STUDENT PAPER

Differences between Stochastic and Deterministic Modeling in Real World Systems using the Action Potential of Nerves.

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ABSTRACT

The paper discusses the differences between deterministic models and stochastic models in calculus. deterministic models offer very good representations of natural occurring phenomenon but they do not represent everything. Stochastic representation takes into account random probability that is inherit in all real world events and thus represents more then its counter-part. I explain this by using the action potential of nerves as a specific example and show that the deterministic model that Alan Hodgkin and Andrew Huxley does not properly represent the firing of action potential in nerves at threshold voltages. Creating a stochastic model of the action potential takes into account that probability of the gates opening and closing and at threshold levels mimics the true reaction of an action potential at threshold voltages.

INTRODUCTION

The real world is made up of minute random events yet a majority of real world systems are explained using deterministic models. Some such models include various population models and the modeling of action potentials in nerves. In mathematics, deterministic models are explained as a set of states which are predetermined depending on the initial conditions. Thus, as long as the initial conditions never change, the outcome will always be the same. In other words, deterministic models introduce no randomness into the system.[1] Even though these models give seemingly correct outcomes, they go against the nature of real world systems. This is because the majority of real world systems are

1 Deterministic vs. Probabilistic (stochastic), "Mathematical Model", http://en.wikipedia.org/wiki/Mathematical_model

2 Lodish, Harvey et al., *Molecular Cellular Biology* (New York: W. H. Freeman & Co.; c1999), Chapter 21

only affected by randomness in amounts small enough to not notice. This of course depending on the initial conditions.

In order to get an accurate portrayal of a system, the whole system must be modeled accurately, not just certain cases. This is where stochastic models come in. Stochastic models depend on some predetermined and random variables to transition from one state to another.[1] With those random variables comes a way to represent the randomness involved in real world systems. The rest of this paper will discuss in detail the limitations and advantages of stochastic and deterministic models to represent real world systems using the action potential of nerves as the primary example.

BIOLOGICAL BACKGROUND

The human neural system is comprised of excitable cells spread throughout the body that lead to the spine and up to the brain. nerves are a type of excitable cell and the type this paper will use. The way signals are transferred through nerves is by sending electrical impulses starting at the dendrites and down the axon body. Once the electric impulse gets to the axon terminal it will induce a rise in calcium ions in the cytosol. This rise causes vesicles to fuse with the plasma membrane and releases its contents into the synaptic cleft. The neurotransmitters bind to the receptors on the next cell creating an electrical disturbance. If that disturbance is high enough then that cell triggers its own electrical impulse.[2]

The electrical impulse is created by a rapid increase and decrease in electrical membrane potential in the cell. The change in electric potential is caused by the passing of Na^+ and K^+ ions through voltage-gated channels that were open. As the potential increases, more Na^+ channels open. The opening of the channels further increase the potential and depolarize the membrane. When the membrane is depolarized to a certain level it will open enough channels to have a landslide effect and create a spike in the electric potential. This occurrence is called the Action potential.[2]

The action potential has a very unique feature in that it has an all-or-nothing response. This means that once the electric potential gets to a certain level the action potential will always fire. This voltage (which is electric potential) level is called the threshold voltage. The action potential in cells has been studied for quite some time and extensive research has been done on the topic which makes it a perfect medium to compare stochastic
and deterministic modeling.

Arguably the most famous model for action potential is the one that Alan Lloyd Hodgkin and Andrew Huxley came up with in 1952. Their model was described by a set of differential equations and will be used as the example for deterministic modeling. The work on this topic that was done by both Professor Eric Jakobsson from the University of Illinois and myself will be used as the example for stochastic

modeling.

Alan Hodgkin and Andrew Huxley published a series of papers in 1952 on their work describing important properties of ionic conductances in nerve action potentials. They conducted their experiments on a squid axon. The squid axon was a good platform for research because it was large enough to visibly see and also the squid axon basically has two types of voltage-dependent conductances unlike more complex systems.[3] From the research done they came up with a set of differential equations to model action potential in nerves.

$$C_m \frac{dV}{dt} = -g_L\left(V - V_L\right) - \overline{g}_{Na} m^3 h\left(V - V_{Na}\right) - \overline{g}_K n^4\left(V - V_K\right)$$

$$\frac{dm}{dt} = \alpha_m\left(V\right)\left(1 - m\right) - \beta_m\left(V\right)m$$

$$\frac{dh}{dt} = \alpha_h\left(V\right)\left(1 - h\right) - \beta_h\left(V\right)h$$

$$\frac{dn}{dt} = \alpha_n\left(V\right)\left(1 - n\right) - \beta_n\left(V\right)n$$

Figure 1.1: Differential equations discovered by Alan Hodgkin and Andrew Huxley.[4]

According to the differential equations that Hodgkin and Huxley came up with the change in electric potential (voltage) across the membrane is based on three factors; the electric current of Na^+ ions, K^+ ions, and Cl^- ions (leakage). According to Hodgkin and Huxley the leakage current is negligible compared to the Na^+ and K^+ currents. The electric currents of the Na^+ and K^+ currents are determined by multiplying the current conductance of those ions at that voltage with the voltage difference between the current voltage and the ion's electric potential. Each of those factors change as the current system voltage changes. The conductance changes based on how many voltage-dependent channels are open which in turn are controlled by voltage gates inside of the channel. There are three types of voltage gates that determine how many channels are open. The Na^+ channels are controlled by three m gates and one h gate while the K^+ channels are controlled by four n gates. The change in these gates are determined by the three lower differential equations.[4] The alpha and beta functions are listed in the table below. The alpha function determines the percentage of gates that go from open to close whereas the beta function determines the opposite.

3 Mark Nelson and John Rinzel, "Hodgkin Huxley Model" in *The Book of GENESIS: Exploring Realistic Neural Models with the GEneral NEural SImulation System, Second Edition*, James M. Bower and David Beeman (TELOS/Springer-Verlag; 1998), Chapter 4

4 A.L. Hodgkin and A.F. Huxley, "A Quantitative Description of Membrane Current and its Application to Conduction and Excitation in Nerve", J. Physiol 117 (1952), 500-544

Table 2.1: The parameters of the Hodgkin-Huxley equations. The membrane capacity is $C = 1\,\mu\text{F/cm}^2$. The voltage scale is shifted so that the resting potential vanishes.

x	E_x	g_x
Na	115 mV	120 mS/cm^2
K	-12 mV	36 mS/cm^2
L	10.6mV	0.3mS/cm^2

x	$\alpha_x(u\,/\,\text{mV})$	$\beta_x(u\,/\,\text{mV})$
n	$(0.1-0.01\,u)\,/\,[\exp(1-0.1\,u)-1]$	$0.125\exp(-u\,/\,80)$
m	$(2.5-0.1\,u)\,/\,[\exp(2.5-0.1\,u)-1]$	$4\exp(-u\,/\,18)$
h	$0.07\exp(-u\,/\,20)$	$1\,/\,[\exp(3-0.1\,u)+1]$

Figure 1.2: Alpha and Beta functions for the n, m, and h gates. Voltage = u.[5]

These equations were discovered by Hodgkin and Huxley by performing patch clamp experiments on the squid axon. They clamped the voltage at a certain level so it would not change as they stimulated action potentials in the axon. This was done so they could measure the change in conductance independent of voltage change. They proceeded to run these at various voltage levels to acquire accurate data.[4]

DETERMINISTIC MODEL

With the equations above we were able to replicate Hodgkin and Huxley's data, including the patch clamp experiments through simulations run on Octave software. We did this in order to later compare our data from the stochastic model simulations. Once we confirmed that our results were same as the graphs presented by Hodgkin and Huxley in their 1952 paper we changed the parameters to test how accurate it simulated the all-or-nothing response that action potentials have.

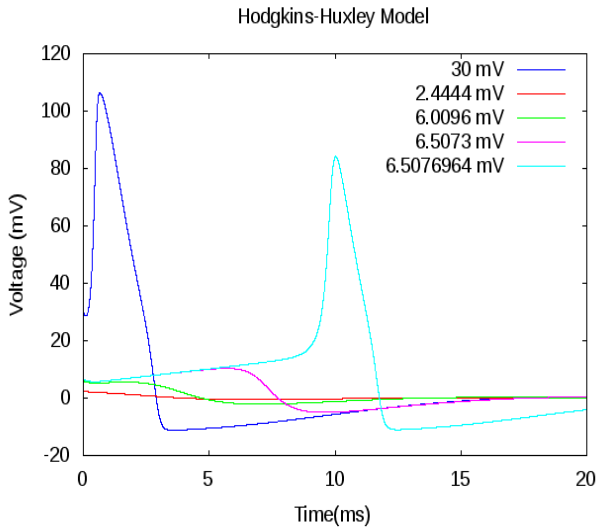


Figure 1.3: Graph of the Hodgkin-Huxley model simulations at various voltages

We noticed that as the input voltage changed the action potential peak and curve changed also. The lower the input voltage the smaller the peak and the more wide spread the curve which is not similar to how action potentials fire. With this we found our limitations of the deterministic model we used. The closer we got to the threshold voltage the more the model deviated from the correct representation of an action potential. The reason for this is because the model created by Hodgkin and Huxley does

4 A.L. Hodgkin and A.F. Huxley, "A Quantitative Description of Membrane Current and its Application to Conduction and Excitation in Nerve", J. Physiol 117 (1952), 500-544

5 Wulfram Gerstner and Werner N. Kistler, "Spiking Neuron Models". http://icwww.epfl.ch/~gerstner/SPNM/SPNM.html

not take into account the random chance for a gate to switch states. Depending on the current voltage of the system any gate has a vary chance to switch from open to close or close to open. This random factor gave us the idea for the stochastic model we used.

STOCHASTIC MODEL

For the stochastic model we simulated a patch of nerve membrane by created an array of n,m, and h gates that would either be in the open or closed state. Every iteration of the simulation we would check to see if the state of the gate would randomly change. We determined the state change by comparing the value of the alpha or beta function to a random number created from a random number generator. If the state was previously closed and the value of the alpha function for that input voltage was greater then the random number the gate is set to open, otherwise it stays closed. The same concept is used for the beta function except it determines if an open gate should close. Once all the gates in the iteration were checked we took the average of all the n,m, and h gates separately and using the first differential equation in figure 1.2, calculated the change in voltage. That change was then added to the previous voltage passed in and all of new information was passed into the next iteration. This simulation was run for over 1000 iterations with several hundred gates being simulated for each gate type. The results we got were conclusive with what we had expected for both the voltage clamp experiments and the action potential curves. The results below show side by side comparisons of the deterministic results (left) and the stochastic results (right).

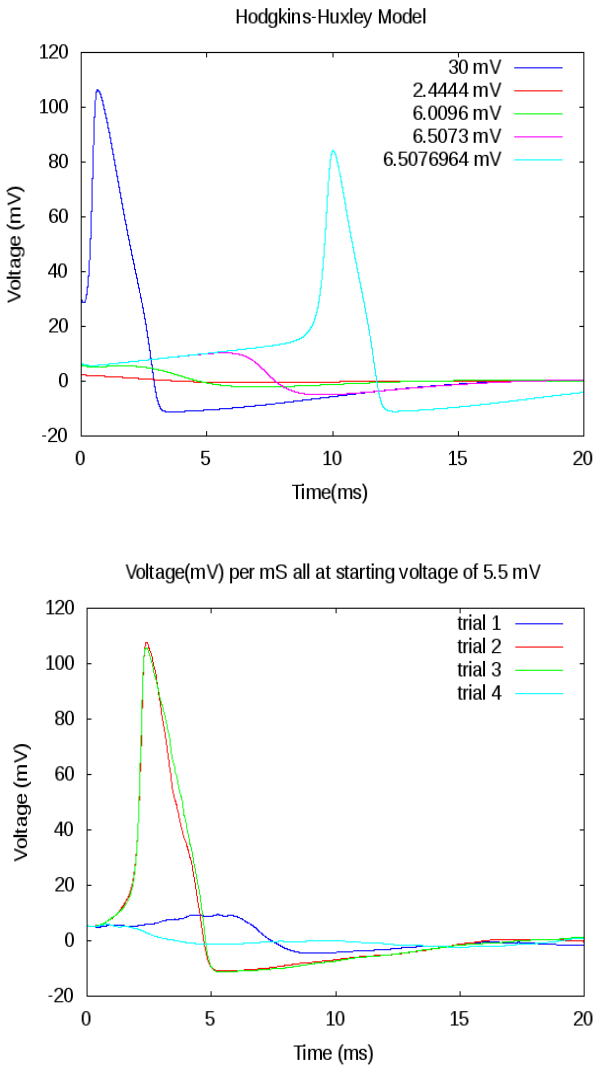


Figure 1.4: Hodgkin-Huxley model run at various voltage (top) and stochastic model run at 5.5 mV (down)

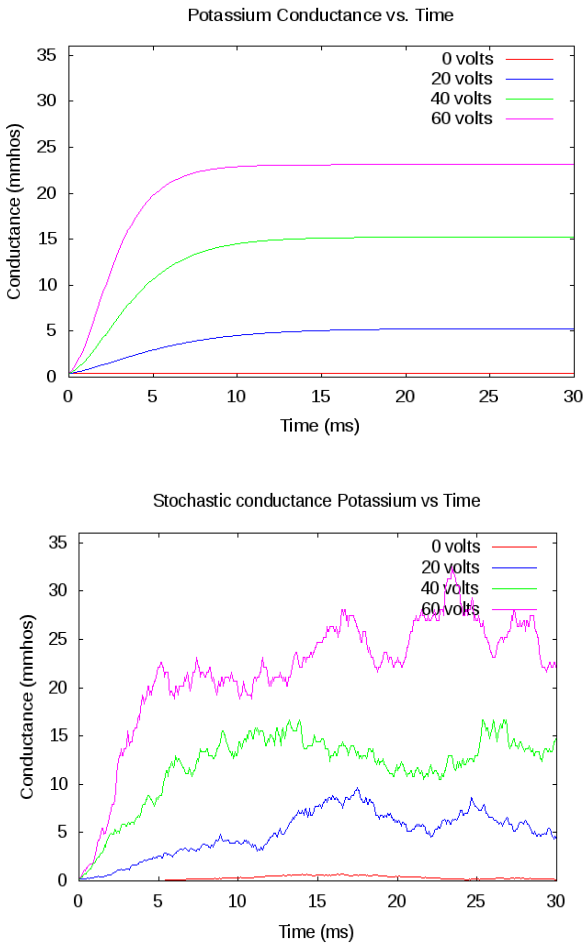
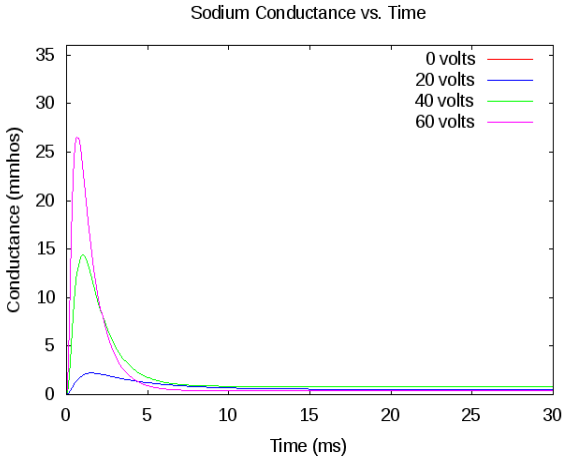


Figure 1.5: Hodgkin-Huxley potassium patch clamp results (top) and stochastic model results (bottom)



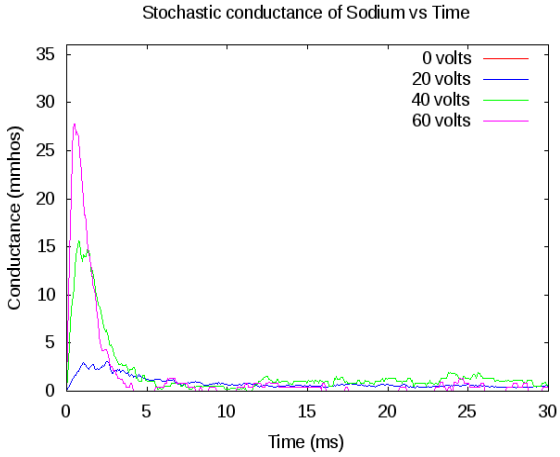


Figure 1.6: Hodgkin-Huxley sodium patch clamp results (left) and stochastic model results (right)

SUMMARY

The stochastic model produced more accurate data then that of the deterministic model but it was not without its limitations. Running the simulations for the stochastic model was extremely slow compared to the deterministic model. Some simulation runs took almost ten minutes to finish. Changing the parameters to do less iterations sped the simulation up but also increased the noise to a point where the data is useless. This can be attributed to the way in which we designed our model though and is not true of all stochastic models.

In the end the deterministic model did not give us as much data as the stochastic model but what it lacked in information it made up for in runtime. When dealing with real world systems however that lack of randomness can far outweigh the speed gained. The ultimate goal of

this paper is to show that stochastic processes are important and should be taught side by side with differential equations and deterministic modeling topics. Einstein discovered the correlation between a random walk and the diffusive process in 1905 yet 105 years later probability is taught separate from calculus and differential equations still.

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REFERENCES

[1] Deterministic vs. Probabilistic(stochastic), "Mathematical Model", http://en.wikipedia.org/wiki/Mathematical_model

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[4] A.L. Hodgkin and A.F. Huxley, "A Quantitative Description of Membrane Current and its Application to Conduction and Excitation in Nerve", J. Physiol 117 (1952), 500-544

[5] Wulfram Gerstner and Werner N. Kistler, "Spiking Neuron Models". http://icwww.epfl.ch/~gerstner/SPNM/SPNM.html