

A rule-based firing model for neural networks

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Abstract—Full multi-compartment multi-channel neuron models are state of the art for single neuron modeling but are CPU intensive. This makes them unsuitable for network modeling, where simulation of 10,000 or more neurons is desirable. For this reason, most network models utilize highly simplified models such as single state-variable integrate-and-fire units. This compromise has the disadvantage of eliminating most biological detail, much of which can be expected to lead to interesting and important network behavior. To reconcile these opposing computational and biological demands, we developed a rule-based firing (RBF) model incorporating a number of synaptic and cellular responses which are activated as needed. The rules produce effects that include adaptation, bursting, depolarization blockade, Mg-sensitive NMDA conductance, and post-inhibitory rebound. By utilizing pre-calculated waveforms and avoiding linked differential equations, network simulations are entirely event-driven, with no integration overhead. The model has been further optimized by use of table look-ups in lieu of run-time calculation.

Keywords: neural networks, computer models, simulation

I. INTRODUCTION

Classical artificial neural network (ANN) models utilize simple sum-and-squash analog units which add their inputs linearly and then pass them through a nonlinear function to produce a bounded output. Networks of these units can produce many interesting behaviors. However, the utilization of ANNs as direct models of the nervous system is limited by their use of a single continuous state variable. This state-variable is assumed to be a stand-in for the rate of firing of nerve cells. Although rate coding is likely to be important in the brain, these simple ANN models do not readily capture other coding schemes, such as those involving synchronization and oscillation, that are also likely to be essential.¹

Integrate-and-fire neurons provide the critical missing detail: spike generation. They can therefore be utilized to design networks which show these additional properties that require clear signal timing. A number of interesting results regarding oscillation and phase locking have been obtained with such model neurons.^{2],[3}

The ultimate level of network modeling realism is to utilize full compartment models with multiple voltage-sensitive ion channels in all compartments. However,

such models are extremely expensive computationally. Additionally, these models produce complex, difficult-to-understand dynamical behaviors that makes them very hard to tune to produce particular input/output responses. Altering the many internal parameters of these models will typically change several of the neuron response patterns that one wishes to individually explore in a network setting.

For these reasons, we have developed a rule-based firing model that reproduces some of the complexity of real neurons with little computational overhead and with ready access to parameters that are likely to be critical for network dynamics. The basic rule remains the same as that of the integrate-and-fire model: fire when the state variable exceeds a fixed threshold. Additional rules are then added as needed to capture a variety of biological details.

II. METHODS

We have developed the RBF model to be entirely event driven: state variables are only updated when an event is received. These events can be 1. external synaptic events from another neuron or a stimulator; 2. internal events indicating that the unit must now update some state. A simple example of the latter is a refractory period. The unit is refractory (ignores input) during a fixed period of time following spike generation. At the end of this period, it needs to update its internal state in order to indicate that it is no longer refractory.

Most external inputs produce a step increment in one of the internal state variables. These state variables then decay exponentially back towards resting state. By using table look-up, we avoid run-time calculation of these exponentials as well as other response waveforms. Additionally, random variables are precalculated and stored in arrays so as to avoid calls to computationally expensive pseudo-randomization routines.

The techniques and simulations described here are implemented in the NEURON simulator (www.neuron.yale.edu).^{4],[5],[6} Although NEURON is a compartment model simulator, it features an efficient event queue utilizing a splay-tree algorithm.^{4],[7],[8} The NEURON integrator can be turned off during

event-driven simulations so as to offer no time- and minimal space-overhead. Individual neuron integrator can also be turned on to run hybrid networks with both compartmental and rule-based cells.⁹

III. RESULTS

As noted above, the primary rule is that of the integrate-and-fire neuron: the neuron fires when the activation state crosses a fixed threshold. However, in the RBF model, the activation state is not itself an independent variable but is instead taken as a total membrane voltage V_m that is the sum of four state-variables that represent various types of input as well as an additional state which responds to spiking. The four external state variables correspond to the major types of synaptic inputs: the excitatory AMPA and NMDA inputs; and the inhibitory GABA_A and GABA_B inputs. (AMPA, NMDA as used here do not refer to the actual chemicals but to the excitatory synaptic connections associated with their associated receptors.) The internal state variable corresponds to a summed afterhyperpolarizing potassium current (AHP) which is triggered following spike generation. The spike itself does not need to be internally represented at all but is simply an event that can be added to the event queue for delivery to postsynaptic cells to which the current cell is connected.

The response to an individual input is a voltage jump after an axonal delay. Weight W_{AMPA} determines the size of the voltage step whose amplitude is also proportional to the distance from the E_{AMPA} reversal potential: $V_{AMPA}^{step} = W_{AMPA} \cdot \frac{V - E_{AMPA}}{E_{AMPA}}$ (E_{AMPA} in the denominator is a normalization). Note that W_{AMPA} is a unitless weight, not a conductance. W_{AMPA} converts a driving force to a step voltage increment due to the AMPA activation. This step is added to a calculated ongoing V_{AMPA} which represents the summed AMPA EPSP and is maintained as a separate state variable. Following a step, V_{AMPA} decays with time constant τ_{AMPA} . For convenience, parameters are expressed in biological units, so that for example resting membrane potential and E_{AMPA} can be different in different cells.

As noted above, the model maintains separate V_{syn} synaptic state variables for V_{NMDA} , V_{GABAA} and V_{GABAB} with suitable time constants and reversal potentials and an intrinsic AHP “current,” augmented whenever a spike occurs. The AHP is a negative current that not only adds into the global V_m but is also used to directly augment the refractory period. An additional adaptation mechanism is provided by decrementing the synaptically driven V_{syn} state variables after each spike. Because the units are rule-based, their firing tends to be

highly regular which in a network setting could produce unwanted coincidences. As a symmetry-breaking procedure, jitter can be added as a small additional random delay in spike firing time.

At least two kinds of burst spiking are commonly seen in neurons: driven bursts riding on top of powerful synaptic stimulation and an intrinsic bursts produced by the intrinsic mechanisms of the neuron itself. Both of these burst types can be produced by the RBF model with the latter emerging from a rule that determines burst length and frequency. Here again, the bursts can be varied by adding jitter or by varying the length or frequency.

Depolarization blockade of spiking occurs in a Hodgkin-Huxley model neuron, as in reality, where the voltage rises beyond the domain where sodium channel activation and deactivation occur, preventing the characteristic action potential oscillation. In the RBF model, depolarization blockade occurs when a fixed upper threshold is reached. RBF rules also emulate the influence of NMDA activation, with its tendency to produce longer and stronger depolarizing effects in the presence of postsynaptic depolarization. In the RBF model, this influence is instantiated using the standard Mg⁺⁺ unblocking equation: $1/(1 + \exp(0.062 \cdot -V_M) \cdot Mg/3.57)$.¹⁰ Note that the use of realistic units (mV) for voltage rules allows us to use the standard Mg⁺⁺ dependence equation. We have not yet implemented learning rules associated with NMDA activation.

NMDA shows cooperativity based on postsynaptic voltage: increased activation leads to greater depolarization leads to further activation. Hippocampus shows an intriguing image of this postsynaptic cooperative effect: GABA_B, a prolonged, inhibitory input, demonstrates a cooperativity based on the strength of the presynaptic burst.^{11],[12} Thus a large presynaptic burst can produce a very substantial inhibition. However, the effect of inhibition is often dual, since it effects an immediate cessation of activity but also encourages a subsequent facilitation of firing through an anode-break mechanism. This rebound effect is particularly prominent in thalamo-cortical cells but can be seen to a lesser extent in many cell types.¹³

In the RBF model, increasing presynaptic burst size produces larger IPSP and greater rebound firing. This complex phenomenon is regulated though a set of rules: 1. a delay between presynaptic burst firing and inhibitory postsynaptic potential (IPSP) initiation (based on the delays required for second messenger transmission); 2. burst size cooperativity¹⁴ 3. post-IPSP rebound as a percentage of the IPSP size.

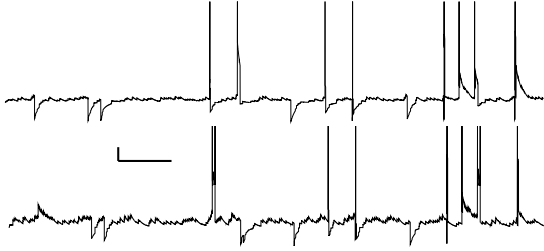


Fig. 1: Activity in a network of 1000 excitatory and 40 inhibitory cells. Representative inhibitory (top) and excitatory (bottom) cell voltage traces (scale:10 mV;100 ms)

We have begun to utilize these simulacra in network models (Fig. 1). Since these simulations have no integrator overhead, they can run arbitrarily fast, depending on the amount of spiking in the model. As spike frequencies increase, queue overhead imposes increasing computational burden. This dependency on activity patterns makes it difficult to benchmark the simulation against other model types, requiring that the average firing of two implementations be matched on a per-cell-type basis (compartment models of some cell types will be far more computationally intensive than those for others). In general, we can expect substantial speed ups over integrated simulations unless event frequencies approach the inverse of the time-step required for numerical integration of compartment models. A typical time-step for a fixed time-step integration would be 0.025 ms corresponding to a 40 kHz integration frequency. Such an event frequency would occur in a network with a convergence of 1000 cells each actively spiking at 40 Hz. Although pyramidal cells have order 10000 synaptic boutons, the convergence is considerably less due to redundant connectivity. Additionally, under most conditions the several thousand presynaptic cells would not be expected to all be simultaneously strongly activated.

IV. DISCUSSION

In addition to advantages of speed, the RBF model lays out neural parameters explicitly so as to permit easy manipulation. By contrast, in a compartment model, phenomena such as adaptation and post-inhibitory rebound are dependent on several voltage-sensitive ion channels, each of which has its own complex parameterization,¹⁵ two-steps removed from the phenomenon of interest. Alteration of one of these channel-level parameters will typically have multiple effects, altering not only the neuron-level phenomenon of interest but often profoundly altering other neuron responses as well. For

example, altering adaptation by changing the strength of one or more of the many potassium channels responsible for adaptation will likely change burst patterns as well.

The RBF model provides a framework that can incorporate other rules as needed in particular systems where they are thought to be important. For example, some neurons have prolonged bursts with characteristic firing patterns.¹⁶ These patterns can be incorporated into the rule based either by constructing an analytically calculable dynamical rule or by providing a simple cut-and-paste spike-form. In the latter case, jitter and length variation rules would then be added to prevent stereotypy.

An interesting, and difficult, additional rule-set would incorporate input/output relations from dendritic inputs. There is considerable debate as to whether dendrites simply provide reach, with all inputs being handled equally, or provide substantial signal processing. In the latter case, it is possible that the dendrites make the cell into the equivalent of an entire neural network of simplified units.¹⁷ In this case, it might be possible to represent dendritic fields as individual RBF units with specialized rule base. Alternatively, the dendritic transform might be a complex mapping that could be simulated by using a multi-dimensional table look-up.

In some cases, additional rules can be incorporated by providing waveforms copied from electrophysiological records. More flexible rules can be arrived at by emulating the behavior of the more complex compartmental models. In this case, RBF units can be run together with compartmental simulations in NEURON with use of a fitting algorithm controlling RBF unit parameters.

These hybrid networks, incorporating RBF units with compartment models at varying levels of complexity will also be valuable for confirming the adequacy of RBF activity patterns by comparing them to compartment model activity within the network context. Compartment models have the advantage of allowing testing of specific ion channel alterations such as occur with the application of drugs and other neuromodulators. Observed neuron-level changes can then be used to develop additional rules to assess pharmacotherapeutic effects.

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- [1] W. Lytton, *From Computer to Brain*. New York: Springer Verlag, 2002.
- [2] N. Brunel, "Dynamics and plasticity of stimulus-selective persistent activity in cortical network models," *Cerebral Cortex*, vol. 13, pp. 1151–1161, 2003.
- [3] —, "Dynamics of networks of randomly connected excitatory and inhibitory spiking neurons," *Journal of Physiology, Paris*, vol. 94, pp. 445–463, 2000.
- [4] M. Hines and N. Carnevale, "Discrete event simulation in the neuron environment," *Neurocomputing*, vol. 58, pp. 1117–1122, 2004.
- [5] —, "Expanding NEURON's repertoire of mechanisms with NMODL," *Neural Computation*, vol. 12, pp. 995–1007, 2000.
- [6] —, "Neuron: a tool for neuroscientists," *The Neuroscientist*, vol. 7, pp. 123–135, 2001.
- [7] D. Jones, "An empirical comparison of priority-queue and event-set implementations," *Comm. ACM*, vol. 4, pp. 300–311, 1986.
- [8] D. Sleator and R. Tarjan, "Self adjusting binary trees," *Proc. ACM SIGACT Symposium on Theory of Computing*, pp. 235–245, 1983.
- [9] W. Lytton and M. Hines, "Independent variable timestep integration of individual neurons for network simulations," *Neural Computation*, vol. in press, 2005.
- [10] C. Jahr and C. Stevens, "A quantitative description of nmda receptor-channel kinetic behavior," *Journal of Neuroscience*, vol. 10, pp. 1830–1837, 1990.
- [11] P. Dutar and R. Nicoll, "A physiological role for GABA_B receptors in the central nervous system," *Nature*, vol. 332, pp. 156–158, 1988.
- [12] C. Davies, S. Davies, and G. Collingridge, "Paired-pulse depression of monosynaptic GABA-mediated inhibitory postsynaptic responses in rat hippocampus," *J Physiol (Lond)*, vol. 42, pp. 513–531, 1990.
- [13] W. Lytton, A. Destexhe, and T. Sejnowski, "Control of slow oscillations in the thalamocortical neuron: A computer model," *Neuroscience*, vol. 70, pp. 673–684, 1996.
- [14] A. Destexhe and T. Sejnowski, "G-protein activation kinetics and spillover of gamma-aminobutyric acid may account for differences between inhibitory responses in the hippocampus and thalamus," *Proc Nat Acad Sci USA*, vol. 92, pp. 9515–9519, 1995.
- [15] L. Borg-Graham, "Modeling the non-linear conductances of excitable membranes," in *Cellular and Molecular Neurobiology: A Practical Approach*, H. Wheal and J. Chad, Eds. NY: Oxford, 1991, pp. 247–275.
- [16] A. Destexhe, D. Contreras, M. Steriade, T. Sejnowski, and J. Huguenard, "In vivo, in vitro and computational analysis of dendritic calcium currents in thalamic reticular neurons," *J Neurosci*, vol. 16, pp. 169–185, 1996.
- [17] P. Poirazi, T. Brannon, and B. Mel, "Arithmetic of subthreshold synaptic summation in a model ca1 pyramidal cell," *Neuron*, vol. 37, pp. 977–987, 2003a.