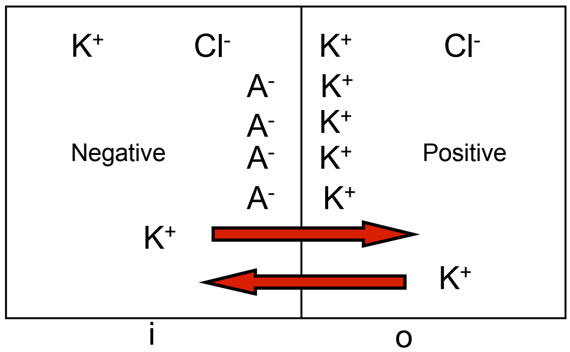
Donnan Equilibrium



We can define the electrochemical potential as:

$$\mu_1 = \mu_o + RTLn\alpha_1 + zF\psi_1$$

$$\mu_2 = \mu_o + RTLn\alpha_2 + zF\psi_2$$

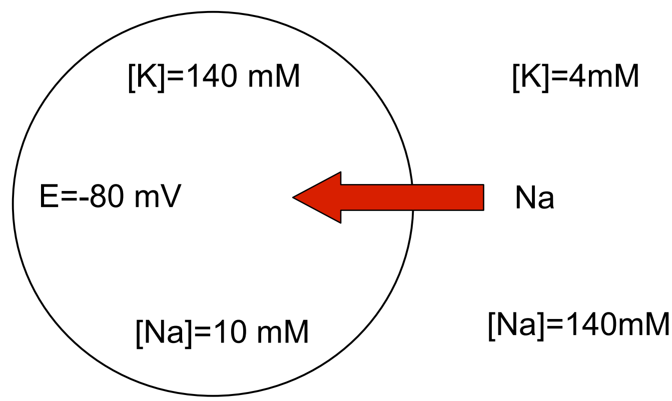
At equilibrium $\mu_1 = \mu_2$

$$\therefore RTLn\alpha_1 + zF\psi_1 = RTLn\alpha_2 + zF\psi_2$$

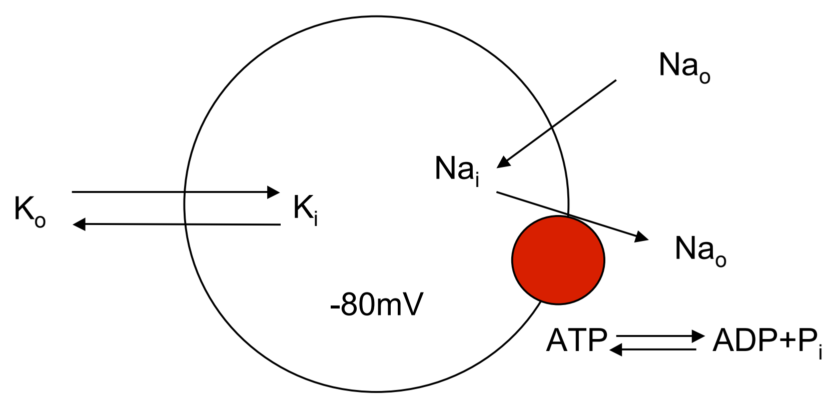
$$\psi_1 - \psi_2 = E = \frac{RT}{zF} Ln\frac{\alpha_1}{\alpha_2} = \frac{RT}{zF} Ln\frac{C_1}{C_2}$$

$$E = \frac{RT}{zF} Ln\frac{C_1}{C_2}$$ *Nernst equation*

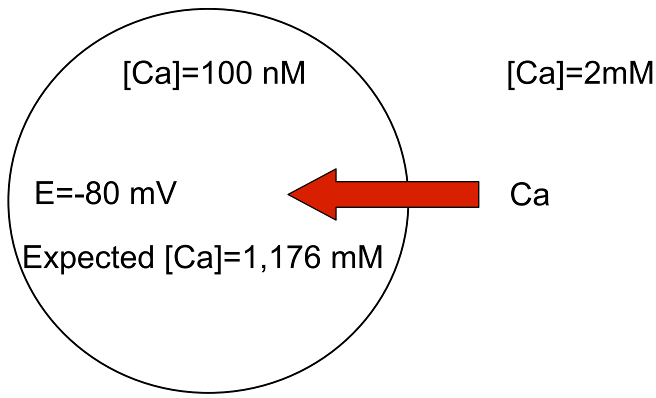
Calculations with the Nernst equation indicate that [Na_i] should = 3,434 mM if it is at electrochemical equilibrium.



Na Pump Maintains the Inward Na Gradient

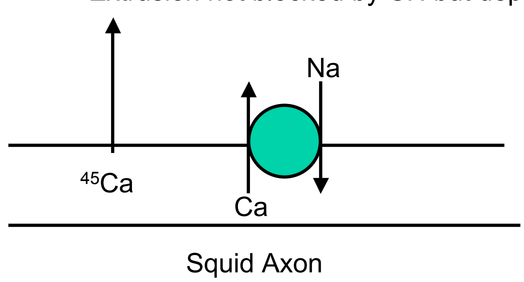


Calculations with the Nernst equation indicate that $[Ca_i]$ should = 1,176 mM if it is at electrochemical equilibrium.



Blaustein and Hodgkin (1969)

Extrusion not blocked by CN but depended on Na_o

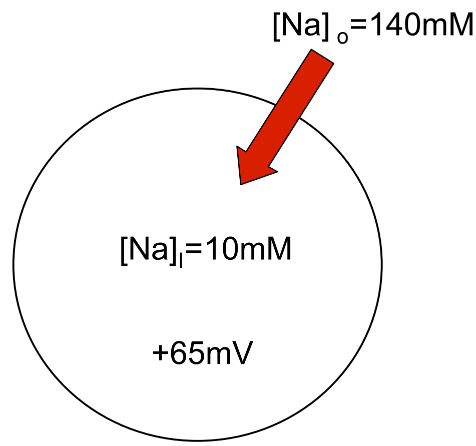


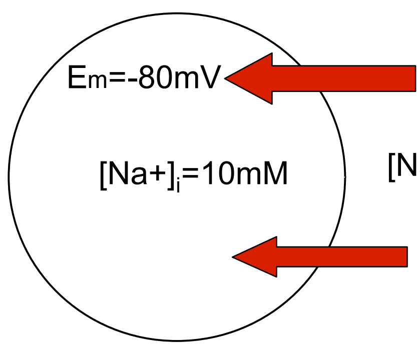
Driving Forces

Ohms Law I=gV

$$E_{Na} = \frac{RT}{zF} \ln \frac{[Na+]_o}{[Na+]_o}$$

E_{Na}=+65mV





Electrical Driving Force =E_m (mV)

$[Na^+]_o$=140mM

Force Driving Diffusion=-E_{Na}

Net Driving Force(mV)=E_m+(-E_{Na})
Or E_m-E_{Na} (mV)

Ohms Law and Electrophysiolgy

Net Driving Force(mV)=E_m-E_{Na} (mV)

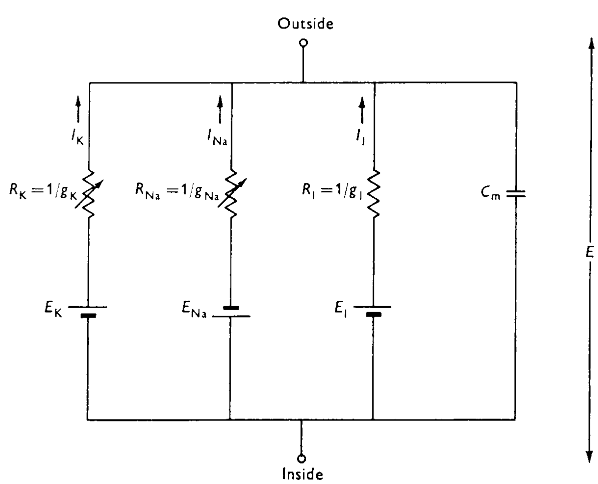
From Ohms Law Na current ,I_{Na} (ion flux) will be given by:

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

When $E_m=E_{Na}$ $I_{Na}=0$

By changing E_m until $I_{Na}=0$ we can find E_{Na}.

Conceptual model of a patch of electrically excitable membrane. (After Hodgkin and Huxley, 1952*d*.)



At the steady state (resting membrane) when there is no net current:

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

For K, Na and Cl:

$$I_K=g_K(E_m-E_K)$$
$$I_{Na}=g_{Na}(E_m-E_{Na})$$
$$I_{Cl}=g_{Cl}(E_m-E_{Cl})$$

$$\therefore E_m=\frac{g_k}{\sum g}E_k+\frac{g_{Na}}{\sum g}E_{Na}+\frac{g_{Cl}}{\sum g}E_{Cl}$$

Where $\sum g=g_K+g_{Na}+g_{Cl}$

An action potential recorded intracellularly from a squid giant axon. The vertical scale shows the potential (mV) of the internal electrode with respect to the external sea water. The action potential is preceded by small stimulus artefact. The sine wave at the bottom is a time marker, frequency 500 Hz. (From Hodgkin and Huxley, 1945.)

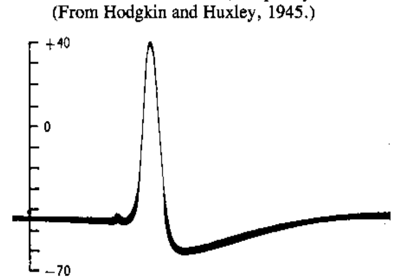
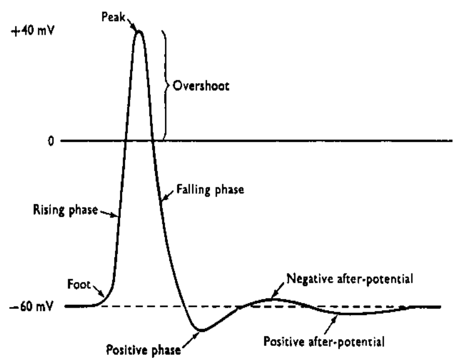
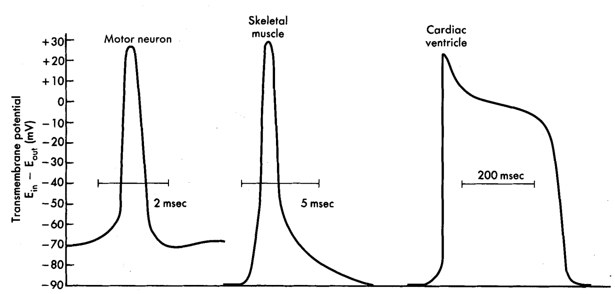


Diagram to show the nomenclature applied to an action potential and the after-potentials which follow it.



Action Potential from Different Cells

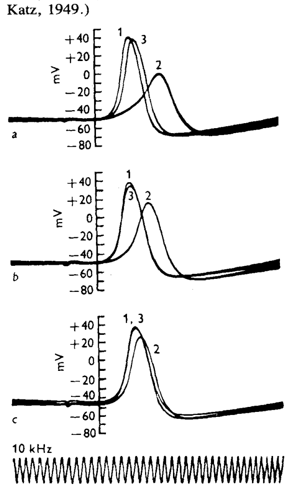


Action potentials from three vertebrate cell types. Note the different time scales.
(Redrawn from Flickinger CJ et al: *Medical cell biology,* Philadelphia, 1979, WB Saunders.)

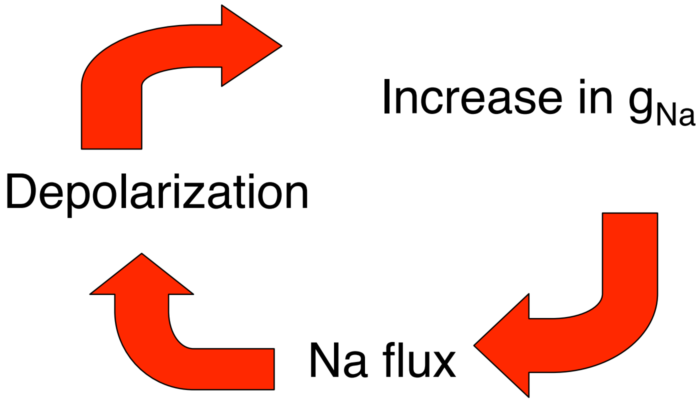
The “sodium theory” of the action potential

Action potentials exhibit an overshoot. Thus the peak of the action potential is well above zero. Hodgkin and Katz suggested (in 1949) that this was due to a rapid and selective increase increase in the permeability towards sodium.Thus g_{Na} transiently becomes much greater than g_k .How can this idea be tested?

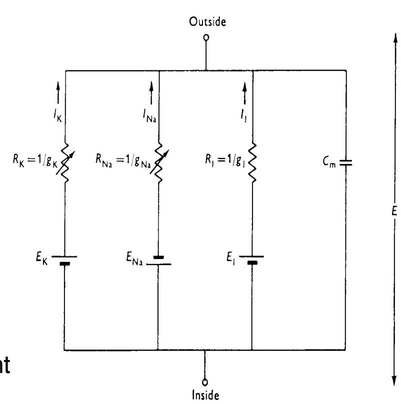
The effect of reducing the external sodium ion concentration on the size of the action potential in a squid giant axon. In each set of records, record 1 shows the response with the axon in sea water, record 2 in the experimental solution, and record 3 in sea water again. Experimental solutions were made by mixing sea water and isotonic glucose solutions, the proportions of sea water being *a*, 33%; *b*, 50%; and *c*, 70%. (From Hodgkin and Katz, 1949.)



Positive Feedback



Conceptual model of a patch of electrically excitable membrane. (After Hodgkin and Huxley, 1952*d*.)

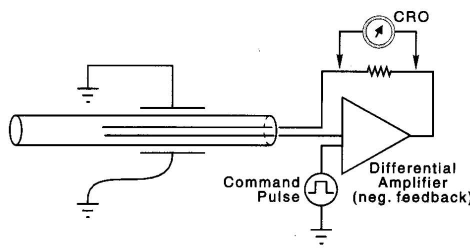


Current flowing through the axon membrane is assumed to consist of capacity current and Ionic current.

$$I = C_m \frac{dE}{dt} + I_i$$

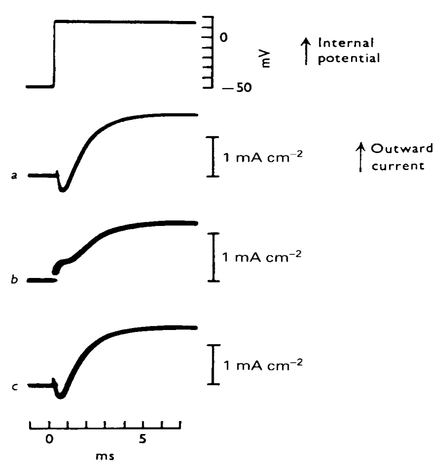
If the voltage is held constant i.e
The membrane is clamped dE/dt=0
and the membrane current =ionic current
i.e $I = I_i$

Voltage Clamp

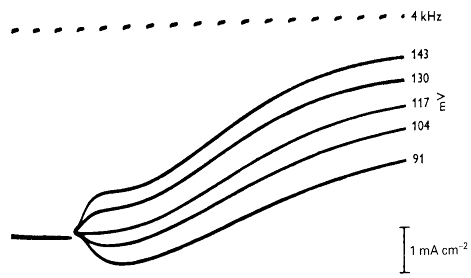


The voltage clamp method used in a squid giant axon. The two wires inserted into the axon are used to measure membrane potential (V) and to pass current (I). The high-gain negative-feedback amplifier compares the command pulse with the membrane potential, and outputs the amount of current necessary to hold the membrane potential constant (or "clamped"). The magnitude of the feedback current can be measured as the IR voltage drop across a resistor and displayed on a cathode-ray oscilloscope (CRO).

Typical records of the membrane current during a voltage clamp experiment. *a* and *c*: In sea water; *b*: in a sodium-free choline chloride solution. (From Hodgkin, 1958, after Hodgkin and Huxley, 1952*a*.)

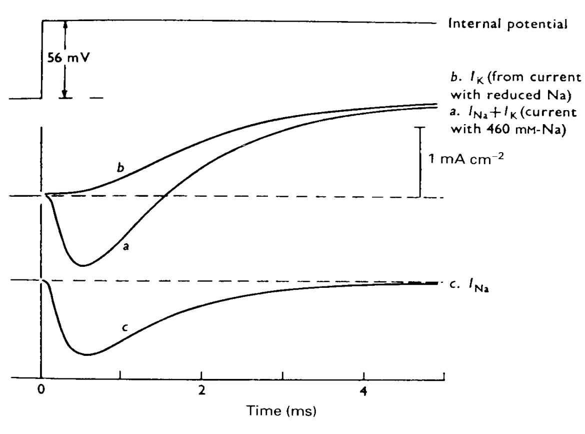


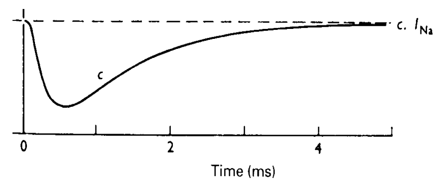
Membrane currents at large depolarizations. Values of V are shown at the right of each record. (From Hodgkin, 1958, after Hodgkin, Huxley and Katz, 1952.)



The potential at which the initial (Na current) is neither inward nor outward is the reversal potential E_{Na} for the Na current i.e about 117 mV.

Analysis of the ionic current in a *Loligo* axon during a voltage clamp. Trace *a* shows the response to a depolarization of 56 mV with the axon in sea water. Trace *b* is the response with the axon in a solution comprising





From traces of Na current as a function of time we can obtain g_{Na} by using the equation $I_{Na}=g_{Na}(E-E_{Na})$. E_{Na} is the potential at which the current is nulled.

Ionic conductance changes during a clamped depolarization, derived from the current curves shown in fig. 5.12. The broken curves show the effects of repolarization. (From Hodgkin, 1958, by permission of the Royal Society.)