Appedix C: Hodgkin-Huxley Equations

The Hodgkin-Huxley equations belong to conductance-based compartment model. Physiologically just like other cells, neurons are surrounded by double-lipid membranes separate cytoplasm from extracellular space. Ion pumps maintain concentration gradients across membranes and thus electrical potential. The basic scheme of single compartment models is shown in Figure C.1-1 [1].

C.1 Conductance-based compartment model

Neuronal cell membranes have been modeled as capacitors separating electric charge. The ion channels across the membrane act as conductance that allows ionic current flow between intracellular and extracellular space. The transmembrane current flow perturbs electrical balance and may initiate action potentials. The reverse potentials E_{Na}, E_K, and E_L exist due to the concentration gradients of ions across the membrane maintained by ion pumps. The current balance equation according to Kirchoff's Law can be written as follows:

$$C\dot{V} = -I_{Na} - I_K - I_L + I_{ex} \tag{A.1}$$

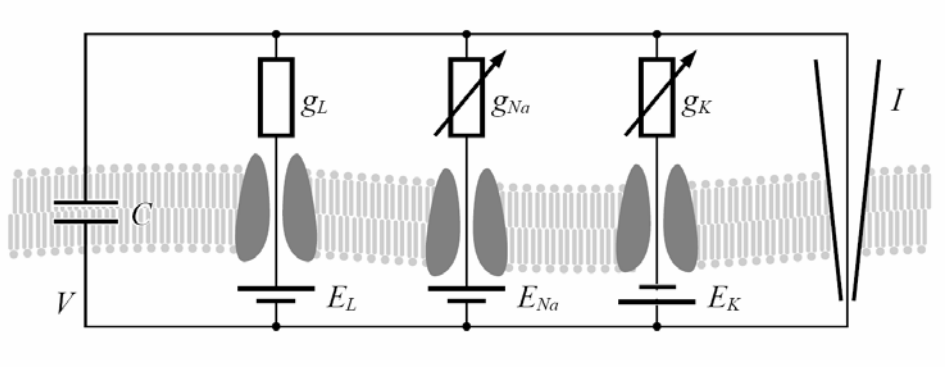

Figure C.1-1 The representation of compartment model

C.2 Ion channels

For Hodgkin-Huxley model, the types of channels considered include sodium, potassium, and leakage [3]. Each ion channel is selective to specific type of ion. Ionic current through ion channel is determined by the opening and closing of ion channels. The gating variables represent the degree of opening of a certain ion channel and they follow first order kinetics with voltage-dependent rate constants α (V) and β (V). The voltage dependence was determined experimentally and has been formulated into equations [2]. The detailed model for each ion channel is described below. With the system of ordinary differential equations (ODEs) fully defined, four variables with four equations, the ODEs can be integrated to get the response of membrane potential. The resting membrane potential is approximately -65 mV.

Sodium channels are controlled by two gating variables: m and h, both of which depend on the membrane potential. The activation variable m increases with membrane potential while inactivation variable decreases with it. The dynamics of sodium channels are described in Eq. (A.2).

$$
\begin{aligned}
&I_{Na} = g_{Na} m^3 h (V - E_{Na}) \\
&\dot{m} = \alpha_m(V)(1-m) - \beta_m(V)m \\
&\dot{h} = \alpha_h(V)(1-h) - \beta_h(V)h \\
&g_{Na} = 120\ mS/cm^2;\ E_{Na} = -50\ mV \\
&\alpha_m(V) = 0.1(V+40)/(1-\exp(-(V+40)/10)) \\
&\beta_m(V) = 4\exp(-(V+65)/18) \\
&\alpha_h(V) = 0.07\exp(-(V+65)/20) \\
&\beta_h(V) = 1/(1+\exp(-(V+35)/10))
\end{aligned}
\tag{A.2}
$$

Potassium delayed-rectifier current flows through potassium channels which are controlled by one single gating variable n. The variable n grows with respect to membrane voltage. The overall dynamics of potassium channels are described in Eq. (A.3).

$$
\begin{aligned}
&I_K = g_K n^4 (E_K - V) \\
&\dot{n} = \alpha_n(V)(1-n) - \beta_n(V)n \\
&g_K = 36\ mS/cm^2;\ E_K = -77\ mV \\
&\alpha_n(V) = 0.01(V+55)/(1-\exp(-(V+55)/10)) \\
&\beta_n(V) = 0.125\exp(-(V+65)/80)
\end{aligned}
\tag{A.3}
$$

The leakage current, I_L, approximates the passive properties of the cell has linear relationship with the membrane voltage.

$$
\begin{aligned}
&I_L = g_L(E_L - V) \\
&g_L = 0.3\ mS/cm^2;\ E_L = -54.38\ mV
\end{aligned}
\tag{A.4}
$$

C.3 Modulation by using building blocks in Simulink

We used individual modules in Simulink to incorporate the dynamics of ionic channels into the hierarchical model. Modulation can facilitate the reuse of the building blocks and make debugging simpler. There are three levels of model complexity introduced as shown in Figure C.3-2. The top one outlines the input and output signals. The second level describes the ion channels as conductance and neuronal membrane as capacitor. The connections between building blocks with transfer functions embedded are drawn

based upon Hodgkin-Huxley equations. The third level includes the detailed dynamics of both sodium and potassium channels. There are two channel variables (h and m) controlling sodium channels and only one (n) influencing potassium channels.

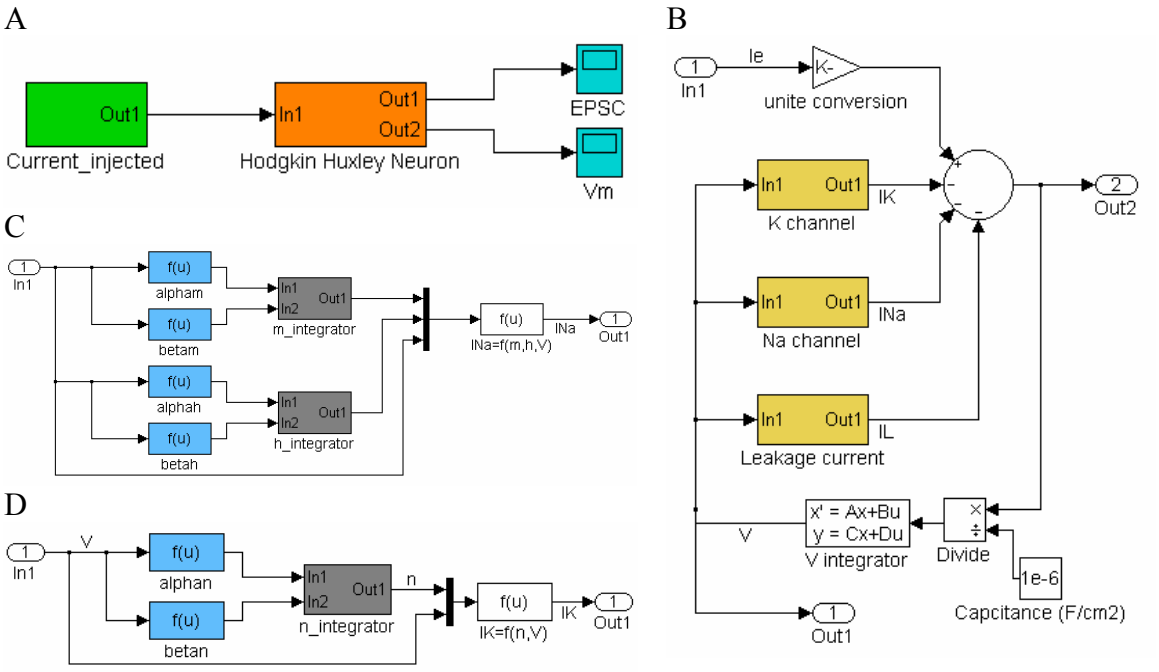

Figure C.3-2 The hierarchical Simulink structure to implement Hodgkin-Huxley equations. (A) The main directory that takes the current injected as input and exports the excitatory postsynaptic current and membrane potential. (B) The ion channels embedded in the conductance-based model. (C) The detailed structure describing the dynamics of sodium channels. (D) The detailed structure describing the dynamics of potassium channels .

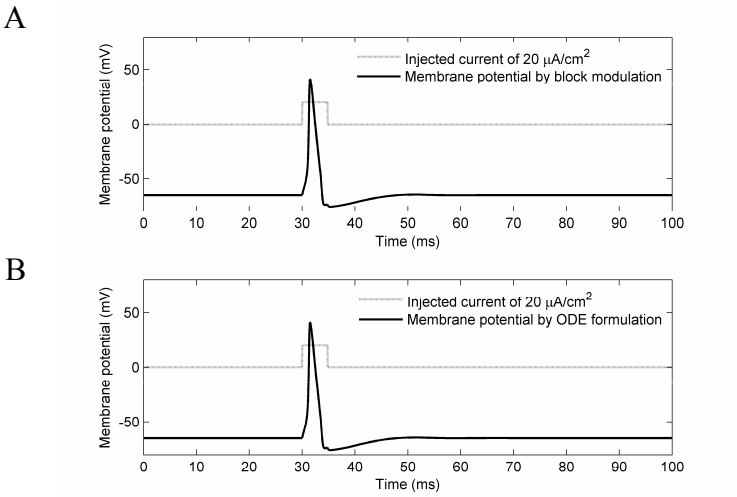

Figure C.3-3 The input current and output membrane potential based on Hodgkin-Huxley equations. (A) The response based on standard H-H model. (B) The response based on hierarchical model implemented in Simulink.

C.4 Modification of H-H model

The shapes of action potentials vary significantly, depending on the types and locations of neurons. Although the output of Hodgkin-Huxley equations represents one major type of action potential, it cannot account for all the classes of action potential. Therefore, various spiking models have been developed independently or based on the H-H equations. To model the responses from various types of neuron, a precise simulation of action potentials initiated at the neurons of interest is necessary. There are two aspects of H-H model that we modified for the modeling work of spike timing dependent plasticity. The first is the kinetics of potassium channels and the second is the depolarization after potential behavior.

C.4.1 Change the kinetics of K channels

The recovery rate of potassium channels is described by the two ion channel rate constants $\alpha_n(V)$ and $\beta_n(V)$. While $\alpha_n(V)$ is the opening rate constant, $\beta_n(V)$ is the closing rate constant; both of them are voltage dependent. The potassium current flow through rectifier potassium channels recovers the membrane potential from the hyperpolarization state. Since different kinds of neurons demonstrate different length of the tail after action potential, to control the rate of the recovery, the values of $\alpha_n(V)$ and $\beta_n(V)$ need to be adjusted. As shown in Figure C.4.1-4, slow K channels result into long post action potential tail and fast K channel render swifter recovery. For the classical H-H equations (fast K channel), the value pre voltage terms constant of $\alpha_n(V)$ and $\beta_n(V)$ are 0.032 and 0.5, respectively, based on Eq. (A.3). As for slow K channel, those values are adjusted to 0.15; for medium K channel, 0.32.

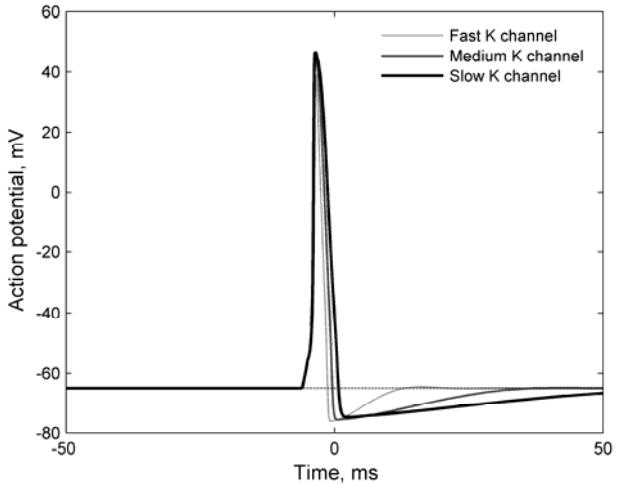

Figure C.4.1-4 The output of Hodgkin-Huxley equations with different rates of potassium channel kinetics.

C.4.2 Introduce depolarization after potential

Several types of neurons mentioned in the manuscript demonstrate depolarization after potential (DAP) behavior. These neurons, at the repolarization stage, depolarize instead of hyperpolarize once reaching the resting potential, which is -65 mV according to H-H equations. Therefore, the level of membrane potential does not drop below the steady state value. To implement the introduction of DAP into H-H model, we decided to reverse the hyperpolarization part of the action potential whenever the membrane potential V_m is smaller than -65 mV. The constant k_{DAP} is added to control the degree of depolarization after potential. The Matlab® codes to execute the algorithms are as follow and the comparison between the output of classical H-H model and that with DAP behavior is shown in Figure C.4.2-5.

```
IF  Vm < -65

    THEN Vm = -65 + kDAP * (-65 - Vm)

ELSE

    Vm = Vm

END
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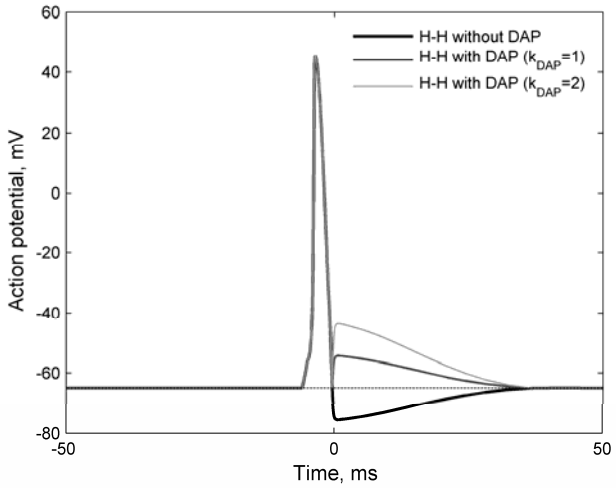

Figure C.4.2-5 The output of Hodgkin-Huxley equations with different degree of depolarization after potential (DAP).

1. Benda J (2002) PhD Thesis: Single Neuron Dynamics Models Linking Theory and Experiment. In: Universität zu Berlin, Berlin, Germany
2. Dayan P, Abbott LF (2001) Theoretical neuroscience: computational and mathematical modeling of neural systems. MIT Press, Cambridge, MA
3. Hodgkin A, Huxley A (1952) A quantitative description of membrane current and its application to excitation and conduction in nerve. J Physiol 117:500-544