BEHAVIORAL MODELING OF NEURONAL ACTION POTENTIALS USING VERILOG-AMS

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ABSTRACT

In this paper, a Verilog-AMS implementation of the Hodgkin-Huxley neuron equations is presented, gradually, focusing on the simulation of every parameter for the comprehension of the entire model and culminating in the generation of an action potential. The behavioral model is in the process of improvement so as to include all the properties inherent to the dynamics of the model for different kinds of stimuli, and it will be used in the test bench of neuromorphic electronic circuits that are bound to come.

1. INTRODUCTION

Nowadays, in order to improve the performance of electronic circuits, the researches about how the biological structures of neuronal cells work have become critical to understand, mainly because the advantage of its application in fault-tolerant systems [1,2,3]. Despite of the complexity of their behavior, several studies have been done [4], some of which with satisfactory results in modeling the cells' action potentials – which are responsible for the mechanisms of the transmission of nervous impulses – such as the Hodgkin and Huxley Model [5] and the Lewis Model [6]. Hence, various studies concerning the implementation of those and other models in Hardware Description or High Level Programming Languages, viz. VHDL, VHDL-AMS, C, C++, are being carried out [7] aiming its appliance in biological inspired circuits [8].

In this paper, an implementation in Verilog-AMS [9] of a single action potential based on Hodgkin-Huxley model is presented, as well as the behavior of its most significant parameters. The purpose of this effort is to build, using a robust language, a reference model for a test bench in which a posterior library of neuromorphic logic gates can be tested.

2. HODGKIN-HUXLEY MODEL OVERVIEW

Throughout a series of experiments with the giant axon of a squid, A. L. Hodgkin and A.F. Huxley have developed a mathematical description for the generation of action potentials (also known as spikes), and applied it by modeling an equivalent electrical circuit.

The overview of their model is presented in the following subsections.

2.1. Electrical circuit

The Hodgkin and Huxley model can be understood as a parallel RC circuit, where the capacitance and variable resistors represent the capacitive and selective permeability feature of the membrane cell, respectively. The resistors can be thought of as the resistance of the cell to the flow of the ions Na^+, K^+ and additional ions (consisting mainly of Cl^-), whose influence is modeled by the leakage current. Such ion currents are responsible for the maintenance of the potentials between the interior and exterior of the cell. The voltage sources connected to each resistor represents the reversal potentials of the ions.

Thus, the circuit that unites all those characteristics previously exposed is presented in Figure 1:

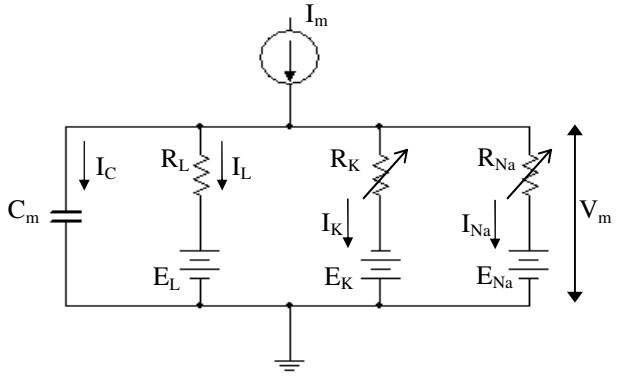

Figure 1 - Schematic diagram of the Hodgkin-Huxley circuit. The subscript *m* and *L* stands for membrane and leakage respectively. This last subscript is due to the leakage current that model the effect of the ions that are not being explicitly considered within the dynamics of the cell membrane depolarization and repolarization.

2.2. Equations

Therefore, the equations that describe the behavior of the system are

$$I_m(t) = C_m \cdot \frac{dV(t)}{dt} + \sum_{1}^{3} I_{ions}(t) \qquad (1)$$

$$I_{ion}(t) = \bar{g}_{ion} \cdot x_{activation}^{p_1} \cdot y_{inactivation}^{p_2} \cdot (V(t) - E_{ion}) \qquad (2)$$

where C_m denotes the membrane capacitance, I_m the total current that flows through the cell membrane, I_{ion} and E_{ion} the current and the reversal potential of a particular ion, respectively. The voltage V is defined as the difference between the membrane potential and the resting potential:

$$V(t) = V_m(t) - V_{resting\ potencial} \qquad (3)$$

Specific ion channels control the flow of the three currents (sodium current, potassium current and leakage current), the resistances that characterize them, can be thought of as conductances as well, thus $\bar{g}$ stands for the maximum conductance achieved by an ion if all the channels are open. The variables of activation and inactivation (x and y, also known as gating variables) stand for the probability of an ion channel to be open or closed to the passage of that ion; hence the range of these variables is between 0 and 1. They obey the differential equation:

$$\frac{dx}{dt} = \alpha_x(V) \cdot (1 - x) - \beta_x(V) \cdot x \quad (4)$$

A similar equation is valid for the inactivation variable. The potassium ion encloses only one variable of activation n, while the sodium ion encloses a variable of activation m, and a variable of inactivation h.

The rate constants α and β are non-linear functions of the potential, that have been adjusted to fit experimental data, so as the exponents of the gating variables (p_1 and p_2). The first ones are then given by:

$$\alpha_n(V) = 0.01 \cdot \frac{10 - V}{e^{\frac{10-V}{10}} - 1} \quad (5) \qquad \beta_n(V) = 0.125 \cdot e^{-\frac{V}{80}} \quad (6)$$

$$\alpha_m(V) = 0.1 \cdot \frac{25 - V}{e^{\frac{25-V}{10}} - 1} \quad (7) \qquad \beta_m(V) = 4 \cdot e^{-\frac{V}{18}} \quad (8)$$

$$\alpha_h(V) = 0.07 \cdot e^{-\frac{V}{20}} \quad (9) \qquad \beta_h(V) = \frac{1}{e^{\frac{30-V}{10}} + 1} \quad (10)$$

2.3. Parameters' values

The values of the parameters used in this implementation are those originally reported by Hodgkin and Huxley as seen in Table 1:

Parameters	Ions		
	Na^+	K^+	Cl^-(Leakage)
Reversal Potential (E)	115 *mV*	-12 *mV*	10.59895 *mV*
Maximum Conductance ($\bar{g}$)	120 *mS/cm²*	36 *mS/cm²*	0.3 *mS/cm²*

Table 1 - Parameters of the Hodgkin and Huxley model.

The capacitance of the membrane is 1 $\mu F/cm^2$, and the resting potential is considered to be zero.

3. VERILOG-AMS IMPLEMENTATION

The high level implementation using the Verilog-AMS language was built in a sequential bottom-up method – which means that a variable present in a specific equation have its behavior tested before its proper inclusion in the model equations –, due to the possibility of verifying the existence of any errors within the parameters of the model and better understanding of its dynamics. This process is illustrated in the subsequent topics.

Solving the Hodgkin and Huxley differential equations, the variables of activation and inactivation have the following aspect:

$$x(V,t) = x_\infty - (x_\infty - x_0) \cdot \left(e^{-\frac{t}{\tau_x}}\right) \quad (11)$$

The steady state value and the boundary conditions that satisfy the equation when $t=0$ are x_∞ and x_0 respectively, τ_x is the time constant of the variable.

3.1. Time constants

Each activation and inactivation variable (n, m and h), has its own time constant (τ_n, τ_m and τ_h that are a function of the rate constants α and β), whose behavior determines how fast these variables reach their steady state values. The basics of the analog process of all the time constants are shown in the Listing 1:

Listing 1 - Verilog-AMS time constants' code. The first piece is for time constant of n, and the second is for the time constants of m and h.

```
//time constant of n
analog begin
an = 0.01k*(10m-(V(tn)-Vrep))/(limexp((10m-(V(tn)-
Vrep))/10m)-1);
Bn = 0.125*limexp(-(V(tn)-Vrep)/80m);
Tn = 1/(an+Bn)*pow(10,-3);
I(tn) <+ Tn;
end

//time constants of m and h
analog begin
ah = 0.07*limexp(-(V(th)-Vrep)/20m);
Bh = 1/(limexp((30m-(V(th)-Vrep))/10m)+1);
am = 0.1k*(25m-(V(tm)-Vrep))/(limexp((25m-(V(tm)-
Vrep))/10m)-1);
Bm = 4*limexp(-(V(tm)-Vrep)/18m);
Tm = 1/(am+Bm)*pow(10,-3);
Th = 1/(ah+Bh)*pow(10,-3);
I(tm) <+ Tm;
I(th) <+ Th;
End
```

Note that the flows of the branches have as contributions the time constants; this routine simplifies the act of visualizing the behavior of the parameter of this subsection, since it is needless to create new disciplines and natures.

Therefore, the time constants dependence of voltage achieved is presented by Figure 2:

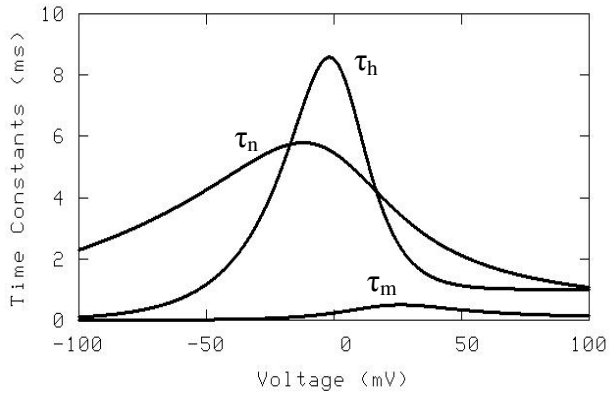

Figure 2 - Time constants for the gating variables m, n and h.

3.2. Steady state values

Since there are three variables, there are also three different steady states values (similar to the time constants, they also are a function of α and β). They dictate the magnitude of the activation and inactivation variables for a certain voltage when the time tends to infinity. A piece of the analog process is presented in the Listing 2 (n_∞ followed by m_∞ and h_∞):

Listing 2 - Fragments of the Verilog-AMS codes extracted from the scripts containing the behavior of the steady state values of *m*, *n* and *h*.

```
// steady state of n
analog begin
...
ninf = an/(an+Bn);
I(x) <+ ninf;
end

// steady state of m and h
analog begin
...
minf = am/(am+Bm);
hinf = ah/(ah+Bh);
I(x) <+ hinf;
I(y) <+ minf;
End
```

The same observations made for the time constants apply also for the steady state values of the variables *n*, *m* and *h*.

The result of the simulation can be seen from Figure 3:

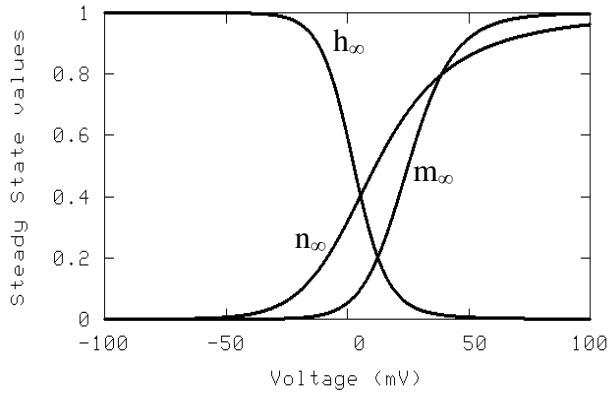

Figure 3 - Steady states values for the gating variables *n*, *m* and *h*.

3.3. Activation and inactivation variables

As a result of the appropriate behavior of the time constants and the steady states values, it was likely to simulate the *n*, *m* and *h* (setting initial condition for every variable). The Listing 3 presents the main additions to the code of the preceding subsection.

Listing 3 - Verilog-AMS code of the sodium activation and inactivation variables. Once the implementation of the potassium variable has a very similar code structure, it will not be presented.

```
//sodium variables
analog begin
...
if ($abstime <= tdf) begin
Vo=0;
aho= 0.07*limexp(-(Vo-Vrep)/20m);
Bho=1/(limexp((30m-(Vo-Vrep))/10m)+1);
amo=0.1k*(25m-(Vo-Vrep))/(limexp((25m-(Vo-Vrep))/10m)-
1);
Bmo=4*limexp(-(Vo-Vrep)/18m);
mo = amo/(amo+Bmo);
ho = aho/(aho+Bho);
end
if ($abstime > tdf) begin
Vo=50*pow(10,-3);
aho= 0.07*limexp(-(Vo-Vrep)/20m);
Bho=1/(limexp((30m-(Vo-Vrep))/10m)+1);
amo=0.1k*(25m-(Vo-Vrep))/(limexp((25m-(Vo-Vrep))/10m)-
1);
Bmo=4*limexp(-(Vo-Vrep)/18m);
mo = amo/(amo+Bmo);
ho = aho/(aho+Bho);
end
tdr = td;
tdf = td + width;
if (($abstime > tdr)&&($abstime <= tdf)) begin
t = $abstime - tdr;
end
else if ($abstime > tdf) begin
t = $abstime - tdf;
end
else begin
t = 0;
end
m = minf - (minf-mo)*limexp(-t/Tm);
h = hinf - (hinf-ho)*limexp(-t/Th);
I(x) <+ m;
I(y) <+ h;
End
```

Thus, the response of these activation and inactivation variables to a single pulse of 50 *mV* (depolarization of the membrane) with a 30 *ms* width is presented in Figure 4:

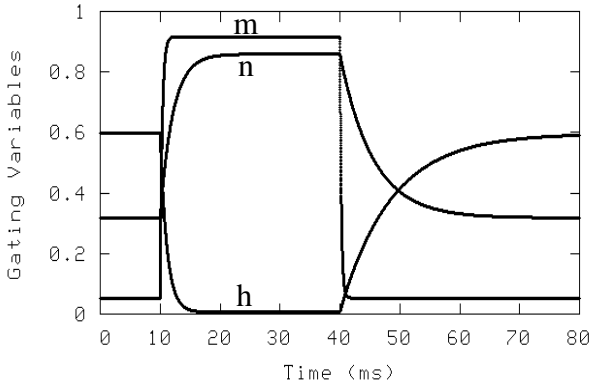

Figure 4 - Activation and inactivation variables *n*, *m* and *h*.

3.4. Conductances

The conductance of each ion Na^+ and K^+ may now be replicated, as follows the most important changes in the analog interface code of the last subsection (the leakage conductance will not be presented since it is modeled as a constant):

Listing 4 - The main difference between the Verilog-AMS codes of the activation and inactivation variables and the conductances of the ions.

```
analog begin
...
gna = gnamax*pow(m,3)*h;
I(x) <+ gna;
end

analog begin
...
gk = gkmax*pow(n,4);
I(x) <+ gk;
end
```

For an input of a single pulse of 26 *mV* with a 50 *ms* width, the result obtained is shown in Figure 5:

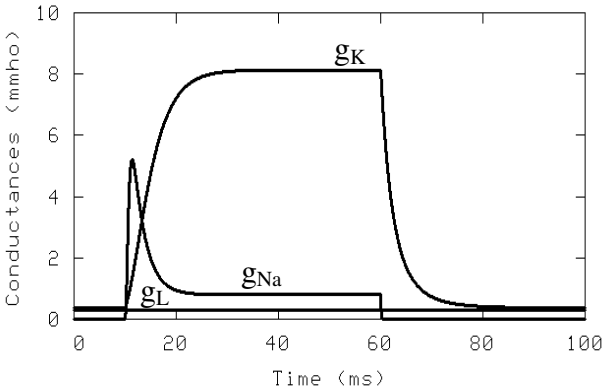

Figure 5 - Transient analysis of the conductances of Na and K and the leakage conductance.

3.5. Spike generation

The formal action potential simulated by combining all those previous built behavioral modules had as a stimulus a single pulse of current with width of 1 *ms*. The Figure 6 presents three action potentials generated with currents of magnitude of 2.5 μA, 5 μA and 10 μA.

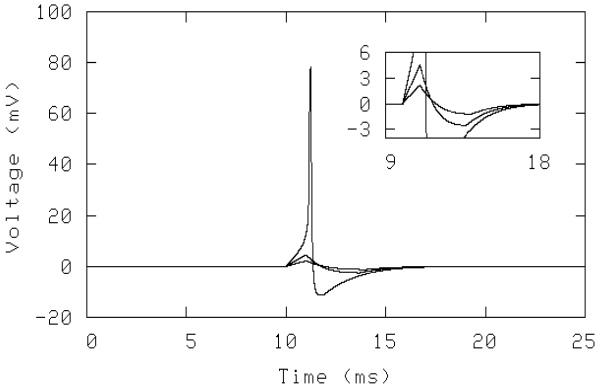

Figure 6 - A current of 10 μA generates a spike about 80 *mV*. On the other hand, currents of 2.5 μA and 5 μA are insufficiently strong to generate an action potential, then, there is merely a slight voltage variation above the resting potential of the membrane (see insert in the top right of the figure).

As can be seen in Figure 6, the spike model does not include the refractory period yet - even though it does incorporate the hyperpolarization period, in which the potential is below the resting potential - or a clearly defined firing threshold for a spike generation. Since the work of modeling the Hodgkin and Huxley equations in Verilog-AMS is still in development, efforts are being made in order to accurately model the behavior of the biological spike.

4. CONCLUSIONS

Throughout this paper the behavior of all parameters and variables of a single action potential of the Hodgkin and Huxley model was shown, as well as how they can be implemented in Verilog-AMS so as to simulate a spike.

The others aspects of the dynamics of this model, such as a more efficient description of the neuronal refractoriness and the threshold effect are the subject of ongoing research at the Federal University of Rio Grande do Norte.

5. ACKNOWLEDGEMENT

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6. REFERENCES

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