Electronic Model of Neural Adaptation

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Introduction

The behavior of neurons has been modeled with circuit elements for a long time. Hodgkin and Huxley developed their theory of action potential generation through circuit elements with active variable conductances that generated the non-linear dynamics of the action potential. Luckily for Hodgkin and Huxley, the squid axon which they studied only contained two types of active channels. It is known now that neurons can contain many different types of channels, all of which can play a substantial role in the firing properties of the neuron.

One property of neuronal firing patterns that has attracted much attention recently is neural adaptation. Adaptation was first observed when neurons would change their firing rates in the presence of a constant stimulus (ref). Originally, it was thought that this process was mediated by a single exponential time constant – a property which could easily be explained by a simple "adaptation" channel. However, evidence shows that the process of neural adaptation has different time-constants dependent on the history of the input stimuli. This history-dependent modification of neuronal firing patterns could be a useful computational tool in the nervous system – neuron firing rates are not based on local stimulus information, but on history thus providing memory on a longer timescale. Rather than exponentials, evidence shows that neurons follow a power-law based mechanism. Several computational advantages, such as time-scale independence, of power-law dynamics are discussed in Drew and Abbott.

One mystery of power-law adaptation dynamics is the implementation of such dynamics. Several implementations have been suggested (Drew and Abbott, Fairhall, Gilboa) as the biophysical mechanism for power-law adaptation. Here we show a circuit model of neuronal dynamics – based on Guy Roy's neuroFET, with an additional adaptation channel that is time-constant independent.

Methods

Spiking Neuron Circuit Implementation

The model of spiking neuron used is based on Guy Roy's neuroFET. This model was developed as an implementation of Hodgkin and Huxley's description of a neuron and uses FET properties in the linear regime to act as the voltage dependent resistors that mimic channels. To implement the dynamics of neuronal channels the voltage across the membrane capacitor is fed into wave-form shaping circuits that act to mimic the dynamics of sodium and potassium channels. These dynamics are fed into the FETs to alter their resistances and effectively open or close the channels (Figure 1).

The model neuron with only the two original channels behaved similarly to real neurons. The resting potential was -45mV, the peak of the AP was 30mV, and the half-width of the AP was 2.5 ms. For a series of action potentials no changes in firing rate was observed after the first action potential. The initial action potential was typically larger and broader than successive action potentials. After each action potential there was a hyperpolarization of the voltage across the membrane capacitor that had a peak of -60 mV and decayed back to the resting potential with a time-constant of approximately 10ms. The formation of a series of action potentials appeared to follow a Hopf bifurcation.
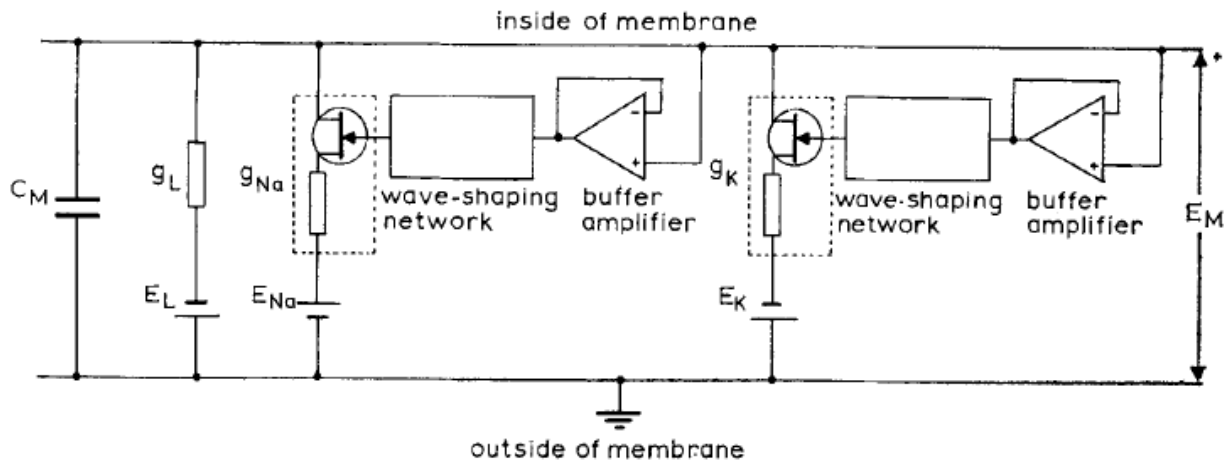
Figure 1: General idea of circuit design - using FETs in the linear regime to act as variable conductances. Wave-shaping network circuits are used to mimick the dynamics and voltage dependence of the channels.

Implementation of Adaptation

In order to implement a time-constant independent adaptation in the circuit, we first created an additional channel to serve as the adaptation channel. This channel was driven in a similar way by a wave-shaping circuit. To make the channel time-constant independent, the channel is itself driven by an RC circuit where R is in part determined by a FET acting as a variable resistor. The FET is driven by an integrator circuit which keeps track of a long time range of the circuit history. The change in the FET's conductance will change the R in the RC circuit leading to a change in the time constant of this circuit. The RC circuit's output drives the FET channel that causes the neuron to adapt.

In order for the properties of the voltages driving the FET's conductances to be appropriate, we had to amplify and bias these voltages so that they fall in the right range to alter the FET's resistances. The amplification was done so that the voltage would fall in a dynamic range spanning between 5 and 10 volts, and the bias was added so that this range would be mostly positive. In order to fine tune the parameters variable voltage dividers were added as the bias parts of the Op-Amp circuits and were set to find optimal ranges of the driving voltages.

The RC circuit that drives the adaptation channel originally used the amplified voltage as the source of the short-term channel dynamics. However, this voltage is large and tended to saturate the transistor. Instead a voltage divider was added to weaken the voltage across the source and drain of the transistor to keep it in the linear regime. Later this voltage was amplified by another Op-Amp circuit in order to return the voltage to a level that appropriately modifies the conductance of the FET regulating the adaptation channel.

Results

After the new channel was implemented and the parameters of the circuit were tweaked, the circuit showed adaptive properties. There was a clear difference between the initial firing rate and the firing rate near the end of a stimulation. The extent of adaptation could be varied by changing many of the parameters – such as the bias of the voltage driving the adaptation channel, the resistances that are in parallel and in series with the adaptation channel (these are effectively the minimum and maximum
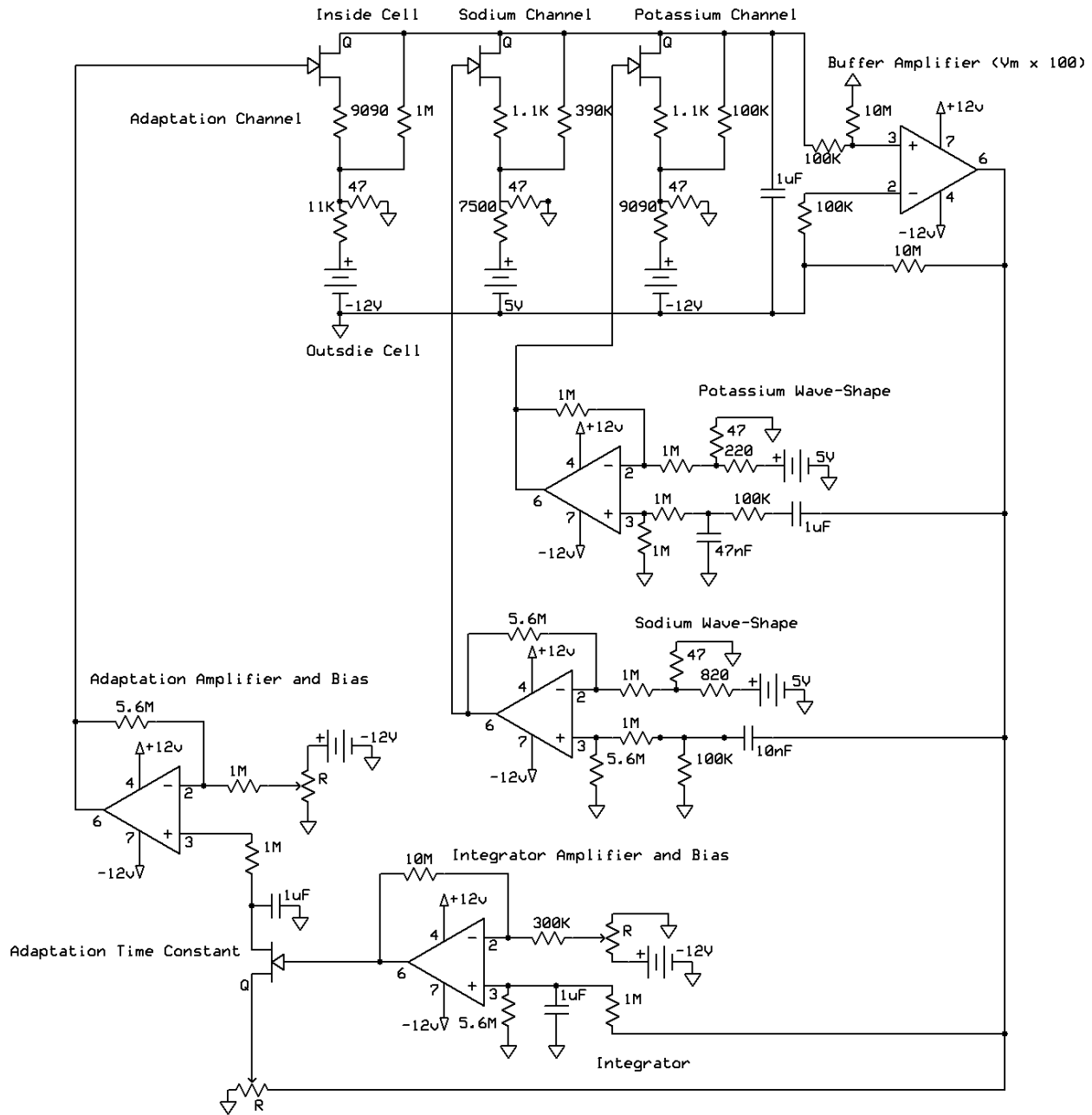
Figure 2: Complete circuit diagram used to implement adaptation dynamics

conductance values for the channel), the bias of the integrator, as well as the voltage driving the variable RC circuit. Typically, the circuit would quickly jump from the minimum and maximum adaptive rates leaving little in the duration of the more variable part of the adaptation. The dynamic range of the adaptation times is likely to improve with a more refined parameter search of the resistances and capacitances that make up the adaptation circuit.

A further problem is the tendency for the adaptation channel to completely kill the generation of action potentials. Increasing the strength of the adaptation channel (by increasing the conductance in series with the adaption FET), would often lead to the opening of the adaptation channel preventing the initiation of action potentials.
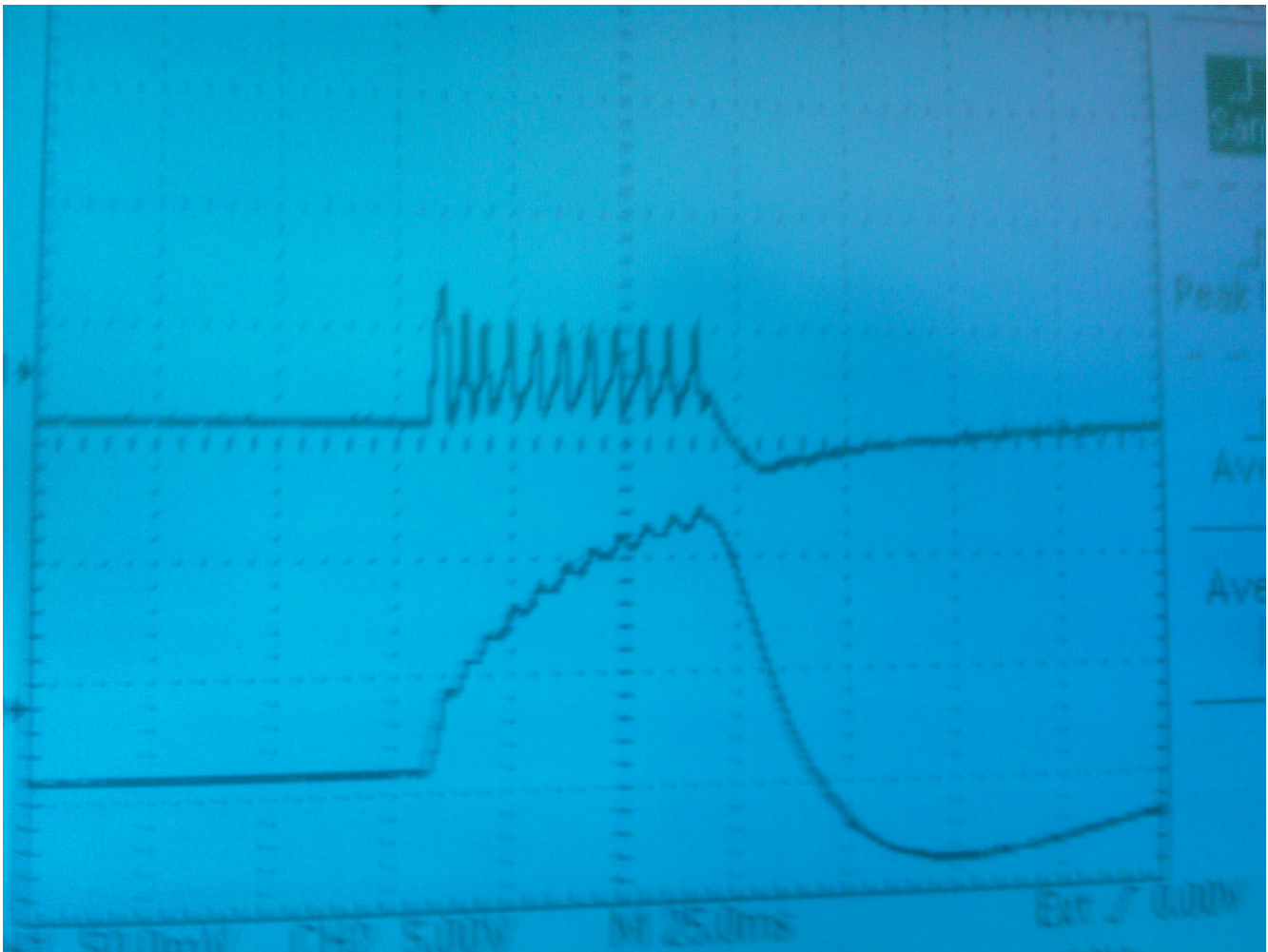
Figure 3: Adaptation of spike frequency. This neuron was given a square wave stimulation. The top trace is the membrane voltage, clearly the action potential firing rate is increasing over time. The bottom trace is the voltage driving the adaptation FET. This trace was used to calculate the time-constant of the adaptaion process.

We tested whether the circuit displayed time-constant independent neural adaptation by stimulating the circuit using a square pulse of constant duration at different frequencies – i.e. stimulation would consist of a 75 ms square pulse at 1 Hz, 2 Hz, etc. This would have a large effect on the history of the neuron, but locally each stimulation would be completely identical. We see in Figure 3 that as the stimulation frequency increases the time-constant of the adaptation circuit decreases, which corresponds to results seen in real neurons (higher-frequency stimuli leads to faster adaptation). The time constant measured was that of the voltage driving the opening of the adaption FET in what is considered to be the "cell membrane". This gave the cleanest and most sensitive measurement.

Under the same stimulation protocols we also simply counted the number of spikes that would happen for a given 75 ms square wave. Below 3 Hz the neuron fired 15 times, at 4 Hz the neuron fired only 14 times, and at 5.5 Hz the neuron fired 10 times. However, the reason the neuron only fired 10 times at 5.5 Hz was not due to adaptation, rather it was due to the adaptation current completely inhibiting the generation of action potentials. There was a clear, but slight, showing of adaptation though at 3-4 Hz as 1 less action potential was generated during the same stimulus duration.
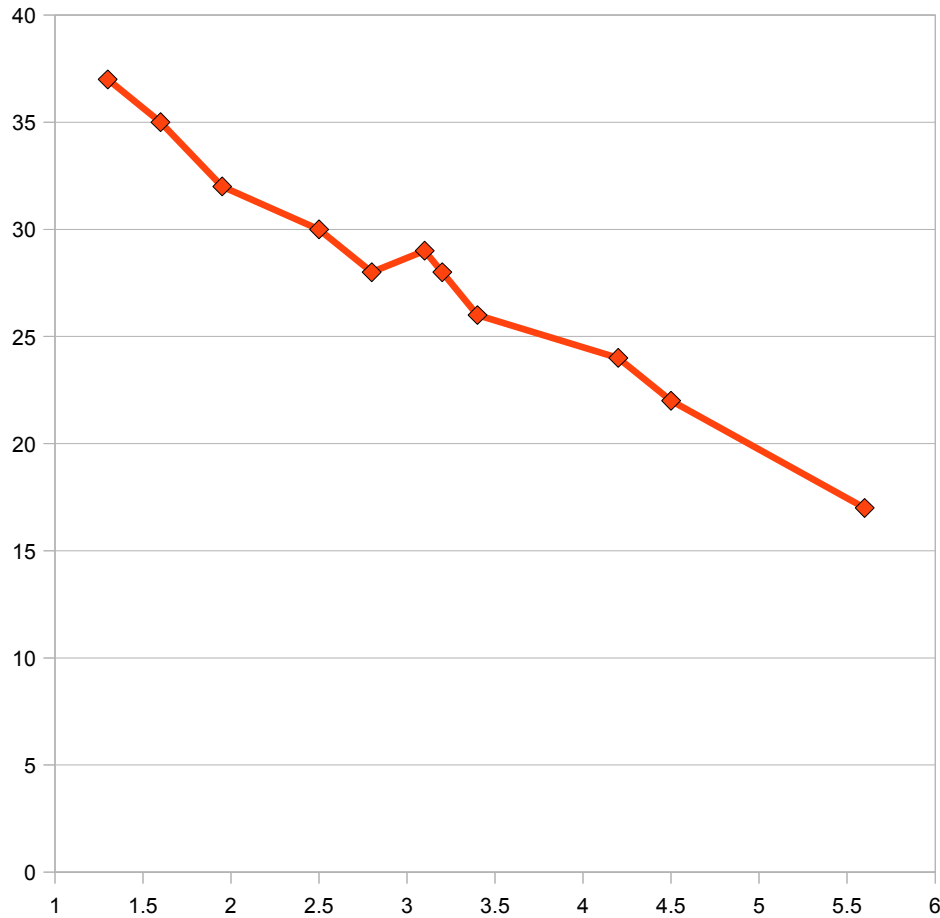
Figure 4: Time constant as a function of stimulus frequency. The same 75 ms square pulse was delivered as a stimulus to the neuron at different frequencies. At higher frequencies the time-constant which governs the inhibitory voltage regulating the adaptation FET decreases.

Discussion and Future Directions

We presented here a circuit implementation of time-scale independent neuronal adaptation. However, the sensitivity and dynamic range of the properties of the circuit were limited and could be much better refined through modification of several parameters. The spiking dynamics also can be improved, as the ion driving potentials were calculated based on voltage sources of 5, 15, and -15 Volts, where as in reality these voltages were not accurate. This may play a role in the oddity of the first action potential.

The dynamics of the system covered three qualitative regimes (2 bifurcations). The lower regime was non-spiking. The membrane dynamics act oscillatory around the equilibrium value determined by the input current. This implies that the eigenvalues of the underlying dynamical system are not real. This behavior of the circuit is unlike what is considered to be typical of a neuron – comare with the integrate and fire model. The oscillatory behavior prevented the neuron from acting as a classical integrator and long weak pulses of current would not lead to action potentials. The second regime (which may or may not really be a bifurcation), was when the neuron fired it's single, larger and wider action potentials. After the first action potential, the neuron would then oscillate and decay to

equilibrium. The third regime, was a Hopf bifurcation. The neuron now oscillated around an unstable point and entered a limit cycle, where each loop was an action potential. Without the adaptation current, once the bifurcation was reached the neuron would fire action potentials as long as the stimulation was held. The oscillatory nature of the system may have also contributed to the low-levels of sensitivity of the adaptive properties. If the intrinsic dynamics could be changed such that the eigenvalues become real, then the neuronal dynamics may behave more like the commonly accepted class of neurons. *(Looking further at the dynamics of the circuit would be a really good idea – I guess the state variable are the voltages across the capacitors? The spike-generation system has 4 capacitors (one holding the state variable of membrane voltage), and I guess looking at high-dimensional dynamical systems is typically a problem. It seems that the system could also be simplified to just 2 state variables a-la Morris-Lecar and Fitzhugh-Nagumo. It would be interesting to see if we could get the system to not oscillate in the subthreshold regime, and look at the reasons how it would get into the more classical neuron mode.)*

Our implementation of neuronal adaptation is not very biologically plausible. Simulations of adaptation suggest other possible mechanisms that may be easily implemented in a similar circuit. Lundstrom et al suggest that the multiple time-scales are due to the interaction of several time-scales overlapping. A circuit implementation could have several adaptation channels each with their own characteristic time-constants spanning over a large range. They suggest that this mechanism does not completely account for all of the effects of adaptation, and that slow inactivation of sodium currents may also be needed to create power-law dynamics. This could be implemented through another wave-shaping circuit that acts to slowly close the sodium FET, which could be added with the current wave-shaping circuit for the sodium FET.

References

Lundstrom, B. N., Higgs, M. H., Spain, W. J., Fairhall, A. L. (2008) Fractional differentiation by neocortical pyramidal neurons. Nature Neuroscience 11(11): 1335-1342.

Gilboa, G., Chen, R., Brenner, N. (2005) History-Dependent Multiple-Time-Scale Dynamics in a Single-Neuron Model. The Journal of Neuroscience 25(28): 6479-6489.

Drew, P. J., Abbott, L., F. (2006) Models and properties of power-law adaptation in neural systems. 0Journal of neurophysiology 96(2): 826-833.

Hodgkin, A., Huxley, A. (1952) A quantitative description of membrane current and its application to conduction and excitation in nerve. Journal of Physiology 177: 500-544.

Roy, G. (1972) A simple electronic analog of the squid axon membrane. IEEE Trans Biomed Eng. 19(1): 60-63.