Application of Data Science and Information Technologies in Neurosciences
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Prof. Kostas Vekrellis, Prof. Eleftherios Ouzounoglou

The Hodgkin-Huxley Model as an Oscillator

Aspasia Vozi

Contents

1 Exercise 1

For the purpose of this assignment, we deal with one of the most popular conductance-based model, the Hodgkin-Huxley model (HH model). The HH model is a mathematical model that describes how action potentials in neurons are initiated and propagated. Similar to the LIF (Leaky integrate-and-fire) neuron model, it consists of a set of nonlinear differential equations that approximate the electrical characteristics of a neuron cell. The model was first described in 1952 by Alan Hodgkin and Andrew Huxley to explain the mechanisms underlying the initiation and propagation of action potentials in the squid giant axon.

The simulation of the HH model is based on four variables, the membrane potential, V, and three gating variables, the sodium activation variable, m, the sodium inactivation variable, n and the potassium activation variable , h. The gating variables range between 0 and 1, representing the fraction of channels in a particular state. By multiplying together, all such variables for a type of channel indicates the fraction of the channels that are open and able to transmit current.

With respect to the gating variables, each gating variable has a voltage dependent steady-state value that is reached if the membrane potential is fixed and a voltage-dependent time constant that determines the rate of approaching the steady-state. The voltage-dependent functions are usually obtained by fitting to empirical data.

We are given a code, where the four variables, sodium activation, m, sodium inactivation, h, potassium activation, n, and membrane potential, V, are updated on each time step, since they depend on each other. Initial conditions are 0 for all gating variables and E_L (leak reversal potential) for the membrane potential.

$$C_m \frac{dV_m}{dt} = G_L(E_L - V_m) + G_{Na}^{(max)} m^3 h(E_{Na} - V_m) + G_K^{(max)} n^4 (E_K - V_m) + I_{app} \tag{1}$$

$$\frac{dn}{dt} = \alpha_n(V_m)(1 - n) - \beta_n(V_m)n \tag{2}$$

$$\frac{dm}{dt} = \alpha_m(V_m)(1 - m) - \beta_m(V_m)m \tag{3}$$

$$\frac{dn}{dt} = \alpha_n(V_m)(1 - n) - \beta_n(V_m)n \tag{4}$$

parameter	Symbol	Value
Leak Conductance	G_L	$30\mu S$
Maximum sodium conductance	$G_{Na}^{(max)}$	$12\mu S$
Maximum delayed rectifier conductance	$G_K^{(max)}$	$3.6\mu S$
Sodium reversal potential	E_{Na}	$45mV$
Potassium reversal potential	E_K	$-82mV$
Leak reversal potential	E_L	$-60mV$
Membrane capacitance	C_m	$100pF$
Applied current	I_{app}	$variable$

Table 1: Parameters used to simulate the HH model.

Gating variable	Steady state	Time constant	Rate constants
m	$\frac{\alpha_m}{\alpha_m+\beta_m}$	$\frac{1}{\alpha_m+\beta_m}$	$\alpha_m = \frac{10^5(-V_m-0.045)}{exp[100(-V_m-0.060)-1]}$ $\beta_m = 4\times10^3 exp\frac{-V_m-0.070}{0.018}$
h	$\frac{\alpha_h}{\alpha_h+\beta_h}$	$\frac{1}{\alpha_h+\beta_h}$	$\alpha_h = 70exp[50(-V_m-0.070)]$ $\beta_h = \frac{10^3}{1+exp[100(-V_m-0.040)]}$
n	$\frac{\alpha_n}{\alpha_n+\beta_n}$	$\frac{1}{\alpha_n+\beta_n}$	$\alpha_n = \frac{10^4(-V_m-0.060)}{exp[100(-V_m-0.060)-1]}$ $\beta_m = 125exp\frac{-V_m-0.070}{0.008}$

Table 2: Gating variables steady-state, time constant and rate constants used to simulate the HH model.

We simulate the model for $0.35s$ using the aforementioned equations and parameters, and setting the applied current to zero. We present in the Figure 1 below the results, and we note that the membrane potential initially produces a spike, after of which a small increase is observed and then the membrane potential stabilizes in $-0.0702V$ as expected. The spike that occurs immediately after the application of the zero current, could be attributed to the ion conductances and their constants. Since HH model takes into consideration these parameters as well, it is possible for a spike to occur even when zero current is applied to the model neuron.

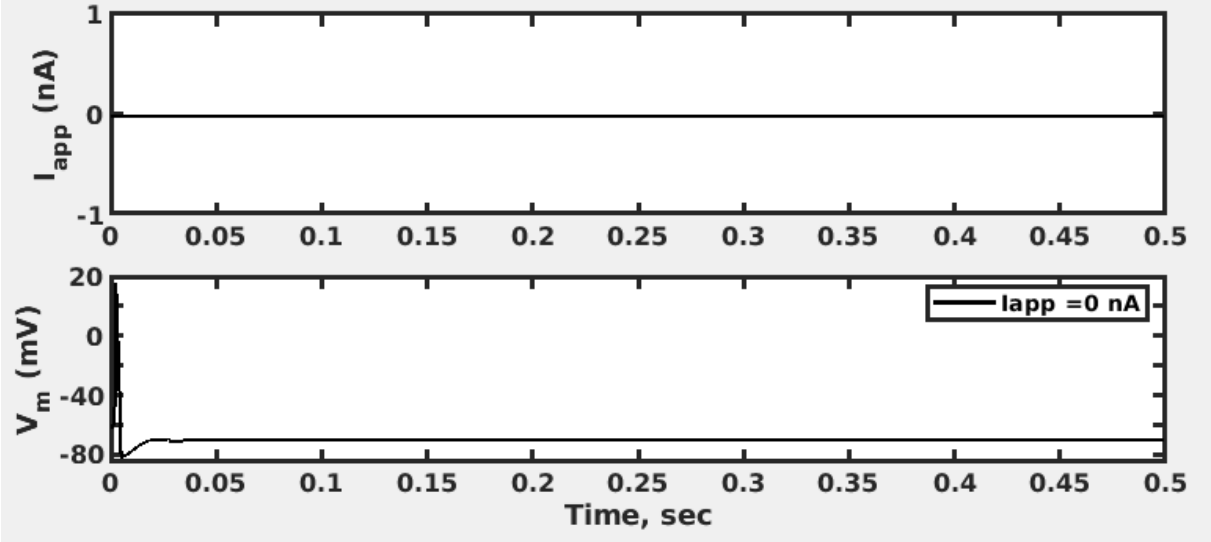

Figure 1: Membrane potential vs. time after the application of $I_{app} = 0$.

2 Exercise 2

For the purpose of this exercise and using the same parameter values for the model, several current values, below $0.22nA$, were applied for $100ms$, beginning at $100ms$. The applied current values are: $0.05, 0.10, 0.15, 0.20$ and $0.22nA$. These are shown in Figure 2 A. Regarding the membrane potential plots for each current, presented in Figure 2 B-F, we note that in every case, a spike is observed at the beginning of the simulation, as expected since no parameters are changed compared to exercise 1. It is noteworthy that even the highest current value does not produce spikes. Moreover, subthreshold oscillations are observed while the values increase. These oscillations appear at the first milliseconds of current applications, and then disappear as expected, since the system stabilizes over time.

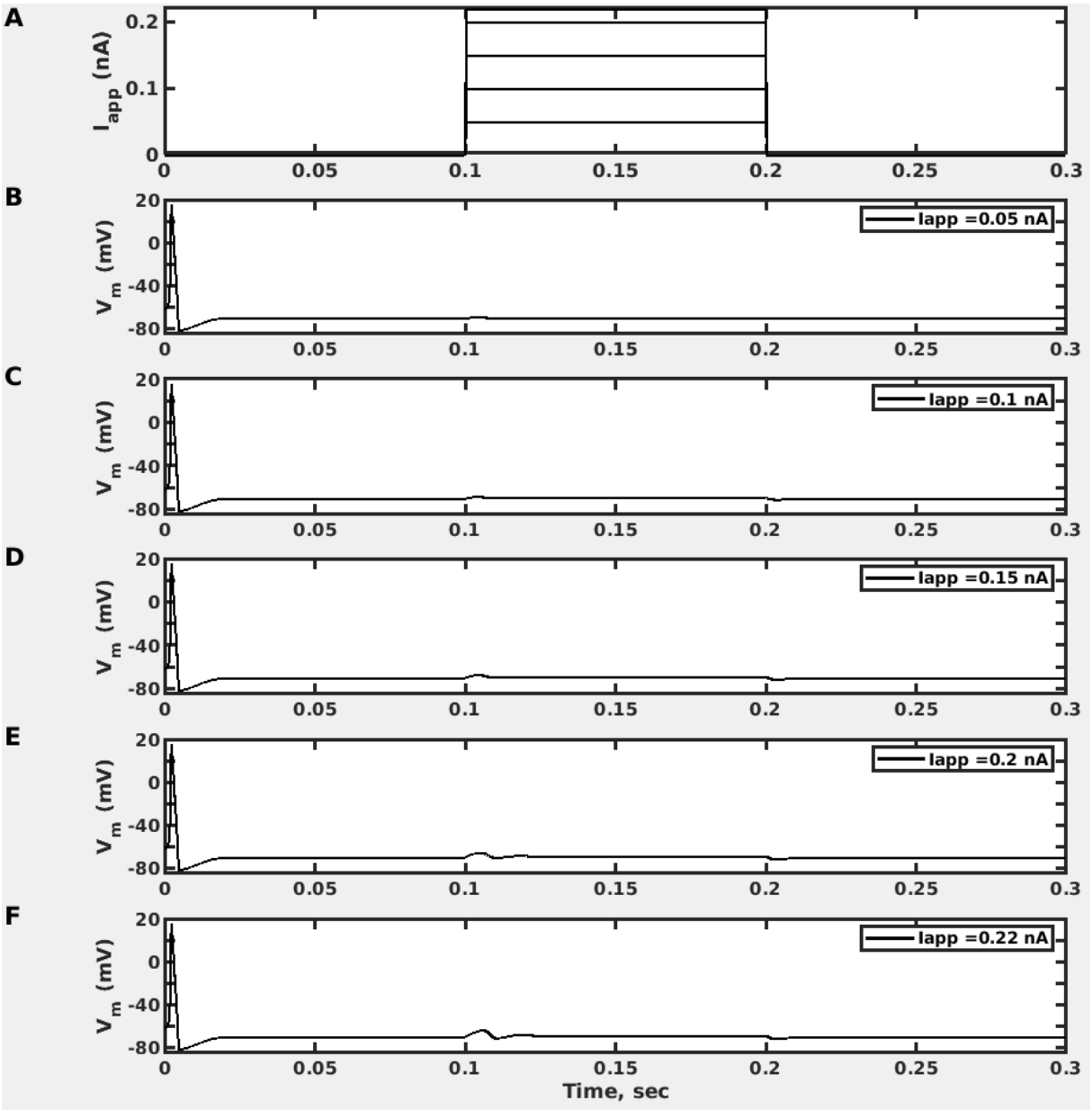

Figure 2: Input of various current values (A) and the changes in membrane potential (B-F).

3 Exercise 3

For the purpose of this exercise, ten pulses of the same current, $0.22nA$ were applied in every trial, with a different interval, delay, of the two plots. This delay varies from 5 to $25ms$. All current pulses last $5ms$ and are shown in the plot at the top of Figure 3. It is noted that spikes occur only when this delay revolves around the value of $15ms$. Although in the previous exercise it was observed that a current of $0.22nA$ is not enough to produce spikes, it is noted here that when this current is applied every $15ms$, spikes occur. These spikes could be attributed to the sum of overall inward current.

Furthermore, it is observed that for the delays of 20 and $25ms$, only subthreshold oscillations take place. This may be due to the inability of the charge to sum up and produce the rapid activation of sodium channels, since the oscillations are probably too far temporally. Regarding the interval that lasts $10ms$, subthreshold voltage increases occur again, probably because the pulses happen too frequently. The membrane potential does not reach the threshold to produce spikes, and one would expect for spikes to be generated more frequently according to the pulses. However, the slower but longer reaction of potassium channels activation does not allow spikes to occur. This is more prominent, when the delay is of $5ms$, when only one small voltage increase is observed, and after that the system stabilizes. In this case, we could consider the applied current to be constant, since the delay between the pulses' onsets is equal to the duration of the pulse.

To that end, it is observed that the model produces spikes only when the input frequency is near the neuron's natural frequency, which is called resonant frequency. Therefore, the resonant frequency of this model could be considered to be close to the one where input is given every $15ms$.

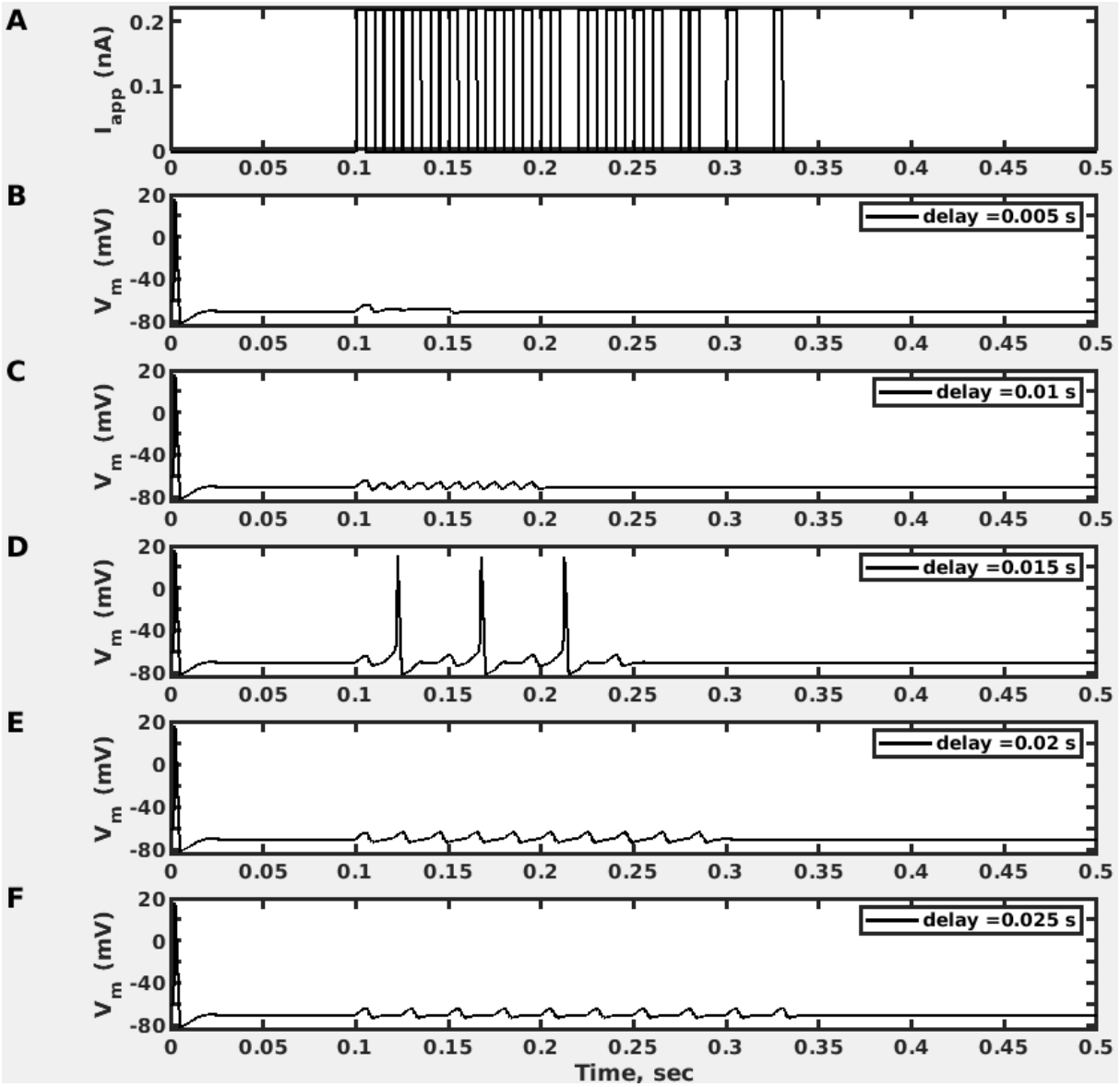

Figure 3: Current and membrane potential over time, for 10 pulses of 0.22 nA with varying frequencies.

4 Exercise 4

In this case, a constant current of $0.6nA$ is applied in our model, as well as 10 inhibitory pulses of 0 current that elicit its hyperpolarization. Moreover, the leak potential is decreased at $-0.065V$ and the initial value of sodium channels inactivation constant (h) is lowered at 0.5. As it is shown in Figure 4, no spikes occur before or after the current pulses. However, right after one inhibitory pulse occurs, a spike is produced every time. This phenomenon is known as the anode break potential, where a spike is produced after release from a hyperpolarization event. Anode break potential is the result of hyperpolarization, that increases h close to 1 and enables the generation of spikes. Moreover, during hyperpolarization, potassium channel activation (n) approaches zero, resulting in the decrease of the potassium current that could counteract spikes.

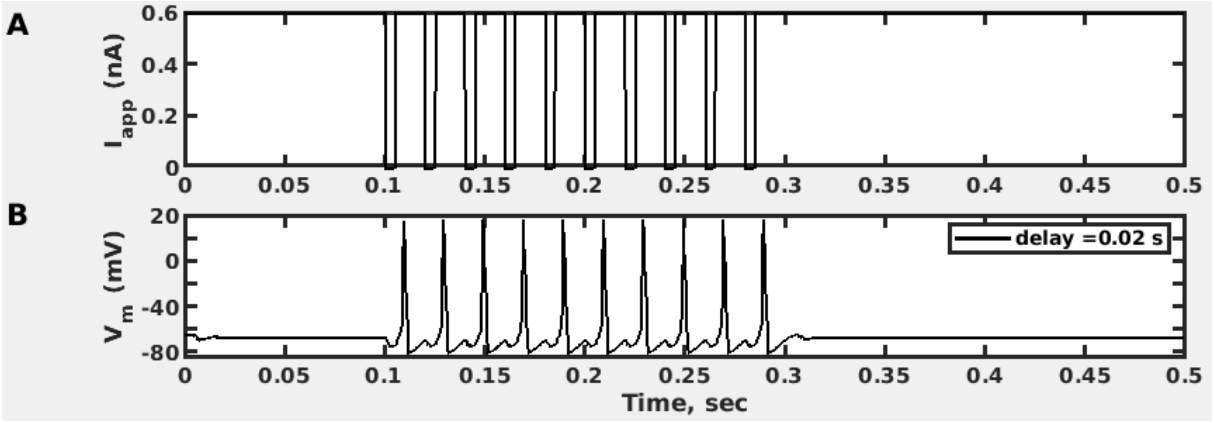

Figure 4: Anode break action potentials, occurring after hyperpolarization of the membrane.

5 Exercise 5

For the purpose of Exercise 5, there is constantly a current input of $0.65nA$ and a current pulse of $1nA$ occurs at $100ms$ for a duration of $5ms$. The parameter values are the same as in exercises 1-3. The results of this simulation are shown in Figure 5. We observe that the constant current input of $0.65nA$ produces spikes, but after the pulse takes place, there are no spikes produced.

This observation could be expected, since the production of a spike, given the current, depends on the state of gating variables and not just on the membrane potential. Therefore, it could be assumed that the sudden rise of the current probably affects the gating variables of the ions and does not allow spike production.

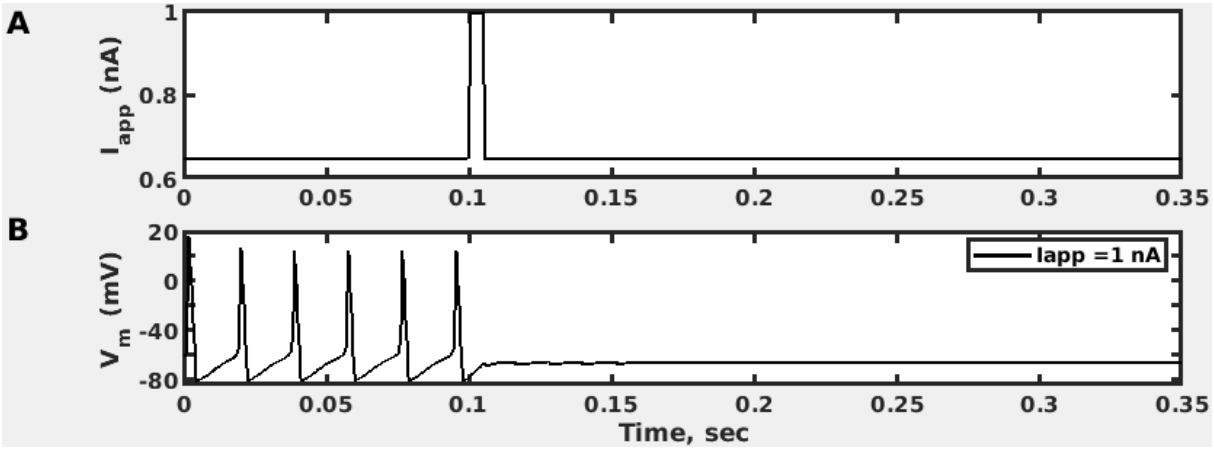

Figure 5:

6 Exercise 6

For the purpose of exercise 6, constant current is $0.7nA$ and the initial values of the gating variables are set to zero. When the simulation starts, a spike is shown, that could be attributed to the fast activation of sodium channels, the high value of current and the lower membrane potential, that is $-0.065V$.

As it is shown in Figure 6, after the produced spike, the system reaches an equilibrium and no more spikes occur, until the current pulse. During the pulse, a spike occurs and after that, a few subthreshold oscillations that decay rapidly are observed.

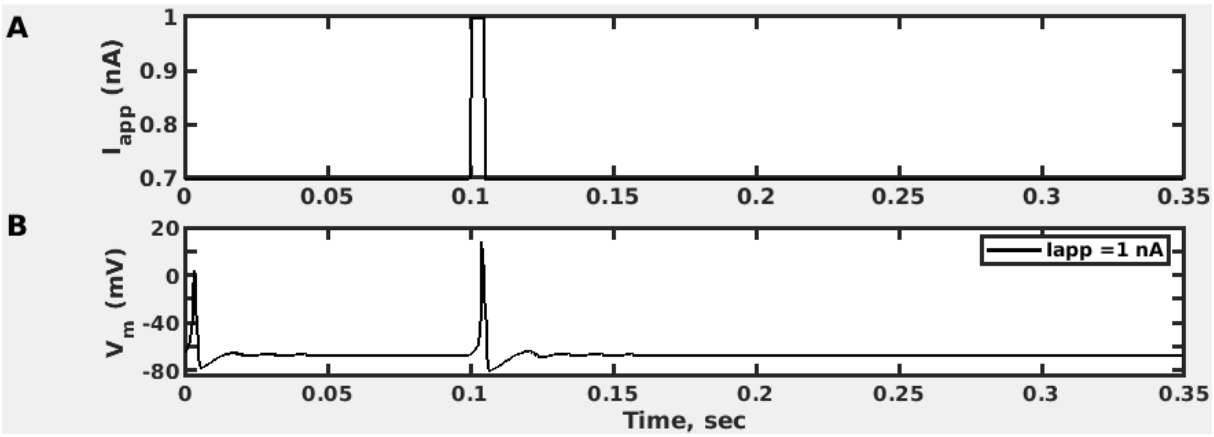

Figure 6: HH model simulation with a current pulse of $1nA$ at $100ms$, lasting $5ms$.