Ion Channel Modeling with Analog Circuit Evolution

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ABSTRACT
We propose that analog electrical circuits are a natural representation for modeling the dynamical systems that arise in neuroscience. Here we use analog circuit evolution, a reverse engineering technique designed to search through analog circuit space, to automatically design circuit models of ion channel behavior. Results comparing several different multiobjective and coevolutionary techniques demonstrate the importance of evaluating the fitness of evolved circuits under multiple behavioral conditions.

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Algorithms, Design, Performance, Reliability, Experimentation

Keywords
Analog Circuit, Dynamical Systems, Evolutionary Algorithms, Circuit Evolution, Ion Channel, Neuroscience, Physiology, Hodgkin and Huxley

1. INTRODUCTION
Inspired by the classic work of Lapicque, Hodgkin and Huxley [5,7], we propose that analog electrical circuits are a natural representation for many classes of dynamical systems that arise in neuroscience. Further, we observe that analog circuit evolution by genetic programming is a powerful and well-established technique for reverse engineering electrical systems [6]. Here, we consider the natural combination of these ideas and apply analog circuit evolution to the reverse engineering of neurophysiological systems. In contrast with our previous work exploring a similar reverse engineering approach [2], here we evaluate the performance of several different evolutionary techniques, most of which have not been previously applied to circuit evolution. In addition, we consider the need to robustly model ion channel behavior under many physiological conditions instead of just one, and how this need can be balanced against the computationally expensive Spice simulations necessary for nonlinear analog circuit evolution.

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2. METHODS
Ground truth Hodgkin-Huxley potassium ion channel data was obtained using NEURON 7.0 [4]. To evaluate the fitness of a candidate circuit produced during evolution, we simulated the circuit using Spice, probed it with the same stimulus used in NEURON, and compared the resulting voltage responses. We defined the “universe” as consisting of six possible physiological conditions, or six stimulus waveforms: step pulses of amplitude 0.3 nA, 1 nA, and 3 nA, and 500 Hz sinusoidal pulses with amplitudes of 0.3 nA, 1 nA, and 3 nA.

For automated circuit design, we employed a variation on Koza’s analog circuit evolution technique [6]. Initially, a population of candidate sub-circuits was randomly created and placed in a variable portion of an otherwise invariant embryonic circuit as shown in Figure 1. We represented circuits with a direct schematic-based encoding, in which components and their connections are stored as flat lists. Seven electrical components were used as the building blocks with which evolution operated. For full details on the representation, see [2].

We evaluated the performance of six different multiobjective and coevolutionary algorithms for circuit evolution, which we refer to as the “primary evolution techniques”. In addition, four secondary variations on each of the six primary techniques were employed, giving a total of 24 distinct analog circuit evolution algorithms.

The six primary evolution techniques were 1) Single Objective, 2) Active Coevolution, 3) Multiobjective Simple Fitness, 4) Multiobjective Pareto Fitness, 5) Incremental Simple Fitness, and 6) Incremental Pareto Fitness. The Single Objective technique employed a single stimulus waveform to probe a candidate circuit, whereas in the Active Coevolution technique, the stimulus antagonistically coevolved in order to maintain selection pressure on the circuit population [1]. In the Multiobjective Simple Fitness and Multiobjective Pareto Fitness techniques, all six possible targets were used to evaluate the fitness of every circuit in every generation. In the Multiobjective

Simple Fitness technique, the fitness of a circuit was quantified as the sum of the difference between the circuit’s behavior and the target behavior for each of the six targets. For the Multiobjective Pareto Fitness technique, the six fitness cases were considered to be distinct, equally important objectives. We used the NSGA-II multiobjective optimization algorithm to optimize for all six fitness objectives simultaneously [3]. For the Incremental Simple
Fitness and Incremental Pareto Fitness techniques, an evolutionary run started with a single target. After N generations a second target was added, after N more generations a third target was added, and so on. For the Incremental Simple Fitness technique, when targets were added, they were combined into one fitness score and for the Incremental Pareto Fitness technique, targets were added as separate objectives as in Multiobjective Pareto Fitness above.

The secondary evolution techniques were inspired by recent work showing that using genotypic age as an explicit objective is a powerful way to reduce bloat and maintain diversity [8]. Here we tried four variations on this idea: fitness, age-fitness, size-fitness, and age-size-fitness optimization. Age is defined as in [8] and size is defined simply as the number of components in the circuit. Like age, size is to be minimized.

RESULTS

We tested the ability of analog circuit evolution to reverse engineer the Hodgkin-Huxley potassium ion channel by performing 10 trials for each of the 24 circuit evolutionary algorithms. Each trial lasted for a total of 7200 circuit evaluations. Stimuli were changed every 1200 generations for Active Coevolution and added every 343 generations for the incremental techniques. All population sizes were 256. We found that age-fitness optimization performed as well as or better than any other secondary evolution technique for each of the six primary evolution techniques; these results are shown in Figure 2. The error plotted in each panel of Figure 2 is the sum of the errors for each of the six training stimuli. Like age, size is to be minimized.

The Multiobjective Simple Fitness and Incremental Simple Fitness techniques appeared to outperform the other techniques for this difficult hardware evolution problem. This suggests that fitness evaluations including several different input/output targets are important to prevent overfitting for any one target. However, there is no clear advantage to presenting these multiple targets incrementally or all at once from the beginning of the evolutionary run. As we scale the problem to encompass the fully automated design of complex neuromorphic circuits used in biomedical applications, understanding the advantages and disadvantages of the incremental vs. “all at once” approaches will likely be of increasing importance.

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