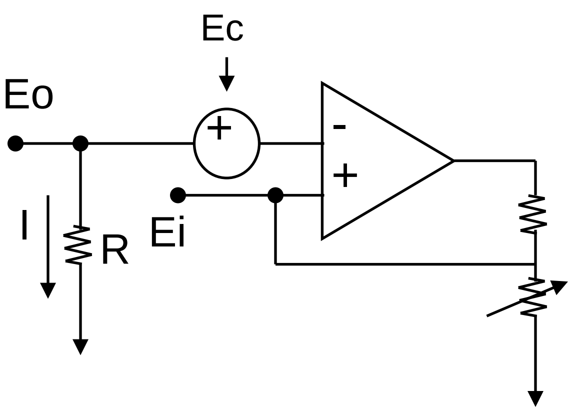
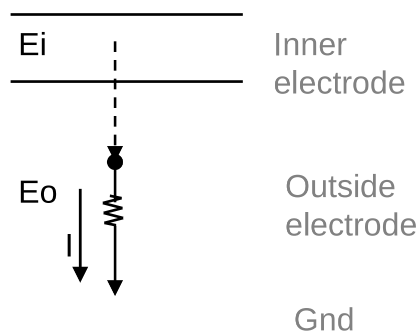
3-3. Bioelectric Phenomena

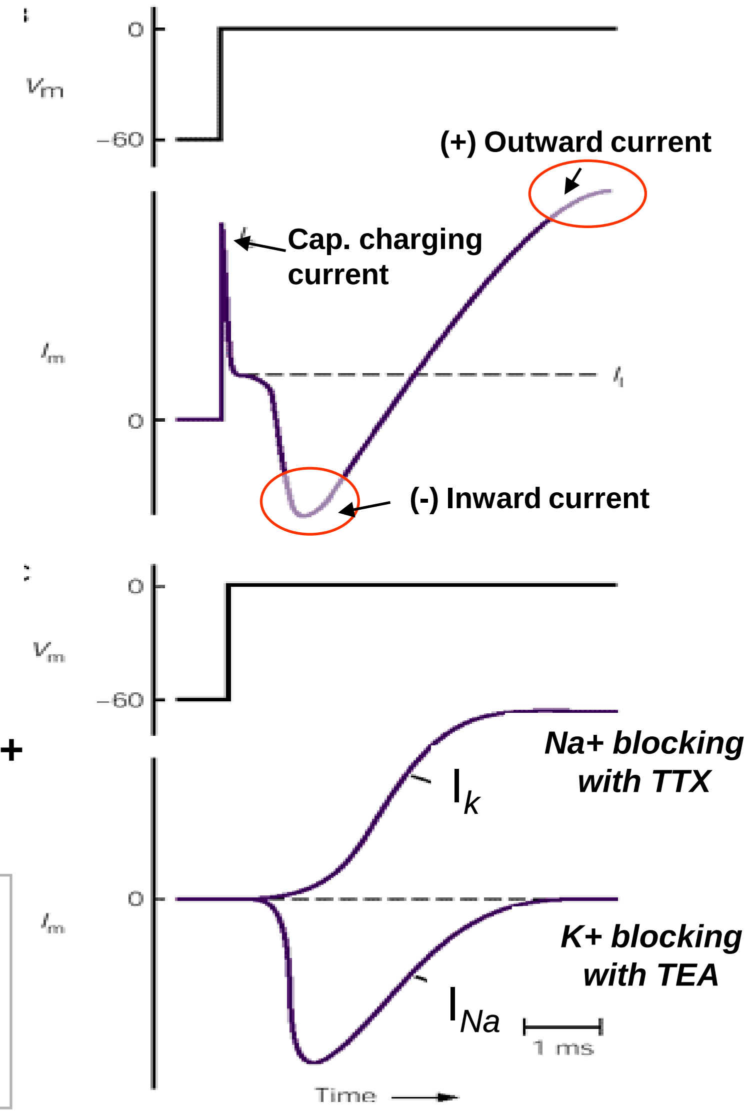
Theoretical Modeling

The H-H Model
Hodgkin-Huxley Model

Their Method:Voltage clamp







− This can be obtained by measuring the transmembrane current at below threshold.

− Subtracting both the capacitive and leakage current from I_m leaves only the Na+ and K+ currents.

− To separate the Na+ and K+ currents, they chose a Na+ free solution.

Pure K+, Na+ current

I_c: Cap. charging current

I_l: leakage current

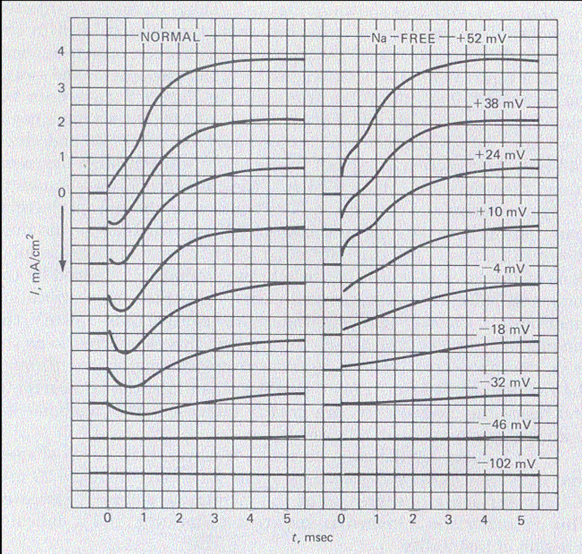
I_k: K+ current

I_{Na}: Na+ current

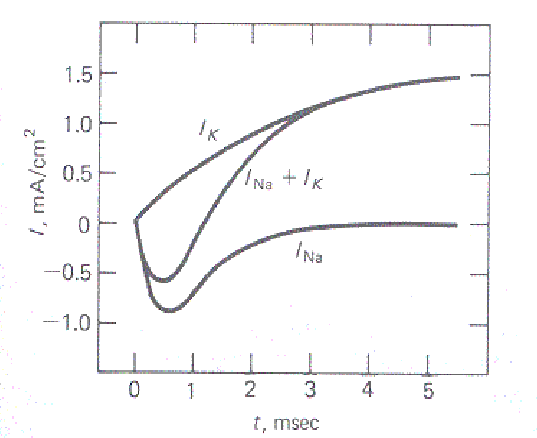
The independent Na+ and K+ channels

- From the Voltage clamp experiments:
  - The ionic current is divided into the initial Na+ influx and the later K+ outflux and these are independent.

Normal vs. Na free solution



Currents measured in normal (left) and sodium-free solutions (right). Membrane potential held at −60 mV, then stepped to potentials shown on right. (After Hodgkin and Huxley, 1952*a*.)



Voltage-clamp currents in squid axon measured in normal ($I_{Na} + I_K$) and sodium-free (I_K) solutions. I_{Na} calculated as difference between above two curves. (After Hodgkin and Huxley, 1952*a*.)

(inward current is negative)

- To explain the sigmoidal (S-shaped) kinetics of the rising phase of the sodium and potassium currents, Hodgkin and Huxley proposed that the Na channels were controlled by three activation (m) gates and one deactivation gate (h) and the K channels were controlled by four activation (n) gates. Here m,h,and n are probabilities of opened gates. Using maximum conduction values of each channel,

  - Sodium $$G_{Na} = \overline{G}_{Na} m^3 h$$

  - Potassium $$G_K = \overline{G}_K n^4$$

i.e., maximum channel conductance multiplied by rate constants.

Circuit model and Equation

- Equation of the time dependence of the membrane potential.

$$g_{Na} = G_{Na}(\max) \cdot m^3 \cdot h$$

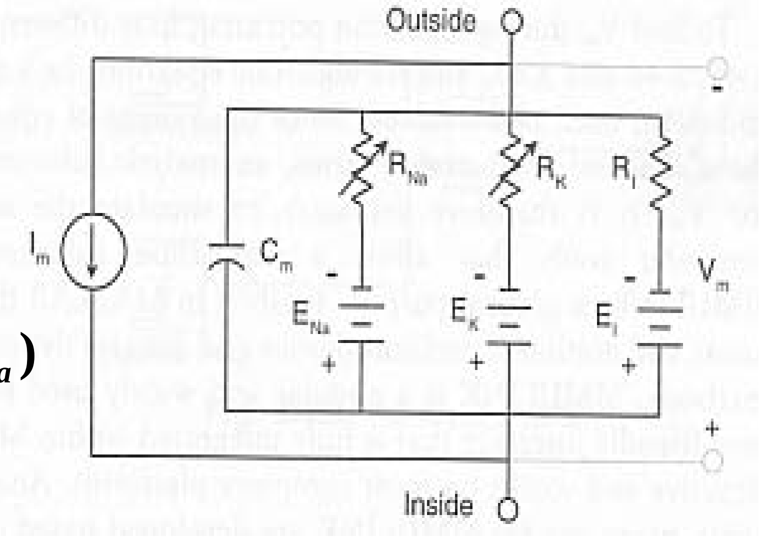
$$g_K = G_k(\max) \cdot n^4$$

$$I_{Na} = g_{Na}(V_m - E_{Na}) = G_{Na}(\max) \cdot m^3 \cdot h \cdot (V_m - E_{Na})$$

$$I_k = g_k(V_m - E_k) = G_K(\max) \cdot n^4 \cdot (V_m - E_K)$$

$$I_L = g_L(V_m - E_L) = G_L(\max) \cdot (V_m - E_L)$$

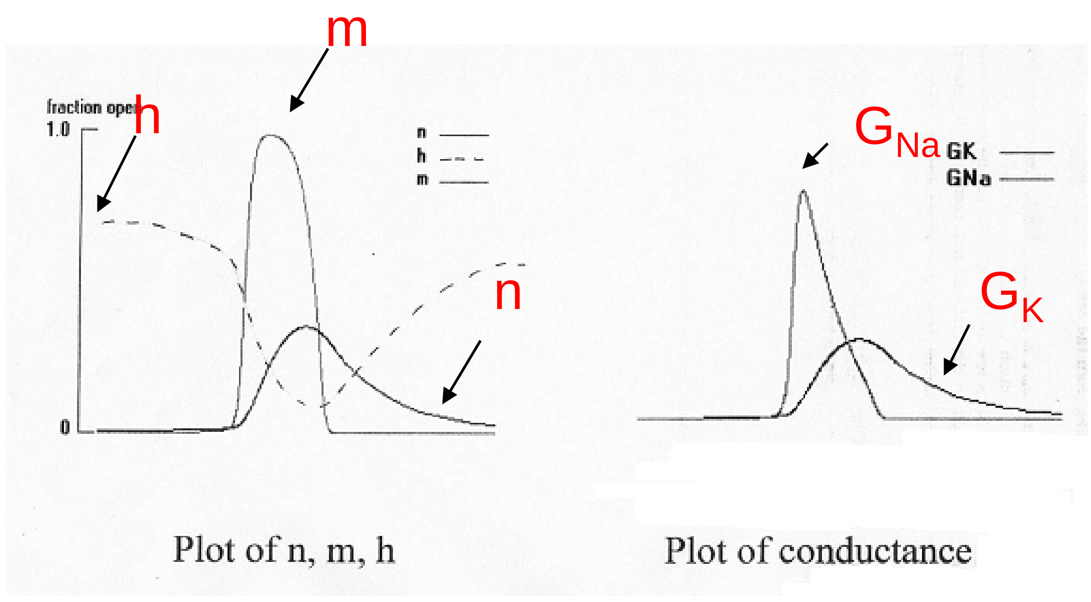
$$I_C = C\frac{dV_m}{dt}$$



Circuit model of an unmyelinated section of squid giant axon..

$$I_{ext} = I_{Na} + I_k + I_L + I_C$$

Hodgkin Huxley model



$$C\frac{dV}{dt} = \bar{g}_{Na}\, m^3 h\,(V_{Na} - V) + \bar{g}_K\, n^4\,(V_K - V) + g_L(V_L - V) + I_{ext}$$

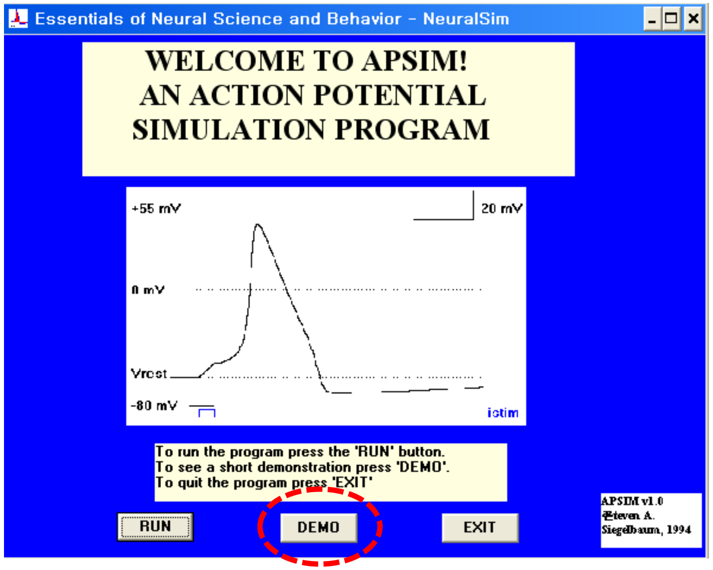
How to simulate using APSIM

APSIM: Action Potential SIMulator

- Neural signal simulation software
- To investigate the quantitative behavior of APs in response to different membrane properties and ion concentrations
- Squid giant axon membrane
- Current pulse stimulation with an intracellular electrode
- Based on the Hodgkin-Huxley equations
- Measure the threshold potential & refractory period

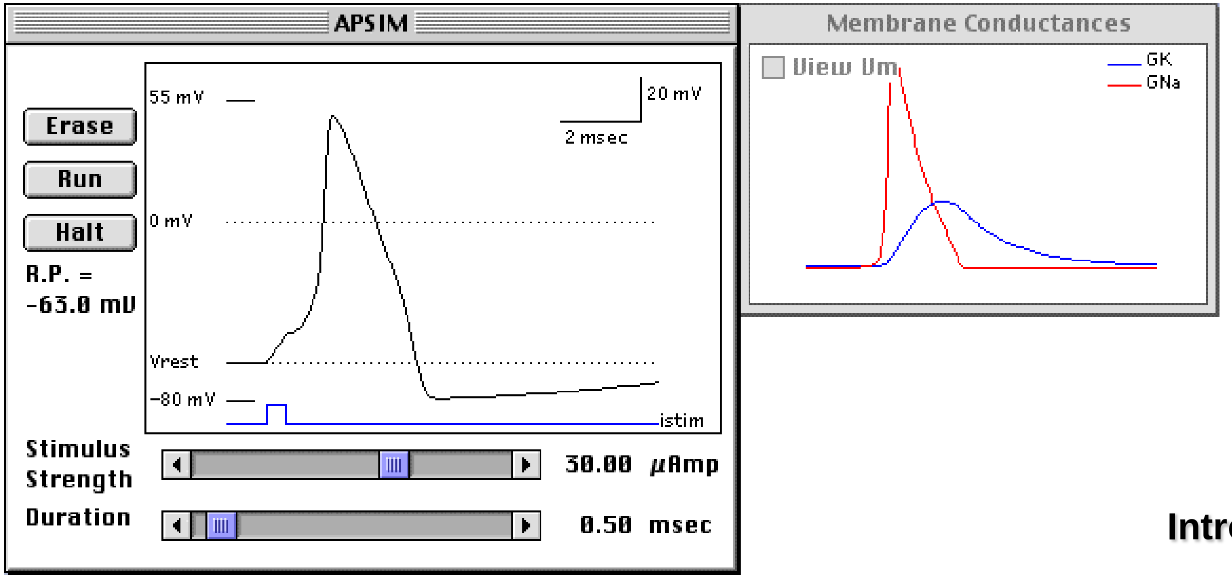
1. Run the APSIM DEMO program

- Launch the APSIM program.
- Click the DEMO button to launch a demonstration of intracellular recording.
- In addition to the intracellular recording, there are plots of the conductances that Hodgkin and Huxley calculated.



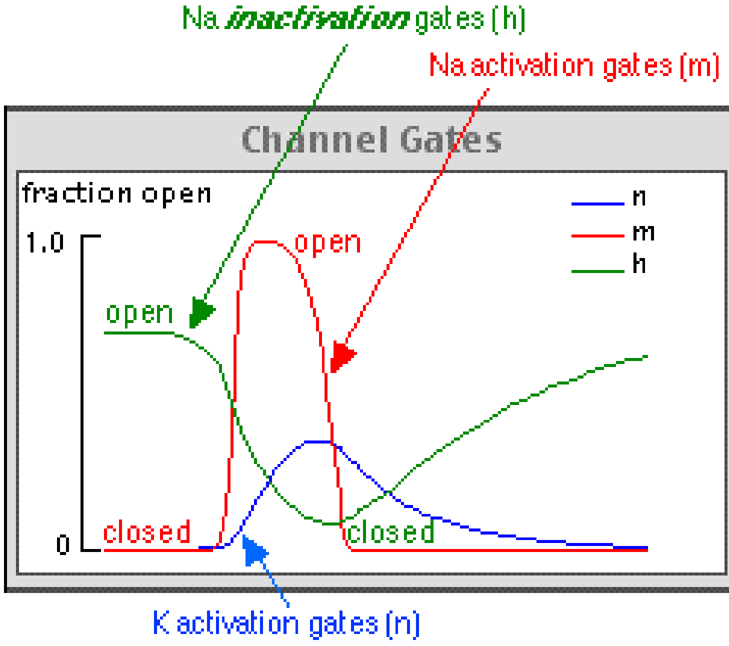
1. Run the APSIM DEMO program

- At the end of the DEMO program three windows will be open.
  - Main window: Action potentials
  - Second window: Membrane conductances for Na and K channels



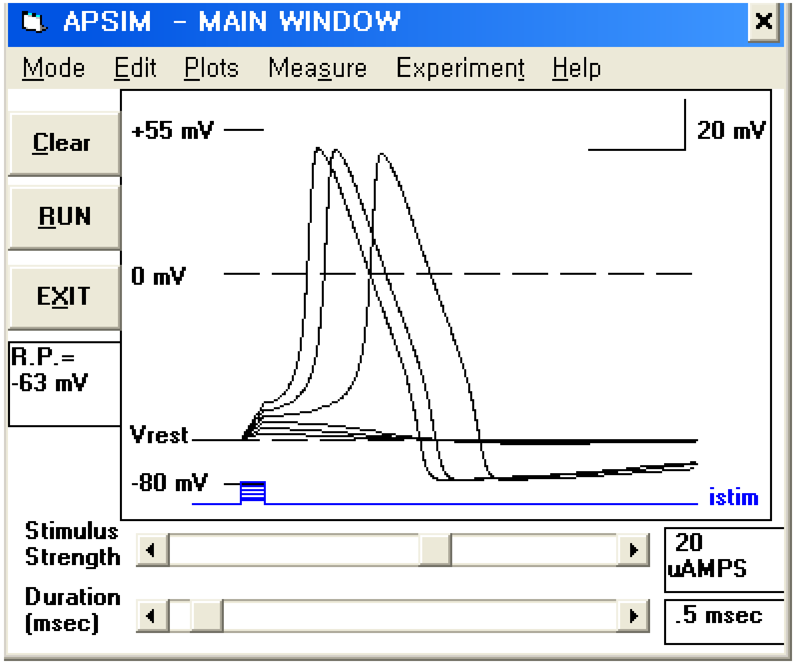
1. Run the APSIM DEMO program

– Third window: state of channel gates (Na-channel activation gates and inactivation gates)
  - These gates are given the labels m, h, and n, respectively, which are the variables that Hodgkin and Huxley used in their original equations.



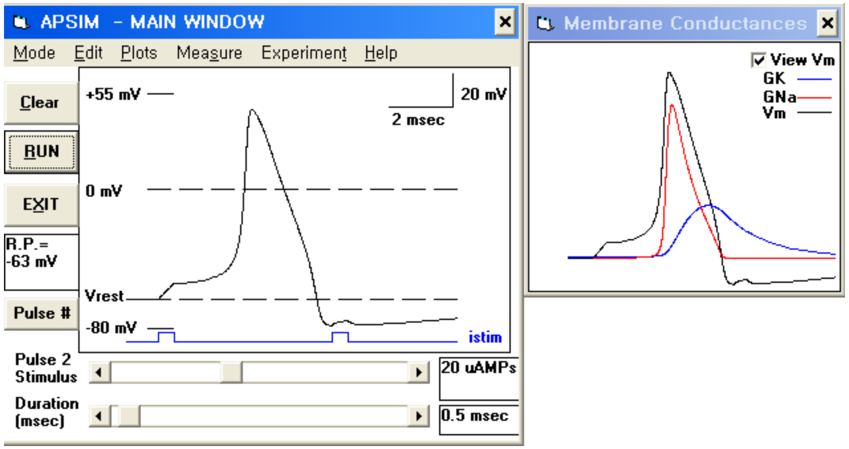
2. Run the threshold demonstration

- When the main demo is over, select " experiments menu -Threshold" and watch the demonstration.
- Press Run to stimulate the axon with the default stimulus strength.
- Drag the stimulus slider slightly to increase the stimulus strength.



3. Run the refractory period demonstration

- Select "Refractory Period" from the Experiments menu and watch a demo of twin-pulse stimulation.
- Open the Membrane Conductances window and re-run the refractory period demonstration.
- Examine the conductances for Na and K as you change the interpulse interval.



4. Explore the effect of increasing external K^+ concentration

- We know that increasing external potassium leads to a depolarized resting potential.
  - Re-establish single pulses. From the Params menu, select "Ion concentrations."
  - In the dialog box that appears, adjust the external concentration for potassium on the upper control.
  - Run one stimulus to get a spike from the default concentration(10 mM) to 20 mM.
  - NOTE: The simulation becomes unpredictable if you raise the external K+ beyond 20 mM.

5. Explore the effect of the number of channels

- The channel density (the total number of channels per area of membrane) is reflected in the Maximal Conductances setting (Params menu).
- Test what happens to the spike as you decrease the number of Na channels, G(Na), and K channels, G(K).
  - The units of conductance are milliSiemens.
  - Decreasing the maximal conductance is equivalent to having fewer channels of that type in the membrane.

Simulate mini-project

Assignment #3