- **How do we change the membrane potential in a cell?**

- **Ohm's law** ⇒ \( I = \frac{V}{R} \)  
  In cell physiology we use:

\[
\frac{\text{ion}}{\text{mol}} \quad I_{\text{ion}} = g (V_{m} - V_{\text{ion}}) =
\]

where \( g = N A \)

- Now, suppose that we have a number of \( K^+ \) selective ion channels and we now add \( Na^+ \) selective ones to our vesicle.

\[
V_{k} = -84 \text{ mV} \\
V_{Na} = +84 \text{ mV}
\]
The equivalent circuit for the muscle becomes,

\[ I_{C} + I_{Na} + I_{K} = 0 \]

Unless external sources are connected to our cell, it is always true that,

\[ I_{C} = C_{m} \frac{dV_{m}}{dt} = 0 \text{ in the steady state.} \]

\[ I_{Na} = g_{Na} (V_{m} - V_{Na}) \]

\[ I_{K} = g_{K} (V_{m} - V_{K}) \]

\[ g_{Na} (V_{m} - V_{Na}) = -g_{K} (V_{m} - V_{K}) \]

\[ g_{Na} V_{m} - g_{Na} V_{Na} = -g_{K} V_{m} + g_{K} V_{K} \]

\[ V_{m} (g_{Na} + g_{K}) = g_{Na} V_{Na} + g_{K} V_{K} \]
\[ V_m = \frac{g_{Na}V_{Na} + g_k V_k}{g_{Na} + g_k} \]

\[ V_m = \frac{V_{Na} + \left( \frac{g_k}{g_{Na}} \right) V_k}{1 + \left( \frac{g_k}{g_{Na}} \right)} \]

so then, when \( g_k \gg g_{Na} \) \( \implies \) \( V_m = V_k \) !
and
\( g_k \ll g_{Na} \) \( \implies \) \( V_m = V_{Na} \).

What is an action potential?

\( C_m \)

\( \begin{array}{c}
\text{outside} \\
S_1^* \\
\left( \text{Na}^+ \text{channel gate} \right) \\
S_2^* \\
\left( \text{K}^+ \text{channel gate} \right) \\
1 \\
\text{inside} \\
\end{array} \)

\( V_m \)
Action potential in excitable cells.

Current clamp.

\[ I_0 = I_R + I_C = \frac{V_m}{R_m} + C_m \frac{dV_m}{dt} \]

So

\[ \gamma \frac{dV_m}{dt} = I_0 R_m - V_m \]

Solution

\[ V_m = I_0 R_m \left(1 - e^{-t/\tau}\right) \]
- In a cell, current injection changes the membrane potential like,

\[ V_m \]

- the AP is due to membrane \( g_{Na} \) and \( g_{K} \) which are voltage and time dependent.

- In order to study the ionic basis of voltage dependent conductances we need to use a technique known as "voltage clamp" which was invented here at Columbia University by K. S. Cole in the 1940's.
- Voltage clamp and I/V relationships.

\[ V_0 \sim I_m \cdot R_f \]

\[ V_m \sim V_c \]

- A "whole cell" patch clamp recording of a chromaffin cell from the adrenal medulla of a cow may look like,

- Each current is the result of the current through many ion channels that form an "ensemble average".

- Currents can be separated with TTX and TEA.
- Voltage clamp experiments allow us to precisely measure "current-voltage" relationships.

\[ I = \frac{V}{R} \]

\[ I = g_{ion} (V_m - V_{ion}) \]
A voltage dependent ionic conductance will look like...

\[ \frac{1}{g(v)} \]

\[ \text{where } g(v) \]

\[ \text{rectification} \]

\[ I \]

\[ V \]

In a real cell we have:

\[ \frac{1}{g_k(v)} \]

\[ V_k \]

\[ \frac{1}{g_{Na}(v)} \]

\[ V_{Na} \]

\[ I_k = g_k (V_m - V_k); \quad I_{Na} = g_{Na} (V_m - V_{Na}) \]
Peak K⁺ current I-V

\[ I_k \quad V_{m} = -85mV \quad -30mV \]

Peak Na⁺

\[ V_{m} = -35mV \quad V_{Na} \]

From the I-V relationships, we can determine \( g(u) \)

\[ g_k = \frac{I_k(V_m)}{V_m - V_k} \quad g_{Na} = \frac{I_{Na}(V_m)}{V_m - V_{Na}} \]

- Armed with these facts, we can roughly explain the A.P. as an event resulting from the opening and closing of Na⁺ and K⁺ ion channels.
However, as you could see from the ionic currents, both $\text{Na}^+$ and $\text{K}^+$ conductances are not only voltage dependent but are also, time dependent. To understand this we need rate equations and simple differential equations. We will follow the reasoning of A. Hodgkin and A. Huxley.

Ion channel gating is a probabilistic event that depends on the membrane potential.

$$I_{\text{ion}} = N_0 \cdot f (V_m - V_{\text{ion}})$$

but $N_0$ depends on $V_m$ and on $t$

$$N_0 (V_m, t) = N_{\text{Total}} \cdot p_0 (V_m, t)$$

$$\therefore I_{\text{ion}} = N_{\text{Total}} \cdot p_0 (V_m, t) (V_m - V_{\text{ion}})$$
- Let's make a really simple kinetic model for an ion channel.

\[ \alpha(V) \rightarrow \ \text{Open} \quad \beta(V) \]

Closed

- where \( \alpha \) and \( \beta \) are the opening and closing rate constants.

- what is a rate constant you ask? Well.....