

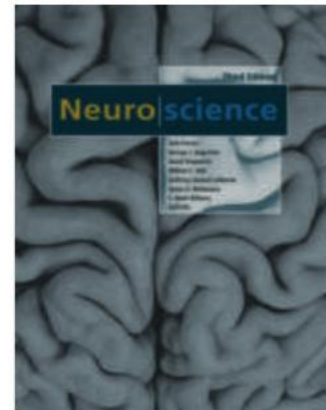
# Action Potential

Finally Something  
is Happening...

Topics I	Topics II
Introduction	Synaptic Transmission
Electrochemical Gradients	Electrophysiology Techniques
Passive Membrane Properties	Basic Circuits (Spinal Cord)
Action Potential	Sensory Systems Overview
Voltage-Gated Ion Channels	Synaptic Plasticity
Ligand-Gated Ion Channels	Recapitulation

# Study Material

- NEUROSCIENCE Third Edition
  - Dale Purves
- Chapter 2 pages 31-46
  - In particular pages 43-45
- Chapter 3 pages 47-67



**THE COVER**  
Dorsal view of the human brain.  
(Courtesy of S. Mark Williams.)

NEUROSCIENCE: Third Edition  
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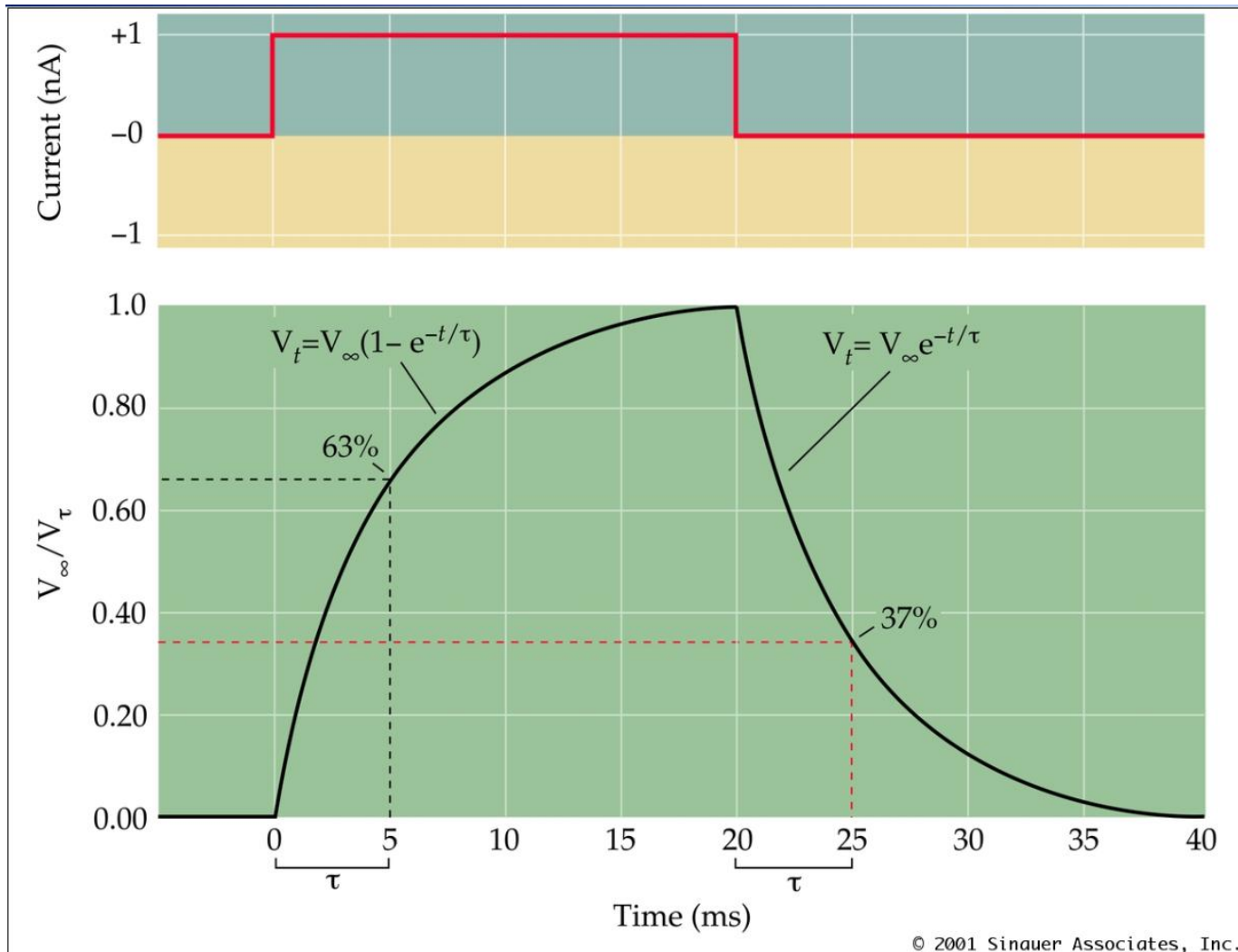
# Aims for this Lecture

- Understand the action potential as an all-or-none signal with a threshold.
- Know the underlying ion conductances and their specific kinetics.
- Understand how positive and negative feedback mechanisms shape the action potential.
- Know how action potentials propagate.

# Recapitulation L3

- Cell membranes are thin isolators separating conducting media. As such they behave as capacitors.
- Changing the voltage across the membrane therefore requires the movement of charges.
- These charges (ions) move through channels with a certain resistance.

# Recapitulation L3



# Recapitulation L3

$$V(t) = V_{\infty} (1 - e^{-t/\tau}) \quad \tau = RC$$

Tau is the membrane time constant. It is proportional to the capacitance of the neuron and the membrane resistance.

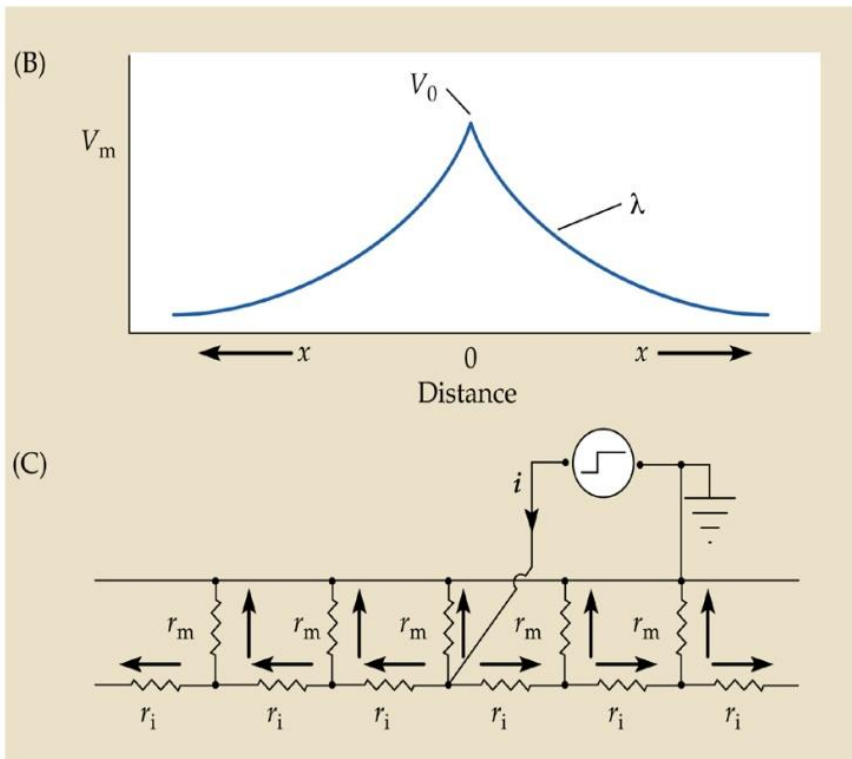
The capacitance is given by the amount of cell membrane and depends on the size (surface area) of the neuron.

The membrane resistance at rest is also likely a function of the size of the neuron (larger neuron -> smaller resistance), but it is very dynamic and can change, since channels can open and close.

# Recapitulation L3

- Neuronal processes are not very good conductors.
- Neural membranes are not ideal isolators and the cytoplasm inside the process has a relatively high resistance.
- Moreover, if we want to change the membrane potential we again have to move charges just to charge the membrane capacitance.
- The hydraulic equivalent is a leaky, elastic garden hose.

# Recapitulation L3



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$$\lambda = \sqrt{\frac{r_m}{r_i}}$$

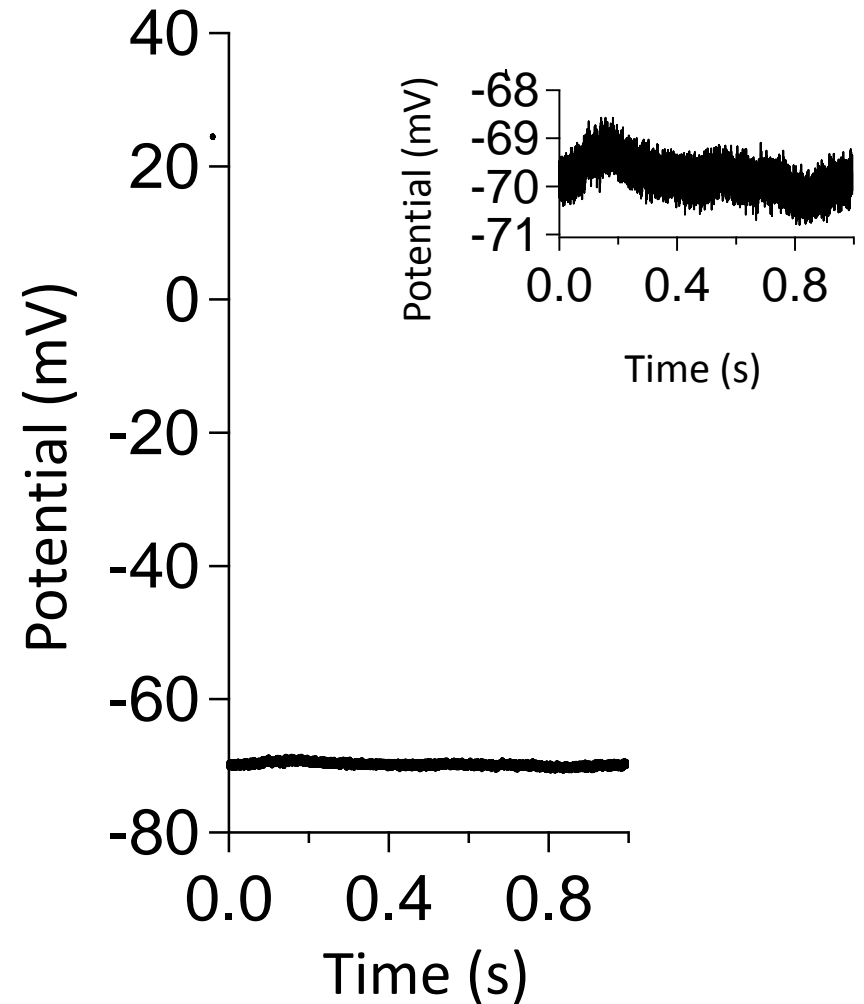
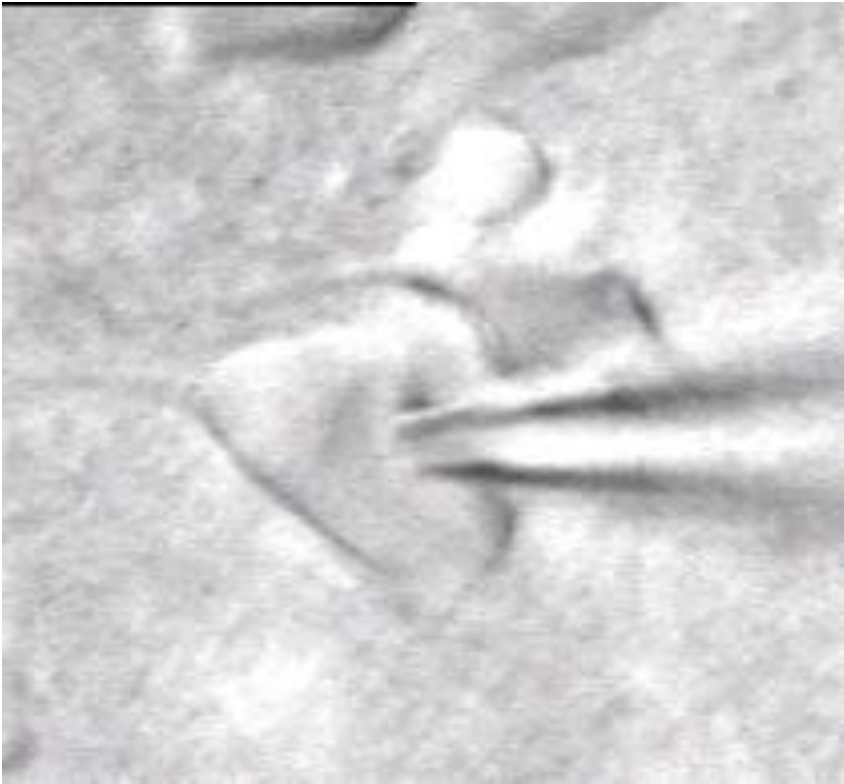
The length constant describes the signal loss along a neuronal process. After one length constant we only have 1/e or about 37% of the signal. Typical length constants range from 100 micrometers to a millimeter.

$r_m$  is the membrane resistance (across).  
 $r_i$  is the cytoplasmic resistance (lengthwise).

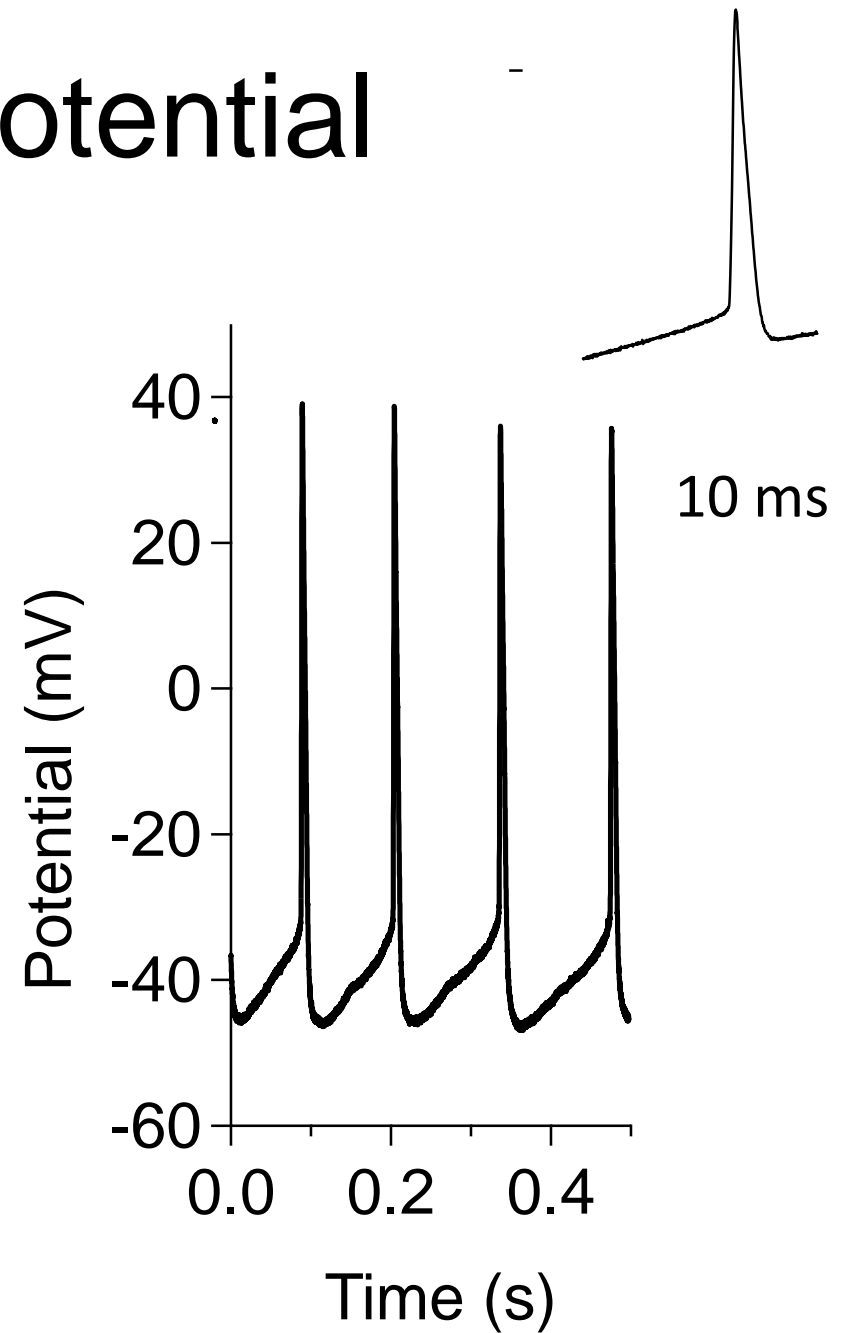
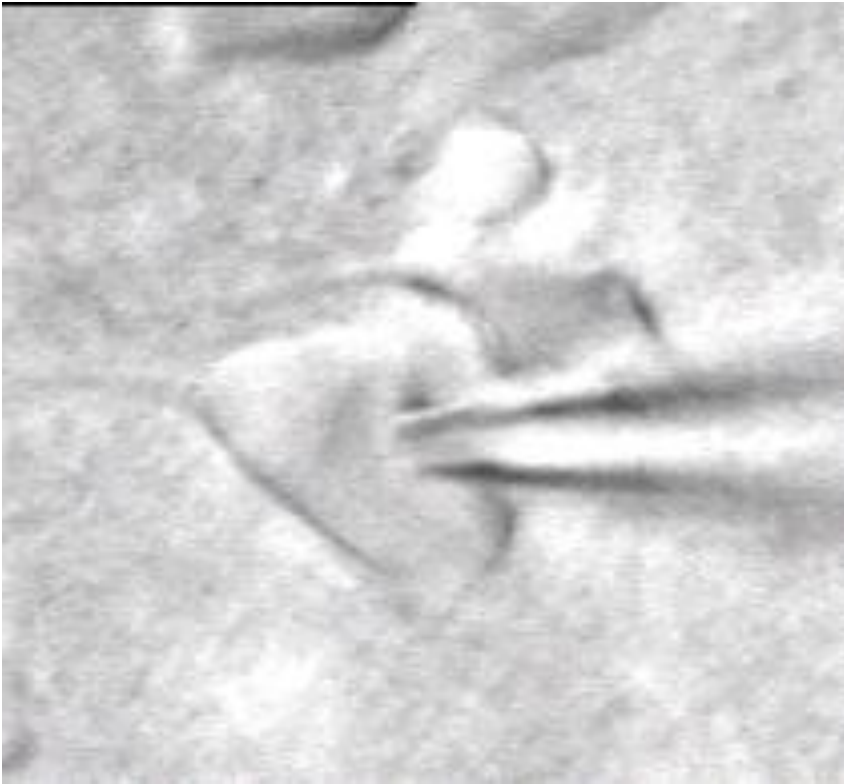
This simplified version is only valid for steady signals (and is the best case).



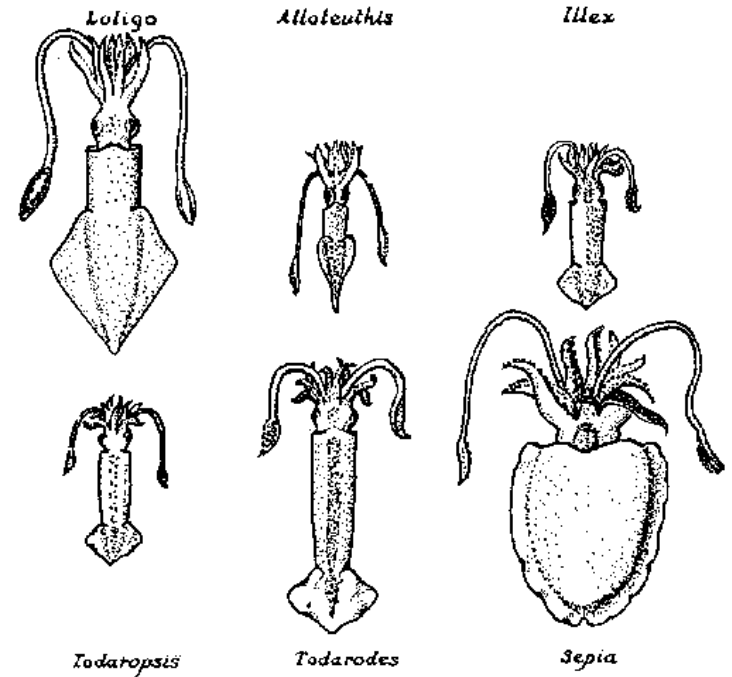
# Resting Membrane Potential



# Action Potential



# Loglio forbesi



# Squid Giant Axon

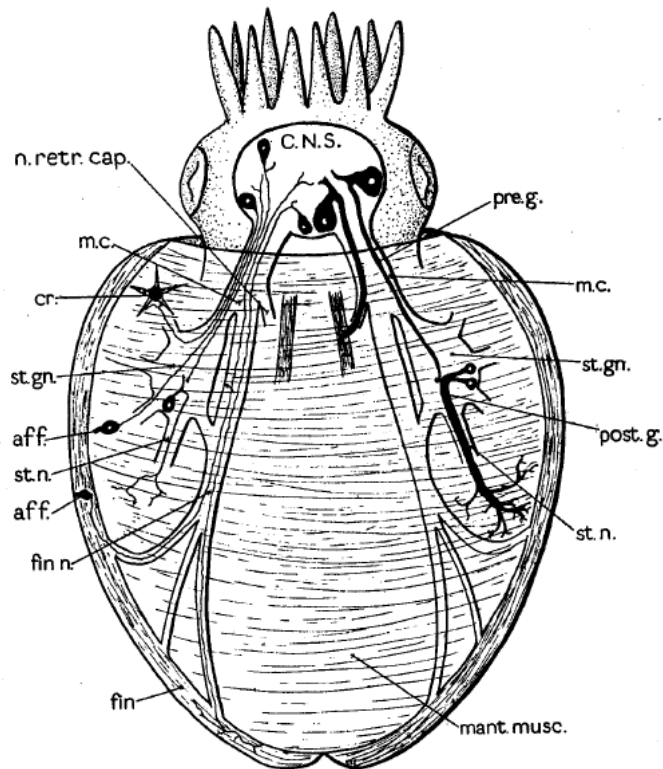
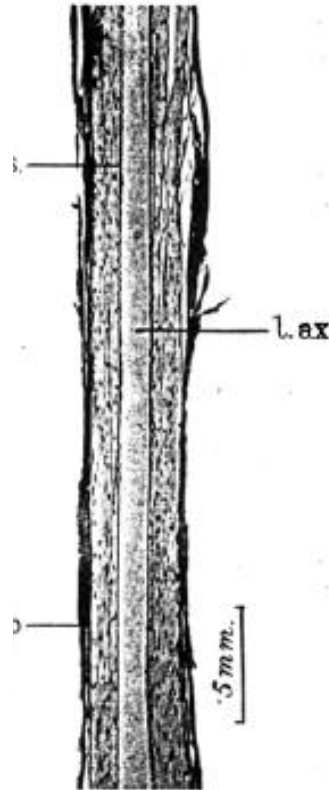


FIG. 1.—Diagram of the innervation of the mantle in *Sepia officinalis*. The details of the connexions of the giant fibres are not known; *pre. g.*, represents the "pre-ganglionic" fibres, which arise in the palliovisceral ganglion; *post. g.*, the "post-ganglionic" fibres, which take origin from the fusion of the processes of several cells. For further explanation see text.



611.018.83:595.3  
611.018.83:594.5

## The Structure of Nerve Fibres in Cephalopods and Crustacea

By J. Z. YOUNG, Department of Zoology and Comparative Anatomy and  
Magdalen College, Oxford

(Communicated by Sir Henry Dale, F.R.S.—Received 20 May, 1936)

# Intracellular Recording

NATURE

OCT. 21, 1939, Vol. 144

## Action Potentials Recorded from Inside a Nerve Fibre

NERVOUS SYSTEM

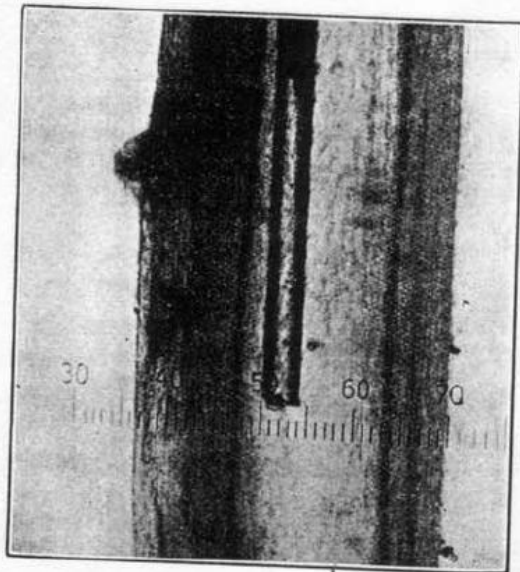


Fig. 1.

PHOTOMICROGRAPH OF ELECTRODE INSIDE GIANT AXON. 1 SCALE DIVISION =  $33 \mu$ .

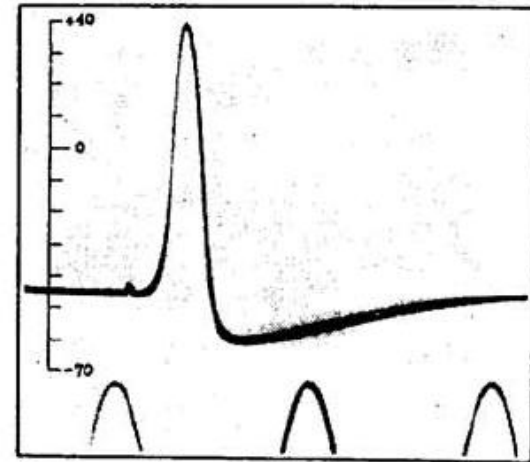
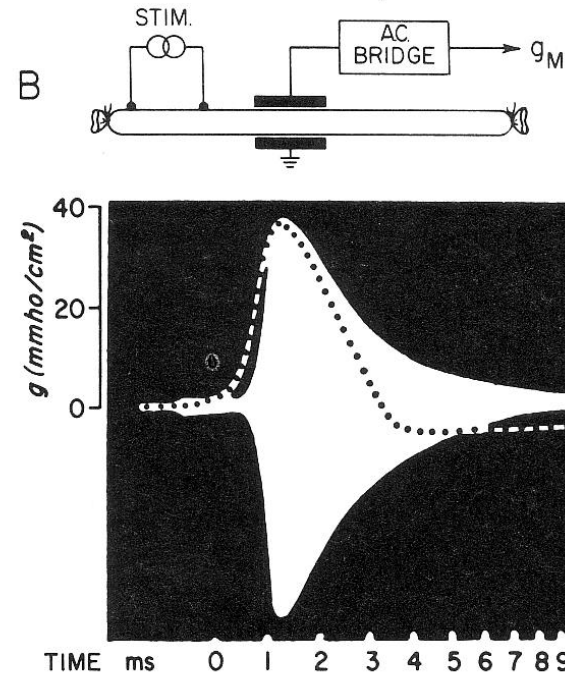
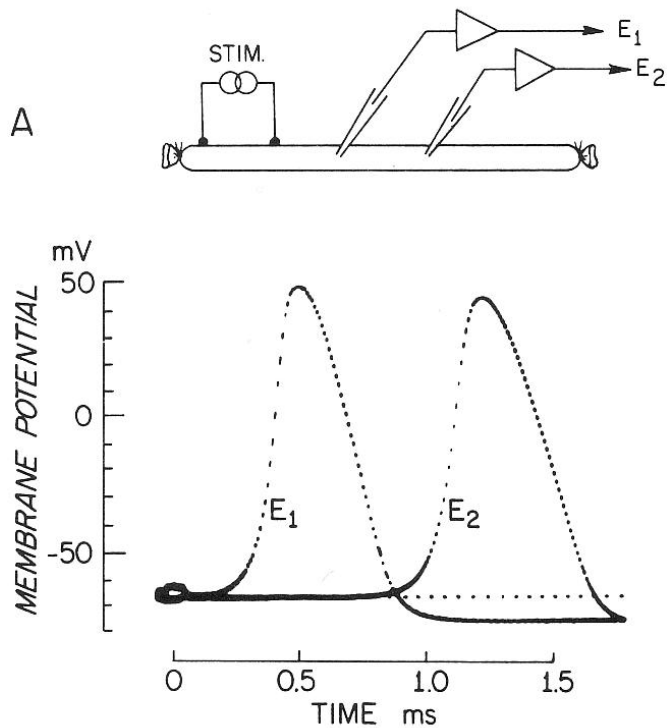


Fig. 2.

ACTION POTENTIAL RECORDED BETWEEN INSIDE AND OUTSIDE OF AXON. TIME MARKER, 500 CYCLES/SEC. THE VERTICAL SCALE INDICATES THE POTENTIAL OF THE INTERNAL ELECTRODE IN MILLIVOLTS, THE SEA WATER OUTSIDE BEING TAKEN AT ZERO POTENTIAL.

These results are important for two reasons. In the first place they prove that the action potential arises at the surface, and in the second, they give the absolute magnitude of the action potential as about 90 mv. at  $20^{\circ}\text{C}$ . Previous measurements have always been made with external electrodes and give values which are reduced by the short-circuiting effect of the fluid outside the nerve fibre.

# Increased Permeability



# Depolarization is Na-dependent

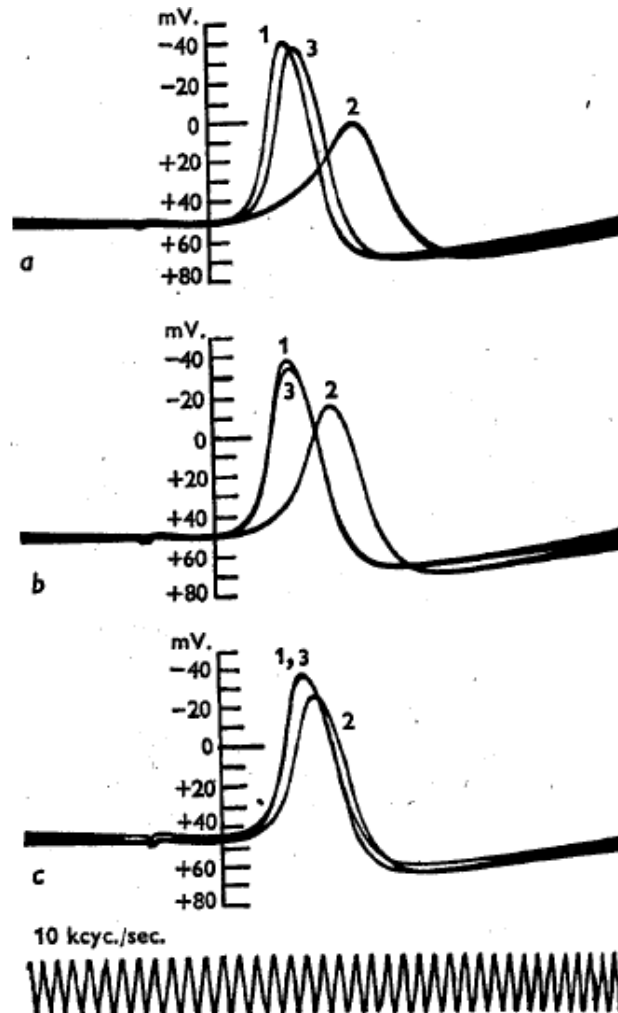
J. Physiol. (1949) 108, 37-77

612.813

## THE EFFECT OF SODIUM IONS ON THE ELECTRICAL ACTIVITY OF THE GIANT AXON OF THE SQUID

By A. L. HODGKIN AND B. KATZ

*From the Laboratory of the Marine Biological Association, Plymouth, and the Physiological Laboratory, University of Cambridge*

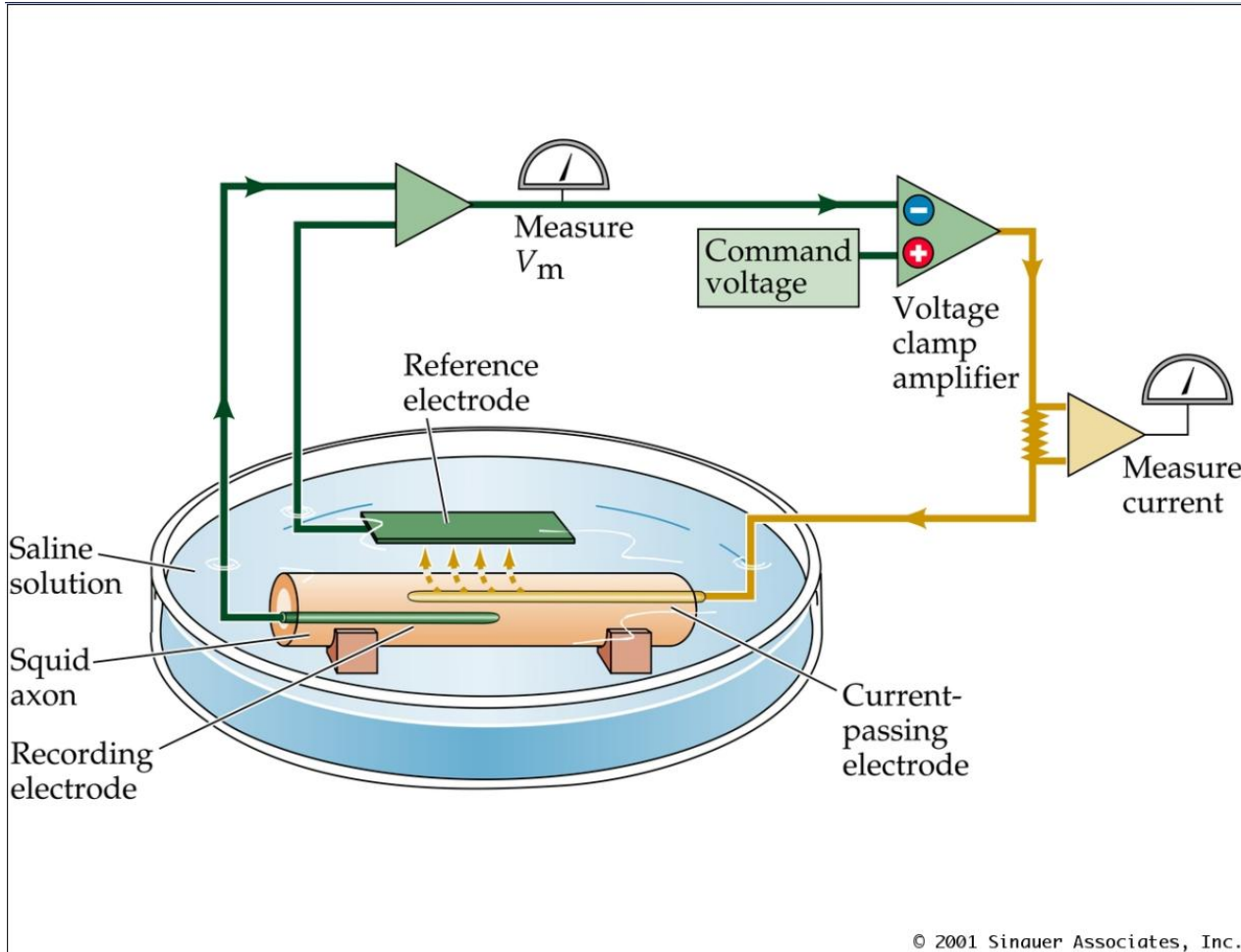


Replacing Na-ions in the extracellular solution with impermeant ions reduces the action potential amplitude.

Fig. 4. Action of sodium-deficient solutions on the resting and action potential. *a* 1, response in sea water; *a* 2, after 16 min. in 33% sea water, 67% isotonic dextrose; *a* 3, 13 min. after reapplication of sea water. *b* 1, response in sea water; *b* 2, after 15 min. in 50% sea water, 50% isotonic dextrose; *b* 3, 6 min. after reapplication of sea water. *c* 1, response in sea water; *c* 2, after 16 min. in 71% sea water, 29% isotonic dextrose; *c* 3, 7 min. after reapplication of sea water. The scale gives the potential difference across the nerve membrane (outside - inside) with no allowance for the junction potential between the axoplasm and the sea water in the microelectrode.



# Voltage Clamp



J. Physiol. (1952) 116, 424-448

## MEASUREMENT OF CURRENT-VOLTAGE RELATIONS IN THE MEMBRANE OF THE GIANT AXON OF *LOLIGO*

By A. L. HODGKIN, A. F. HUXLEY AND B. KATZ

From the Laboratory of the Marine Biological Association, Plymouth, and the Physiological Laboratory, University of Cambridge

(Received 24 October 1951)

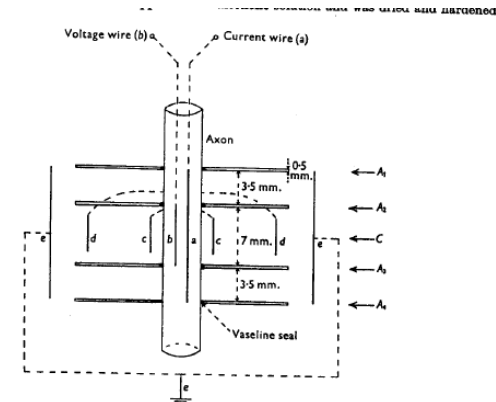
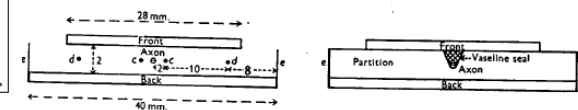


Fig. 1. Diagram illustrating arrangement of internal and external electrodes.  $A_1, A_2, A_3$  and  $A_4$  are Perspex partitions.  $a, b, c, d$  and  $e$  are electrodes. Insulated wires are shown by dotted lines. For sections through  $A$  and  $C$ , see Figs. 2 and 3.



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Membrane voltage is held constant and the current is measured.



# Action Potential Currents

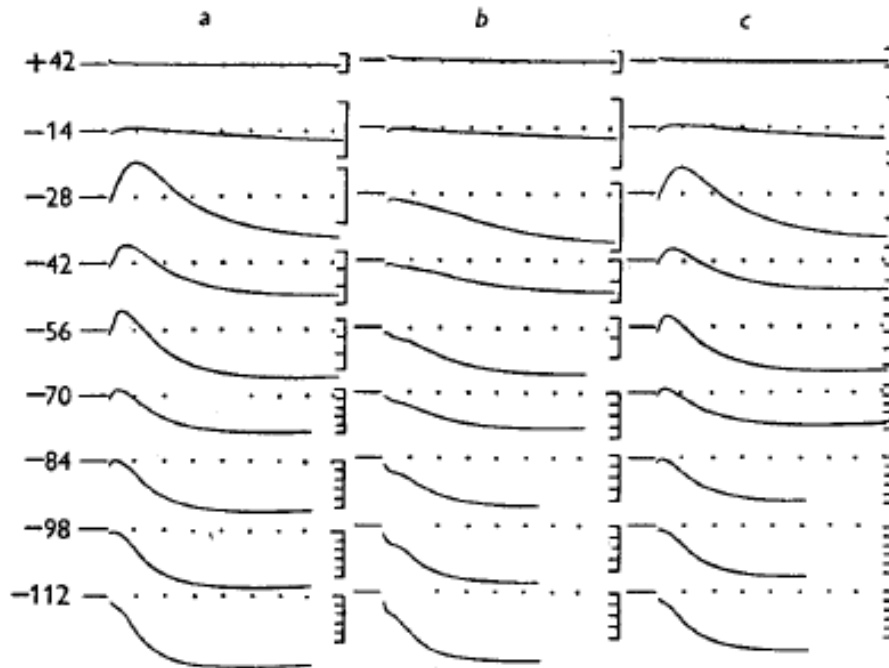


Fig. 2

J. Physiol. (1952) 116, 449-472

## CURRENTS CARRIED BY SODIUM AND POTASSIUM IONS THROUGH THE MEMBRANE OF THE GIANT AXON OF *LOLIGO*

By A. L. HODGKIN AND A. F. HUXLEY

From the Laboratory of the Marine Biological Association, Plymouth,  
and the Physiological Laboratory, University of Cambridge

(Received 24 October 1951)

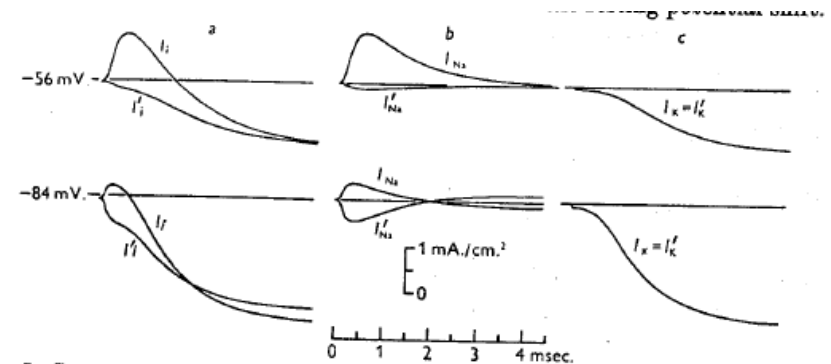
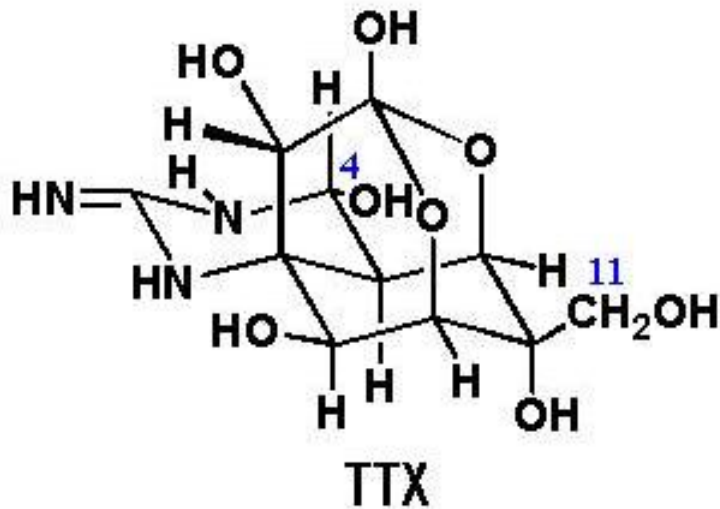


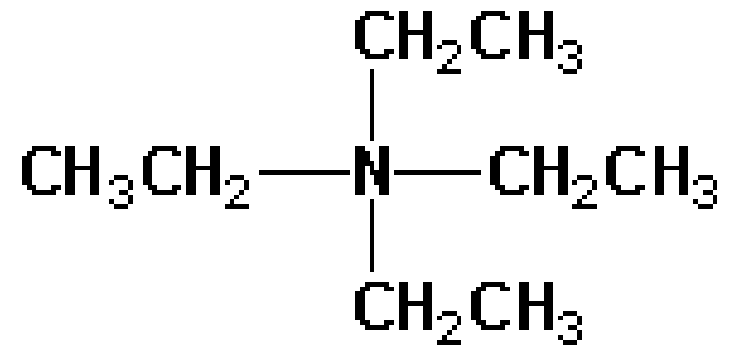
Fig. 5. Curves illustrating separation of ionic current into  $I_{Na}$  and  $I_K$ . Upper part of figure. a, ionic currents:  $I_i$ , axon in sea water, membrane potential lowered by 56 mV.;  $I'_i$ , axon in 10% sodium sea water, membrane potential lowered by 60 mV. (average of curves taken before and after  $I_i$ ). b, sodium currents:  $I_{Na}$ , sodium current in sea water;  $I'_{Na}$ , sodium current in 10% sodium sea water. c, potassium current, same in both solutions. Lower part of figure. Same, but membrane potential lowered by 84 mV. in sea water and 88 mV. in 10% sodium sea water. Current and time scales same for all curves. Axon no. 21; temperature 8.5° C.

Sudden depolarization causes the opening of conductances and flow of current.  
Graphical representation is not according to today's conventions.

# Channel-Blockers



Sodium (Na) channels

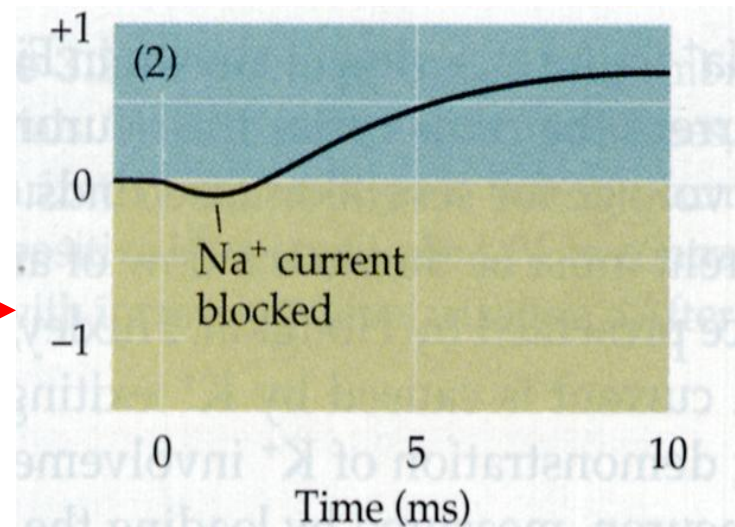
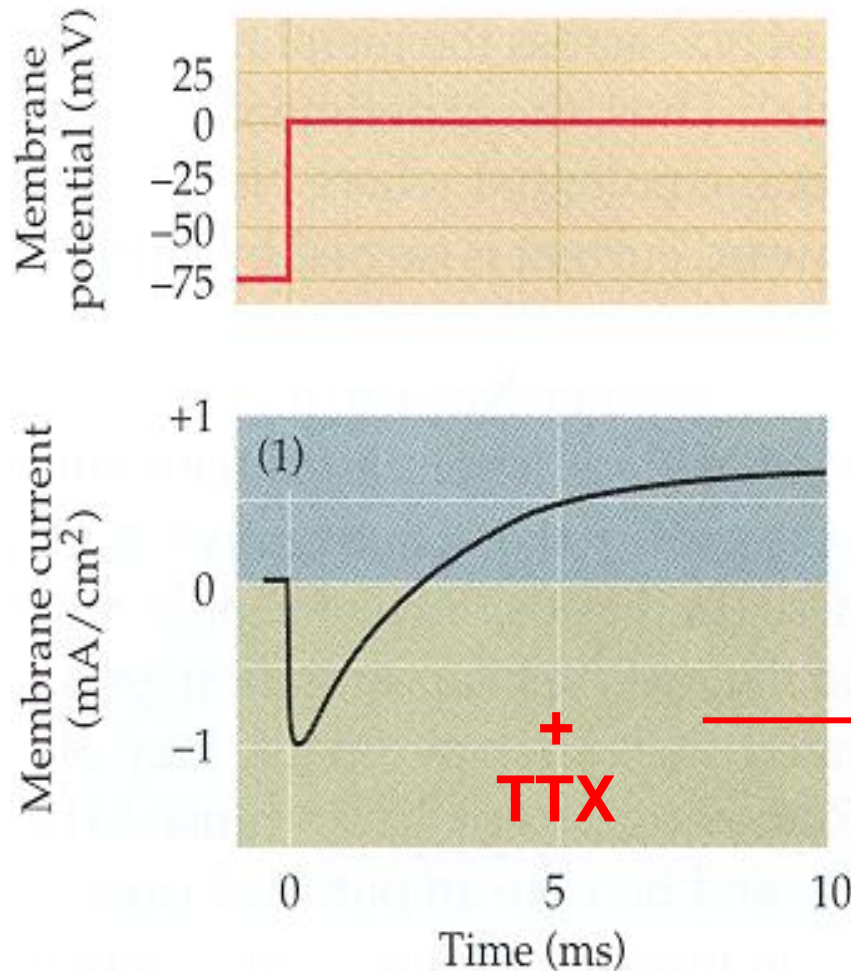


TEA

Tetraethylammonium

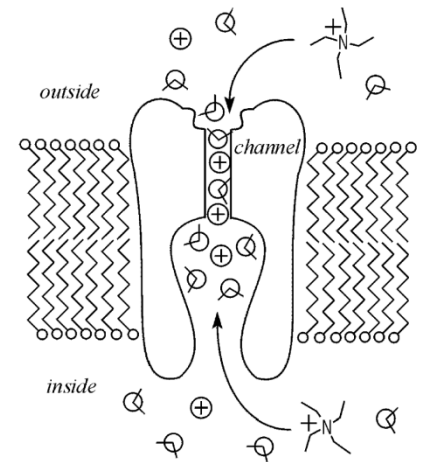
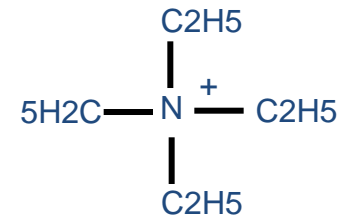
Potassium (K) channels

# After Block of Na-Channels

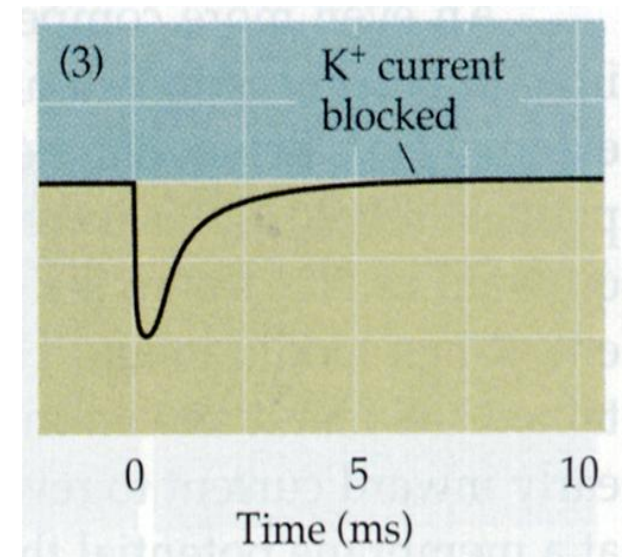
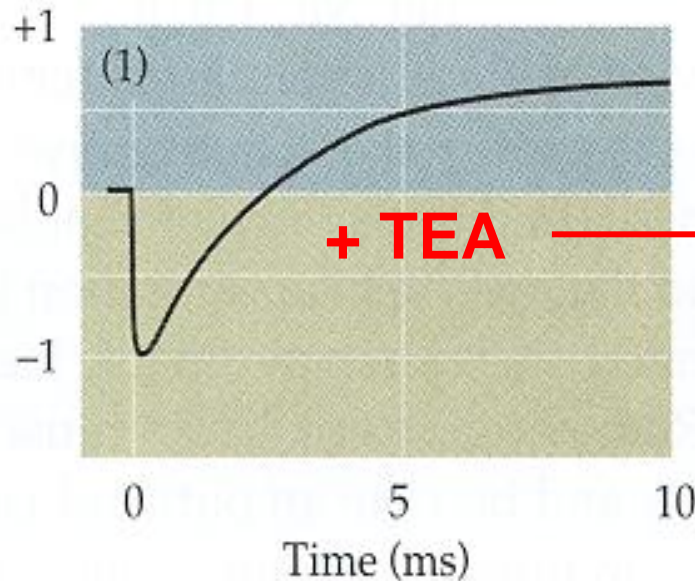


# After Block of K-Channels

Membrane potential (mV)



Membrane current (mA/cm<sup>2</sup>)

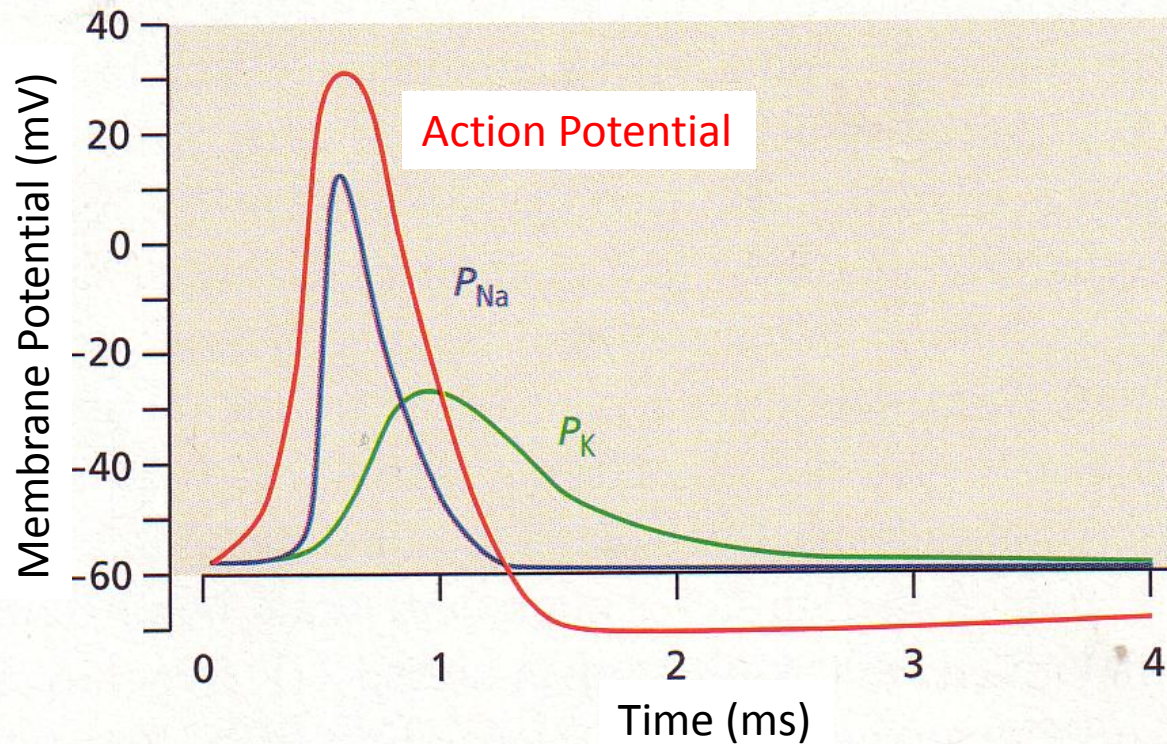




# Conductances

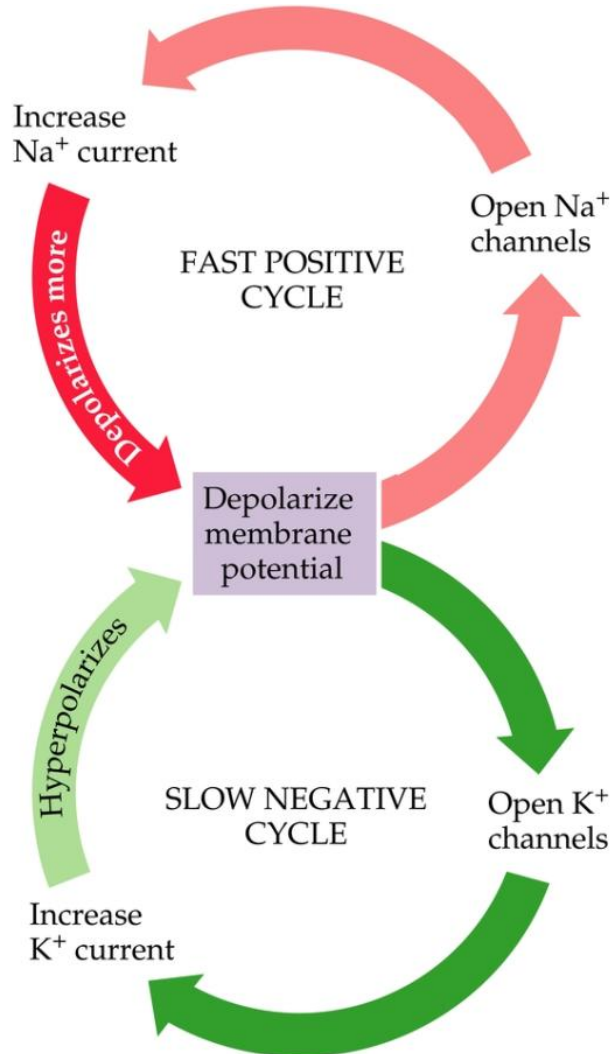
Goldmann, Hodgkin, Katz

$$E_i = \frac{RT}{F} \ln \left( \frac{P_K [K^+]_a + P_{Na} [Na^+]_a}{P_K [K^+]_i + P_{Na} [Na^+]_i} \right)$$



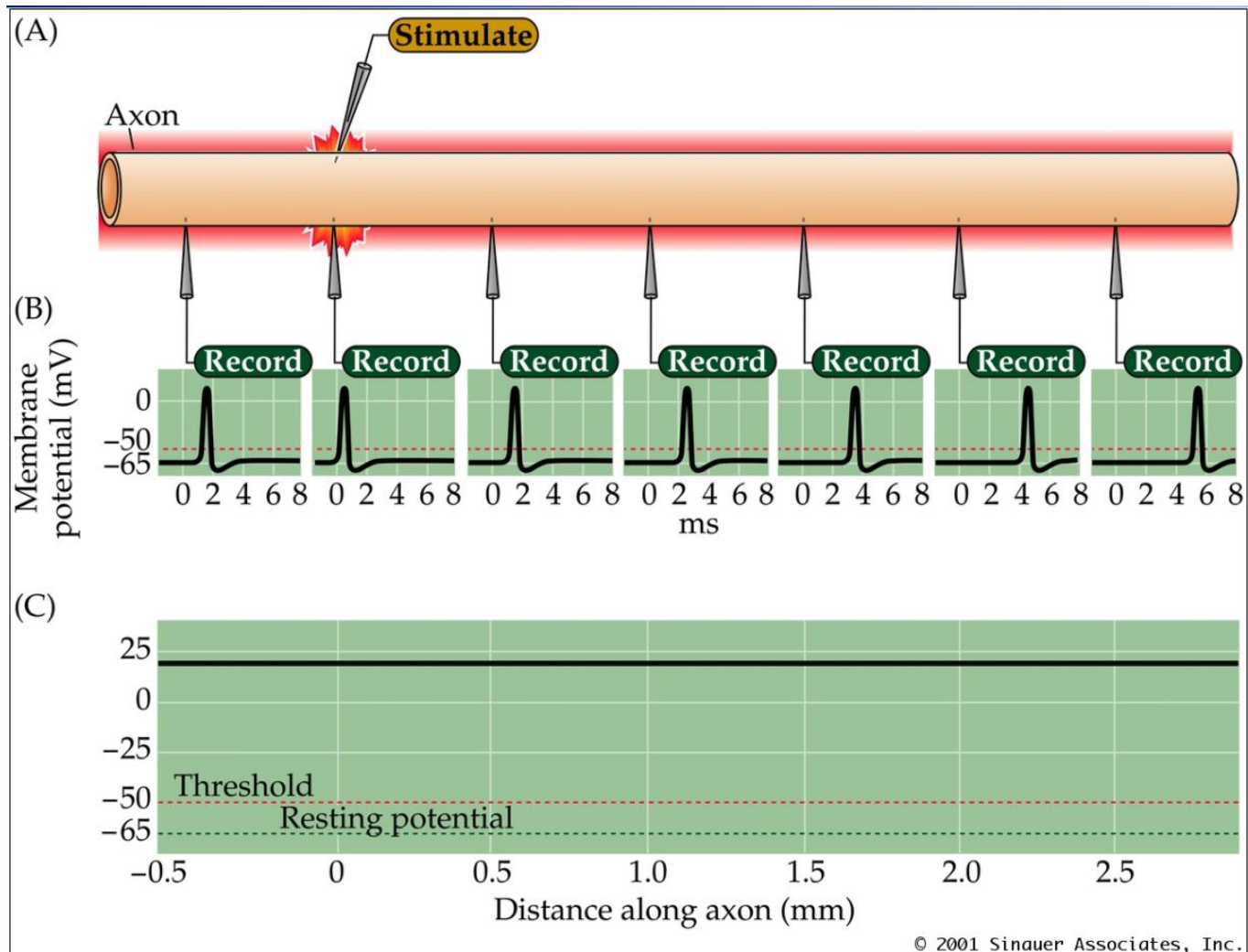
b

# Feedback Mechanisms

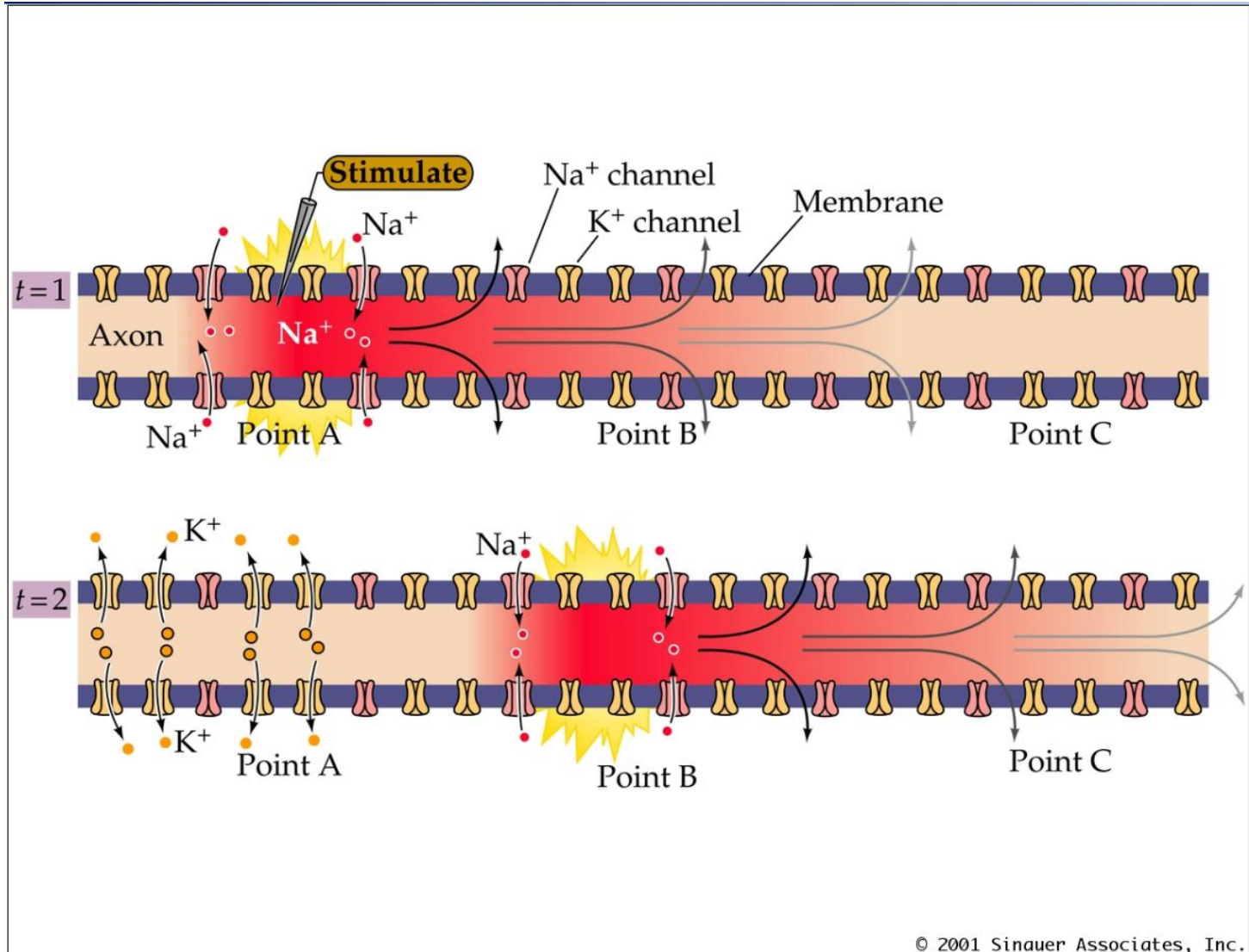


- Positive feedback of voltage dependent Na-conductance
- Negative feedback of voltage dependent K-conductance
- Explosive depolarization and subsequent repolarization

# Action Potentials Propagate

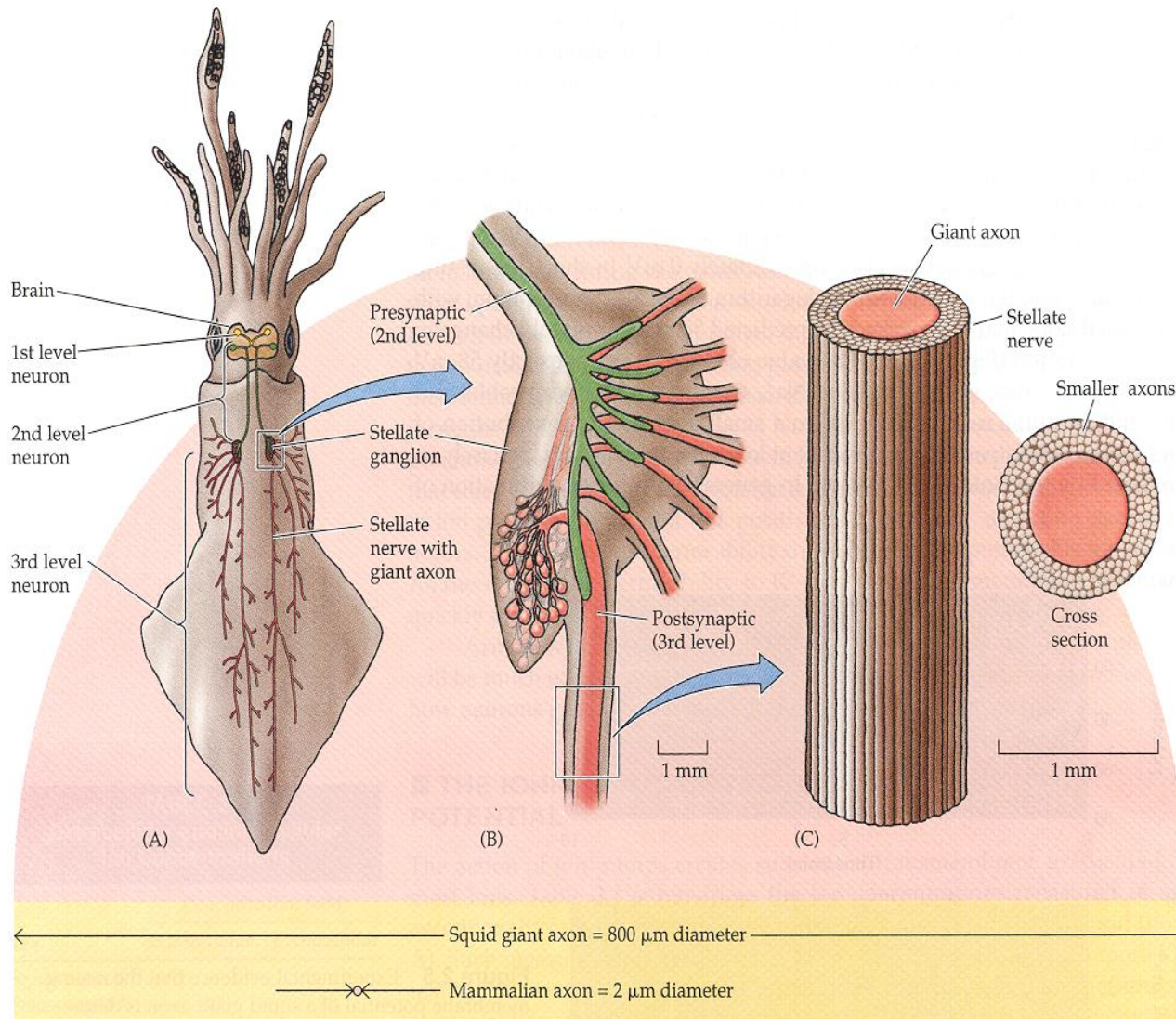


# AP Propagation





# Make It Fast



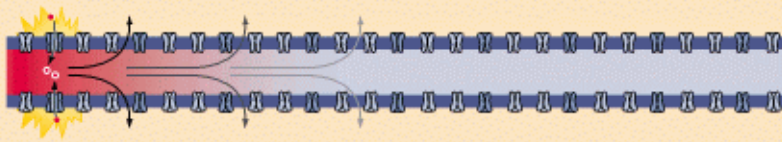
$$v = \sqrt{\frac{r_m}{r_i}}$$

$r_m$  scales linearly with the diameter, while  $r_i$  scales with the square of the diameter

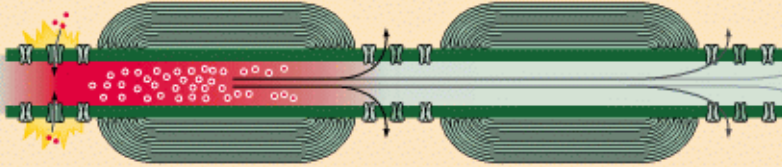
Big axons are faster

$t = 1$

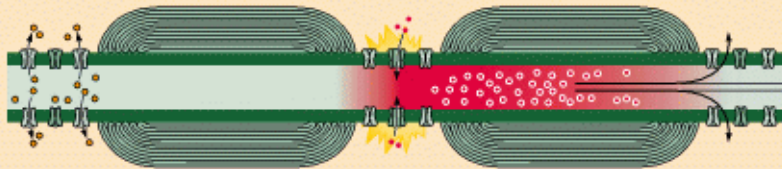
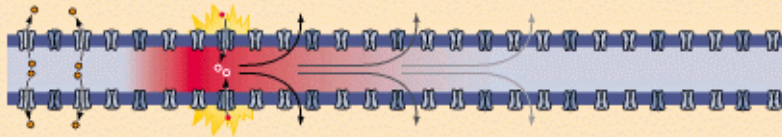
Unmyelinated axon



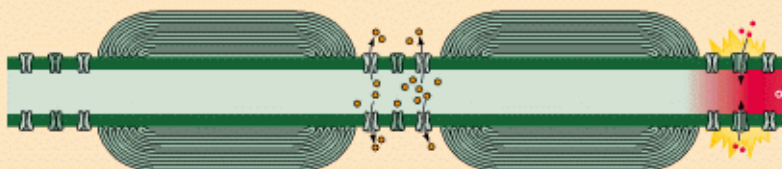
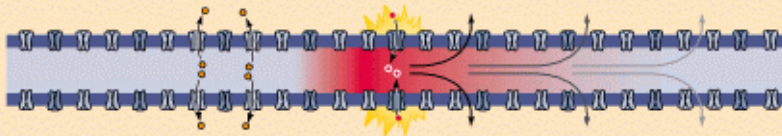
Myelinated axon



$t = 2$



$t = 3$

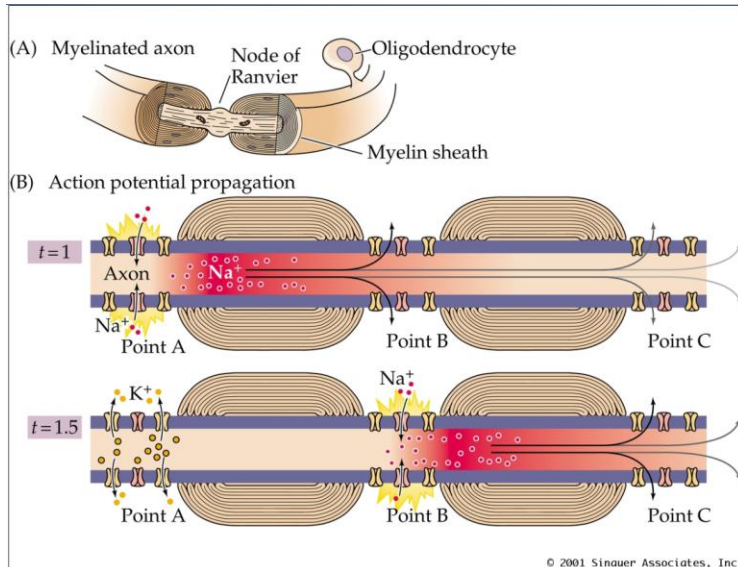


# Myelin

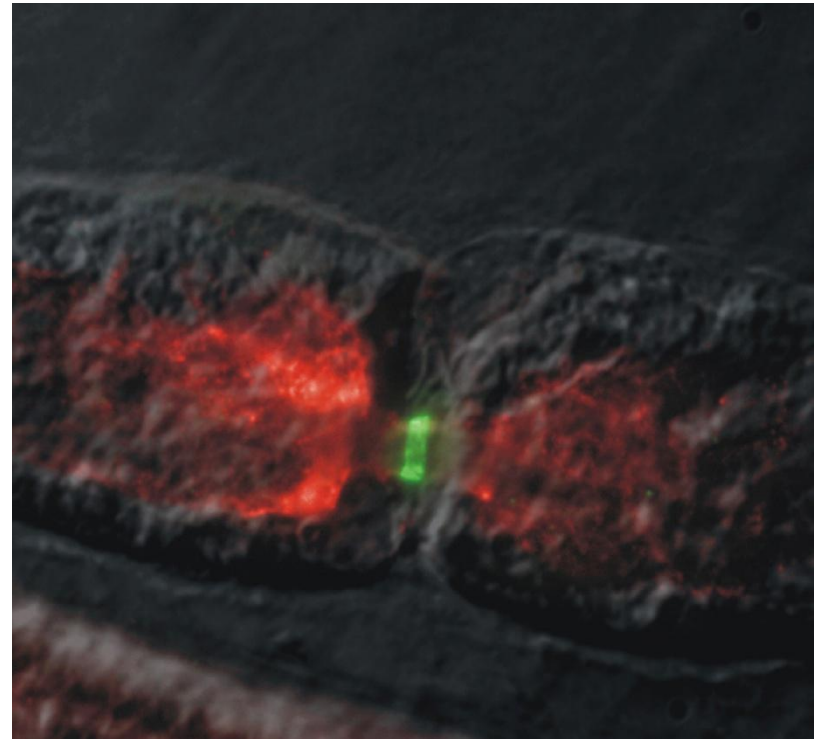
Myelination reduces both  $r_m$  and the capacitance of the membrane. This greatly improves the performance of the 'leaky flexible garden hose'.

The trigger signal can reach more distant channels more quickly.

# Channels are Strategically Enriched

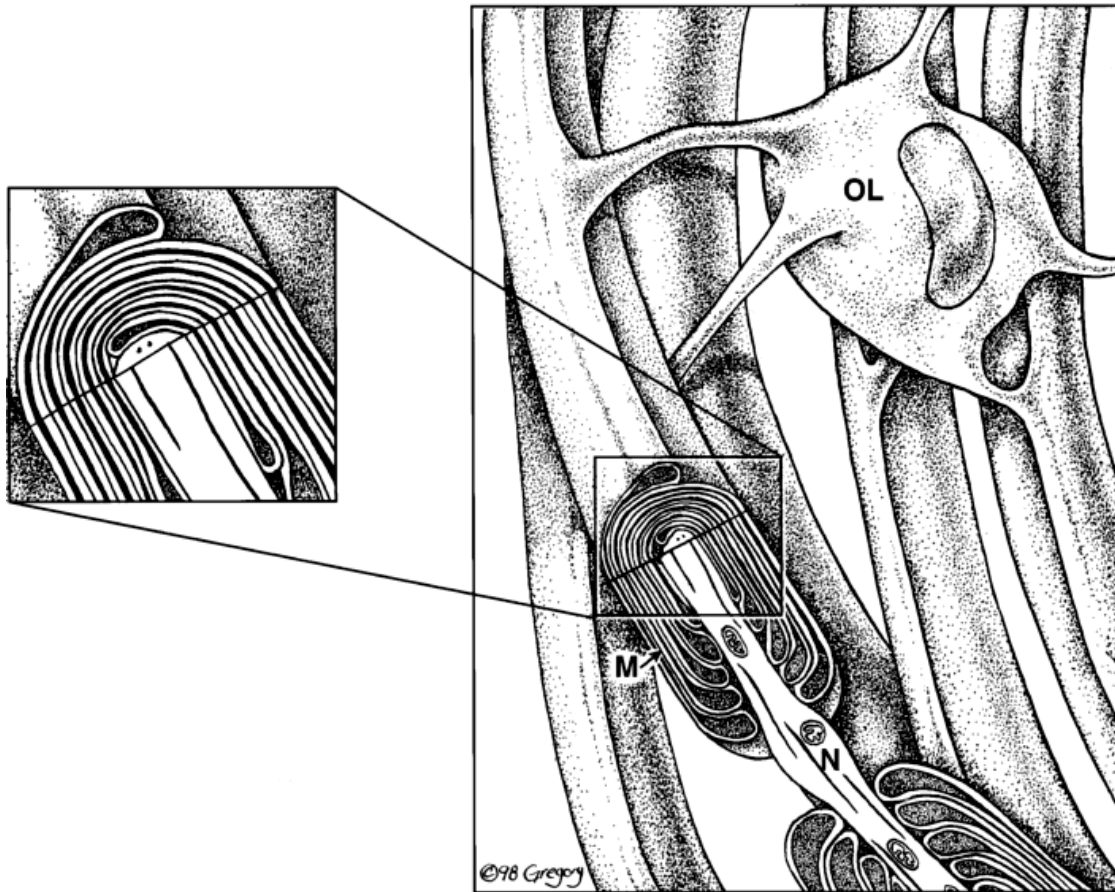


Sodium channels are enriched at nodes of Ranvier -> Saltatory propagation of the AP.



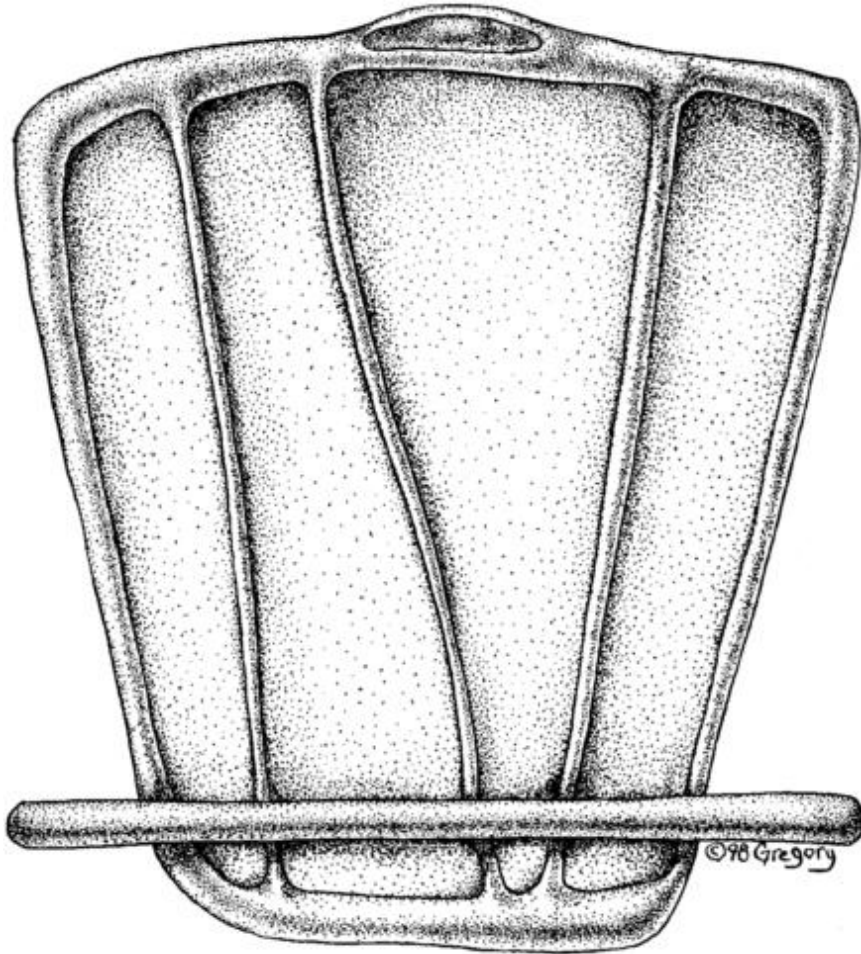


# CNS Myelin



- A single oligodendrocyte forms myelin sheath around many (50) axons.
- Segment length: ca. 1 mm

# PNS Myelin



- An unrolled Schwann cell in the peripheral nervous system (PNS).
- Each Schwann cell only surrounds one axon.