BIOE 302 – Modeling Human Physiology: Hodgkin Huxley Action Potential Model

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Simulink Model

The Simulink model we are going to present is the action potential model developed by Hodgkin Huxley (HH) in 1952. Our simulation was adapted from Hoppensteadt and Peskin (2001), and Murat Saglam's (2008) Hodgkin Huxley models. The HH model demonstrates the electrical properties of a segment of nerve membrane by representing it as an electrical circuit as shown in Figure 1.[3]

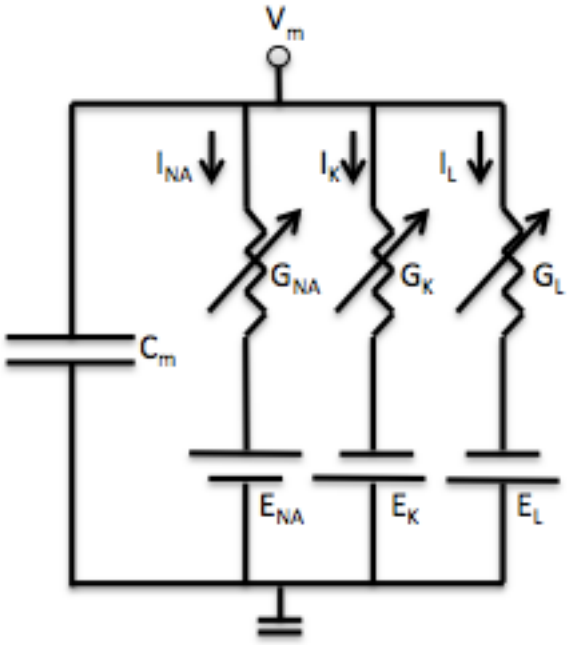

Figure 1: Electrical equivalent circuit proposed by Hodgkin and Huxley for a short segment of a squid axon. The variable resistances represent the voltage dependent conductances.

The circuit in Figure 1 can be described by the following differential equation:

$$C_m \frac{dV_m}{dt} + I_{ions} = I_{ext}. \quad (1)$$

Our model for the behavior of action potentials is based on this differential equation. Before we can begin to analyze it however, we must clear up the conventions we have used in our interpretation of the model. All conventions we use match those found in Hoppensteadt and Peskin (2001).

I_{ions} and I_{ext} have opposite sign conventions, where I_{ions} is the sum of the ionic currents, and I_{ext} is an external current applied to the system. From Equation (1), a positive external current will depolarize the cell (make V_m more positive), whereas a positive ionic current will hyperpolarize a cell (make V_m more negative). This sign convention can be summarized by "outward positive," where an outward flow of positive ions from the cell is considered a positive current. We have defined our resting membrane potential to be -70 mV. This membrane voltage is relative to the outside of the cell, i.e. we have assumed that the potential outside the cell is zero. Finally, we have chosen the sign of our membrane potential such that depolarization makes V_m more positive.

Hodgkin Huxley Action Potential Model

Bioelectricity

Cells utilize charge separation (like a battery) to store energy by exploiting the electrical abilities of their membranes, ion channels and pumps preventing ionic

species from reaching equilibrium. The phospholipid bilayer of cell membranes acts as an insulator, impermeable to ions crossing. Ions can only cross through open ion channels and pumps. This allows the cell to maintain an electric potential difference between the interior and exterior of the cell. This "transmembrane potential" difference is measured in volts and for animal cells varies between 30 – 90 mV.[4] By utilizing the electrochemical properties of its lipid bilayer, ion channels, and pumps, cell membranes can be modeled as a set of resistors (which are voltage dependent), batteries (whose voltage is set by the ion concentration gradient), and a capacitor, all connected in parallel. Voltage-gated ion channels result in dynamic changes to a cell's membrane potential difference. This is what gives neurons the ability to use electrical signaling to encode information and pass it on to other cells.

Ion Channels as Conductors

The flow of electrical charges passing through a point per unit of time is called current, which is measured in amperes (A). Current (I) usually flows through a resistor which may be characterized by resistance (Ω, ohms) or the inverse of resistance, conductance (represented as *g*, with units of siemens (S)). Since ionic current is the result of ions traveling through ion channels, we can imagine the ion channels as resistive elements in an electrical circuit. Membranes have several ion channels, allowing us to describe them as several resistors in parallel. The total resistance of our membrane would be the inverse of the sum of the inverse resistance of each element. However, we just described this inverse relationship as conductance, so we can visualize ion channels instead as conductors, where their total conductance is the sum of the individual conductances of the ion channels.

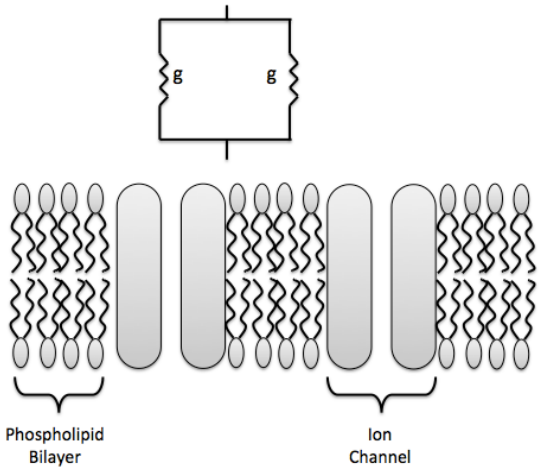

Figure 2: Comparison of resistors in an electrical circuit to ion channels in cell membranes.

A more realistic representation of ion channels has two more circuit components, a switch representing the gates of the channel and a battery representing the reverse potential of the ion current for the particular channel. The reverse potential (E) is defined as the voltage at which the current changes

direction. For a selective ion channel where only one type of ion can pass through it (such as sodium or potassium), the reverse potential equals its Nernst potential. It is important to note that in standard electrical terminology, an open switch represents a short circuit, preventing current from flowing, while in biology an open ion channel permits the flow of ions through it. Be mindful of the subject matter when discussing open and closed gates to prevent confusion on the terminology.

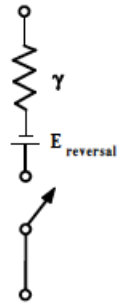

Figure 3: More detailed representation of ion channel. A switch represents the gates to an ion channel, the resistor the conductance of the ion channel and the battery the reverse potential.

The Nernst equation (Equation 2) describes the relationship between the ratio of the concentrations of ions in the interior and exterior of the cell and the electrical potential. It gives the membrane potential required to offset the concentration gradient and achieve equilibrium.

$$V_m = V_{exterior} - V_{interior} = \frac{KT}{zq}\log\left(\frac{c_{interior}}{c_{exterior}}\right) \qquad (2)$$

R is the gas constant (8.314 $\frac{V*C}{K*mol}$), T is absolute temperature (ºK), z is the charge of the ion, and F is Faraday's constant (9.648×10^4 $\frac{C}{mol}$) and V_m is the voltage difference across the cell membrane.

We define the membrane's resting voltage potential as the steady state condition where there is no net flow of electrical current across it. This condition is dependent on the interior and exterior ionic concentration (and hence the Nernst potential for each ionic species), and the relative permeability derived from the ionic conductances. At rest, a cell is much more permeable to potassium than sodium, so we expect its resting membrane potential to approximate potassium's Nernst potential.

Cell membrane as Capacitors

A capacitor (F, Farads) is described as a circuit element with "the ability to store charge Q when a voltage ΔV occurs across its two end"[4] A capacitor is typically described as two parallel plates separated by an insulator. A cell membrane can

thus be compared to a capacitor because of its small thickness, membrane potential across it, and the lipid bilayer acting as an insulator.

$$Q = C\Delta V \quad (5)$$

Much like conductance, when several capacitors are aligned together in parallel their total capacitance is described as the summation of their individual capacitances.

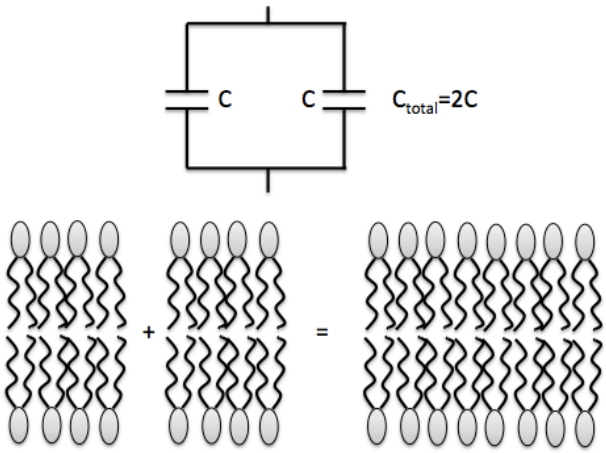

Figure 4: Comparison of Capacitors to the lipid bilayer of cell membranes.

We have defined capacitors as circuit elements which store charge. From our previous definition, we described the flow of charged ions through a given point per unit time as current. Therefore, current can be seen as the time derivative of charge. This means the current flowing through a capacitor (the derivative of Q in Equation 5) must be given by the change in voltage potential across it. Note that the minus sign reflects the sign convention that a positive current is outward directed and hence the membrane potential decreases.

$$\frac{dQ}{dt} = I = -C\frac{dV}{dt} \quad (6)$$

The Voltage Clamp, Ohm's Law and Kirchhoff's Law

We are now closer to understanding Equation 1 from which our model is built. First, we must understand a critical experimental technique used by Hodgkin and Huxley during their original experiment, the voltage clamp.

Using the clamp they were able to maintain the membrane potential at any desired voltage level. It utilized two pairs of electrodes, one pair monitored the voltage across the membrane, and another injected enough current to keep the voltage constant.

This technique can be understood using Ohm's Law. According to Ohm's Law, the voltage difference between two points in an electrical circuit is proportional to the current and resistance between them.

$$V = I \times R \qquad (7)$$

As we increase the voltage to a desired level, we expect the voltage dependent ion channels to open allowing ions to cross the membrane. According to Ohm's law, at a constant voltage if there is a reduction in resistance it needs to be matched with an increase in current. With the reduction of resistance as more ionic channels open up, we need to increase the current allowing the membrane to hold the new voltage level. Therefore, the current being held is directly related to the number of ion channels being opened. In the voltage clamp technique, the current was injected with the second pair of electrodes. While it is difficult to measure ionic current directly, it is easier to measure the clamp current that is necessary to counterbalance it, and you can estimate how many channels are opened.

Now that we understand how a voltage clamp works, and the cellular components with their electrical analogues, we can understand Equation (1). According to Kirchhoff's current law, conservation of electric charges dictate that currents entering a node equal to the sum of the currents flowing out of that node.

$$\sum_{n=1}^{n} I_k = 0 \qquad (8)$$

Thus, the external current applied must equal the sum of the currents traversing the different electrical components that comprise the cell membrane.

$$I_{membrane} + I_{ions} = I_{ext} \qquad (9)$$

Building the model

By combining Equations (6,9), we arrive at Equation (1). When building models from differential equations in Simulink, it is best to arrange the equation and isolate the first order differentials.

$$\frac{dV}{dt} = \frac{I_{external} - I_{ions}}{C_m} = \frac{I_{external} - I_k - I_{Na} - I_L}{C_m} \qquad (10)$$

Equation (10) is the main differential equation Simulink will be solving. In our model, each subsystem calculates their designated ionic currents, which will be discussed later on. We must first begin with the integrator block for $\frac{dV}{dt}$. Typically, neurons have a resting membrane potential of -70 mV. In our model, we apply a current shock at t=0 ms depolarizing the membrane to a value of -55 mV. Thus, the initial condition for our integrator block is defined as V0 (Figure 1). All initialization parameters for our model are pre-loaded into the Simulink file, and are also found in parameters_HH.m.

A subsequent current pulse of 1 ms with an amplitude of *ip* (15 μA) is applied at *t1p* (10 ms). The pulse is found in the Ext Current Subsystem and is created by summing two step blocks.

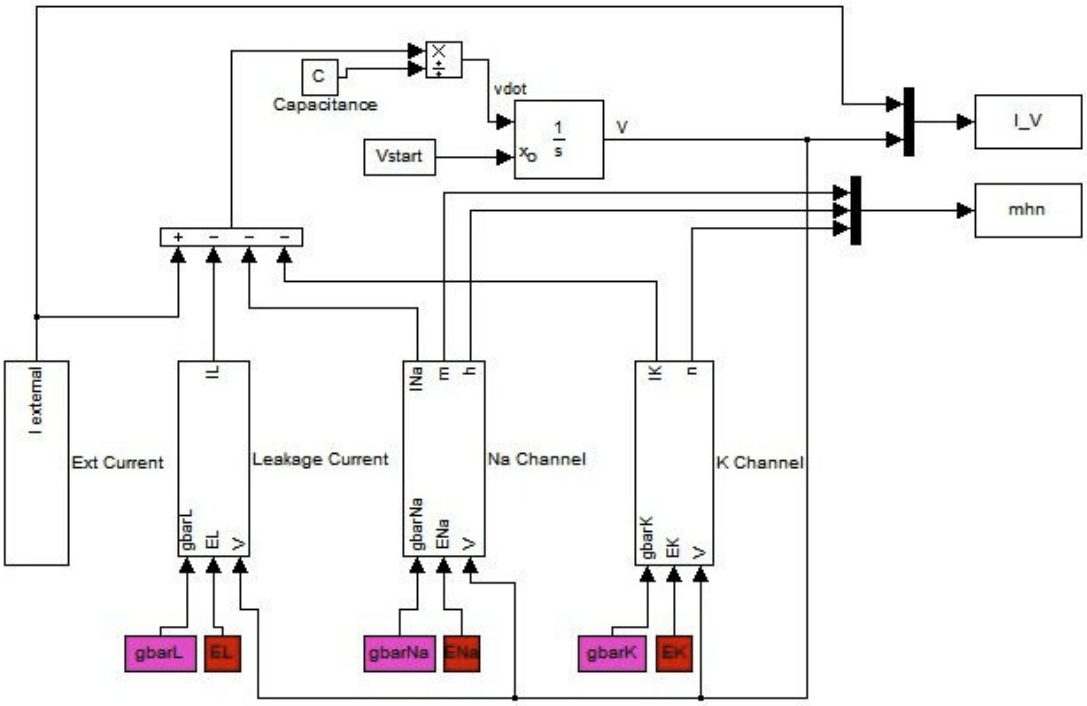

Figure 5: Main Window of Hodgkin Huxley Action Potential Simulink Model

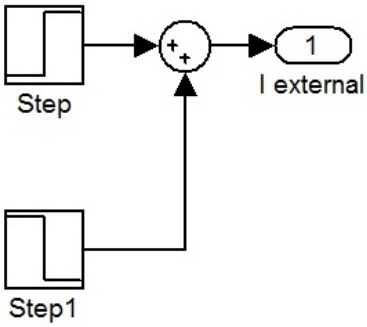

Figure 6: External Current Subsystem. The Step Block has a Step Time of t1p (10 ms), intial value of 0 μA, and a final value of ip (15 μA). The Step1 block has a Step time of t2p (11 ms), initial value of 0 μA, and Final Value of –ip (-15 μA).

Ionic Currents

In Equation (1) I_{ion} represents the algebraic sum of the sodium, potassium and leakage (chloride) ionic currents.

$$I_K = g_K * (V_m - E_K) \qquad (10)$$

$$I_{Na} = g_{Na} * (V_m - E_{Na}) \quad (11)$$

$$I_L = g_L * (V_m - E_L) \qquad (12)$$

Hodgkin-Huxley postulated that the conductances changed as a function of membrane voltage. This voltage dependence can be traced to the properties of the membrane channels which control ion flow across the membrane.

We've described the ionic current through the ion channels as a resistor and a battery in series (Figure 2 and Figure 3). This reasoning flows from the relationship between current and driving force.

There exists a chemical potential difference across the cell membrane (which exists because of the pumping of ions and selectively permeable membrane of the lipid bilayer barrier) and an electrical potential difference, which both serve as a driving force for the flux of ions. The ionic current I, from a single ion species, is proportional to the difference between the membrane voltage and the Nernst of equilibrium potential of the ion, giving:

$$I = g(V_m - V_{Nernst}). \qquad (14)$$

where g is a coefficient of proportionality, which is the conductance per unit area to the specific ion under consideration. We've denoted current as "outward positive", where a flow of positive ions out of the cell is positive current..

Equation (14) is in a general form, and can be applied to the specific ionic currents pertaining to sodium, potassium and chloride, as can be seen in Equations (10, 11, 12). The Nernst potential assumes the role of a battery in series with a resistor, and as can be seen from Equation (7), Equation (14)'s linear relationship between current and voltage follows Ohm's Law. The combination of all ionic currents can be seen as resistors and batteries in series parallel to each other, as can be seen in Figure 1.

Potassium Channel

Each individual ionic channel contains a number of physical gates (represented as switches), which regulate the flow of ions through it. For the remainder of the discussion we will assume the terminology for open/closed channels as allowing/not-allowing ionic flow. We start with the potassium (K+) channel as they are a little more straightforward than the sodium channels.

Each gate can be in one of two states: closed or open. Our model for the channels follows the findings of Hodgkin-Huxley, where a potassium channel has four gates, and each gate can be in either state. The channel will only be considered open if and only if all four gates are open.

If we consider the proportion of a large population of an individual type of gate to be open ranging from 0 to 1, we can represent this proportion that are open to be represented as n. The fraction of gates which are closed will be represented as

(1 – n). The transition between open and closed states follows first-order kinetics:

$$\frac{dn}{dt} = \alpha_n(v) * (1 - n) - \beta_n(v) * n, \qquad (15)$$

where α_n and β_n are rate constants (probability per unit time) for opening and closing a gate, respectively. Each rate is a specific function of voltage, and differs from one another. The following opening and closing functions are given in Hoppensteadt and Peskin:

$$\alpha_n(v) = .1 * \frac{(v+60)/10}{1-e^{\left(-\frac{v+60}{10}\right)}} \qquad (16)$$

$$\beta_n(v) = .125 * e^{\left(-\frac{v+70}{80}\right)} \qquad (17)$$

Therefore, the voltage-dependence of the conductances is incorporated into the model by assuming the probability of opening or closing a gate depends on the value of the membrane voltage. Since each gate is independent of one another, the probability of one gate being open is n, and the probability of all four gates of an ion channel being open, and hence the channel being open, is n^4. Hence, it follows that the conductance be proportional to n^4. This gives us

$$g_K = \bar{g}_k * n^4, \qquad (18)$$

where $\bar{g}_k$ is the constant of proportionality and represents the maximum conductance to K+ when all gates are open. Figure 7 shows the Potassium Channel subsystem modeled in Simulink. The main differential equation is Equation (15). The initial condition for the integrator block was determined by evaluating the MATLAB code provided by Hoppensteadt and Peskin (2001) at t = 0 s. Note that α_n evaluates to 0/0 at a voltage of -60 mV, therefore L'Hospital's rule was used to determine the output of α_n at that voltage, not Equation 16. An if block was therefore used in the evaluation of α_n instead of a fcn block which was used for β_n.

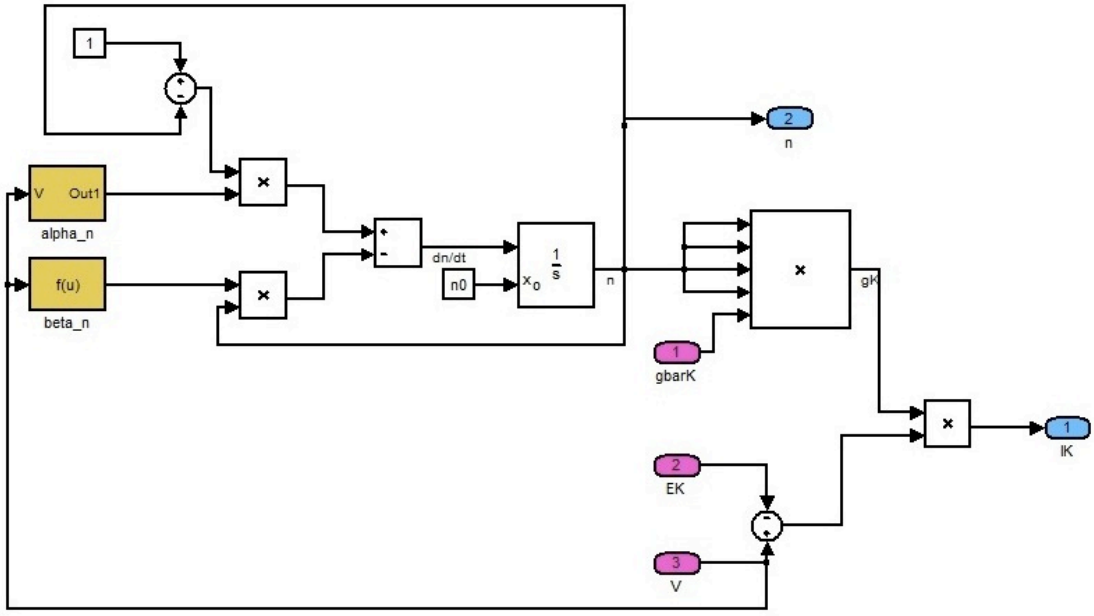

Figure 7: Potassium Channel Subsystem. *Pink blocks denote inputs to the Subsystem, light blue outputs. α_n and β_n are highlighted in yellow. Equations (10, 15, 16, 17, 18) are utilized.*

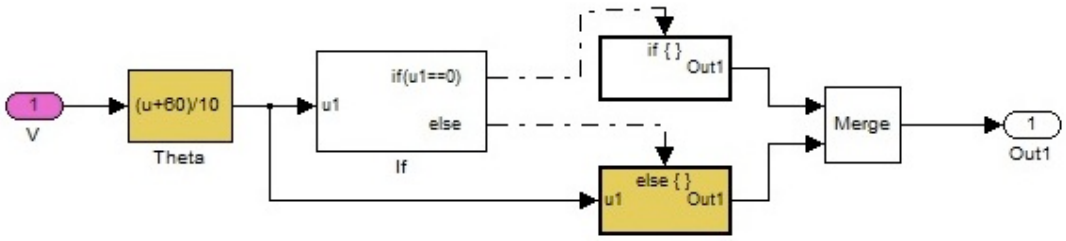

Figure 8: α_n If-Else Control Statement. Theta is the numerator of α_n, and used to determine if a 0/0 condition arises. If it does, α_n has a value of .1 calculated from L'Hospital's rule. If not, the simulation proceeds to calculate it through Equation (16) in the else action port.

Sodium Channel

The sodium (Na+) channel is qualitatively different from the potassium channel. The reason being that sodium has two types of gates, m and h. The m gate reacts quickly to open with an increase in membrane potential, while the h gate reacts slower and in an opposite fashion, closing in response to an increase in membrane potential. Hence, the changes in sodium conductance arise when the m gates have quickly opened, but the h gates have not closed. The lowering of sodium's conductance with further increased membrane voltage is called sodium inactivation.

Like the potassium channel, sodium has four gates, three m gates and one h gate. The sodium channel is open if and only if all the gates are open. All m gates are identical and work independently to one another. All h gates are identical and work independent to one another. The proportions of m gates and h gates that are open are given by expressions similar to those for the n gate found in potassium.

$$\frac{dm}{dt} = \alpha_m(v) * (1 - m) - \beta_m(v) * m \qquad (19)$$

$$\frac{dh}{dt} = \alpha_h(v) * (1 - h) - \beta_h(v) * h \qquad (20)$$

Where α_m and α_h are the opening rate constants for the m and h gates, respectively, and are different from one another. β_m and β_h are the closing rate constants for the m and h gates, respectively, and are different from one another. α_m and β_m are increasing functions of voltage, while α_h and β_h are decreasing functions of voltage. Hoppensteadt and Peskin gives the following functions for the voltage-dependent opening and closing rates of the m and h gates.

$$\alpha_m(v) = 1.0 * \frac{(v+45)/10}{1-e^{(-\frac{v+45}{10})}} \qquad (21)$$

$$\beta_m(v) = 4.0 * e^{(-\frac{v+70}{18})} \qquad (22)$$

$$\alpha_h(v) = .07 * e^{(-\frac{v+70}{20})} \qquad (23)$$

$$\beta_h(v) = 1.0 * \frac{1}{1+e^{(-\frac{v+40}{10})}} \qquad (24)$$

Finally, since each gate is independent of one another, the probability of one m gate being open is m, and one h gate being open h, and there are three m gates and one h gate, the probability of all gates being open is m^3h. The conductance of sodium is then proportional to m^3h where $\bar{g}_{Na}$ is the constant of proportionality representing the maximum conductance to Na+ when all gates are open.

$$g_{Na} = \bar{g}_{Na} * m^3 * h \qquad (25)$$

The Sodium Channel subsystem has a very similar structure than the Potassium Channel subsystem in our Simulink model. The initial conditions for the integrator blocks were determined by evaluating the MATLAB code provided by Hoppensteadt and Peskin (2001) at t= 0s. At a voltage of -45 mV, α_m evaluates to 0/0. L'Hospital's rule was used to determine the output of α_m at that voltage, not Equation 21. An if block was therefore used in the evaluation of α_m instead of a fcn block which was used for β_m.

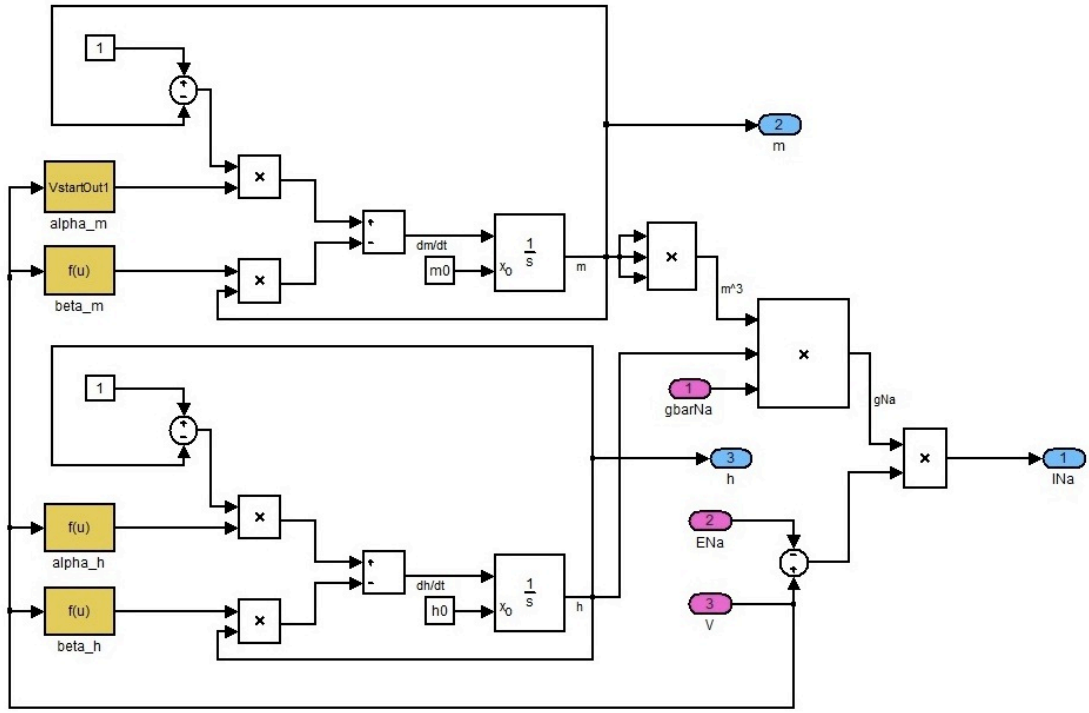

Figure 9: Na Channel Subsystem. *Pink blocks denote inputs to the Subsystem, light blue outputs. α_m, β_m, α_h, β_h are highlighted in yellow. Equations (11,19-25) are utilized.*

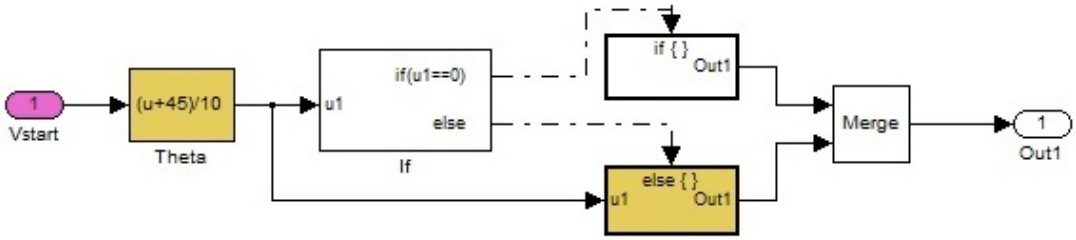

Figure 10: α_m If-Else Control System. Theta is the numerator of α_m, and used to determine if a 0/0 condition arises. If it does, α_m has a value of 1 calculated from L'Hospital's rule. If not, the simulation proceeds to calculate it through Equation (21)

Leakage Channel

In addition to the sodium and potassium channels, a third channel was discovered in the giant squid membrane. The "leakage" channel was found to have a constant conductance of

$$g_L = \bar{g}_L. \quad (26)$$

The leakage channel is a non-specific channel, although it shares similarities to a chloride channel and hence was simulated as such. For a more detailed

explanation on the derivation of the model consult Hoppenstead and Peskin (2001).

Running the Simulation

Now that all elements of the simulation have been explained, we can run it to observe the results.

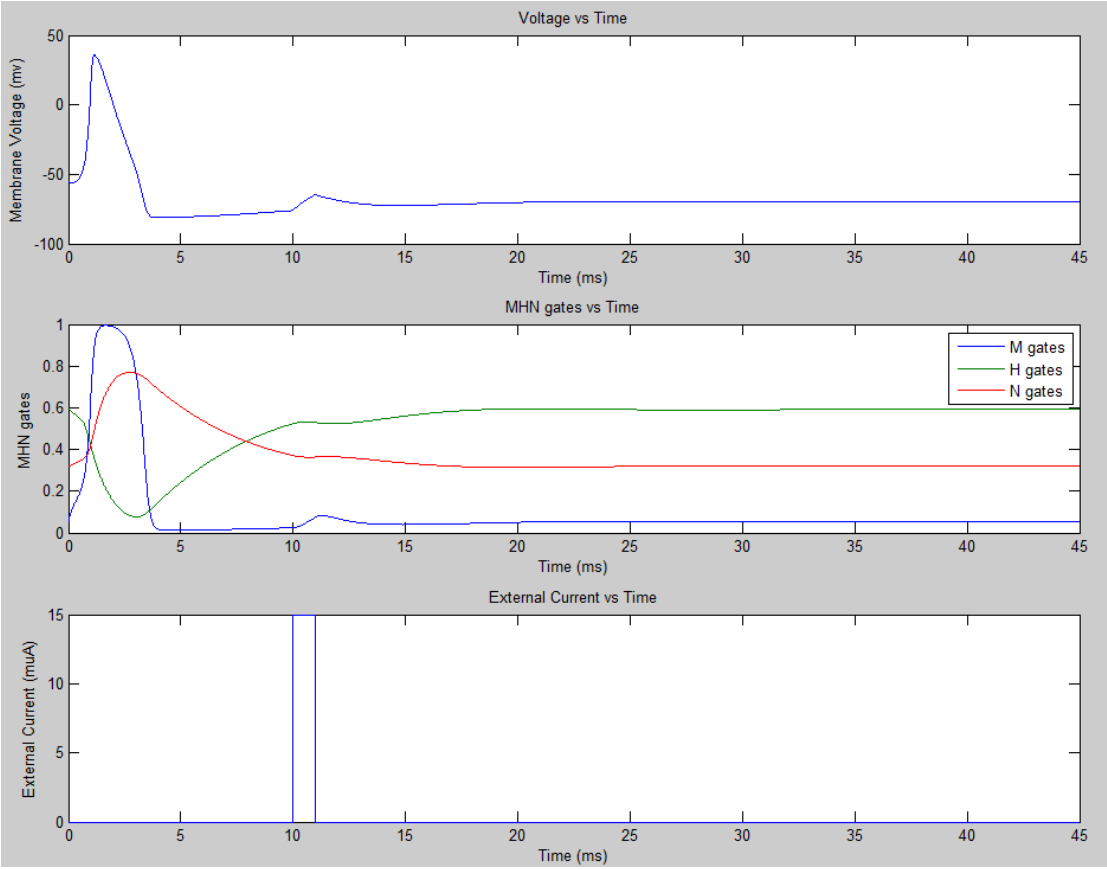

Figure 11: Results of Simulation. Top subplot denotes membrane voltage, middle subplot the gate activities, and the bottom plot is the pulse of the secondary current pulse.

In the top subplot, we have the membrane voltage over time. We defined the cell resting potential to be -70 mV, and at time = 0ms, a current shock was applied raising the potential to -55 mV, which is where we begin our simulation. This shock caused the sodium channels to open, allowing an influx of ions to depolarize the membrane. Remember, an action potential is an all-or-nothing event, if a current shock stimulates the membrane above its threshold value, it will ignite an action potential.

This event allows the cell to reach the Nernst potential of sodium, approximately +58 mV. However, the depolarization also causes the potassium ion channels to open. Once sodium inactivation occurs, the open potassium channels will push the cell to its own Nernst potential of -93 mV. The period where the membrane voltage dips below its resting potential is known hyperpolarization.

All the while, potassium and sodium ion pumps will be actively working to remove three sodium ions from the cytoplasm and accept two potassium ions into the cell. This process will allow the cell to eventually reach its resting potential again. The process of returning to the resting state where the ability of the neuron to fire another action potential is impeded is called the refractory period.

In the middle subplot we observe the voltage dependent gates of the sodium, potassium and leakage channels. The sodium m gates are fast to respond to the current shock at time = 0 ms, quickly opening up as can be seen by the steep slope of the blue graph. This corresponds to the depolarization of the cell membrane, which matches up with the top plot. In the potassium channel we have the n-gates slowly opening up thanks to the depolarization caused by the influx of sodium ions. As potassium leaves the cell, we see the cell membrane repolarizing. At the point where a maximum amount of n-gates are open (and hence potassium channel) we have the steepest slope of repolarization in our action potential. Finally, we have the slow reacting h-gates of sodium. These gates operate opposite to m and n-gates. This phenomenon is called sodium inactivation and once enough h-gates are closed, we see a sudden drop in the m-gate availability.

In the bottom subplot we have a secondary external current pulse of 15 μA lasting 1 ms being applied. It is occurring during the repolarization phase of the action potential. Since the current is being applied during the relative refractory period, only a larger pulse would be able to elicit a response.

Model Applications

We can adjust our model to reflect the effects external agents have on action potential generation. First, we will study the generation of action potentials during the refractory period, and secondly, we will study the effects of the local anesthetic Procaine (Novocaine ®).

Investigating the refractory period: Increasing Second current pulse

By increasing the second current pulse during the relative refractory period, we expect it to generate an action potential. During this period, the potassium channels are open, allowing the exchange of potassium to equilibrate the membrane potential close to its Nernst potential. Action potential during the relative period is possible, but requires a stronger stimulus to overcome the threshold. By doubling our current pulse to 30 μA, we expect an action potential to be generated.

In Figure 12 we can see the larger current pulse does indeed generate an action potential. We also notice the action potential does not begin at the threshold value of -55mV, but a slightly greater value.

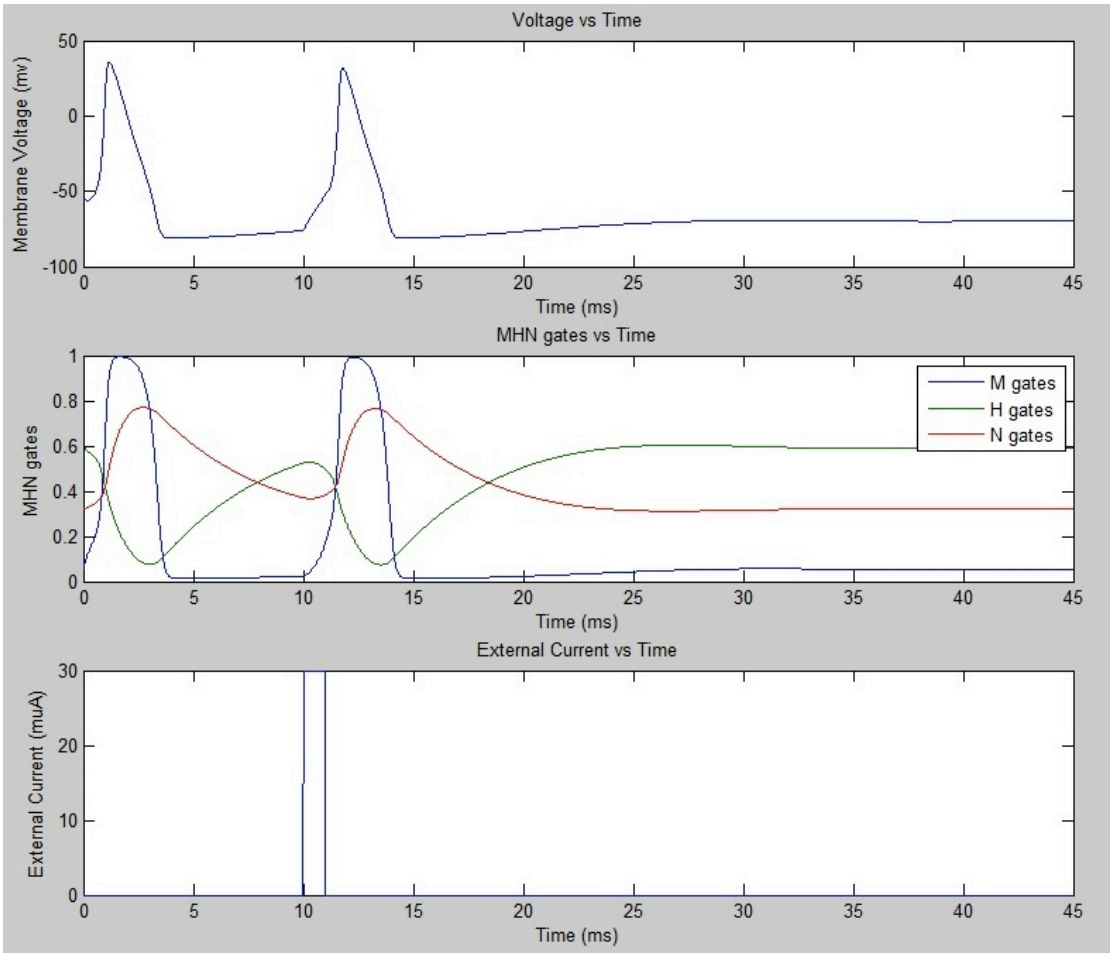

Figure 12: Secondary Current Pulse of 30 μA administered at 10 ms.

Channel Blocking: Local Anesthetic Procaine

A popular local anesthetic used in dental procedures is Procaine, an ester linked drug that blocks sodium channels. Procaine prevents sodium from entering the cell by inactivating a subunit of the channel from the cytoplasm. Without sodium ions, no action potentials are generated, and no pain is registered.

We are interested in observing what effects would simulating a blockage of sodium channels have in our model. We model this by reducing the conductance of sodium, $\bar{g}_{Na}$, to 0 $\frac{mA*ms}{cm^2}$. at 20 ms. We use a switch block to change the value, and initiate a current pulse at 25 ms to verify if an action potential is generated or not.

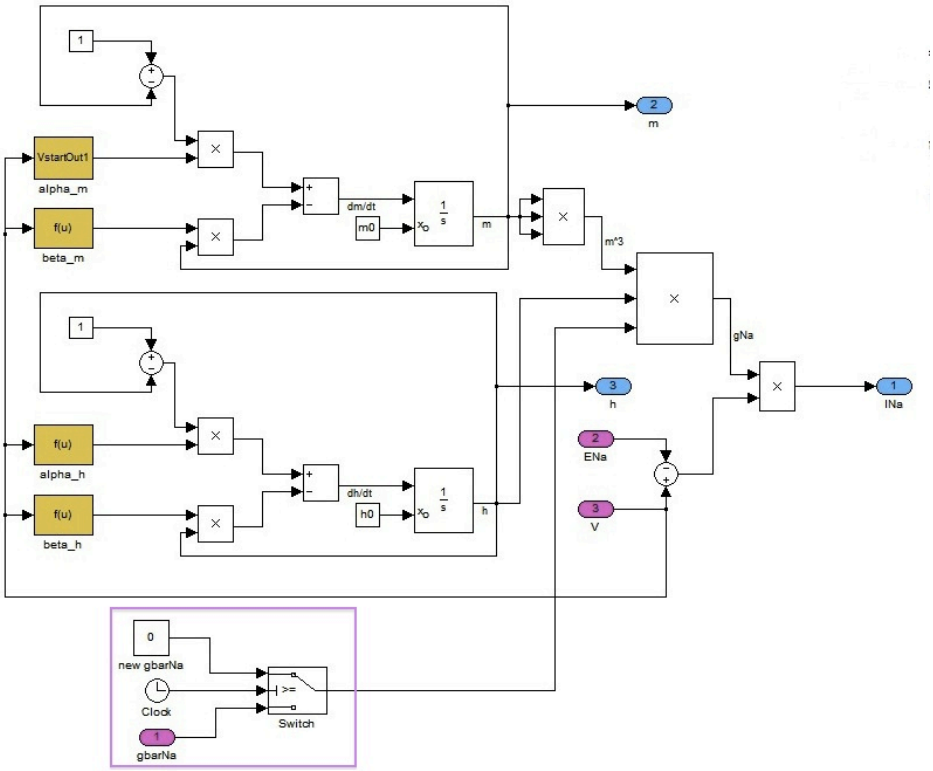

Figure 13: Switch which changes conductance at 20 ms in Na Channel Subsystem

As predicted, no action potential is generated. The blockage of sodium channels prevents any potential from being generated, regardless of the amplitude of the pulse exerted.

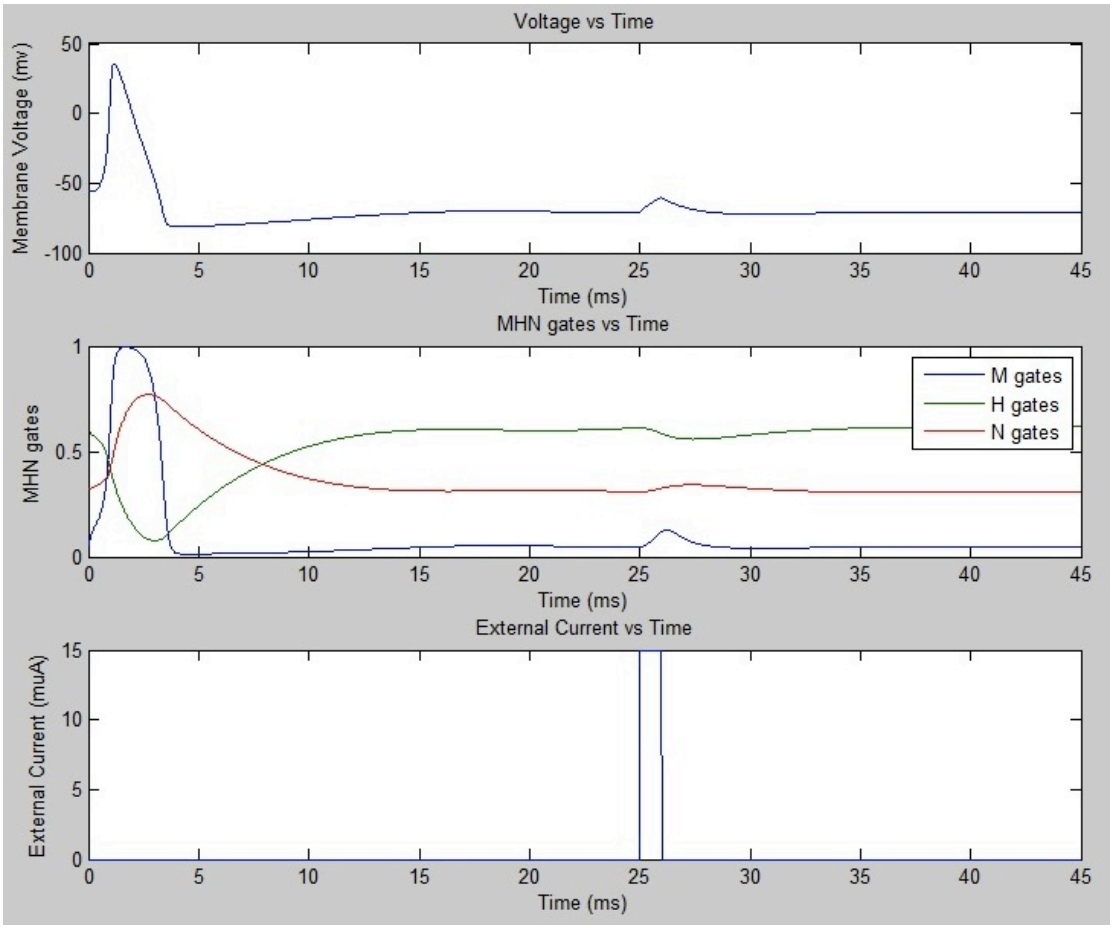

Figure 14: Result Simulating Procaine administered at 20 ms. Current pulse is administered at 25 ms.

Works Cited

[1] Hoppensteadt, Frank C., Peskin, Charles S. Modeling and Simulation in Medicine and the Life Sciences. 2nd Ed. New York: Springer Science+Business Media, Inc, 2001. Print

[2] "Hodgkin-Huxley Model." Matlab Central File Exchange. Mathworks. Murat Saglam, April 22 2008. <http://www.mathworks.com/matlabcentral/fileexchange/19669-hodgkin-huxley-model>.

[3] Nelson, Mark and Rinzel, John. "Ch4: The Hodgkin-Huxley Model." In: *The Book of GENESIS: Exploring Realistic Models with the GEneral NEural SImulation System.* 2nd Ed. Bower, J.M., Beeman, D. New York: Springer-Verlag, 1998. 29-50. Ebook. < http://www.genesis-sim.org/GENESIS/iBoG/index.html>

[4] Axon Instruments, Inc. "Chapter 1 – Bioelectricity." In: *The Axon Guide for Electrophysiology & Biophysics Laboratory Techniques.* Sherman-Gold, Rivka. 1993. 1-16. Ebook. < http://cancer.rutgers.edu/stg_lab/protocols/The%20axon%20Guide.pdf>

[5] Garcia, Hernan G., Phillips, Rob, Kondev, Jane, Theriot, Julia A. "Chapter 17 Biological Electricity and the Hodgkin-Huxley Model." In: *Physical Biology of the Cell.* 1st Ed. 2008. Ebook < http://www.gwu.edu/~phy21bio/Reading/PBOCProofCh17BioElect.pdf>

Appendix 1 – Parameters File

```
%This script has been adapted from Murat Saglam (22.4.2008) and his
%HH action potential Simulink model to better represent the model
%shown in HP.
clear

gbarNa=120; gbarK=36; gbarL=.3; %conductance of ions in hypothetical
%situations where all gates in the channel are open:(mA*ms)/cm^2

ENa=45; EK=-82; EL=-59; %Equilibrium potentials of ions: mV

n0=.3177; m0=.0529; h0=.5961; %initial number of gates open:
%(unitless)
t1p=20; t2p=21; % Beginning and ending current pulse: ms
ip=10;          % Amplitude of current pulse: muA

%Vhold = -70;   % resting membrane volate potential: mV
Vstart=-55;     % membrane voltage potential after initial current
applied: mV
C = 1;          % membrane capacitance per unit area: (muF/cm^2)
```

Appendix 2 – MATLAB Scripts

```
%This script will plot the action potential, the changes in the m,h,n
%gates and the external current applied

%Store the arrays for future plotting:
time=I_V.time;
Iext=I_V.signals.values(:,1);
V=I_V.signals.values(:,2);
m=mhn(:,1);
h=mhn(:,2);
n=mhn(:,3);

%Plot Results
figure(1)
subplot(3,1,1), plot(time,V);
title('Voltage vs Time');
ylabel('Membrane Voltage (mv)');
xlabel('Time (ms)');
subplot(3,1,2), plot(time,m,time,h,time,n);
title('MHN gates vs Time');
ylabel('MHN gates');
xlabel('Time (ms)');
legend('M gates','H gates', 'N gates');
subplot(3,1,3), plot(time,Iext);
title('External Current vs Time');
ylabel('External Current (muA)');
xlabel('Time (ms)');
```

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