Action Potential and Bursting Phenomena using Analog Electrical Neuron

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ABSTRACT
A neuron or nerve cell has passive components due to resistive-capacitive nature of circuitry and active current components contributed by ion channels. Biophysical neurons represent active and passive components by differential equations. The differential equations of the biophysical model were integrated by making arithmetic operations on voltage model circuits. Analog neuronal model using voltage integrator circuits is the main focus of this paper. The work involves two circuit models and also addresses design and passive properties of analog neuron model along with the effects of Na^+ and K^+ ionic channels. In the first simpler circuit, an action potential was generated. In the enhanced second model, sodium and potassium currents were generated separately along with action potential. Impacts of noise and various geometrical signals on the action potential and ionic channels were studied to analyze the effects of membrane resistance and capacitance changes in membrane potential and ionic channels. Besides its use in neuromorphic network research, the model has been successfully in virtual labs and for teaching practice.

Categories and Subject Descriptors
I.5.1 [Pattern Recognition]: Models, Neural nets

Keywords
Electrical analog neuron, neuromorphic engineering, neuronal biophysics

1. INTRODUCTION
There are many reasons for implementing neural models. In computational neuroscience, per say, one studies how some particular neural model performs. In robotics, there has been considerable research into how the neural system attains its capabilities. We have developed hardware neuron models to study real-time processing of information flow in terms of ionic current and also to use the model for teaching purposes. Neurons spike when membrane potential goes beyond a threshold level. .When spiking occurs, it is an 'all-or-none' phenomenon i.e. if a stimulus doesn't exceed the threshold level no action potential result.

However, the design, analysis, and verification of analog circuits to represent aforementioned functionality are a very difficult task due, in part, to the inherent complexities of the basic techniques. There are several analog models that are typically based on prototypical ion conductance models obeying Hodgkin-Huxley (HH) principles [3]. A compromise between the elaborate but bulky conductance-based approach, and the compact but simple I&F models is provided by elaborate models of I & F neurons, with additional neural characteristics, such as spike frequency adaptation properties and refractory period mechanisms [5]. [6,7] have proposed several electronic membrane models that are based on the Hodgkin-Huxley (HH) equations. NeuroFet based models was also based on the Hodgkin-Huxley (HH) model [2,3].

In this paper, we report the design and functioning of a simple neuron model and more advanced neuron models to study and explain biophysical neurons. Another motivation was that analog computation performs non-linear operations using far less power per computation than digital computation. The dynamical reconfigurability of the circuits also provides the realization of robust and adapting systems, which is indispensable in neural systems.

2. MATERIALS AND METHODS
To investigate properties of membrane potential and basic ion channel properties as seen in Granule cells on a hardware platform, analog model was essential. The analog equivalent was adapted from Maeda and Makino model [7, 8]. We implemented the electronic neuron using National Instruments Elvis II (Austin, USA) and a data acquisition device (NI DAQ USB 6221). To investigate properties of membrane potential and basic ion channel properties as seen in Granule cells on a hardware platform, analog model was essential.

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The inputs and outputs were analyzed using the Lab VIEW (NI, USA) software. We constructed the neuron model (adapted from the Maeda and Makino analog circuit [7,8]) on a general purpose board. The circuit had three sections which determined the size and shape of action potential, namely the RC filter circuit and two wave shaping circuits. To investigate effects of membrane resistance and membrane capacitance, the resistance and capacitance in the analog neuron was varied. The effects of noise were studied by adding corresponding noise to the input signals.

2.1 Electrical Circuit Equivalent

Neuronal action potential was modeled in an electrical equivalent circuit using a battery and a resistor. The battery represented the stored potential that was maintained by the sodium/potassium pumps, and the resistor (or conductor) represents the quantity of ions that were allowed to flow in or out of the cell. The more ions channels were opened, the more ions flow.

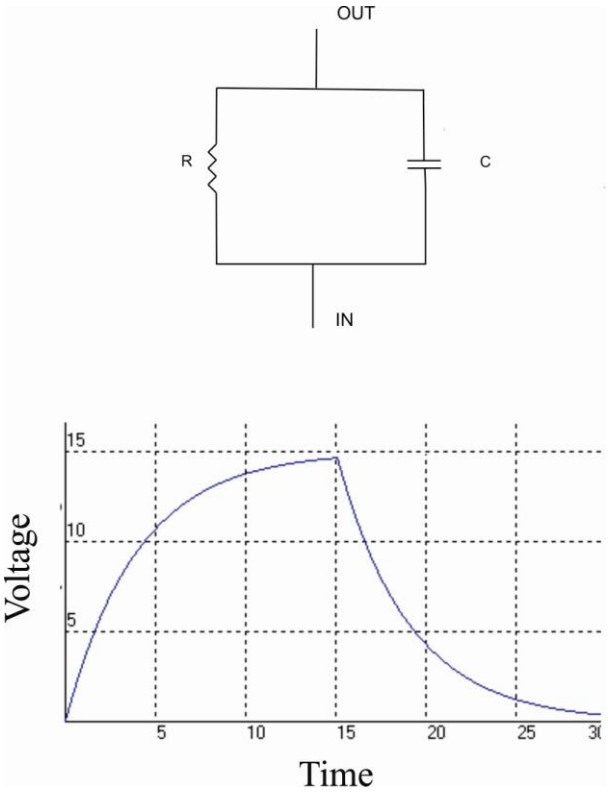

Figure 1: RC circuit and output wave form.

In other words, the resistance to flow for the ions was decreased; conductance was increased, by having more transports open. So the passive transports were basically just variable resistors. Figure 1 shows a simple RC circuit. If a voltage is applied to this circuit then the capacitor begins storing the electricity. Eventually it will reach its maximum storage capacity and simply stay there. Once the external voltage is removed however the capacitor then begins to discharge its stored power across the resistor until it has been fully discharged. The important thing to see here is that the voltage across the capacitor resists change. For example, if this circuit had only a resistor in it then as soon as the power was applied the voltage would change to its steady state value and when removed it would then go to zero immediately. But thecapacitor resists the change because it takes time for it to charge and discharge.

Figure 2 is the neural equivalent circuit with a capacitor that is in parallel with the other variable resistors. It can be noted that the K^+ and Na^+ transports were shown as variable resistors, and that the batteries associated with each were reversed representing reversal potentials of sodium and potassium. This means that current that is generated from the potassium transports flow out of the cell and currents from sodium transports flow into the cell. Another important contributor to the electrical behavior of the cell is the charge separation that is maintained across the cell membrane. This separation of charge by an insulating material causes a capacitive affect on the cell. The small leakage current [4] made up by chloride and other ions. The circuit also has a current called the I_i current, by chloride and other ions. This is the intrinsic current of the neuron.

Figure 3 shows all of the basic elements that are used to simulate a model neuron. Synaptic currents flow inward and out of the cell. The model used does not explicitly simulate every single action potential; it only simulated the overall rate of firing of the neuron at any given moment in time. This was done in an attempt to simply the simulation while still maintaining the important dynamic character of the neuron.

2.2 RC circuit based simple models

RC model based neurons are described by capacitors in parallel to a resistance and use Ohm's law as principle rule.

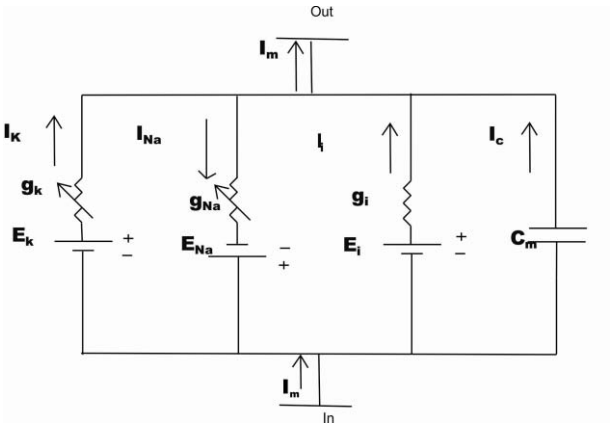

Figure 2: Neural equivalent circuit

2.3 Analog Neuron Models

The motivation behind our model was that by Hoshimiya ([7], see Figure 4). Four branches in the electrical equivalent circuit of HH

equation. V, C, R_l, E_l and I_{ext} represent the membrane potential, membrane capacitance, leakage resistance, leakage Nernst equilibrium potential and the injected DC current input, respectively. The branches (a) and (b) correspond to the V-dependent inward sodium and the delayed outward potassium ionic channels of HH equation, respectively [1, 3] and are shown in Figure 5.

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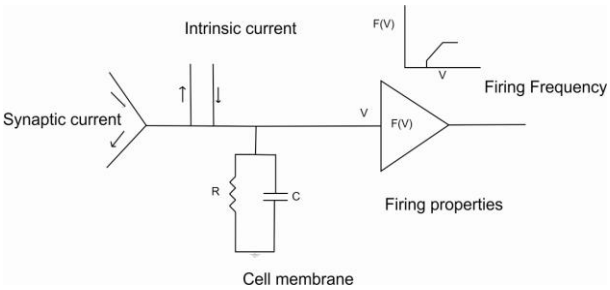

Figure 3: Basic elements of a neuron

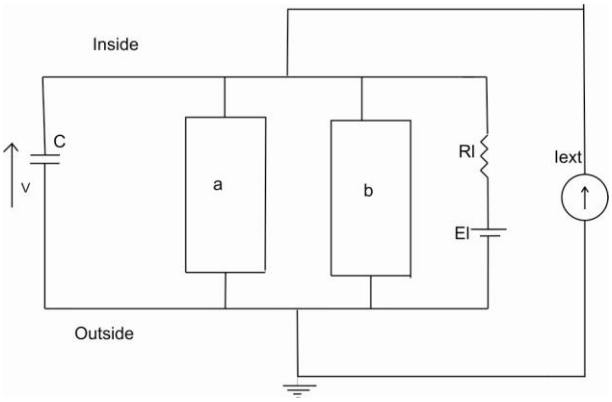

Figure 4: Equivalent circuit of HH neuron proposed by Hoshimiya [7]

Each of the circuit branches consisted of two units, the ionic current sub-circuit and the parallel conductance control circuit. The latter was marked by the dotted square. E_{Na} and E_K correspond to sodium and potassium Nernst equilibrium potentials in HH, respectively. A cut-in voltage of the transistor T1 acted as the excitation threshold. The sodium ionic current I_{Na} was switched on when the membrane potential V exceeded it. The potassium ionic current I_K was switched on when Vn exceeded the cut-in voltage of the transistor T3. In this hardware neuron model, the gating variables m and h of HH equation were not considered. Thus, the hardware neuron model was regarded as a reduced version of HH equation.

The mechanisms of action potential generation in this model are briefly described as follows: (i) I_{ext} charged up C until V exceeds the cut in voltage of T_1; (ii) T_1 was turned on; (iii) T_2 was also turned on; (iv) I_{Na} that was released from the source of E_{Na} to the inside of the membrane charged up C, and as a result, V became more positive toward E_{Na} (action potential generation); (v) I_{Na} charged up Cn slower than C; (vi) V_n shifted upward until it exceeded the cut-in voltage of T_3; (vii) T_3 was turned on; (viii) V rapidly shifted downward from Collector to Emitter of T_3. As a result, V varied suddenly down toward E_K.

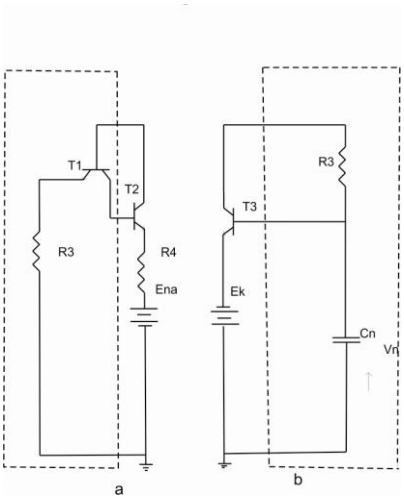

Figure 5: Circuit corresponding to a and b in figure 4.

The model developed as part of this study consisted of 3 transistors, 6 resistors, 2 capacitors and an externally injected DC current intensity (See Figure 6).

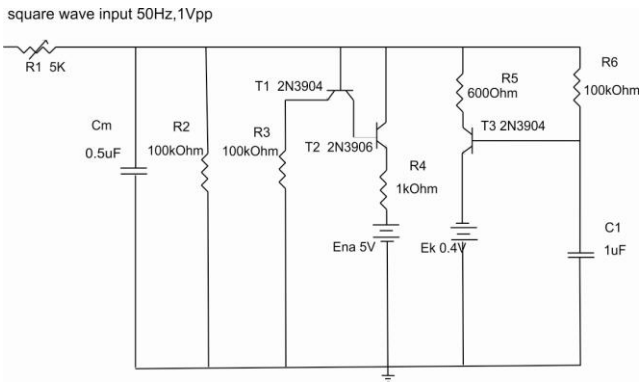

Figure 6: Simple analog neuron model circuit.

The simplified neuronal cell membrane was represented as a resistor in parallel with a capacitor. In a biological membrane, the reversal potential of an ion is the membrane potential at which there is no net (overall) flow of ions from one side of the membrane to the other. Variable parameters were external input voltage and resistance, R_1. C_m and R_1 represented the membrane capacitance and leakage resistance, respectively. The membrane potential V_m, and the refractory equivalent potential V_1 were measured at C_m and C_1, respectively. When external input current raised V_m to exceed the threshold regulated by the voltage 0.8V,

the base and emitter voltage of bipolar transistor T_1 the current flowed from constant voltage source to the capacitor via T_2.Thus an oscillation was produced. The current also flowed into C_1 whose voltage was proportional to the integral of current with respect to time. When V_1 exceeded the threshold regulated by the base emitter voltage of bipolar transistor T_3 the delayed outward current flowed from C_1 to the ground via T_3 such that repolarising phase in an action potential was obtained.

To understand the effects of Na current and K current in the membrane potential, we modified the simple neuron model to add ion channels. To eliminate the voltage E_k a diode was added in the base of transistor T_1 (See Figure 7).

This diode raised the threshold of the model above zero. We made the emitter resistance of transistor T_2 high to obtain the channel currents. The sodium current was measured at the emitter junction of transistor T_3.

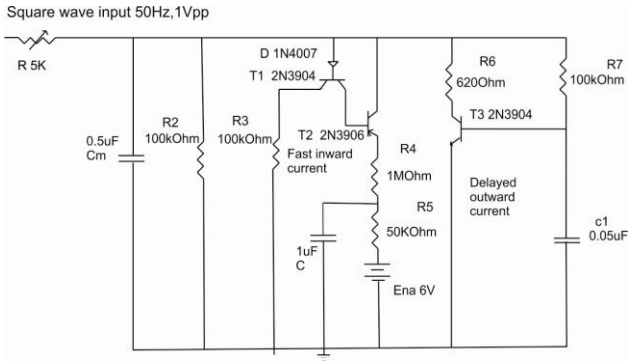

Figure 7: Analog neuron model with ionic channels.

The circuit used an RC combination on the power supply 6V to the fast inward current to limit the current to a short burst to obtain Na current. Potassium current was measured from the base of transistor T_3. We obtained spikes, which was due to the charging effect of capacitor C_3.

2.4 Computer Simulations of HH Neuron Model

Mathematical simulations were also developed for accurate biophysical comparisons. A single-compartmental HH neuron was modeled in NEURON [1] with one HH channel was inserted, R_m = 123Ω, C_m = 1 F. Random noise with mean amplitude =1.4 mV was generated and applied along with the stimulus. Membrane potential was observed in both the cases (with noise and without the noise, see Figure 10 D,E).

3. RESULTS

3.1 Action Potential

We applied a square wave with input frequency of 50Hz, amplitude of 2V peak to peak, offset of 2 and a duty cycle 5% to the analog simple neuron model (Figure 6). We got the membrane potential spikes with 1.65V amplitude with a considerable delay of seconds (see Figure.9). Enlarged single pulse analysis shows a considerable delay of 0.015sec in the output with amplitude of $1.8V_{pp}$ with 0.25 V_{offset}. (Note: All the amplitude is measured in volts and time in sec).

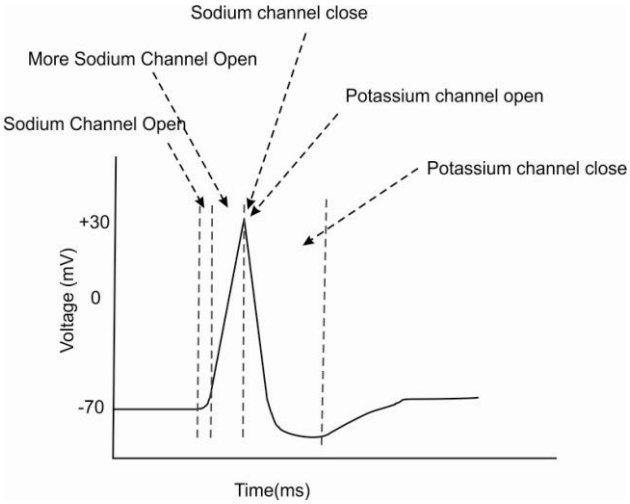

Figure 8: Action potential.

3.2 Effects of Noise on Action Potentials

To understand the impact of noise in action potential we added different types of noises with the input voltage. Figure 10 represent effects of random noise in action potential with spectral amplitude of 0.5 V. Poisson noise (see Figure 11) with mean value 0.5 V distorted the wave in terms of timing while Bernoulli noise (of trial probability=0.5, see Figure 12) distorted the wave shape and timing.

3.3 Passive and Active Properties

Passive properties are intrinsic to that of the membrane. In the analog model, while keeping membrane resistance C_m constant i.e 0.5uF and when the membrane resistance, R_m was varied, membrane voltage amplitude decreased. When the membrane resistance value is varied from 1.4KΩ to 3.6KΩ the amplitude of membrane potential varies from 1.65V to 1.25V. Keeping membrane resistance R_m as constant i.e 1KΩ and varying membrane capacitance, C_m membrane potential amplitude decreased.

Varying ionic properties allowed understanding the active properties of the model. We applied a square wave with input frequency of 50Hz, amplitude of 2V peak to peak, offset of 2 and a duty cycle 5% to the complex neuron model (Figure 7) to study the role of ionic channels in spiking (Figure 13).

Blocking Na and K channels blocked spikes and only passive transients were observed.

3.4 Modeling Bursting

Bursting is an extremely diverse general phenomenon of the activation patterns of neurons in the central nervous system and spinal cord where periods of rapid spiking are followed by quiescent, silent, periods.We adapted [5] to produce bursting phenomena. (See Figure 14) Bursting Hardware neuron model with the simple excitable hardware neuron model shown in the most important difference is that the former has two

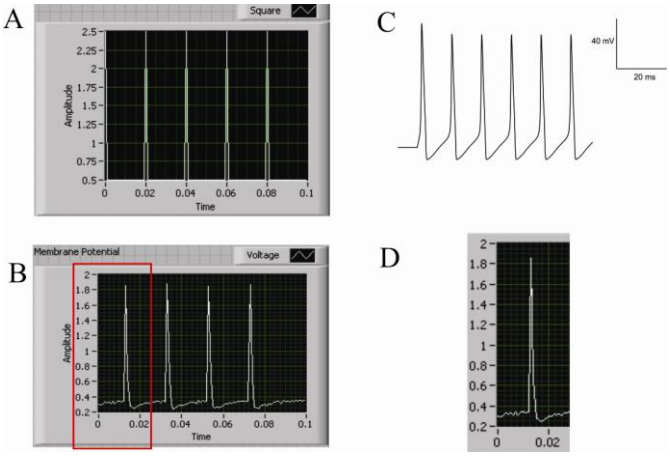

Figure 9: A shows the input stimulus; B shows output (neuronal membrane potential); C shows mathematical simulations of membrane potential recordings; D shows Action potential.

branches (b) and (b') associated with active out ward currents, while the latter has only one branch (b). The branch (b) of the bursting HH model corresponds to the refractory slow system. The branch (b') represents the refractory fast system. Here a transistor T4 is added. T4 completely rectifies the outward current of the branch (b'), since both Base-Emitter and Base-Collector units are located in reverse directions against the inward current. Therefore, the capacitor Cn cannot discharge through T4. So when T3 is turned off, Vn remains constant, leading to the plateau potential. As the result, the excitable and the refractory fast systems are able to regenerate the action potentials until the refractory slow system repolarizes the plateau potential. We obtained a typical bursting (Figure 14) by choosing the capacitor and resistor values as follows:C1:3, Cn-0.5, Cs-1.0 in mF, and RL-100, R1-200, Rs-100 in kV, and ENa-5V.

4. DISCUSSION

The paper proposes an analog neuron model that represents and 'imitates' a biophysical neuron such as a cerebellar granule neuron. The discrete components used in the design offers high flexibility, low productivity, large circuit area, high power consumption, and it can be used only for prototyping purposes

The neuron circuits were capable of aggregating input signals which contribute to the firing of the neuron. The models clearly reproduced basic passive and active membrane properties as seen in real neurons. The most important impact of this model will be its use as a learning tool. We developed the model to be accessible online as an education for undergraduate and postgraduate students. The model is a part of the Neurophysiology virtual labs and will serve as an education tool in courses such as biophysics. The models can be currently accessed from Sakshat Amrita virtual labwebsites:

http://sakshat.amrita.ac.in/VirtualLab/?sub=BIOTECH&brch=NEO&sim=passive-properties-of-a-simple-neuron&cnt=theory and

http://sakshat.amrita.ac.in/VirtualLab/?sub=BIOTECH&brch=NEO&sim=membrane-biophysics&cnt=theory

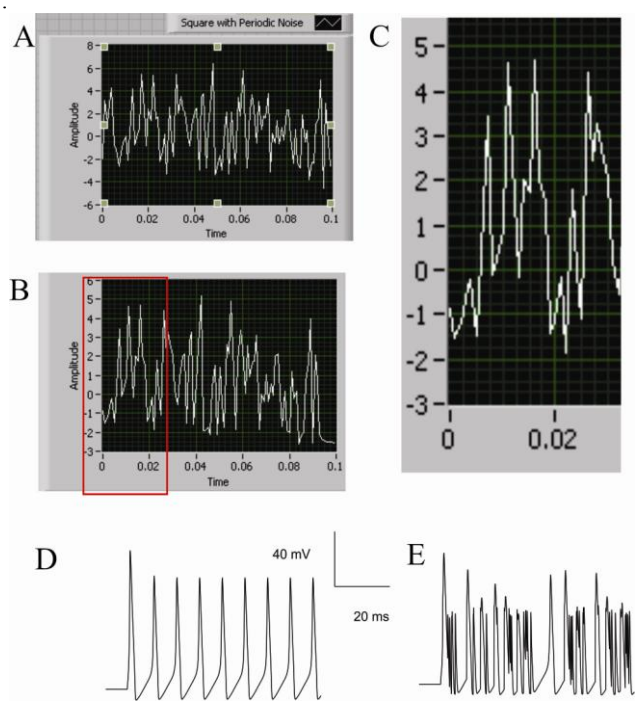

Figure 10: A represent input excitation with Periodic random noise, B the noisy output; C is zoomed output; D shows mathematical simulations of membrane potential recordings without noise; E shows mathematical simulations of membrane potential recordings with noise.

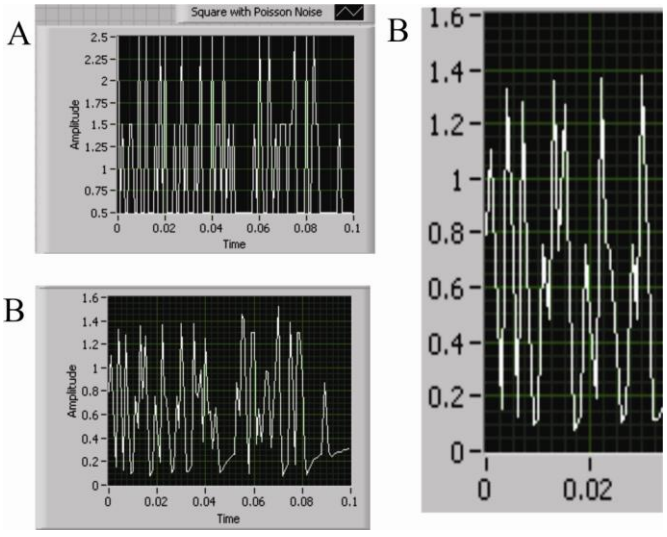

Figure 11: A represent input excitation with Poisson noise. B the corresponding noise and C represent single spike enlarged.

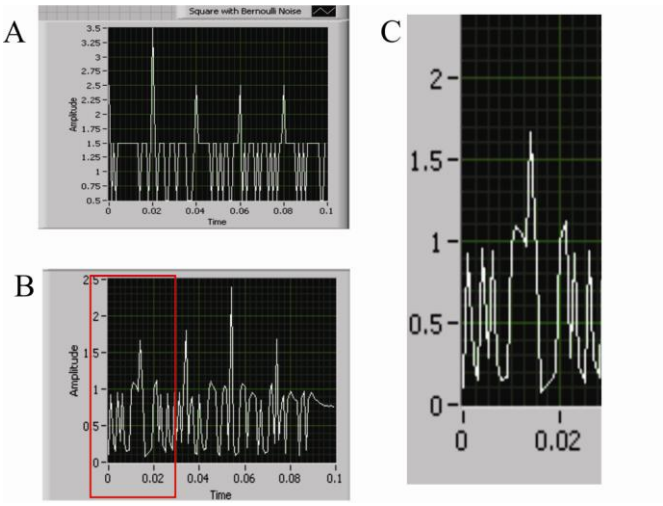

Figure 12: A input excitation with Bernoulli noise; B shows noisy output; C zoomed output.

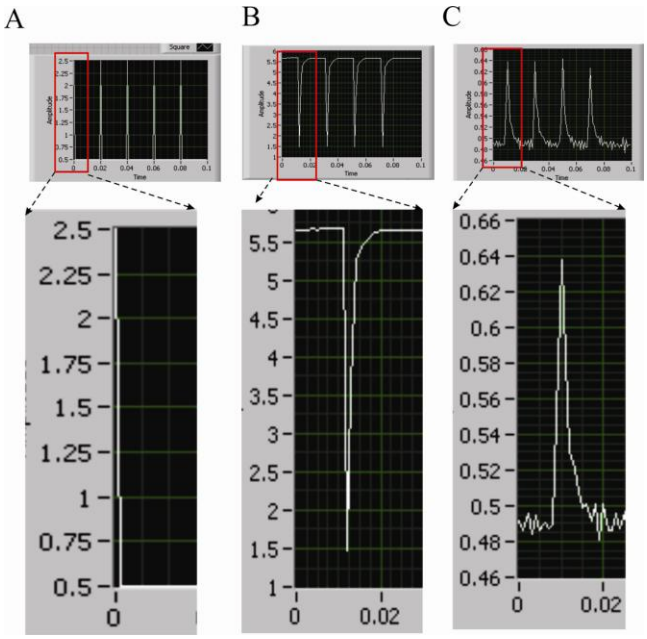

Figure 13: A shows stimulus applied to the neuron model; B voltage corresponding to the Na^+ current; C shows the voltage corresponding to K^+ current.

5. CONCLUSION

It is worthy to point out that the implementation of simple or ion-channel added neuronal circuits using inexpensive discrete components allows a convenient way to construct a prototype circuit to test the functionality of the neural cell under consideration.

Since the models with adaptation, reproduce both spiking and bursting, they can be used to construct several neuromorphic circuits for study of signal processing as in cerebellar circuitry. Cerebellar granule cells form 1011 neurons and are hypothesized

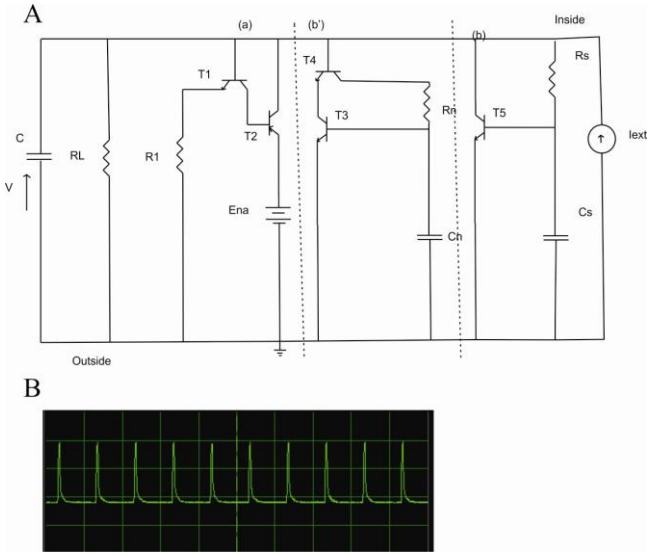

Figure 14: Hardware neuron with periodic bursting.

to perform spatial pattern recoding. Thus such hardware models would allow producing useful neuromorphic computational units for bio-inspired robotics and cognitive articulators.

6. ACKNOWLEDGEMENT

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7. REFERENCES

[1] Hines, M.L., and Carnevale, N. T., The NEURON simulation environment. *Neural Comput.*,9 (1997),1179–1209.

[2] Hodgin, A.L., and Huxley, A.F., Aquanitative discription of membrane current and its application to conduction and excitation in nerve, *J. Physiol*. 2,7 (I952) ,500-544.

[3] Hodgin, A.L., and Huxley, A.F., Currents carried by sodium and potasium ions through the membrane of the gaint axon of lologo,*J. Physiol.* 2, 6 (1952), 449-472.

[4] Hoshimiya, N., Yoshida, S., Shogen, K., and Matsuo, T., Two-terminal electronic circuit neuron model with excitable membrane *V-I-t* characteristic, Biocybernetics 35:125-130,1979.

[5] Leslie, S.S., Implementing neural models in silicon, (May 2004).

[6] Lewis, E. R., Neuroelectric Potentials Derived from an Extended Version of the Hodgkin-Huxley Model, *J. Theoret. Biol.* 10 (1965), 125-158.

[7] Maeda, Y., A Hardware Neuronal Network Model of a Two-level Central Pattern Generator, *Transactions of the*

Japanese Society for Medical and Biological Engineering, 46 (2008), 496-504.

[8] Maeda, Y,.and Makino, H., A pulse-type hardware neuron model with beating, bursting excitation and plateau potential, *BioSystems* 58(2000),93–100.