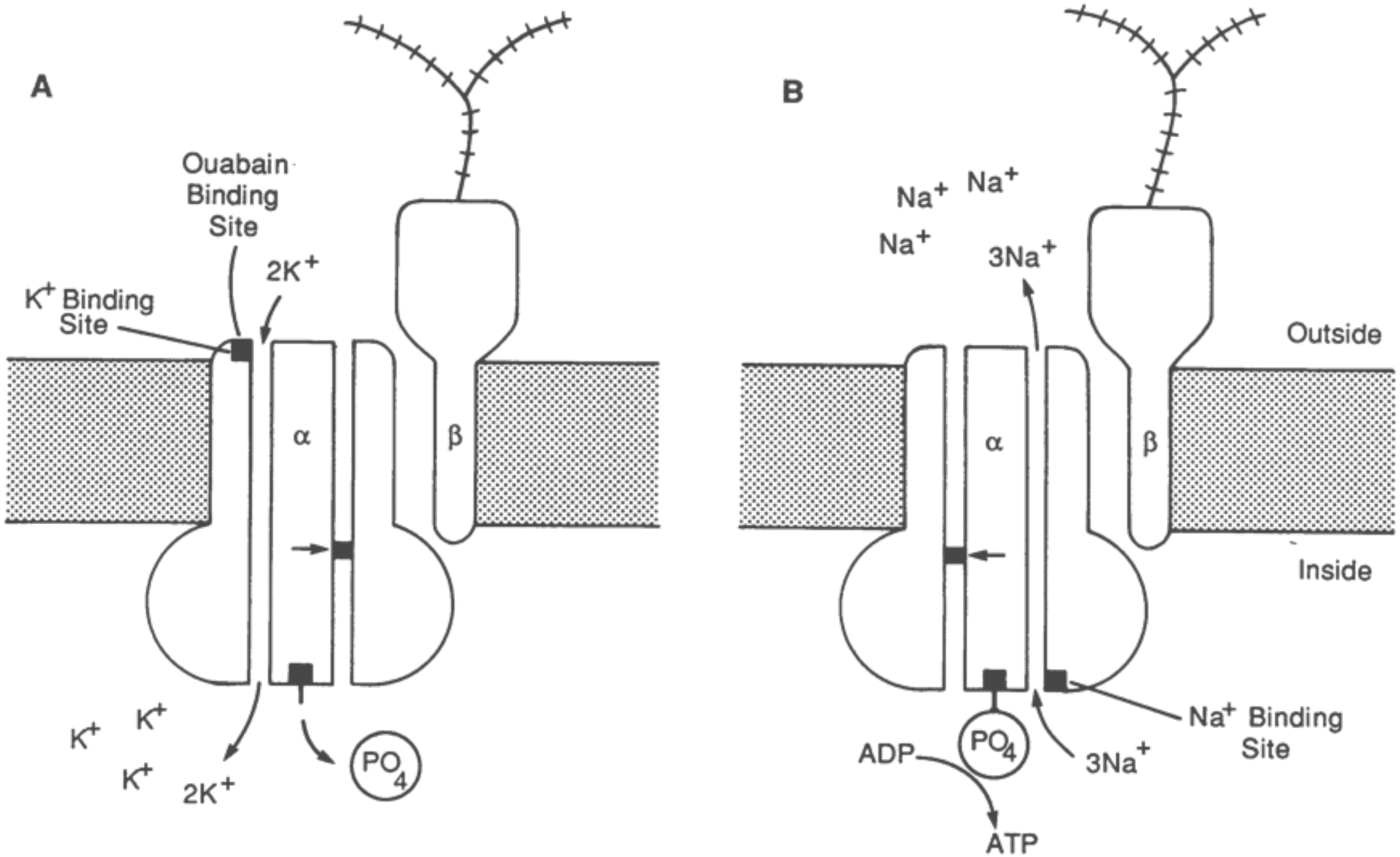
Conductance versus permeability

$$G_K \propto P_K \frac{[K^+]_{OUT}}{[K^+]_{IN}}$$

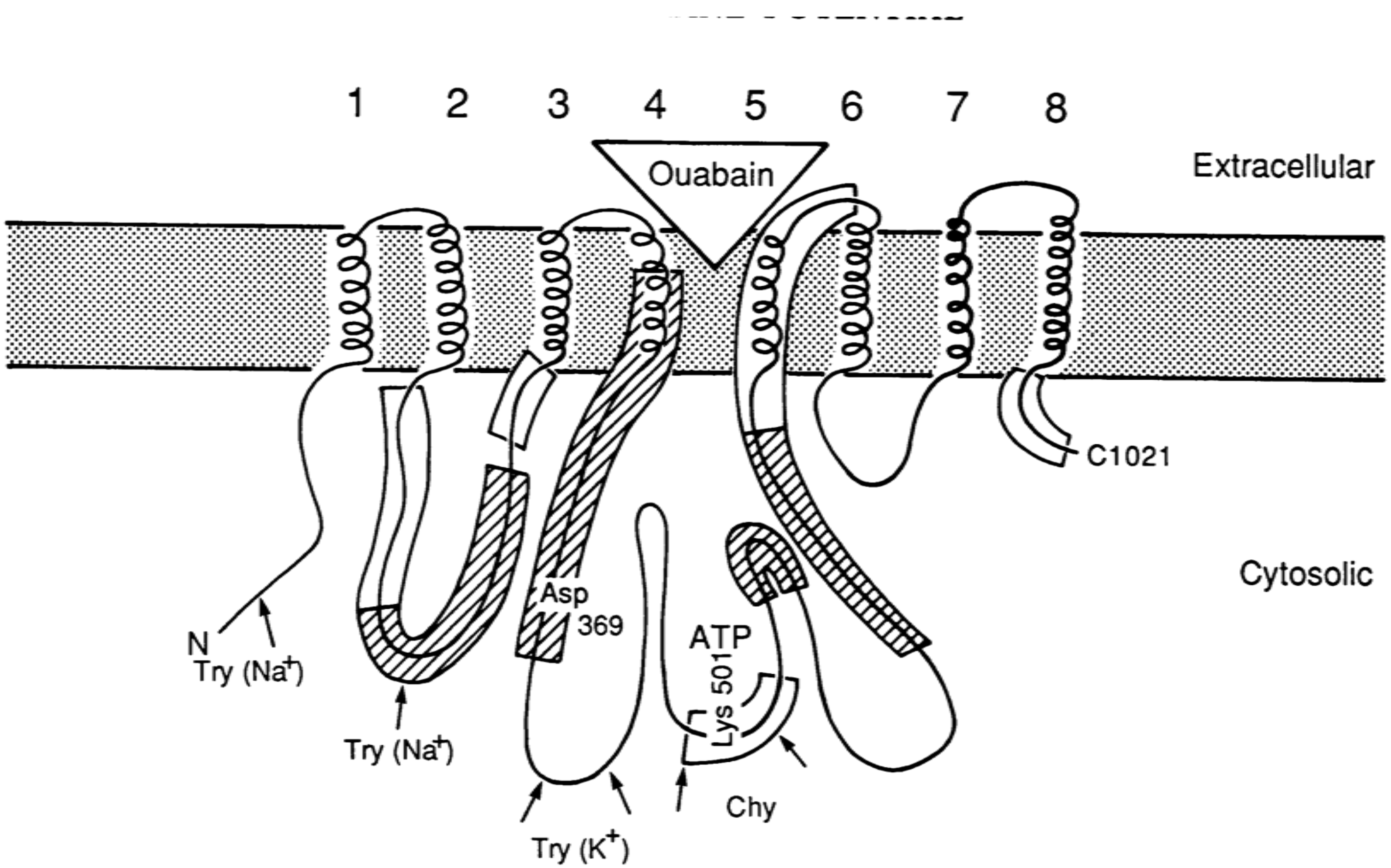
Constant field equation (GHK)

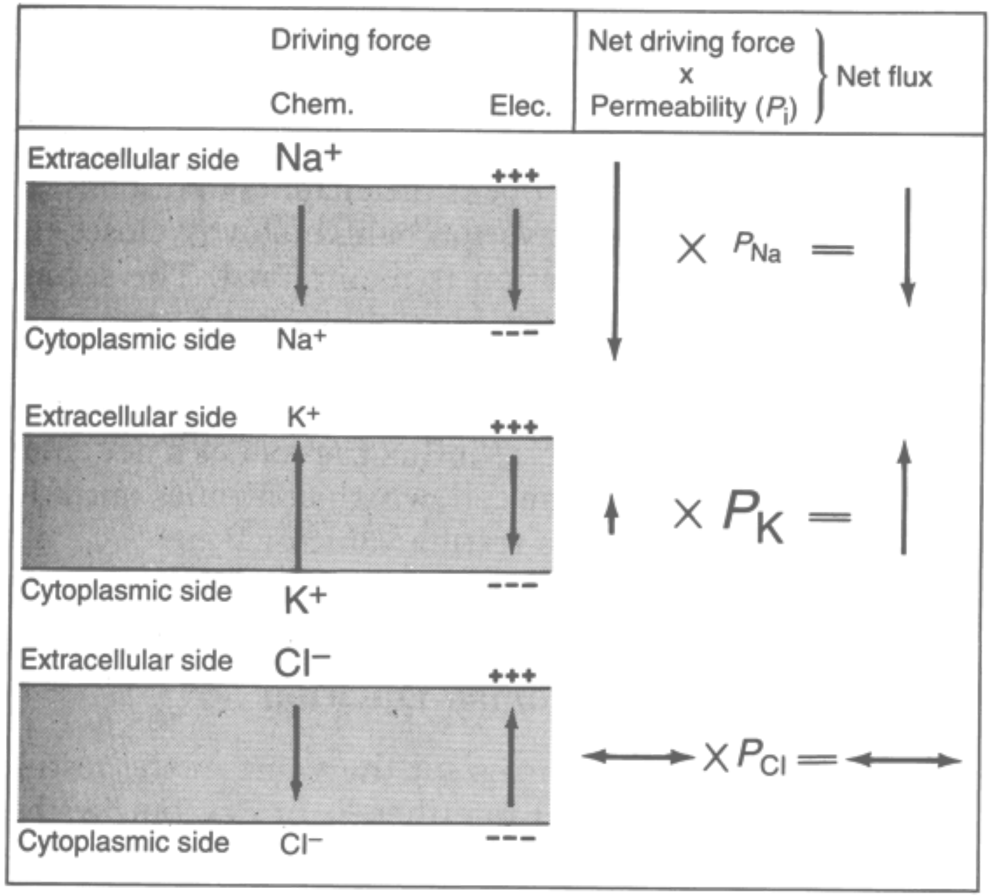
$$V_m = 58 \log \frac{P_K[K^+]_{OUT} + P_{Na}[Na^+]_{OUT} + P_{Cl}[Cl^-]_{IN}}{P_K[K^+]_{IN} + P_{Na}[Na^+]_{IN} + P_{Cl}[Cl^-]_{OUT}}$$

Na^+/K^+ ATP-ase


A
Ouabain Binding Site
2K+
K+ Binding Site
α
β
K+
K+
K+
2K+
PO4
B
Na+
Na+
Na+
3Na+
Outside
α
β
Inside
Na+ Binding Site
ADP
PO4
3Na+
ATP

Na^+/K^+ ATP-ase


1
2
3
4
5
6
7
8
Ouabain
Extracellular
Cytosolic
C1021
Asp
369
ATP
Lys 501
N
Try (Na+)
Try (Na+)
Try (K+)
Chy



The fluxes for Na^+, K^+, and Cl^- across the cell membrane are a result of their chemical and electrical driving forces and the permeability of the membrane. The fluxes shown here are for a cell with a membrane potential of −60 mV and the ionic gradients shown in Table 6–1. (**Horizontal arrows** signify no net driving force or no net flux.)

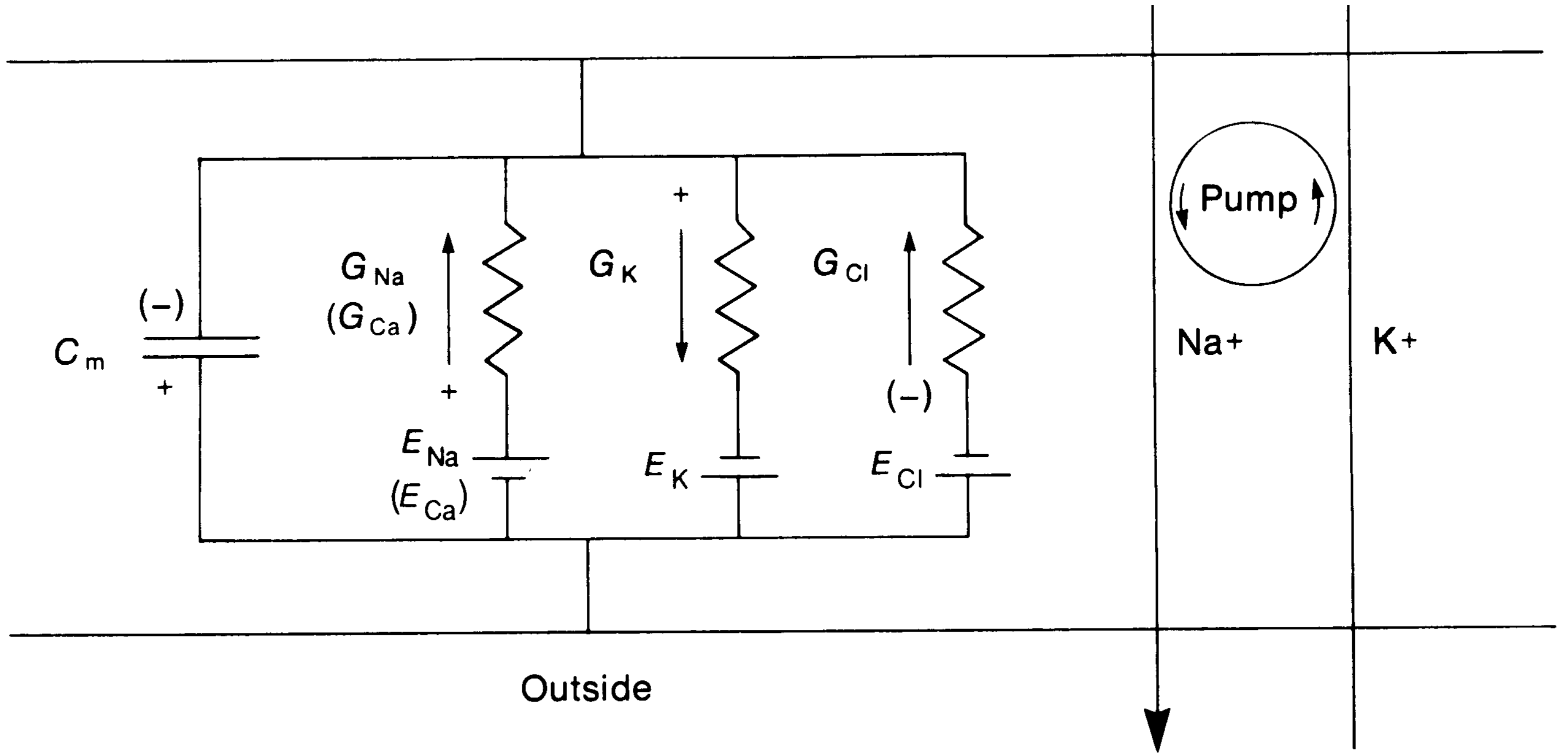


Fig. 4.6 Equivalent electrical circuit for the electrical properties of the nerve membrane.

Early years of modern neurobiology

Armed with his trusty microelectrode,

Don Quijote seeks the secrets of the neuron

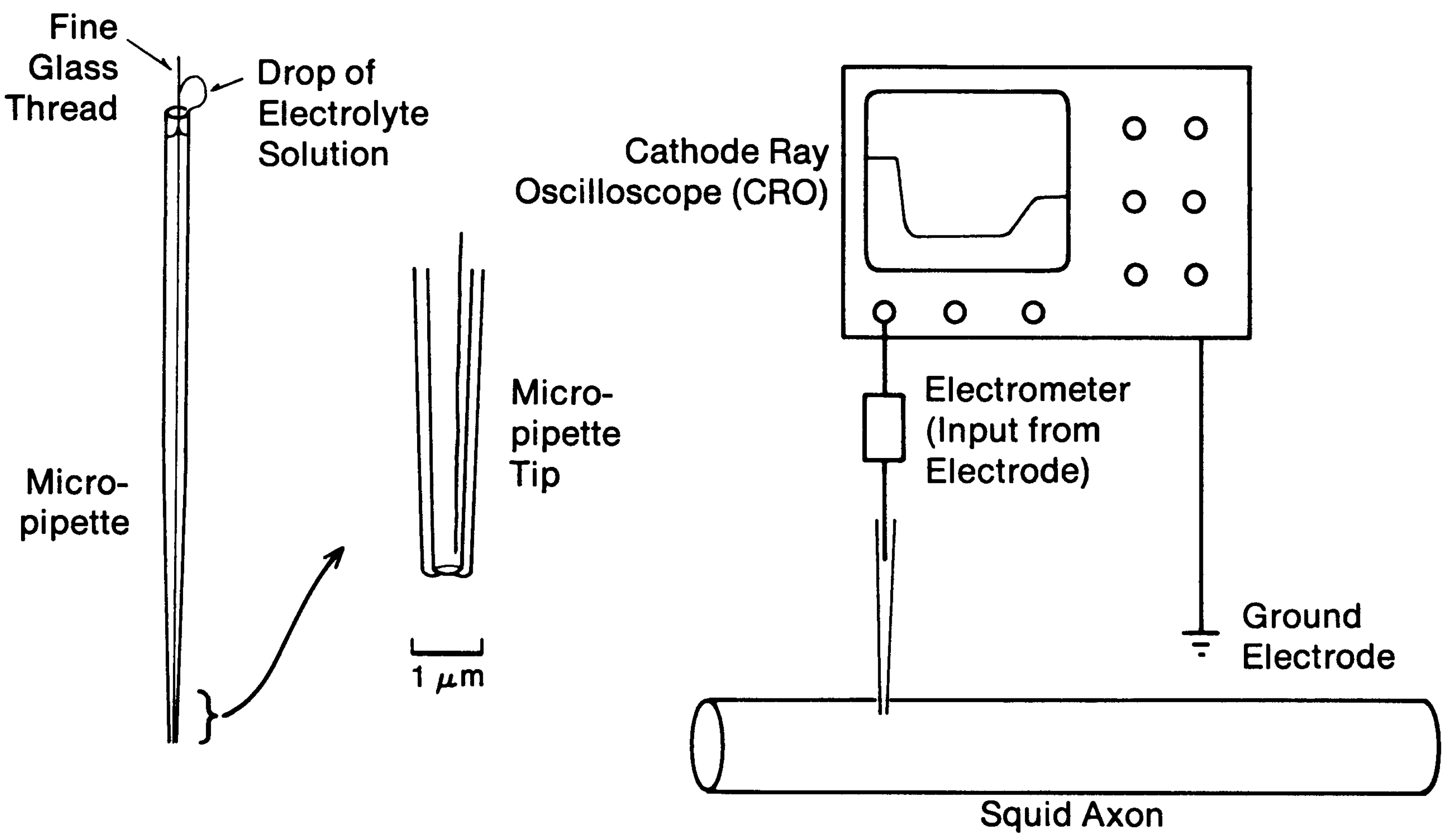
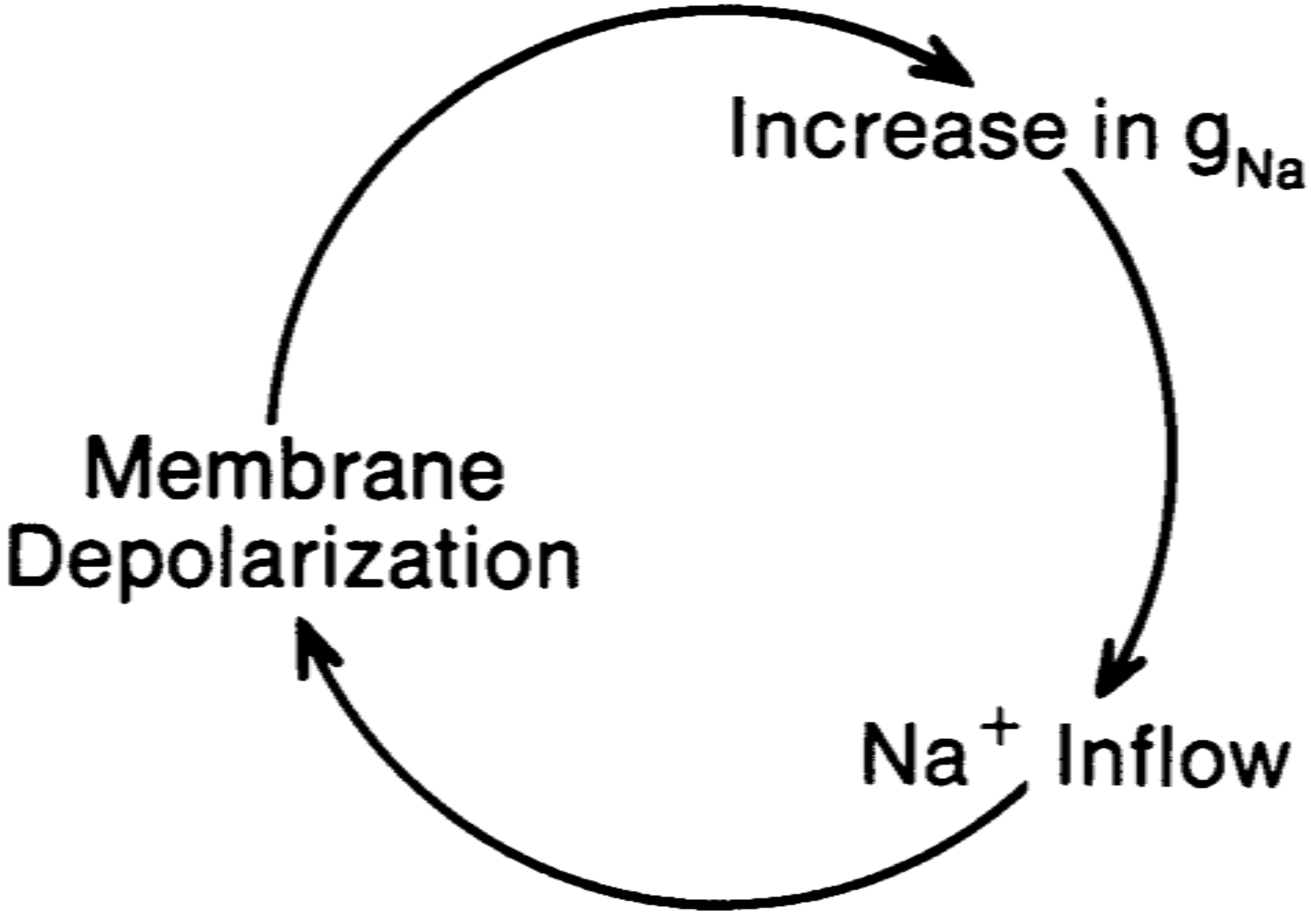
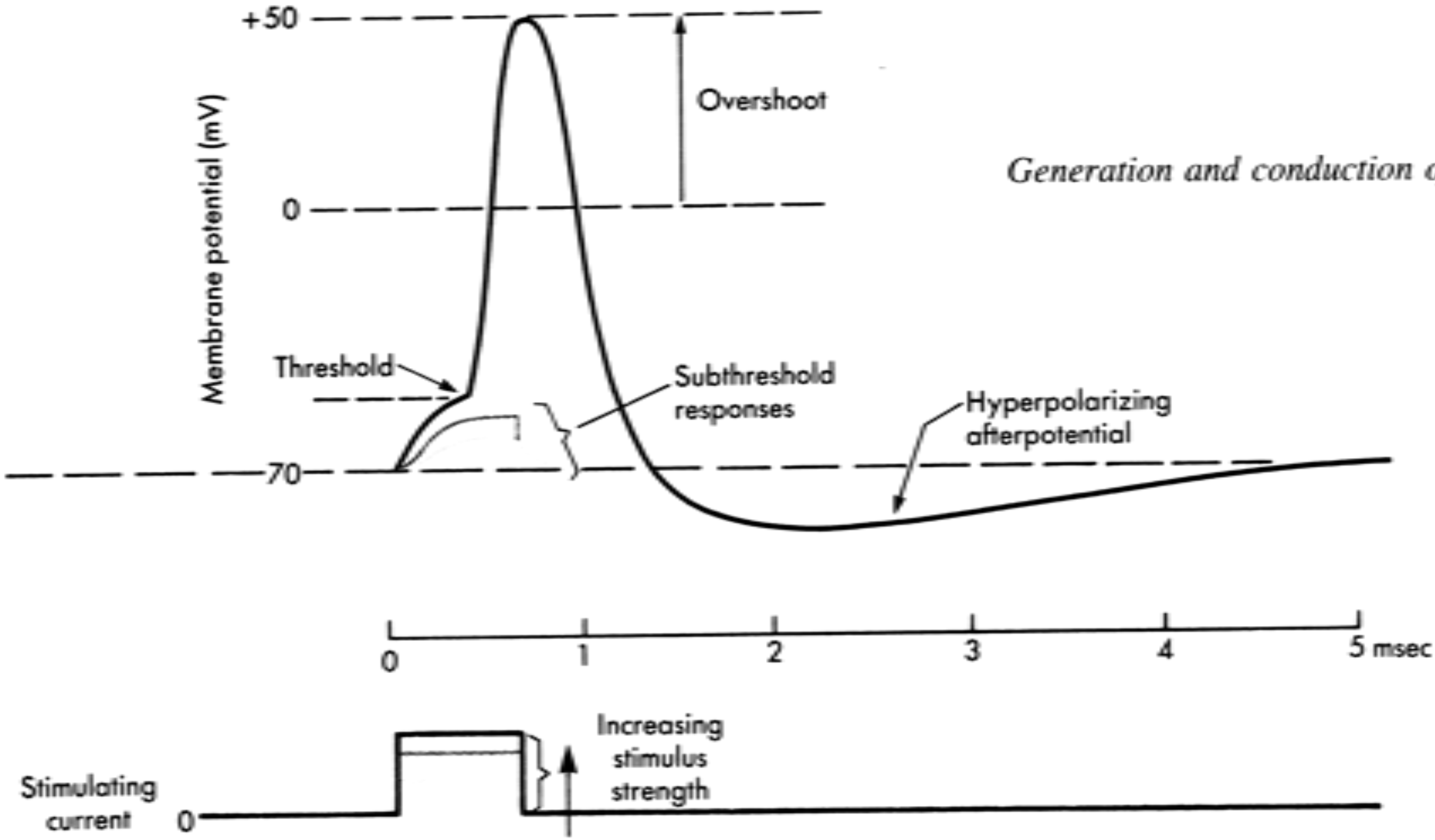


Fig. 4.4 The micropipette is used for electrical recording (extracellular, intracellular, patch), electrical stimulation (current or voltage clamp), or delivery of substances (microionophoresis or pressure ejection). Preparation of an intracellular recording micropipette is shown on the left. The diagram on the right shows the arrangement for recording from a squid axon and observing potentials on a cathode ray oscilloscope (CRO).

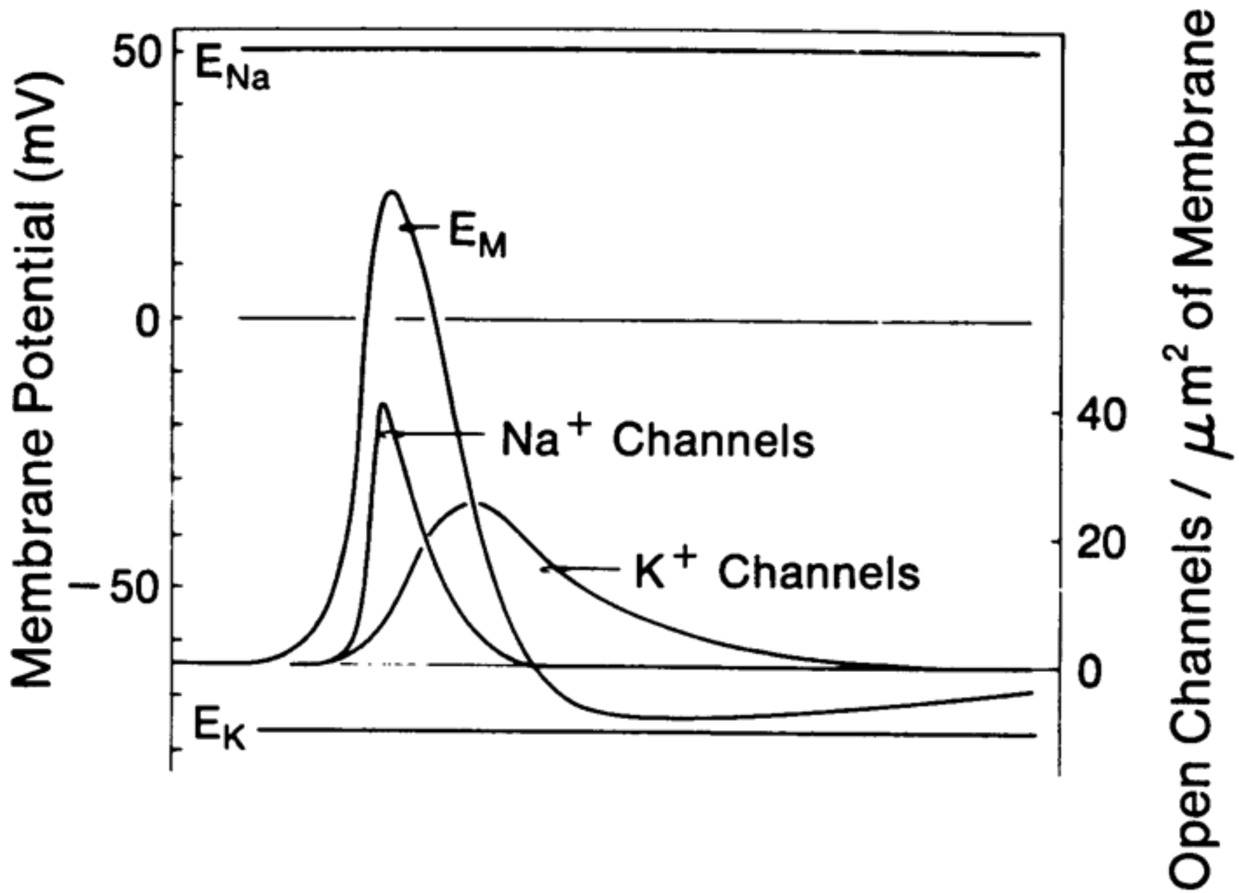

Increase in g_{Na}
Na^+ Inflow
Membrane
Depolarization

Action potential

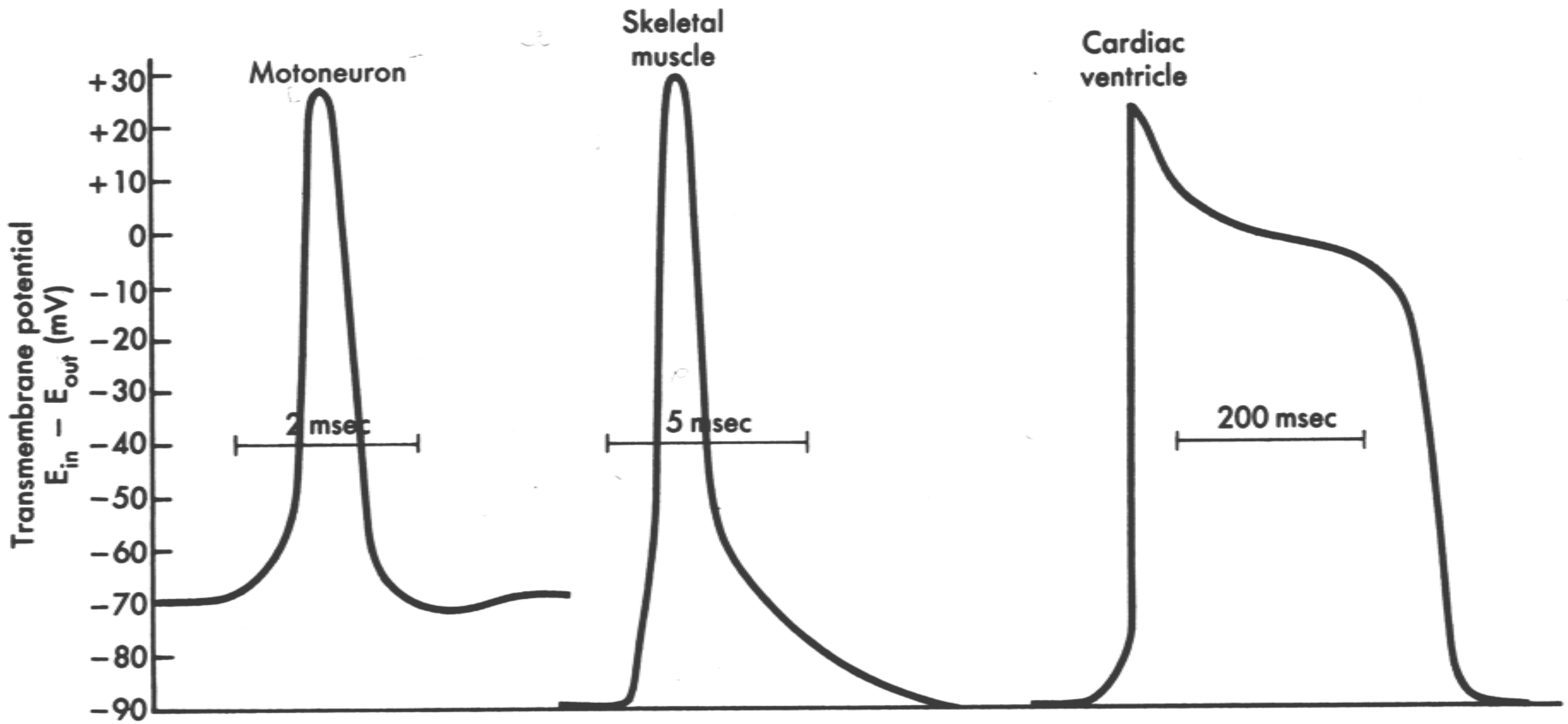


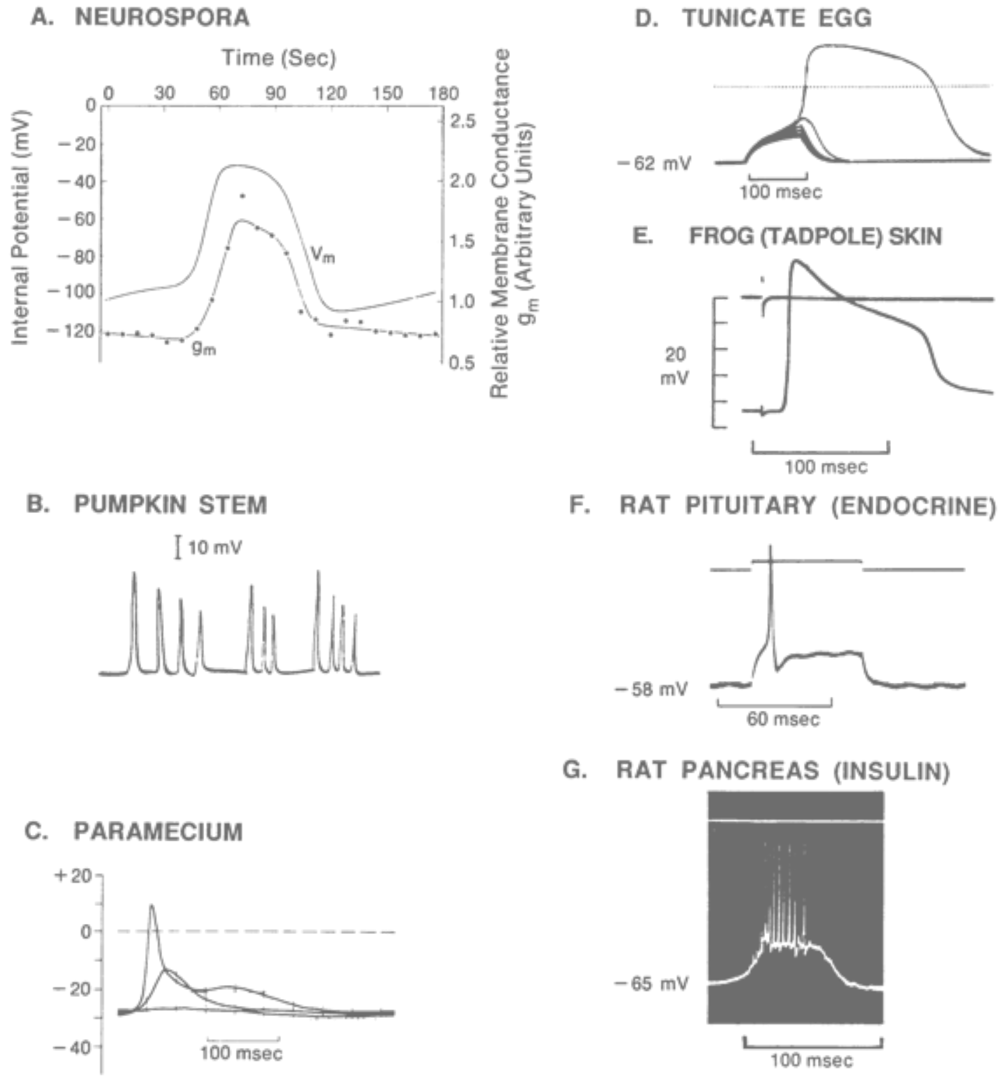
Generation and conduction of action potentials

Changes of conductance during the action potential



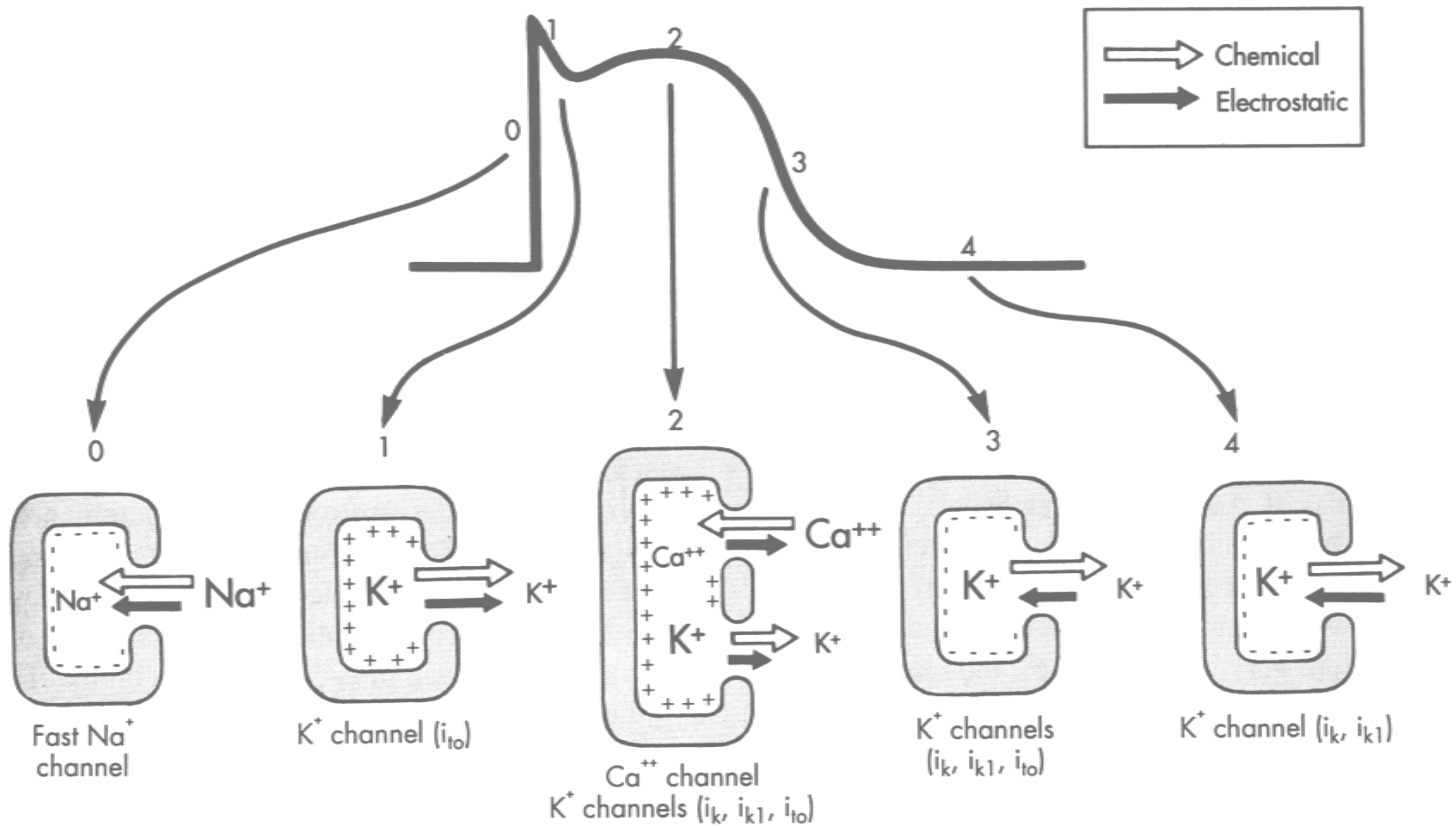
Action potentials





Different action potentials of non-neuron cells

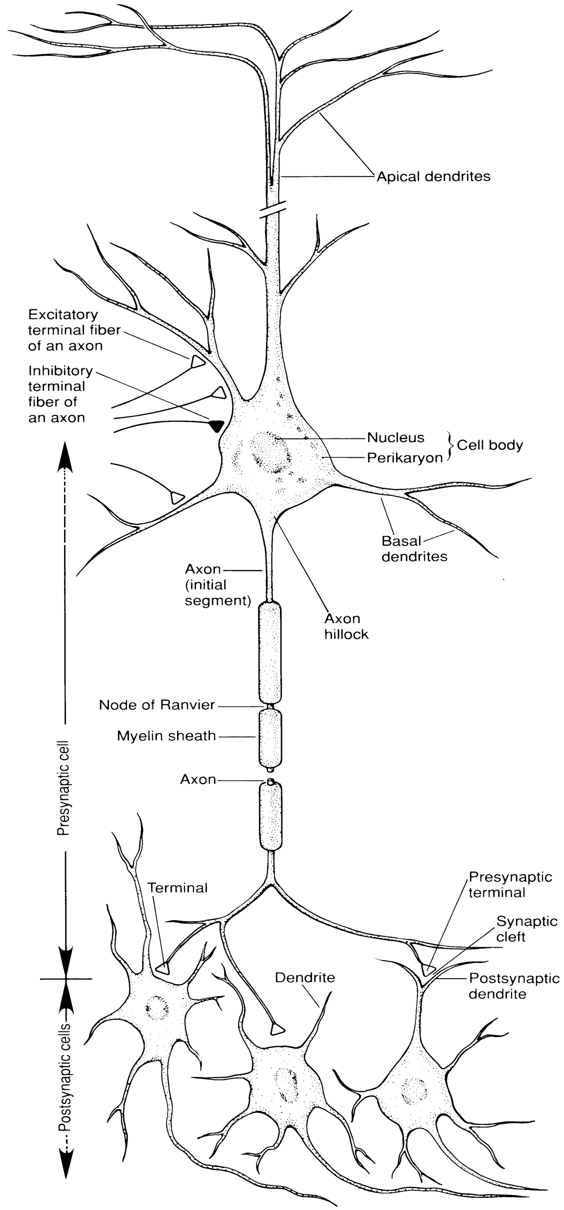
Action potential in a cardiac cell



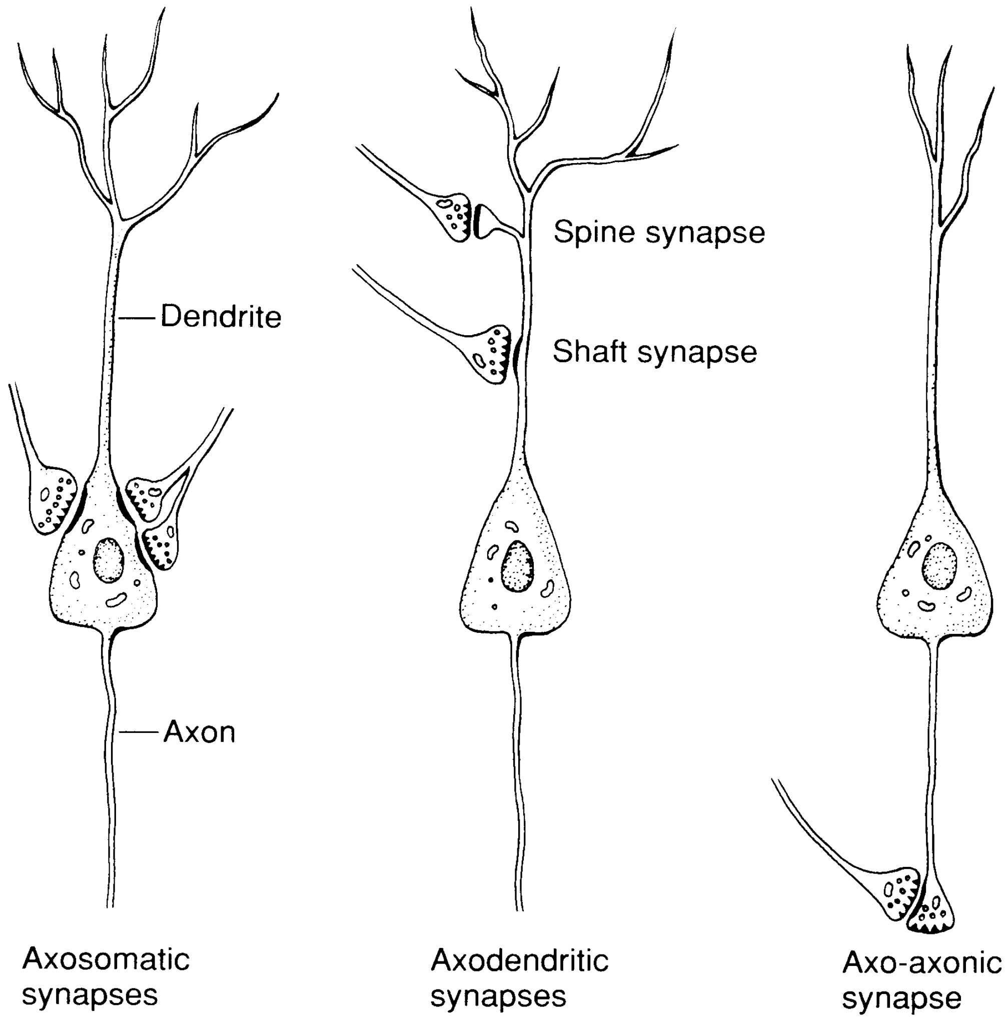
The principal ionic currents and channels that generate the AP

Vertebrate CNS neuron

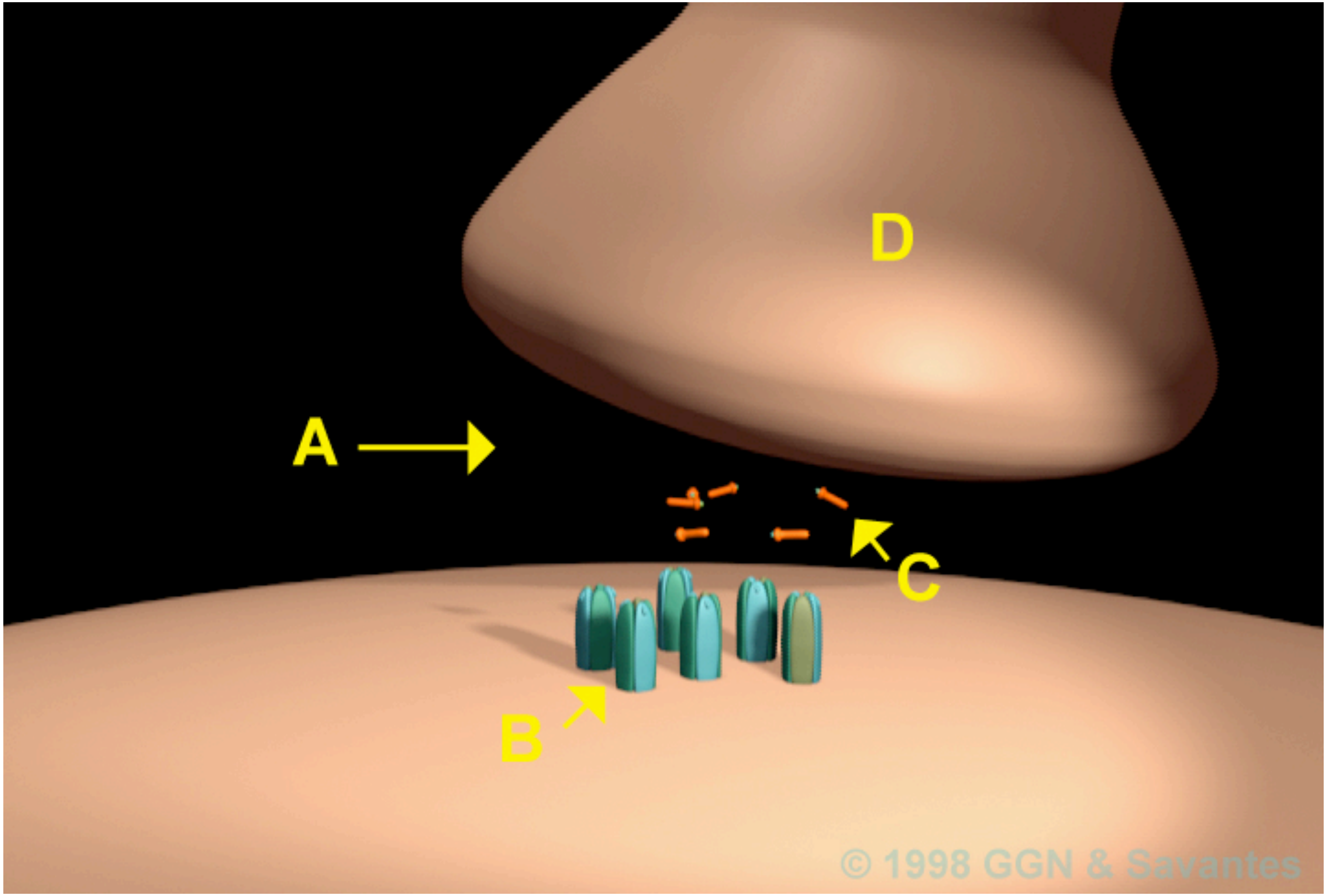
axon branches
can
make synapses
with about 1000
other
neurons



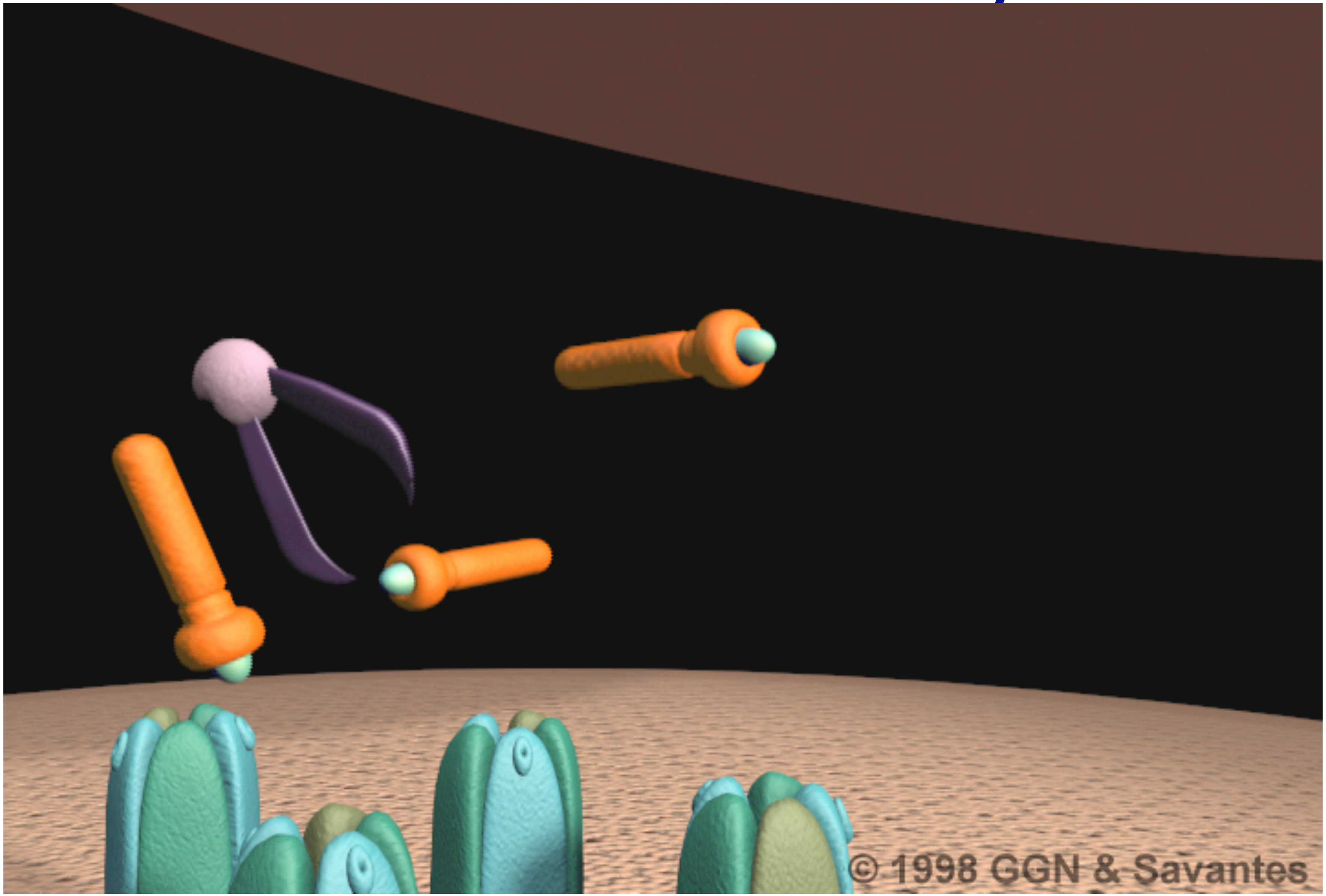
Types of synaptic connections



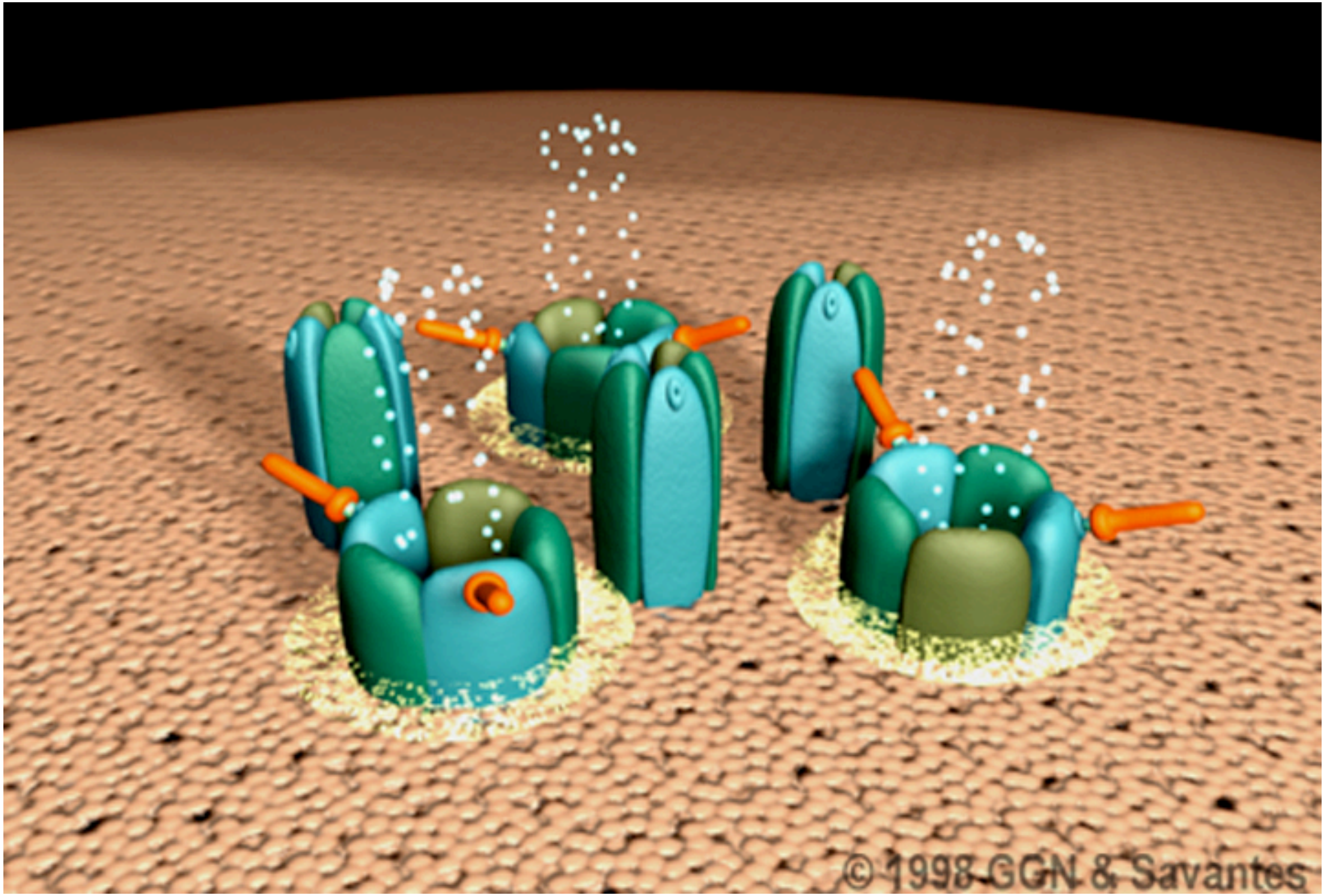
Synaptic connections



Elimination from the syn. cleft



Agonist actions



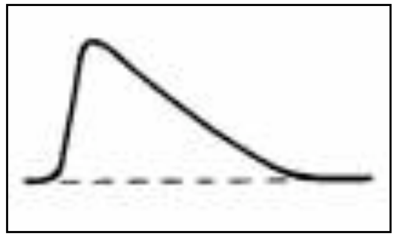
GABA (-)

Inhibitory Amino Acid

IPSP

Hyperpolarization → Inhibition

GLUTAMAT (+)

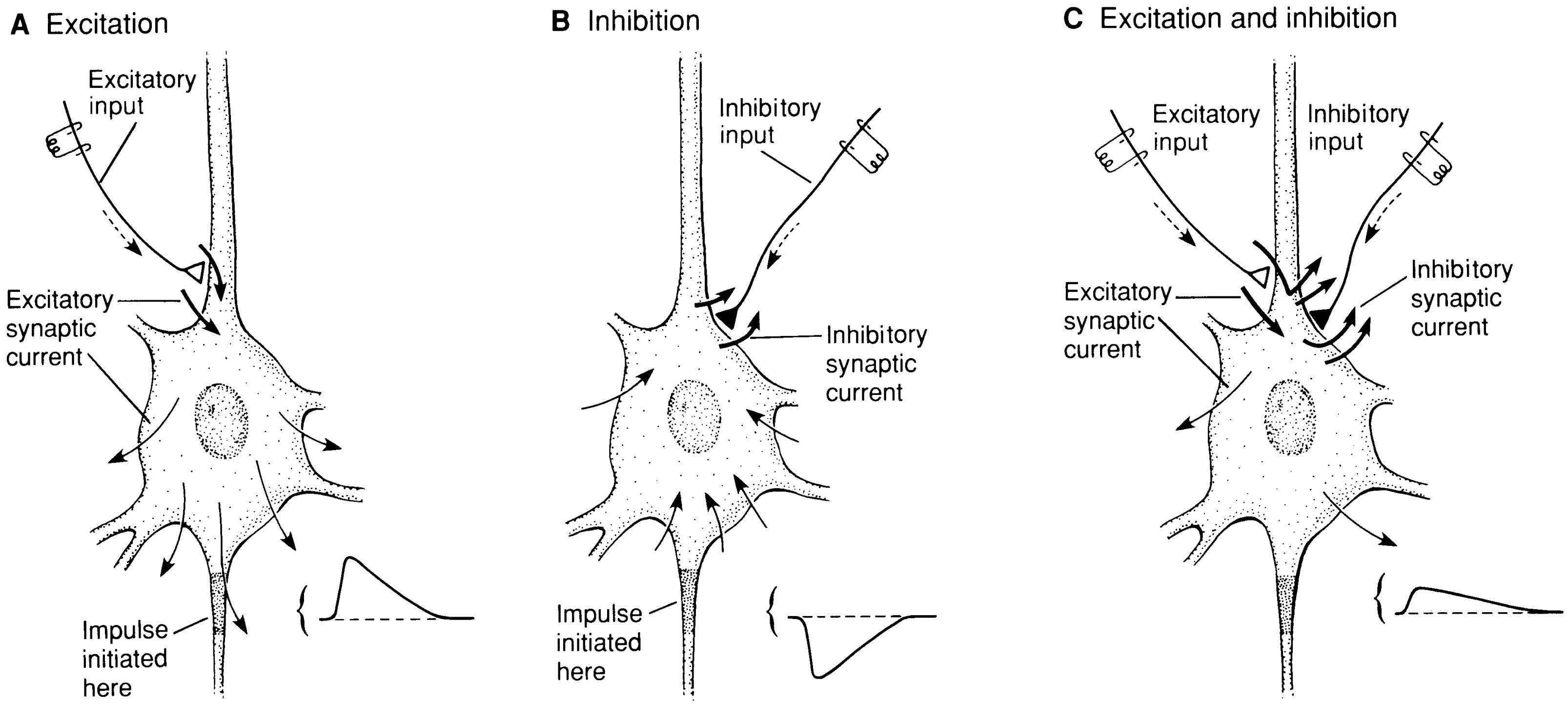


Excitatory Amino Acid

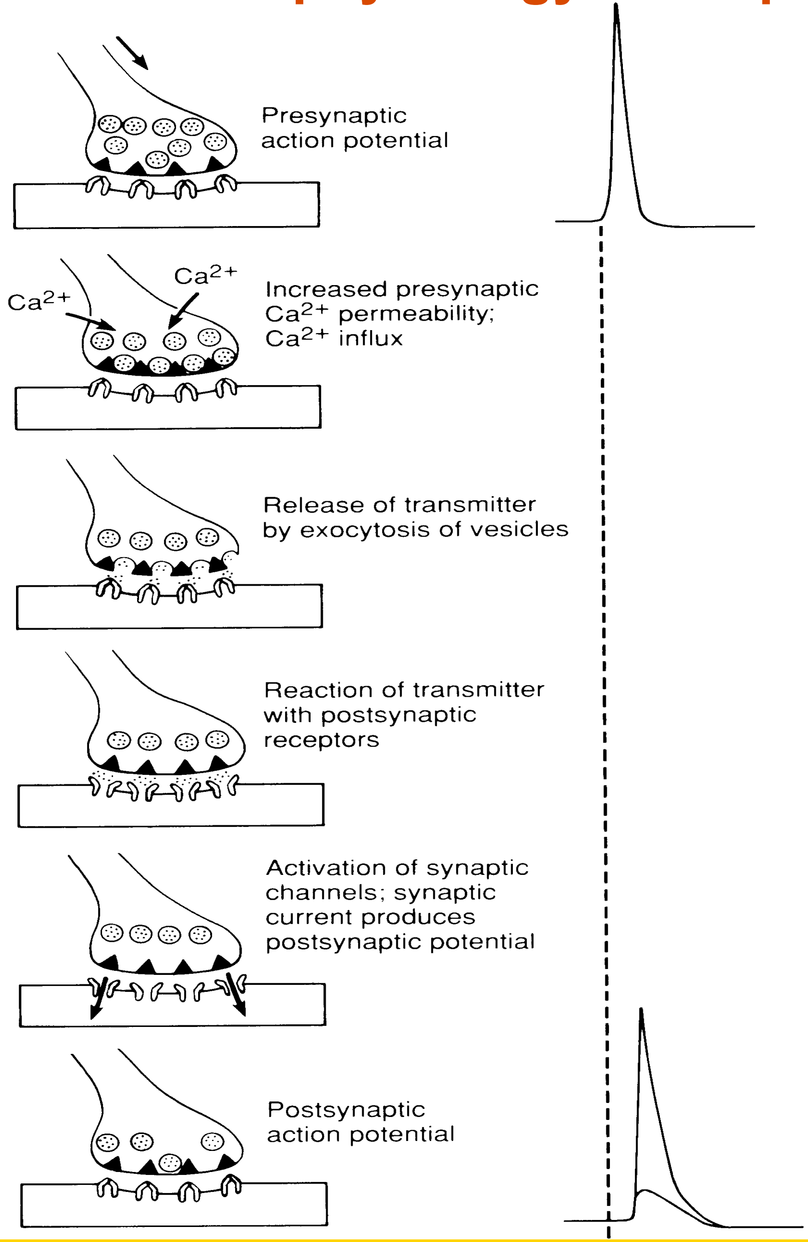
EPSP

Depolarization → Excitation

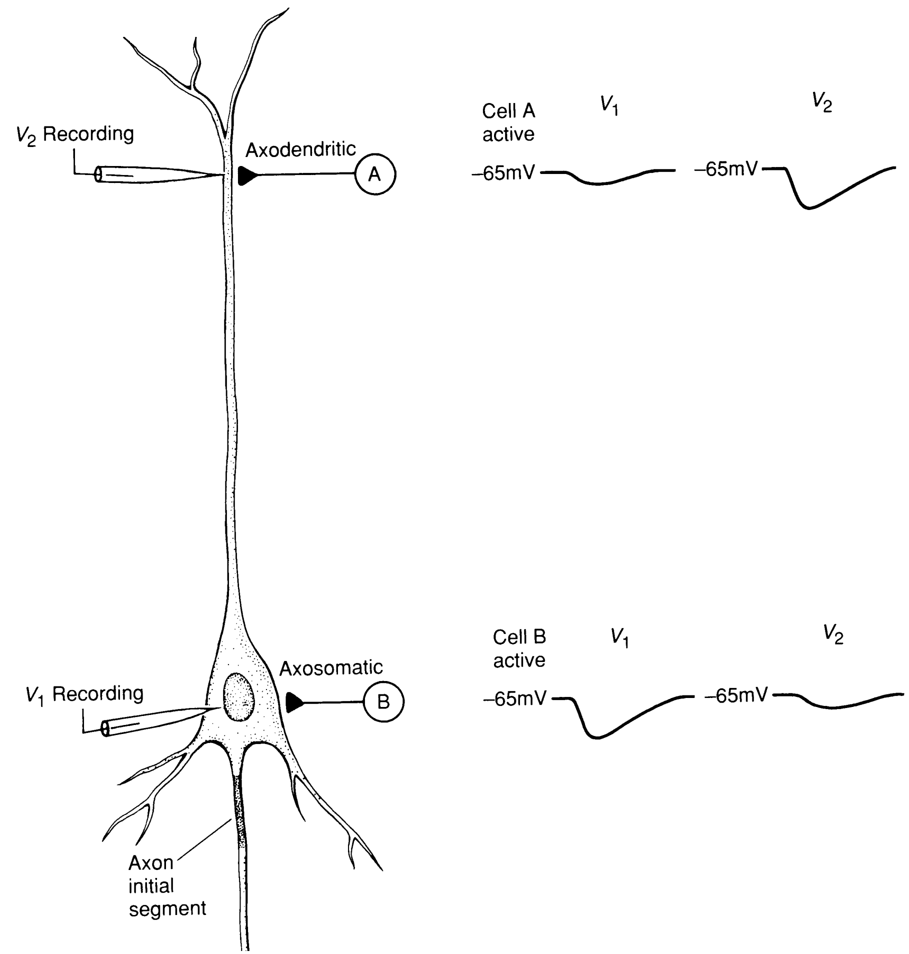
Neuronal integration of “messages”

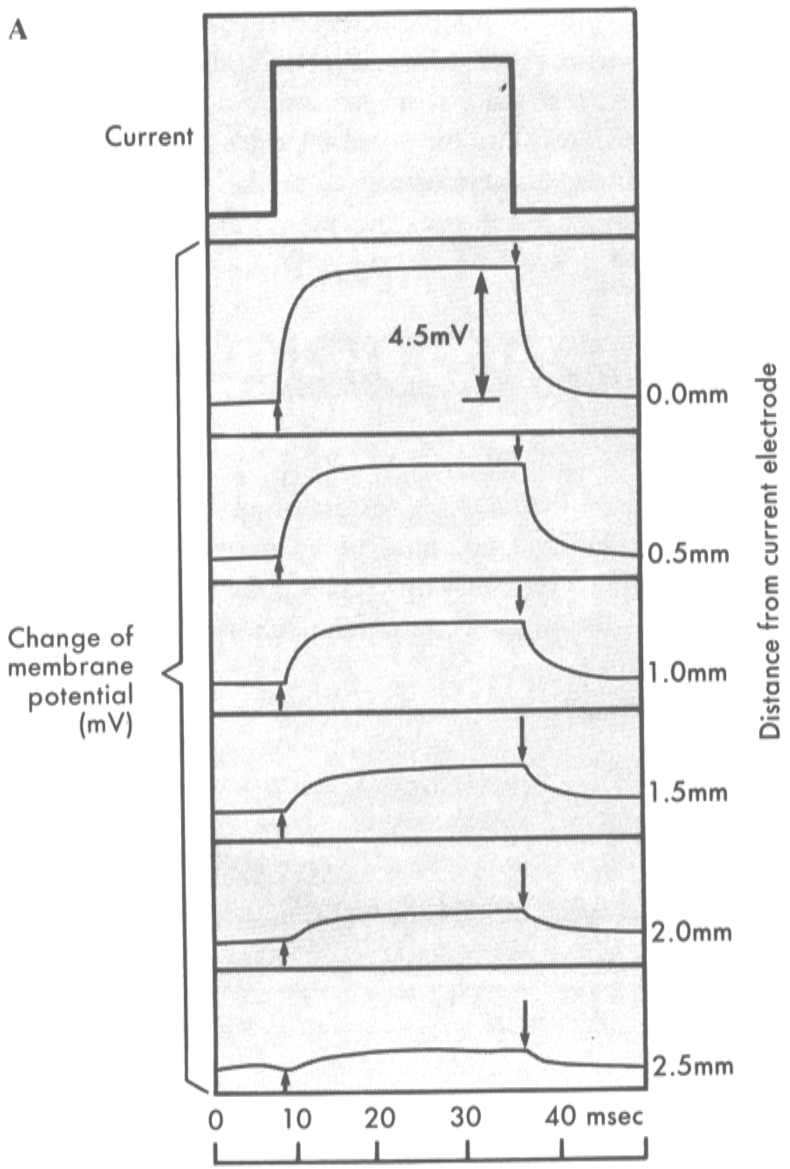


Events during the "talk" of the two neurons

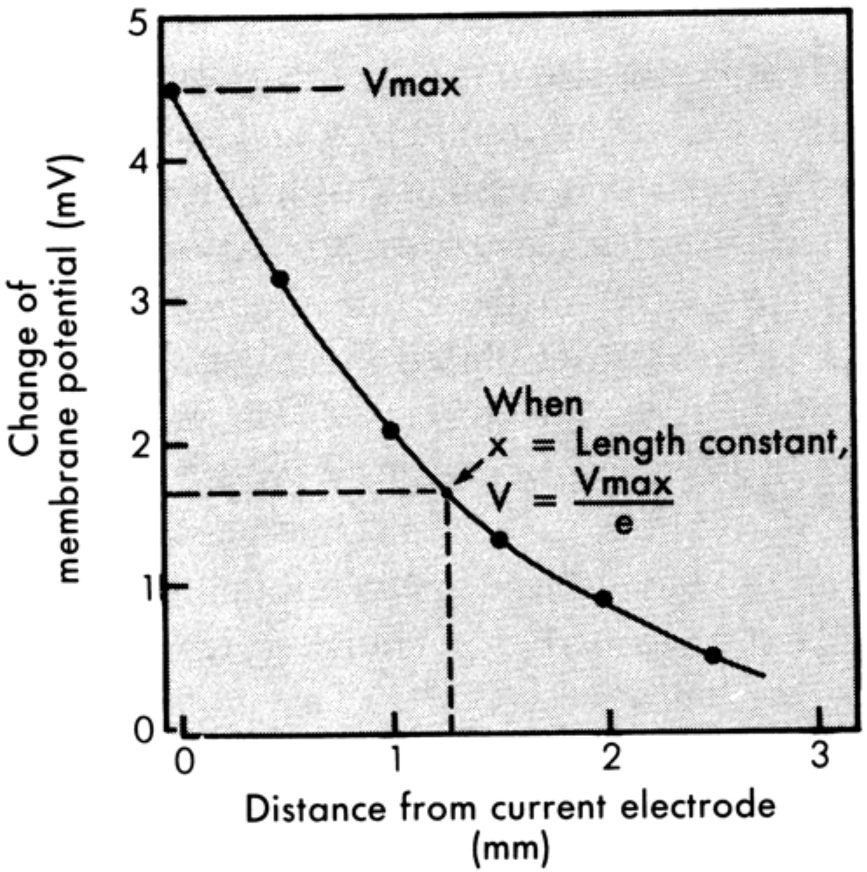


Signal size depends on electrode distance

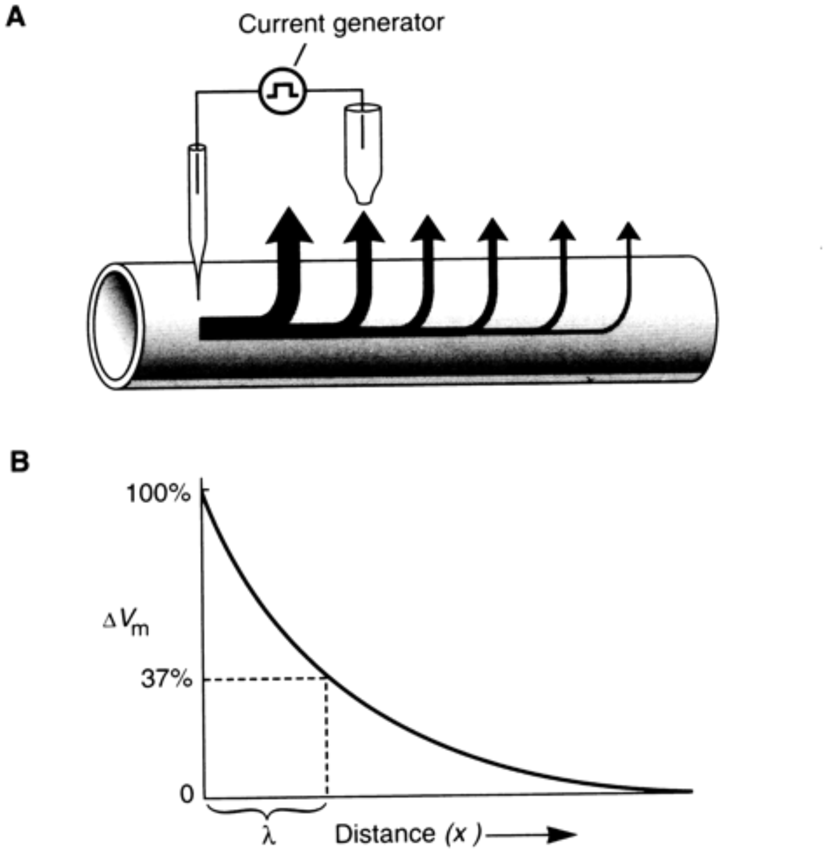



A
Current
Change of membrane potential (mV)
4.5mV
0.0mm
0.5mm
1.0mm
1.5mm
2.0mm
2.5mm
Distance from current electrode
0
10
20
30
40 msec

Space (length) constant

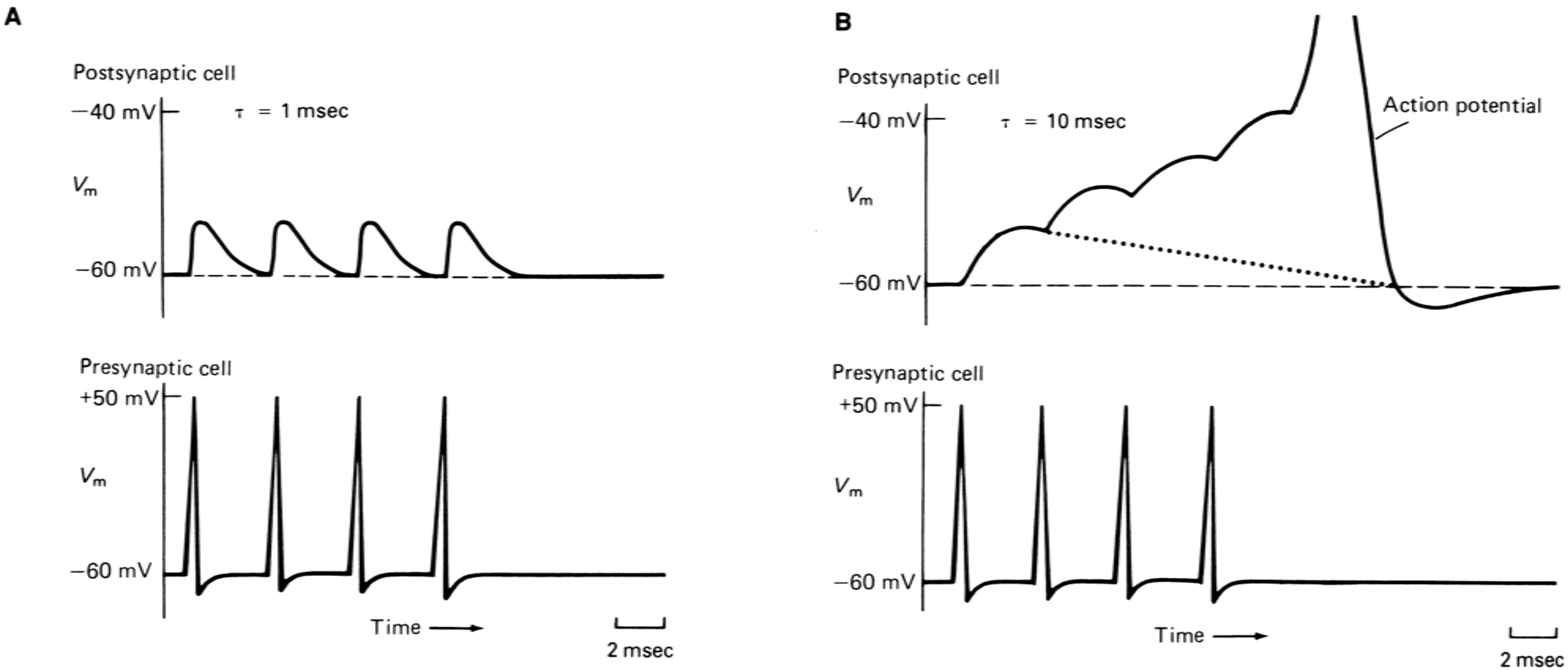


e=2,718281...



Current injected into a neuronal process by a microelectrode follows the path of least resistance to the return electrode in the extracellular fluid (**A**). Under these conditions the change in V_m decays exponentially with distance along the length of the process (**B**).

Temporal summation



Ach receptor (nAChR)

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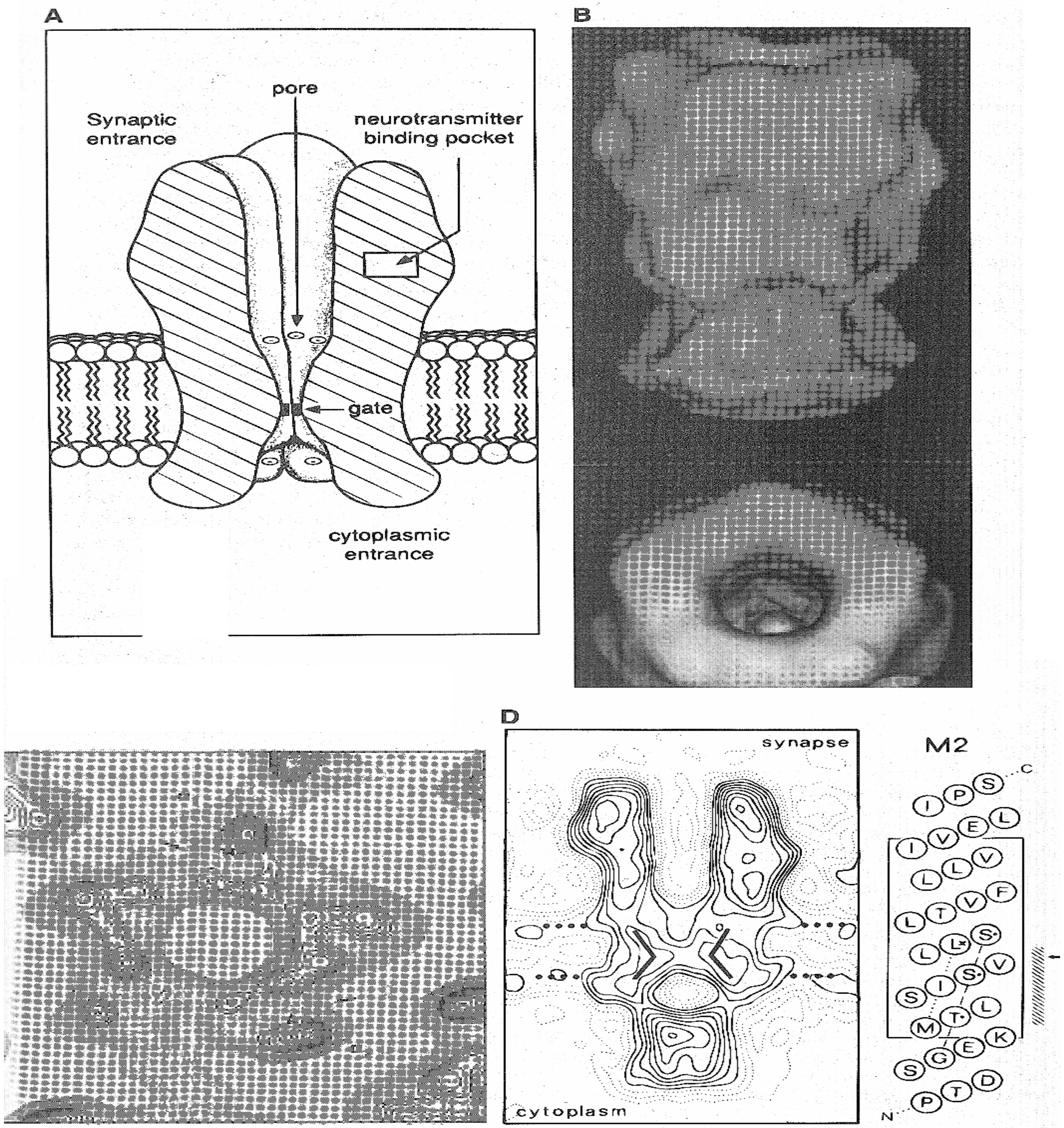
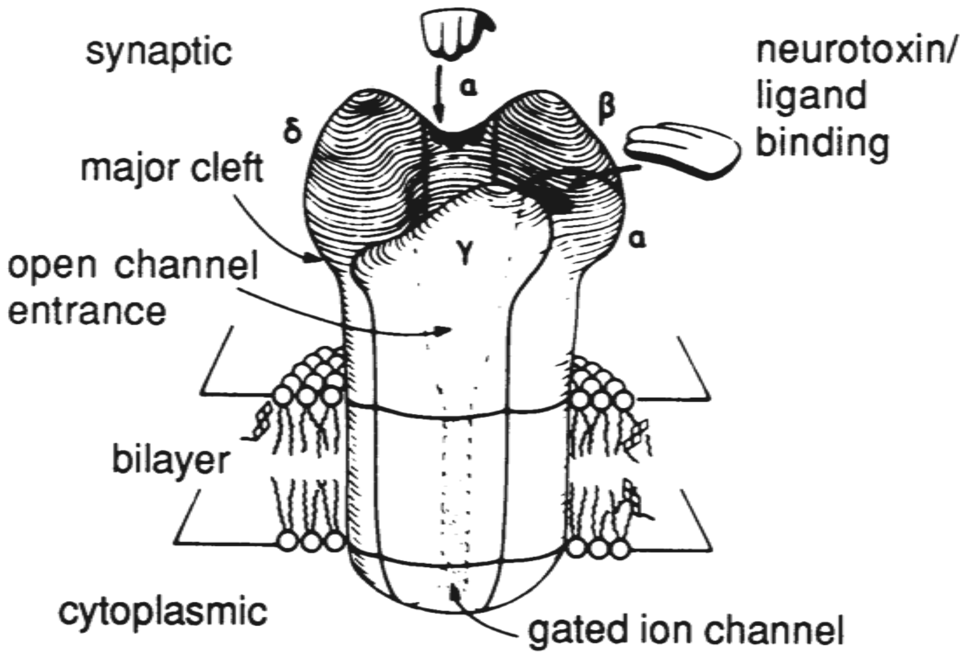
computer rendering imaged by cryo-electron microscopy

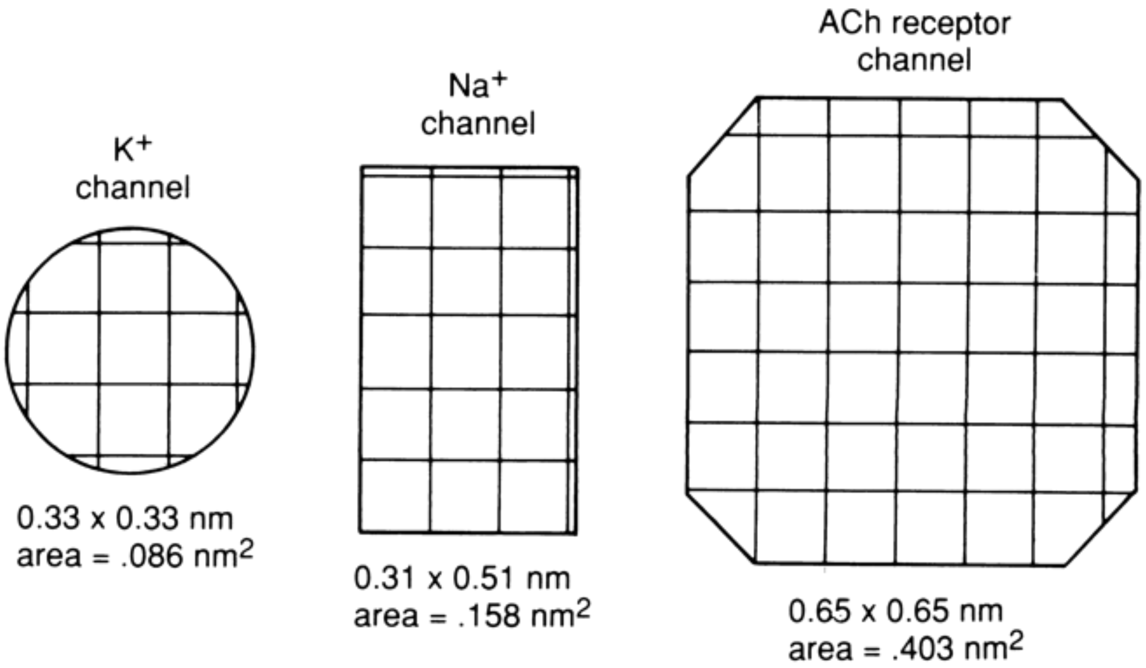

A
B
pore
Synaptic
entrance
neurotransmitter
binding pocket
gate
cytoplasmic
entrance
D
synapse
cytoplasm
M2
C
N

3D protein: ACh receptor-ionic channel



Kistler et. Al., 1982

A comparison of the dimensions of the narrowest points in voltage-gated K^+ and Na^+ channels, and in the ACh-activated channel. The grid size is 0.1 nm (1 Å). Sizes were evaluated by testing channel permeability to several cations and measuring the dimensions of the ions from space-filling models. Note that the ACh-activated channel is quite large compared to the two voltage-gated channels. This explains why the voltage-gated channels are selective for one ion whereas the ACh-activated channel is permeable to both Na^+ and K^+. (From Hille, 1984.)



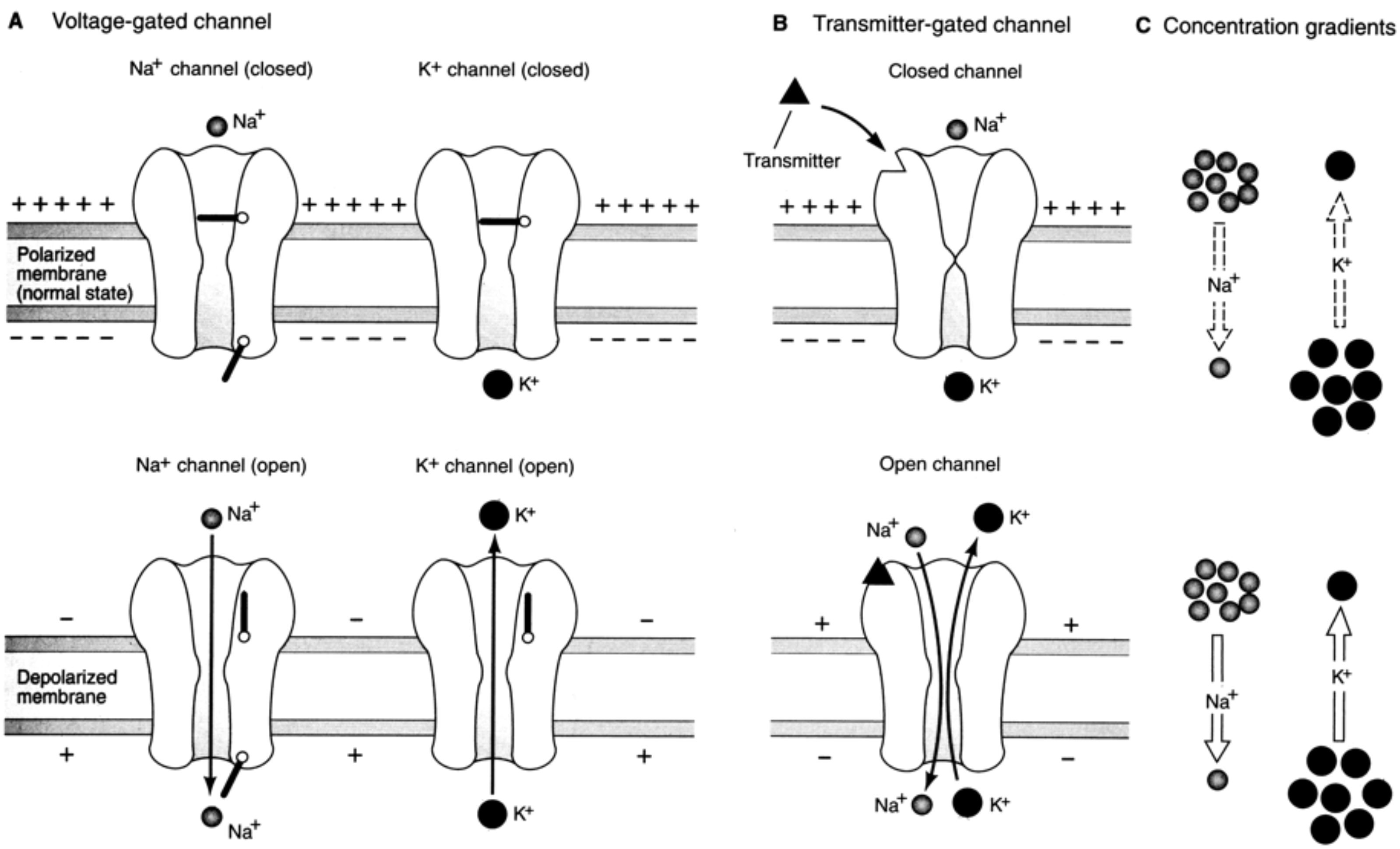


FIGURE 10–8

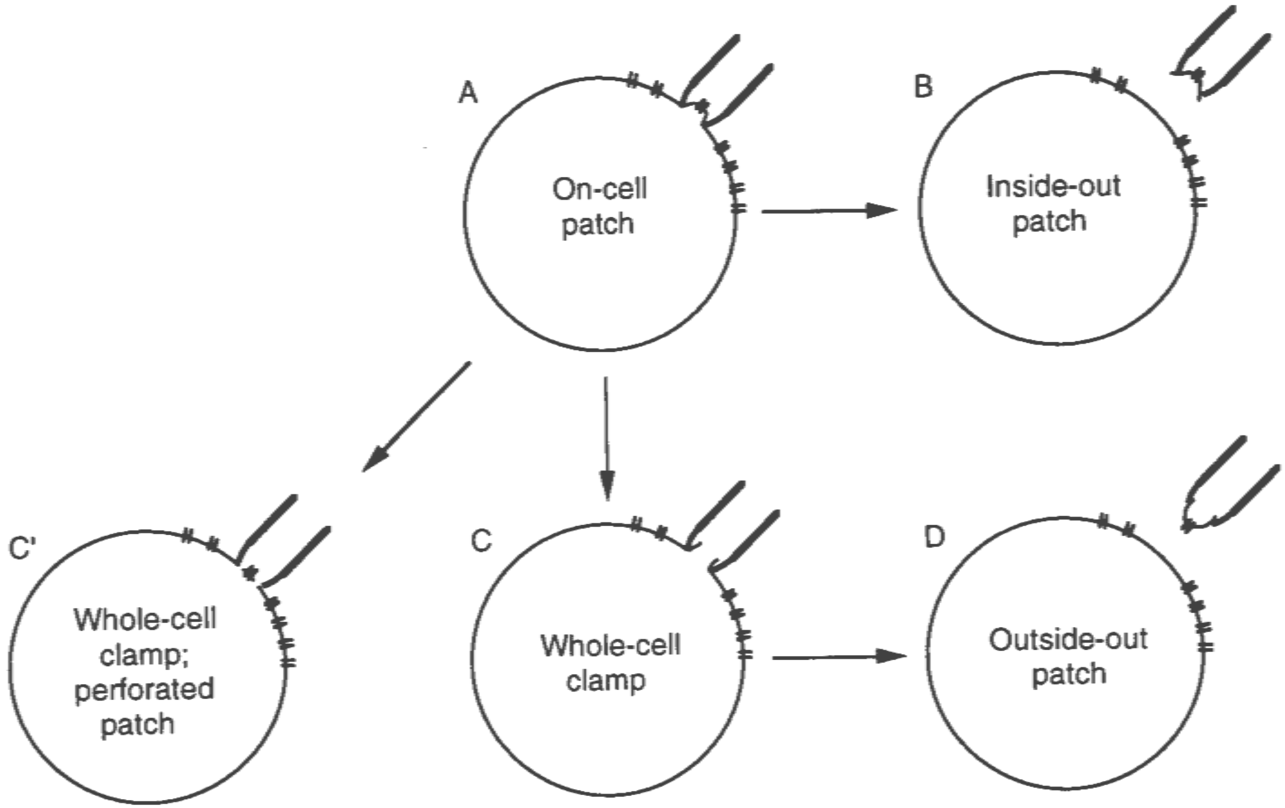
Voltage-gated and transmitter-gated channels operate by different mechanisms. (Adapted from Alberts et al., 1989.)

A. Voltage-gated channels, which contribute to the action potential, are selective for different cations. There are separate channels for Na^+ and K^+.

B. Transmitter-gated channels, which contribute to the synaptic potential, are permeable to *both* Na^+ and K^+.

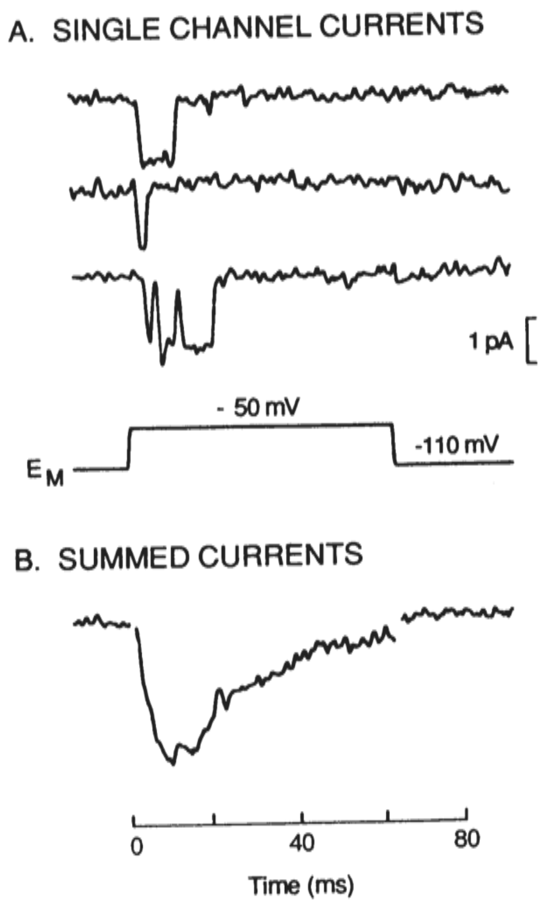
C. The concentration gradients for the ions are the same for both classes of channels.

Patch-clamp technique



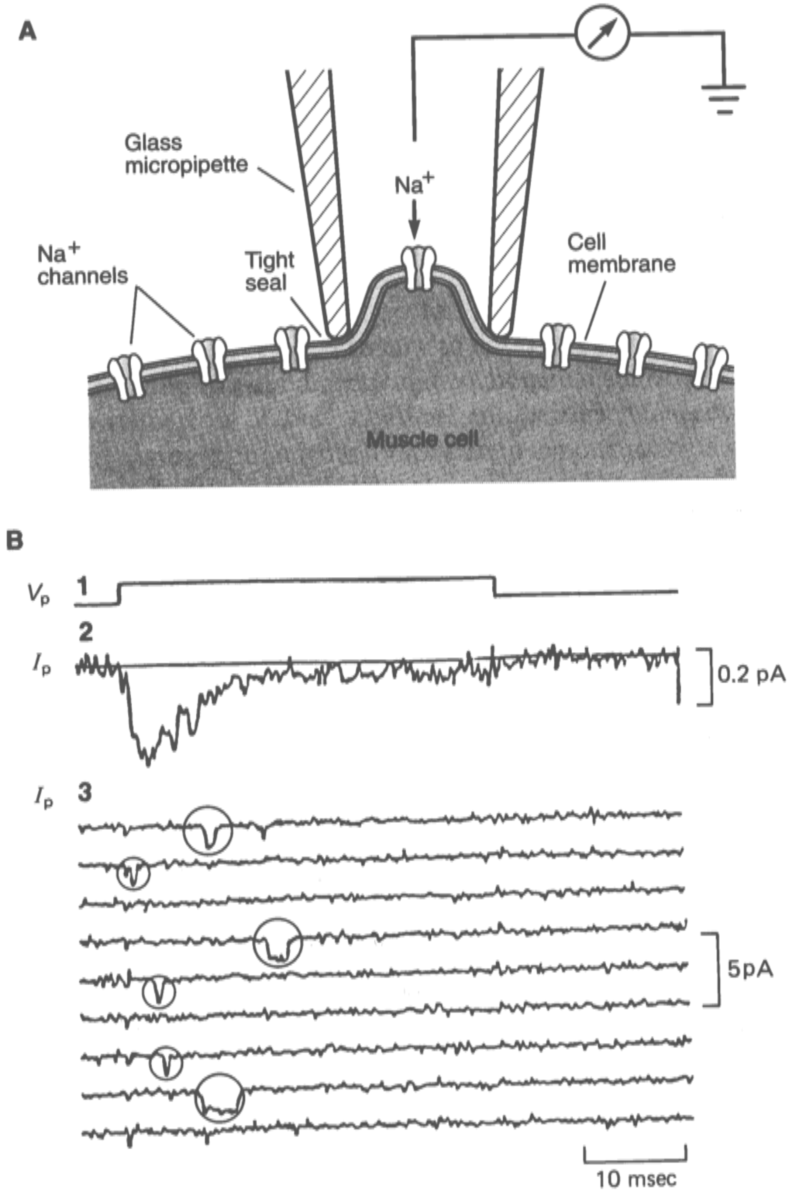
Erwin Naher and Bert Sakman, 1976 *Nobel Price*

Patch-clamp



individual channels

“average” channel

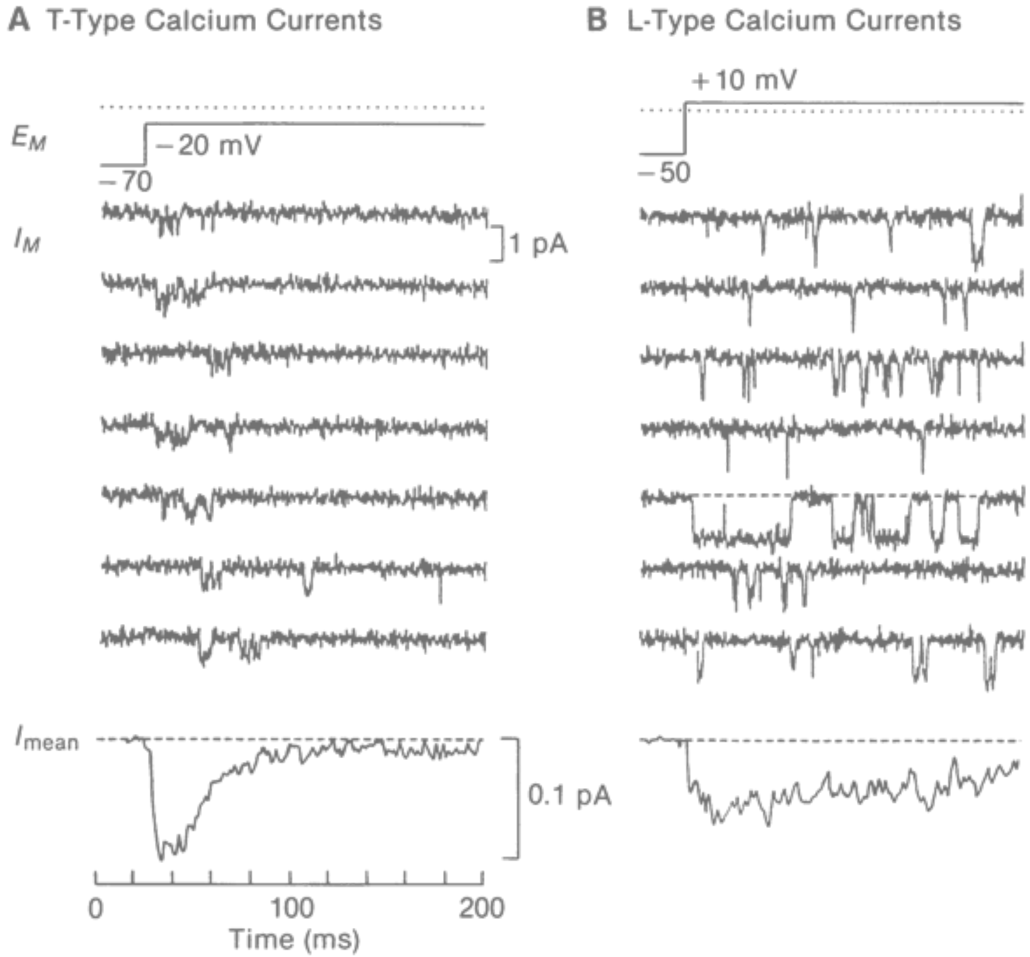


patch-clamp

- *stimulus*
- *sumary of 300 actions*

- *9 individual actions*

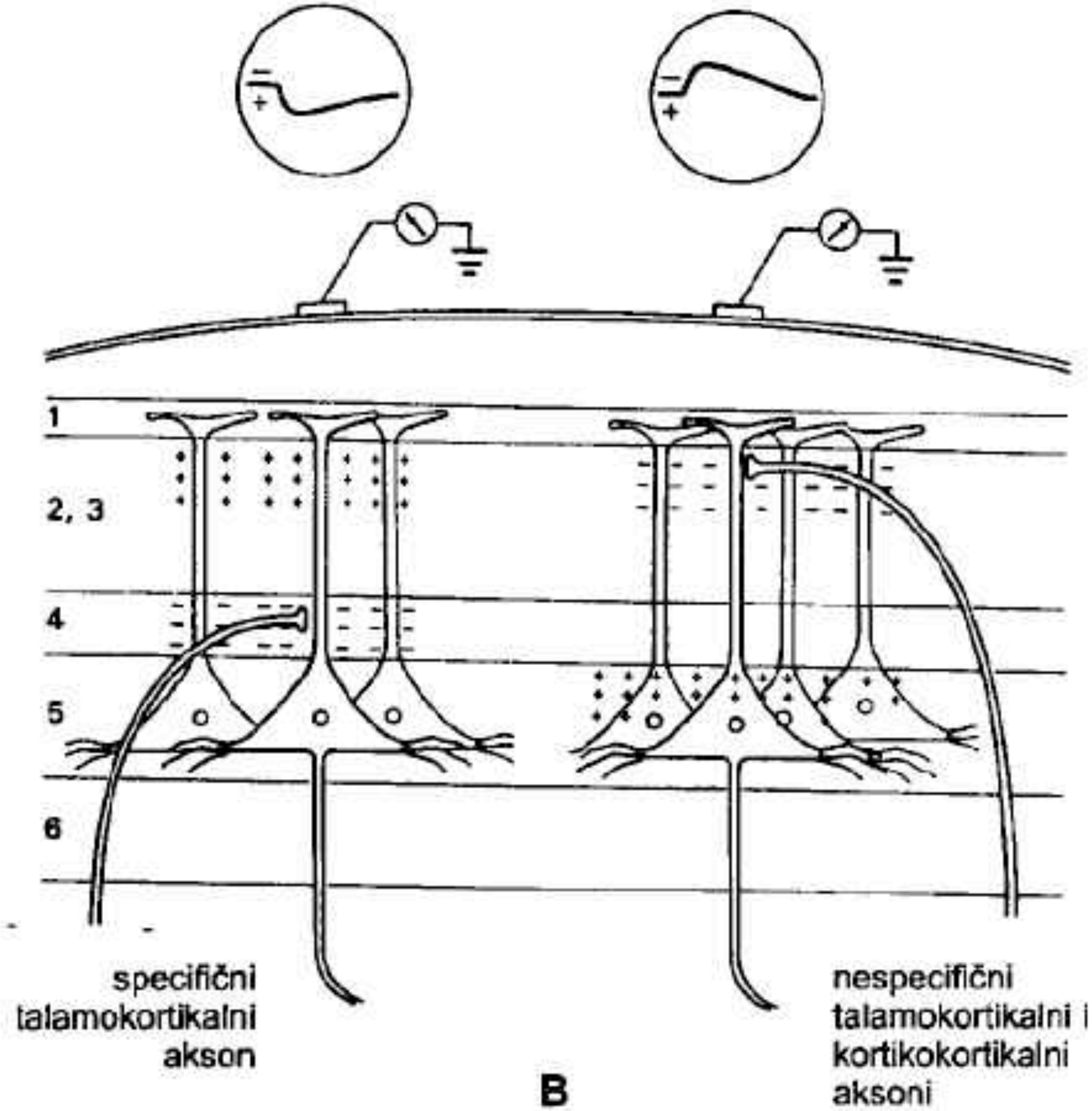
Different Ca^{++}-channels



T-transient

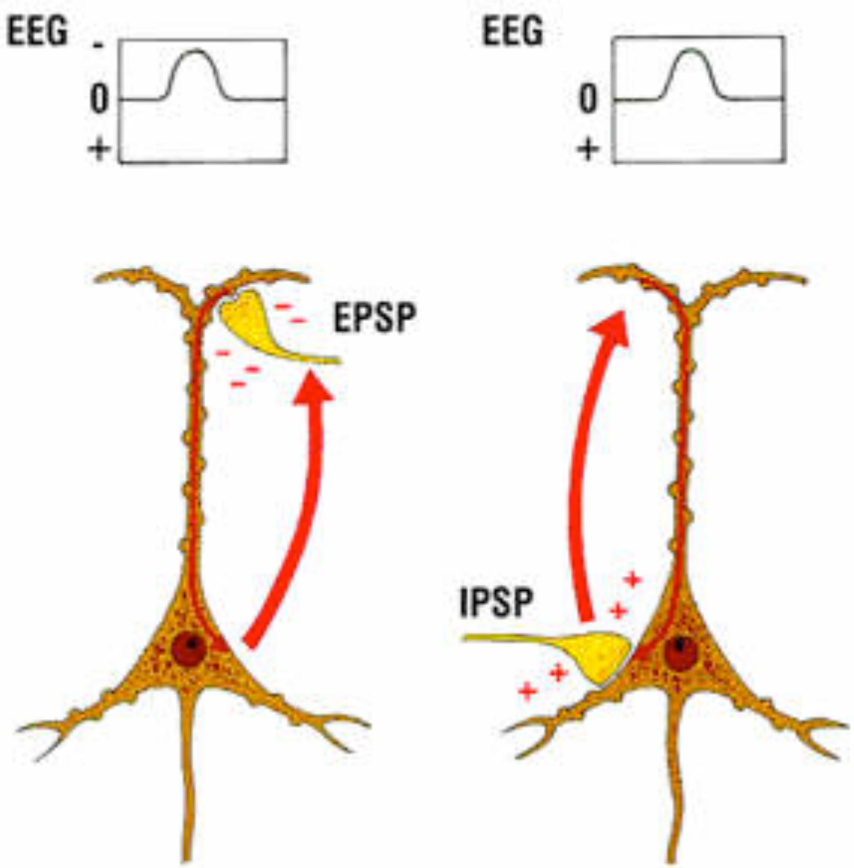
L-long lasting

Basics of EEG



Negative wave on EEG

Basis of the EEG



Illustrates why superficial excitatory post-synaptic potentials (EPSPs) and deep inhibitory post-synaptic potentials (IPSPs) produce the same current flow, hence deflections of the same polarity when recorded by the surface EEG.

From: DS Dinner and H. Luders in Porter, Morselli PL (eds), The Epilepsies, London, Butterworths, 1985.