Easily Adaptable Neuron Emulator Design for Research and Education

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Motivation and Description of the Problem/Need: In the past few decades, it has become clear that neuron research is resulting in more treatments and information on brain disorders. Having a flexible architecture for both education and controlled experimentation would save neuroscientists both time and money while potentially gaining insights that are challenging to obtain by other means. The approach of creating a model to represent the neuron cell has been the main focus of this design when attempting to understand the firing behavior of these different neurons. While some other neuron models dive into the underlying structures, it is difficult to find models that are easily adaptable between neuron types and the constantly changing characteristics of their channels like conductance.

Our planned solution is to attempt to create a flexible model that focuses on parameters and structures that are commonly shared between neurons, like ionic channels. This would allow for modifications to be made to represent multiple different types, as well as develop a further understanding of how different neurons behave. We believe a solution that allows the user to adjust the values and model different neurons would be a valuable asset to both educators and researchers. For educators, it would provide an abundance of models to show students the specific underlying structure of a neuron as well as how minute changes can change the neuron's overall output. For researchers, it would provide a physical electrical model that can be easily used to run tests and apply real-world data. Our model gives the ability to have a well controlled, repeatable test environment and reduce the need for live neuron experimentation which can be time consuming and challenging work, leaving room for error.

Design goals: Our goal for this project is to generate a neuron model base design that can be easily modified, through the use of various circuit components and software, to allow the user to model different types of neuron cells, as well as allow for a deeper understanding of the underlying structures within the neuron, such as the ionic channels. To accomplish this, we used a top-down approach to define the desired adjustable parameters for the neuronal structures and map to a common framework adjustable by software control. Our objective was to generate a block diagram identifying the specialized blocks corresponding to neuron features.

Some of the specific goals derived are as follows:

- Divide specialized neuron functions into separate blocks in a functional diagram
- Develop simple circuits to map specialized neuron functions
- Create a hardware and software solution to adjust neuron parameters
- Package the neuron hardware for use in a lab setting
- Demonstrate flexibility of architecture with multiple neuron types, as shown in Figure 1.

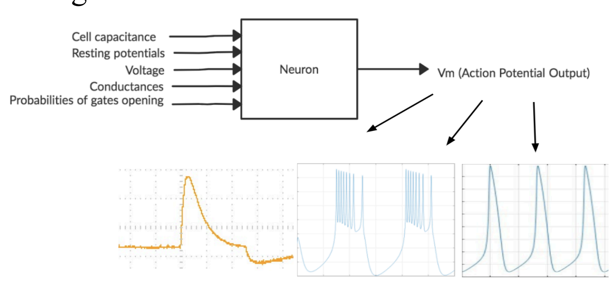

Figure 1. Shown inputs and output of our Neuron model, andexamples of the different action potentials that can be modeled.

Competition and differentiation: In the field of neuron emulation many solutions have been created, some mostly hardware, or others entirely of software in an attempt to help students and researchers understand these complex structures. However, many lack the ability to adapt between different cell types. One neuron electrical framework is the Hodgkin-Huxley model [1]. Examples of particular hardware realizations like the Roy and Lewis membrane models [2] maintain some lower level functional separation, but lack the parameter flexibility of our application to different neuron types and configurations. Another example is the Neuronify model, an educational software program created to represent neurons [3]. Although this model provides the general properties of neurons, their individual modifications are not easily made. Lastly, a fully software model, while more flexible in customization, lacks the ability to work with real test equipment for education.

Design process: In our attempt to rectify the problems within these aforementioned models, we decided to follow along the basis of the Hodgkin-Huxley neuron model [1], however also include a hardware to software interface to adjust parameters of the physical circuit, in order to represent multiple different neuron cells. Particularly, the ionic channel composition and characteristics can be modified.

To begin, we split the project into two main components: software would be responsible for the initial conditions of a neuron and feedback mechanisms relating to neurons, and hardware would consist of various circuit components to represent each of the individual ionic channels. These components were then split to develop summing circuits, voltage dividers, op-amp circuits, sections of code, and analog to digital interfaces conversions in order to improve overall progress as well as reduce chance of error during development. Figure 2 illustrates a higher level functional breakdown of these pieces.

By developing a device in this manner our aim was to target a wider demographic in the educational and research communities, that would be more accessible, adaptable, and multifunctional.

Prototype of the design: The circuit portion of our prototype has been built virtually with Multisim (National Instruments, Austin, TX) to ensure its functionality before building our physical model. Our solution relies on physically representing the smaller ionic channel structures within a neuron with circuitry. This way, the initial values of a cell's environment, such as capacitance, conductance, and voltage that give it its unique behavior and action potential shape can be altered.

Our prototype uses a combination of physical components within a circuit and defined software-based variables to give the user the ability to change these initial values and model any type of neuron. The final action potential is then displayed on a connected oscilloscope. The prototype utilizes a code developed with MPLAB X (Microchip, Chandler, AZ). This code is compiled and programmed onto a PIC18F4525 microprocessor (Microchip, Chandler, AZ). The microprocessor establishes the initial conditions of the cell including current, voltage, and the probabilities of the channels opening.

The control loop, shown in Figure 2, shows the path taken by the signal through the circuit. First converted to an analog signal with a digital to analog converter, it then passes through the many circuit components to compute the necessary activation functions, time constants, and ionic channel currents – just as those of a physical neuron. The signal, in the form of voltage, is converted back to a digital format for the microprocessor to sample and use to update the cell state. This process is repeated to create a feedback loop that shapes into the desired action potential, displayed on a connected oscilloscope.

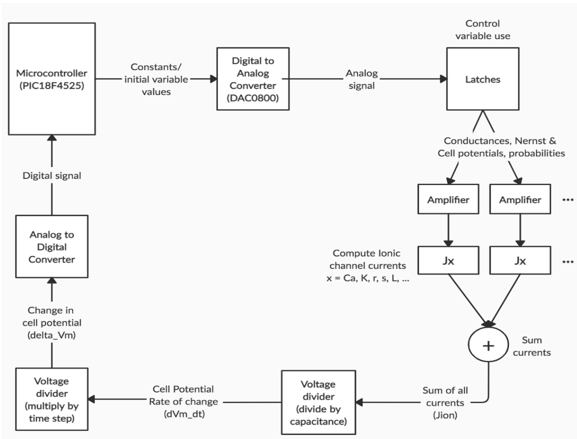

Figure 2. Flowchart showing overall path of circuitry.

Testing and results: We have been able to test our accuracy and precision while developing and integrating each functional block. Two neuron models, a pancreatic beta cell and a sinoatrial node cell, were implemented in MATLAB (Mathworks, Natick, MA) to test the flexibility and accuracy of the design. A comparison between the pancreatic beta cell model [4] and prototype values can be seen in Table 1 below reflecting errors less than 0.2 percent. Furthermore, we confirmed the accuracy of the final shape produced by our model in MATLAB and the prototype design in Multisim. Due to the top down approach, we were able to achieve our initial design goal of building specialized blocks corresponding to a neuron's ionic channels. These specialized block diagrams were then converted into small, basic circuits. We then achieved our goal of combining these together into one larger cohesive circuit that functions with software control. Our next goal is to continue implementing this cohesive circuit onto a breadboard, and finally, create a set-up so it is small and durable for a lab setting.

	Ionic channel		
	Calcium	**'s'**	**'r'**
MATLAB	-2,188.3 mV	514.5 mV	469.9 mV
Multisim	-2,185.0 mV	514.3 mV	469.8 mV
Error (%)	0.15%	0.04%	0.02%

Table 1. Compares MATLAB script values and values produced by Multisim prototype and percent errors. 's' represents ATP activated channel and 'r' represents calcium activated potassium channel.

Value proposition and potential impact: By developing a product that is accessible, small, low cost, and easily tunable to represent the incredibly small biological structures of neurons, our solution provides flexibility for further insight regarding neuron cell structure and behavior. Modifying the neuron characteristics enables further experimentation and development on different neuron cells without the challenges of using live tissue, which set our design apart. Although other neuron emulation models exist, the ability to tune our design sets it apart. Simple software changes would allow for students and researchers to be able to rapidly test and experiment with the many different components relating to these cells, by being able to have hands-on experience, as well as learn about additional types of cells in a shorter time frame.

References:

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4. Bertram R. et al. Biophys J. 79(6):2880–2892, 2000.

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