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S. Saighi, Y. Bornat, J. Tomas, S. Renaud. Neuromimetic ICs and System for Parameters Extraction in Biological Neuron Models. International Symposium on Circuits And Systems 2006, ISCAS06, May 2006, sland of Kos, Greece. pp.4207-4210. hal-00181370

HAL Id: hal-00181370 https://hal.science/hal-00181370

Submitted on 23 Oct 2007

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Neuromimetic ICs and System for Parameters Extraction in Biological Neuron Models

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Abstract—This paper presents an analog neuromimetic integrated circuit and an associated system dedicated for experiments of parameters extraction in biological neuron models. The IC based on Hodgkin-Huxley (HH) formalism computes in real-time and continuous mode. The dedicated system is a PCI board that is able to program dynamically the neuron model parameters in the IC. The full system, which includes the IC and the PCI board, is used to build a new hardware/software technique to extract biophysics parameters from biological neuron. This technique could be helpful for the neuroscientists proposing an alternative to voltage-clamp technique. For that, the new technique will use optimization algorithms to be efficient.

I. INTRODUCTION

Since the first silicon neuron from M. Mahowald and R. Douglas [1], research groups have designed and used analog integrated circuits to integrate neuromorphic systems. Among those neuromorphic items, we can isolate two groups. The first one consists in bio-inspired systems, designed to develop new solutions for engineering questions. The designers use biological principles to build new and more efficient systems about vision [2] [3], attention [4] and learning [5]. The second type are neuromimetic systems that use engineering means and tools; those systems are developed to address neurosciences questions, like the comprehension of central pattern generator [6], rhythmic motor control [7], learning [8] or vision processing [9].

Neuromimetic systems can also be helpful tools for neurophysiology experiments. For example, to specify a biological neuron, neuroscientists use the voltage-clamp technique [10]. This is a long process, where the in-vitro cell activity is measured in a way that it fits one by one ionic channel while measuring the cell surface area and the membrane capacitance. Another technique is to use optimization algorithms to identify the electrical behavior of the observed cell to a mathematical model. When the neuron model is based on the Hodgkin-Huxley formalism, as many as fifteen parameter values have to be fitted for a simple three conductances neuron. If optimization algorithms are computed using a software solution, the computation power of the system [11] becomes quickly a key issue when handling so many parameters. Hardware computation using VLSI ASICs is a solution in such a case. We have already

designed analog neuromimetic integrated circuits based on Hodgkin-Huxley formalism, including the description of calcium-dependent channels [12]. One of the last neuromimetic integrated circuit (IC) that we have designed is a mixed analog-digital chip. Its main features are: it simulates in biological real-time the neuron activity (membrane potential); it is able to process models with onchip dynamically programmable parameters. The ICs are hosted in a custom system, and communicate via a PCI interface with user interface software that controls the neuron models parameters and the simulation progress [13]. In such a system, where the neural activity is computed by dedicated ICs, the host computer is available during the simulation for calculating optimization algorithms.

We will present in this paper the design of analog neuromimetic ICs; results will be shown where analog IC neurons achieve neural simulations in biological real-time but also faster than the biological real-time. This configuration will increase the efficiency of our hardware/software system when identifying a biological neuron. We will end up by the presentation of the complete system developed to process the optimization technique.

II. THE MODEL IMPLEMENTATION

A. The Hodgkin-Huxley formalism

To design neuromimetic IC (in contrast to bio-inspired IC), we chose the Hodgkin-Huxley formalism. The main advantage of this formalism is that it relies on parameters, which are biophysically realistic, by the way of a conductance-based expression of the neural activity (see detailed description of the Hodgkin-Huxley formalism in [14]). We will express here the conductance-based principle and find out generic expressions for these conductance phenomena.

The Hodgkin-Huxley formalism provides a set of equations and an electrical equivalent circuit (Fig. 1) that describe the behavior of separate conductances. Each conductance represents the dynamics of an ionic specie (sodium, potassium or calcium) flowing through the neural membrane. All these ionic currents are integrated on the membrane capacitance following the electrical equation (1),

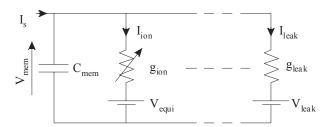


Fig. 1: Neuron electrical equivalent circuit

$$C_{\text{mem}} \cdot dV_{\text{mem}} / dt = -\Sigma I_{\text{ion}} + I_{\text{s}}$$
(1)

where V_{mem} is the membrane potential, C_{mem} the membrane capacitance and Is an eventual stimulation or synaptic current. The generic mathematical expression (2) for each ionic current is:

$$I_{ion} = g_{max} \cdot m^{p} \cdot h^{q} \cdot (V_{mem} - V_{equi})$$
(2)

where g_{max} is the maximal conductance value, m and h are respectively the activation and inactivation function and V_{equi} the ion-specific reverse potential. We will for our implementation integrate current generators that follow expression (2). Synaptic current are based on similar conductance-based model.

B. The implemented analog computation core

Figure 2 describes the organization of the integrated IC gathering ionic current generators as described earlier. To cover the widest possible range of models, while limiting the design complexity, we retained five channel types: leakage, sodium, potassium, calcium and calcium-dependent potassium. A neuron model will be possibly described by any combination of these channel types; associated to the

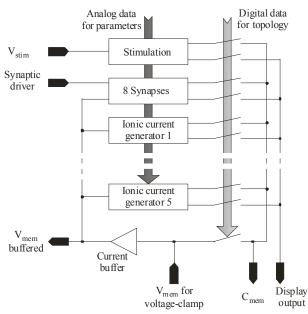


Fig. 2: Analog computation core

chosen set of conductances, 8 input synapses and one stimulation current generator. The analog computation core is configurable through two internal buses. The first one, which is analog, defines the parameter values in the mathematical expression given in (2). The second one is a digital bus used to specify which ionic current generators are active for the simulation. The membrane voltage (via the "Vmem buffered" output) and any ionic current generator switched to the "Display output" can be displayed in real time on an oscilloscope.

III. FROM ANALOG COMPUTATION CORE TO SYSTEM

A. Design principle

We integrated a circuit including two analog computation cores (Fig. 3). The 158 analog parameters that are necessary for the 2 analog cores are stored on-chip, using dynamic analog memories, based on integrated capacitors. The memory cells array receives data from an external ADC, which sequentially refreshes the analog parameters values. This technique allows external modifications of one or more parameters, even during the running of the simulation. Due to internal protocol, one modification necessitates three refreshing cycles (≤ 5 ms), which is compatible with the V_{mem} dynamics in biological real time. To program the parameter memories we use a 3 bits bus (Clock, Reset and Data) and an analog bus (Parameter values). The experimenter chooses a topology before the simulation starts, to define which channels are activated to compute the electrical activity. This topology is stored on built-in dynamic digital memories and programmed by another 3 bits bus (Clock, Reset and Data).

B. The Chip Pamina

The chip was designed in full-custom mode with a BiCMOS SiGe 0.35µm technology process from austria**micro**systems (AMS) under Cadence environment. Figure 4 is a microphotograph of the ASIC called *Pamina*. The ionic current generators have been designed in current mode [15], which means that the internal variables in the model expressions are physically represented by currents. Topology and analog memory cells can also be identified on the figure. *Pamina* contains around 19,000 MOS transistors,

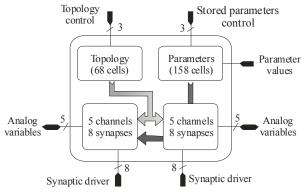


Fig. 3: Integrated Circuit block diagram

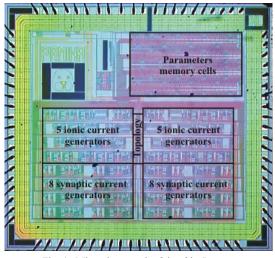


Fig. 4: Microphotograph of the chip Pamina

2,000 bipolar ones and 1,200 passive elements; its area is 4170 x 3480 μ m². Ionic and synaptic current generators, as well as analog memory cells, are designed in full-custom mode; digital cells are from the austria**micro**system's library. Custom implementation is 71% of the 22,200 elements.

C. The system

A complete computer-based system was built to exploit the designed ASICs (see Fig. 5). The experimenter defines the neurons model parameters, using interface software. Theses characteristics include the ionic channels choice between sodium, potassium, leakage, calcium and calciumdependent potassium and the parameters values for each channel. These data are sent to the IC through the analog and digital buses described in the previous paragraph. The analog computation core simulates in real-time the membrane potential, which is digitized through an analog digital converter and sent to the computer for display, storage or further processing.

IV. TOWARDS OPTIMIZATION TECHNIQUE

With the neuromimetic IC called *Pamina* and the communication via PCI-bus with the host computer, we have all components to build a system to determine the set of

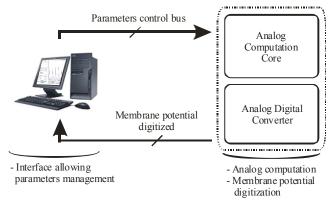


Fig. 5: Structure of the complete simulation system

parameters from a biological neuron, as mentioned in the introduction paragraph.

The parameters extraction by optimization algorithms necessitates to minimize an error function between a reference activity and a current activity. More specifically, this error function compares two membrane potentials, one measured from a biological cell (the reference), and the other from the simulation (the model which parameters are examined). Optimization algorithms do the error function minimization. An error function in temporal domain would have to deal with the arbitrary phase difference that exists between the 2 signals. Synchronizing the reference and simulated activity by adjusting for example the stimulations is not a simple case. We chose to define an error function that compares the membrane potentials evolution in time rather than their static values. Considering the definition of the mathematical expression (1) and (2) for the membrane potentials, we will calculate the phase diagram (3), which specifies the membrane voltage activity on a single period, regardless of the absolute phase. This approach is possible only because we consider periodic activities.

$$dV_{mem} / dt = f(V_{mem})$$
(3)

Figure 6 illustrates plots such a phase diagram in the case of a three conductances neuron model [16]. We plot the phase diagram of the reference activity and the simulated activity, which simulates a set of parameters arbitrary chosen. In that demonstration case, the reference activity is from an already known model card, obtained from voltageclamp experiments, and is software simulated. This plot points out the difference between the two electrical activities, and the "error" is clearly visible. This means that the IC parameters are not well tuned to fit the reference model. The optimization technique will minimize the error function to obtain closer trajectories in the phase diagram. The error function definition and the optimization algorithms choice are discussed in [17].

The main advantages of this technique are that it helps reducing neurophysiology experiments, while giving the opportunity to explore systematically the parameters space of the studied model. With this technique, the neuroscientists need to measure only the membrane voltage, which is easier

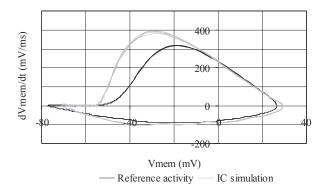


Fig. 6: Phase diagram of reference activity and IC activity

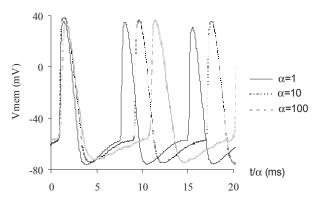


Fig. 7: IC simulation speed increasing for a 3-conductances neuron model

than the ionic channels dynamic with the voltage-clamp technique. The set of parameters exploration will give to the neuroscientists the mathematically possible solutions (possibly more than one). Neuroscientists will then retain the most realistic model card.

V. THE COMPUTATION SPEED

The analog neuromimetic IC present a great advantage over the digital implementations: we can increase the computational speed, and run simulations at a fixed time scale that will be more than the biological real-time. Looking at expression (1), if we arbitrarily divide the membrane capacitor value by a α term, and divide all the kinetics of the activation and inactivation variables by the same α term, we immediately divide the simulation time by the α term (t in the expression is replaced by t/α). We show in fig. 7 test measurements on the ASIC Pamina in the cases $\alpha = 1, 10$ and 100. Each simulation is drawn with its own time scale t/α . This property is limited by the circuit electronic performances, as it was not designed to process higher kinetics than the real-time ones. When $\alpha = 10$, the action potential shape is almost identical to the reference one (α = 1), and the activity frequency slightly increases. When $\alpha =$ 100, we can observe noise during the depolarizing phase of the spike, before the action potential. These results show us that, although the IC Pamina was not designed for increasing the computation speed, we can find an optimum factor to speed up the simulation while keeping an activity identical to the reference one. Applying that property to the software/hardware optimization technique will reduce the simulation time; this can be a key issue when exploring large set of parameters in the Hodgkin-Huxley models.

VI. CONCLUSION

We presented in this paper a custom experimental setup, which includes analog neuromimetic IC modeling the Hodgkin-Huxley formalism, and a PCI interface to dynamically control the IC. The proposed hardware/software technique using this system is an alternative to voltage-clamp experiments for parameters extraction in biological neuron models. We demonstrated that the analog neuromimetic IC can compute neural activity faster than biological time. Additional results including the software implementation of optimization algorithms implementation will be presented during the conference.

ACKNOWLEDGMENT

The authors thank Pr. G. Le Masson (INSERM E 358 – France) for his help on model specifications. This work was supported by E.U. Grant SenseMaker (IST-2001-34712) and E.U. Grant NeuroBit (IST-2001-33564).

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