The phospholipid bilayer imparts capacitance $C$. 
Initial conditions $\rightarrow$ At equilibrium

Initially $V = 0$

$V_{1-2} = -62 \text{ mV}$

10 mM KCl 1 mM KCl 10 mM KCl 1 mM KCl

Net flux of $K^+$ from 1 to 2

Flux of $K^+$ from 1 to 2 balanced by opposing membrane potential
The phospholipid bilayer imparts capacitance C
Kirchhoff’s law: $I_m = I_c + I_i$

$$I_m = C_m \frac{dV_m}{dt} + g_K(V_m - E_K) + g_{Na}(V_m - E_{Na}) + g_{Cl}(V_m - E_{Cl})$$
\[ I_m = I_c + I_i \]
\[ I_i = \Delta V_m / R_{in} \]
\[ I_c = C \cdot \frac{dV_m}{dt} \]

\[ I_m = C \cdot \frac{dV_m}{dt} + \Delta V_m / R_{in} \]
The membrane time constant $\tau$

$$V_m(t) = R_{in} \cdot I_m \cdot (1 - e^{-t/\tau})$$

$$V_m(t) = R_{in} \cdot I_m \cdot e^{-t/\tau}$$

$$\tau = R_{in} \cdot C_{in}$$
Hodgkin & Huxley (1939), Curtis & Cole (1940)
Figure 2.4: Mechanistic interpretation of the resting membrane potential (2.4) as the center of mass. $\text{Na}^+$ conductance increases during the action potential.
Properties of the Action Potential
Stimulus

Squid axon

$E_M$ (mV)

33% $\text{Na}^+$

50% $\text{Na}^+$

Time after shock (ms)

Action potential amplitude (mV)

Resting membrane potential (mV)

$[\text{Na}^+]_{out}$ (mM)

Slope = 58 mV per tenfold change in $\text{Na}^+$ gradient
Hodgkin & Huxley (1952): quantitative description of the voltage and time dependence of Na+ and K+ conductances underlying the action potential
The Voltage Clamp Technique

- Measure $V_m$
- Command voltage
- Voltage clamp amplifier
- Measure current

- Reference electrode
- Saline solution
- Squid axon
- Recording electrode
- Current-passing electrode
Transient Inward

Delayed Outward

Outward

Inward

Voltage V: imposed ("clamped")

Current I: measured

(A) HYPERPOLARIZATION

(B) DEPOLARIZATION

Squid axon

Delayed Outward

Transient Inward

Time after start of test pulse (ms)
Separating Currents

\[ E_M \]

\[ I_K \]

\[ I_M \] (mA/cm²)

\[ I_Na \]

(B) 10% Na⁺

(A) 100% Na⁺

(C) Difference current

Time after start of test pulse (ms)
Current Voltage Relationship (I/V) for $I_{Na}$ and $I_K$
$V_{\text{half}} = -15 \text{ mV}$
Time course of $g_{Na}$ and $g_{K}$
\[ g_{Na} = f(V, t) \]

\[ g_{K} = f(V, t) \]
Activation of $g_K$ depends on $V$ and $t$

**Model**

$$g_K = g_{K(\text{max})} \cdot n^4$$

$n$ = probability that gate is open

$n$ varies between 0 and 1

CLOSED $\leftrightarrow$ OPEN

$$n = f(V,t)$$

$$n = n_\infty \cdot [1 - e^{(-t/\tau_n)}]$$

$n_\infty = f(V); \quad \tau_n = f(V)$

$n_\infty$ is the value of $n$ at a particular voltage when $t >> \tau_n$

$\tau_n$ is the activation time constant
g_Na activates and in activates as a function of V and t

\[ g_{Na} = g_{Na(max)} m^3 h \]

m is the probability that the activation gate is open.

m varies between 0 and 1

CLOSED \( \Leftrightarrow \) OPEN

\[ 1 - m \quad m \]

\[ m = f(V,t) \]

\[ m = m_\infty [1 - e^{-t/\tau_m}] \]

\[ m_\infty = f(V) \quad \tau_m = f(V) \]

\( m_\infty \) is the value of m at a particular voltage when \( t >> \tau_m \)

\( \tau_m \) is the activation time constant
$$g_{Na} = g_{Na(max)}m^3h$$

$h$ the probability that the “inactivation” gate is open.

$h$ varies between 1 and 0

\[ h = f(V,t) \]

\[ h = h_\infty e^{-t/\tau_h} \]

$h_\infty$ is the value of $h$ at a particular voltage when $t = 0$

$\tau_h$ is the inactivation time constant
Important!! $\tau_m < \tau_n$

Squid axon  6.3°C

2.17 Voltage-Dependent Parameters of the HH Model  Time constants $\tau_m$, $\tau_h$, and $\tau_n$ and steady-state values $m_\infty$, $h_\infty$, and $n_\infty$ calculated from the empirical equations of the Hodgkin-Huxley model for squid giant axon membrane at 6.3°C. Depolarizations increase $m_\infty$ and $n_\infty$ and decrease $h_\infty$. The time constants of relaxation are maximal near the resting potential and become shorter on either side.  [From Hille 1970.]
\[ I = C_m \frac{dV_m}{dt} + g_{K(\text{max})} n^4 (V_m - E_K) + g_{Na(\text{max})} m^3 h (V_m - E_{Na}) + g_L (V_m - E_L) \]

\[ g_{Na} = f(V,t) \]

\[ g_{K} = f(V,t) \]