Adjusting the Neurons Models in Neuromimetic ICs using the Voltage-Clamp Technique

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Abstract — **This paper presents an original method to tune a neuromimetic IC based on neuron conductance-based models (Hodgkin-Huxley formalism). This method is well known in electrophysiology as the "voltage-clamp" technique. It consists in measuring the neural conductances while holding the membrane voltage at a clamped level. The voltage- and time-dependent variables of the conductance equations are then interpolated from the measurements. We apply this technique on the neuromimetic IC to extract the exact parameters of the neuron model. This model is computed in software, and results are compared with the hardware simulation. We conclude by mentioning the potential applications of this technique in hardware simulation systems based on neuromimetic ASICs.**

I. Introduction

With more than fifteen years experience, neuromorphic engineering is now well recognized as a research domain. Two applicative fields are identified: the first one is to design artificial systems inspired by biological principles. This research helps developing solutions for engineering questions about vision [1], [2], learning [3] … The second one deals with neuroscience questions, like the understanding of central pattern generator [4], or vision processing [5]. Alternatives to software-based solutions, neuromorphic systems are often based on custom ICs and systems. A neuromimetic ASIC (a circuit computing neurons electrical activity) is designed for a dedicated applicative environment, and computes a theoretical neuron model. The classical way to check the model implementation is to observe the membrane voltage that presents an oscillatory activity. This verification at a behavioral level remains very imprecise.

Neuroscientists have methods to extract from biological neurons current-based models from recordings of their electrical activity. The most popular method is the voltage-clamp technique [6]. During such an experiment, the neuron activity is recorded in vitro using intra-cellular electrodes. The conductance of individual ionic channels (inhibited by injecting specific drugs in the cell) is measured, while the electrode clamps the neuron membrane voltage. After measuring the neuron area and its membrane capacitance, the experimentalist can extract the current-voltage relationships of the ionic conductances, for each type of ionic channel. In a complex neuron model such as the Hodgkin-Huxley enhanced models (3 to 5 ionic conductances) [7], as many as fifteen parameter values have to be fitted for a 3-conductances neuron.

In analog design, the influence of dispersion and mismatch in the fabrication process, added to the influence of the IC electronic environment, implies that some uncertainty remains on the exact equations computed in the circuit. Using a voltage-clamp method like in electrophysiology is a way to extract after the fabrication the exact model implemented on the IC. It the parameters are tunable, it is then possible to adjust the model parameters to obtain a high precision model. These extracted characteristics are also informative for further designs.

We have designed different simulation platforms based on neuromimetic ASICs [8], [9]. The ICs compute in real-time conductance-based neuron models using the Hodgkin-Huxley formalism, and simulate Spiking Neural Networks (SNN). We present in this paper the neuromimetic ASICs, where ionic channels can be isolated to apply the voltage-clamp technique. We explain the IC content and architecture, and show how to apply the voltage-clamp technique. We present experimental results at the conductance level and at the neuron level. Finally, we compare the hardware neuron simulation with parameters with an equivalent software simulation.

II. Implemented Model

A. Hodgkin Huxley Formalism

We chose to implement on the neuromimetic ICs neuron models following 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.

The electrical activity of a neuron is the consequence of the ionic species diffusion through its membrane. The Hodgkin-Huxley formalism provides a set of equations and an electrical equivalent circuit (Fig. 1) that describe these conductance phenomena. The current flowing across the membrane is integrated on the membrane capacitance, following the equation (1).

$$C_{mem}\frac{dV_{mem}}{dt} = -\sum_i I_{ion} + I_S \quad (1)$$

where V_{mem} is the membrane potential, C_{mem} the membrane capacitance and I_s an eventual stimulation or synaptic current.

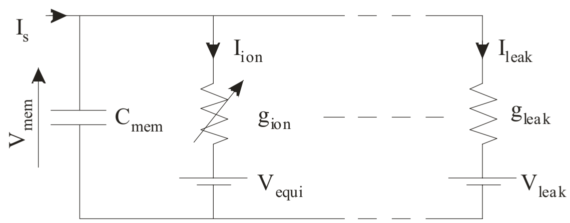

Figure 1: Neuron electrical equivalent circuit

I_{ion} is the current passing through one type of ionic channel, and is given by (2). g_{max} is the maximal conductance value, m and h respectively represent activation and inactivation terms, which are the dynamic functions describing the permeability of membrane channels to the considered ion. V_{equi} is the ion-specific reverse potential and p, q are integers.

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

According to the kinetic function (3), m converges to its associated steady-state value m_∞, which is a sigmoid function of V_{mem} (4). The time constant for the convergence is τ_m. In (4) V_{offset} is the activation sigmoid offset and V_{slope} the activation sigmoid slope. Inactivation h follows identical equations except that the sign of ($V_{mem} - V_{offset}$) is reversed.

$$\tau_m \frac{dm}{dt} = m_\infty - m \qquad (3)$$

$$m_\infty = \frac{1}{1 + \exp\left(\frac{-(V_{mem} - V_{offset})}{V_{slope}}\right)} \qquad (4)$$

B. *Chip design*

Figure 2 describes the architecture of the analog core of the neuromimetic IC (*Pamina*). It gathers ionic current generators that follow the model described in II.A. To cover the widest possible range of models, while limiting the design complexity, we retained five channel types: leak, sodium, potassium, calcium, and potassium calcium-dependent. A neuron model is described by a combination of these channel types; associated to the 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). These parameters are stored on DRAM analog on the chip. The second bus (digital) specifies which ionic current generators are activated for the simulation. The membrane voltage (via the "V_{mem} buffered" output) and any ionic current generator switched to the "Display output" can be monitored in real time.

Pamina is designed in full-custom mode with a BiCMOS SiGe 0.35µm technology process from austria**micro**systems (AMS), using the Cadence CAD suite. The modules computing the ionic current are designed in current mode [10], which means that the internal variables in the model equations are physically represented by currents. *Pamina* includes approximately 19,000 MOS transistors, 2,000 bipolar transistors and 1,200 passive elements; the die area is 4170 x 3480 μm^2. Ionic and synaptic current generators, as well as analog memory cells, are designed in full-custom mode; digital cells are from the AMS standard cells, and the digital block is implemented using an automated place and route. 71% out of the 22,200 elements are placed and routed manually.

C. *System*

A computer-based system was built to run experiments using the *Pamina* ASICs. Using a graphical interface, the user defines each neuron's model. The specifications include the choice of the ionic channels (3 to 5 among the Sodium, Potassium, leakage, modulator conductances) and the parameters values for each channel, as described in (1) to (4). The analog IC simulates in real-time the membrane potentials of the neurons. The user can monitor the neuron membrane voltage, and one ionic current.

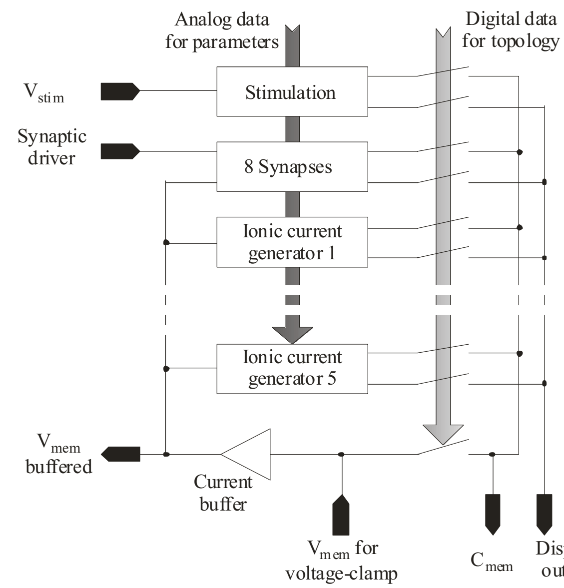

Fig. 2: Analog computation core of the ASIC *Pamina*

III. VOLTAGE-CLAMP TECHNIQUE

Using the voltage-clamp technique, we can identify one by one the parameters of each ionic channel. We open the membrane voltage loop with the switch between C_{mem} output and Voltage-clamp input (see Fig. 2). Then we study the responses of the ionic current generators to successive steps values applied on membrane voltage via the dedicated input. Figure 3.B illustrates the experiment: the membrane voltage steps applied successively to V_{mem} (Fig. 3.A), and the associated response of the isolated Potassium channel. The potassium channel parameters are then extracted from these measurements (see below). In this paper, we study inhibitory neurons, also called Fast Spiking neurons (FS). This class of neurons is modeled by three conductances: sodium, potassium and leak channels.

A. *Potassium channel*

The potassium (K) channel is easy to identify because it has only an activation term n. Equation (2) for this channel is:

$$I_K = g_K n^4 (V_{mem} - E_K) \qquad (5)$$

Results of the voltage-clamp experiment the K channel of *Pamina* are shown in figure 3. For t > 30 ms in Fig. 3.B, I_K current reaches its steady state and $n = n_\infty$. For V_{mem} > 300 mV, $n_\infty = 1$. Thus, (5) gives:

$$I_K = g_K\,(V_{mem} - E_K) \qquad (6)$$

Applying a simple linear regression method to the curves in Fig. 3.B for $t > 30$ ms and $V_{mem} > 300$ mV, we obtain $E_K = -493$ mV and $g_K = 107.2\ \mu S$.

Then for t > 30 ms, we can plot with (5):

$$n_\infty = \sqrt[4]{\frac{I_K}{g_K.(V_{mem} - E_K)}} \quad \text{for each couple } (I_K, V_{mem}) \qquad (7)$$

The resulting $n_\infty(V_{mem})$ curve is fitted by a sigmoid function with $V_{offset\_n} = -186.7$ mV and $V_{slope\_n} = 56.4$ mV.

For the activation kinetic (equivalent to τ_m in (3)), we use a classical approximation method (81.5% of full range at $t = 3.\tau_n$). We obtain $\tau_n = 2.5$ ms.

B. *Sodium channel*

The Sodium channel has an activation term (m) and an inactivation term (h). Then, (2) becomes:

$$I_{Na} = g_{Na}\, m^3 h\,(V_{mem} - E_{Na}) \qquad (8)$$

If we consider $\tau_m << \tau_h$ (a biologically-realistic hypothesis), we can identify separately m and h. With the V_{mem} stimulation steps as in Fig. 3.A, the measured Ina responses are as shown Fig. 4.A. We can identify from those curves following parameters (h is equal to 1): $E_{Na} = 193$ mV, $g_{Na} = 83.7\ \mu S$, $V_{offset\_Na\_m} = -211.8$ mV, $V_{slope\_Na\_m} = 29.3$ mV and $\tau_m = 0.037$ ms.

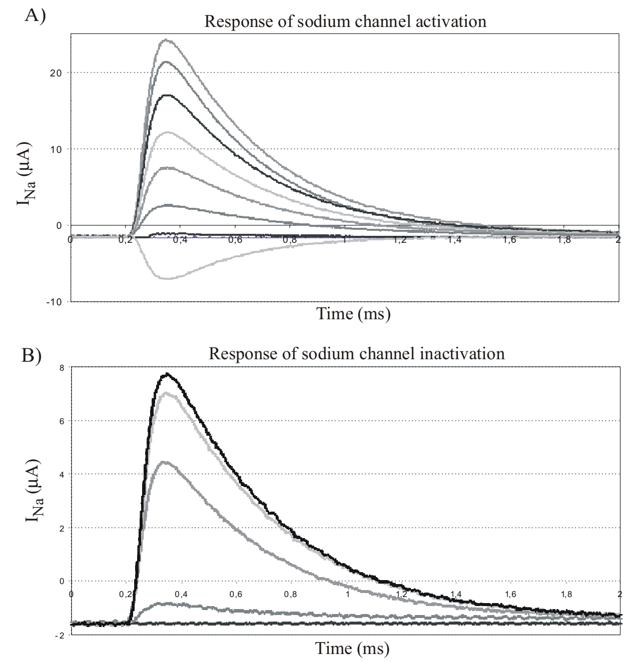

Figure 4: Measurements on the Sodium channel. A) represents the response of Sodium channel activation. B) represents the response of Sodium channel inactivation. Both currents are multiplied per 113.6 from biological value in the chip.

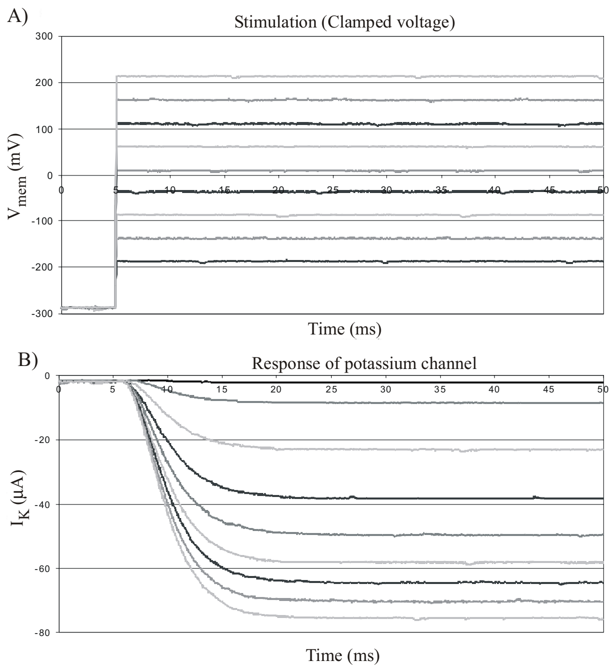

Figure 3: Illustration of the voltage-clamp method on the ASIC, applied to the Potassium channel. A) V_{mem} input steps. During the experiment, steps are applied successively, with a resting period of 50 ms. Y axis scale: V_{mem_ASIC} = 5 x V_{mem_bio}. B) Response current of the Potassium channels to the V_{mem} step of A. The current absolute value for t_∞ increases with V_{mem}. Y axis scale: I_{K_ASIC} = 113.6 x I_{K_bio}. X axis: simulation time is biological real time.

The identification of inactivation term h necessitates a second set of measurements. The stimulation is no more increasing V_{mem} steps with the same initial value, but rather V_{mem} steps, which start from different values with an identical final value. The initial voltage is applied during 10 ms, and then m and h reach respectively steady state m_∞ and h_∞. With the same hypothesis $\tau_m << \tau_h$, when the final value is applied, only the fraction of non-inactivated, i.e. (1-h), appear (m=1) (see Fig. 4.B). We obtain then $V_{offset\_Na\_h} = -231.7$ mV, $V_{slope\_Na\_m} = 19.0$ mV and $\tau_h = 0.42$ ms. We can observe that the hypothesis $\tau_m << \tau_h$ is verified.

C. *Leak channel*

The last channel for the FS neuron corresponds to the leak current. Its model is:

$$I_{Leak} = g_{Leak}\,(V_{mem} - E_{Leak}) \qquad (9)$$

The identification of this equation is obtained by a simple series of voltage-clamp measurements as I_{Leak} depends linearly on V_{mem}. We obtain: $E_{Leak} = -626$ mV and $g_{Leak} = 538$ nS.

IV. Comparison with software simulations

We simulated the FS neuron studied in section III, using the neural simulation software *Neuron* [12]. The model parameters extracted from the measures are translated in their equivalent value in the biological model. The IC is designed to compute voltages and currents with the following gains: $V_{mem\_ASIC} = 5 \times V_{mem\_bio}$; $I_{K\_ASIC} = 113.6 \times I_{K\_bio}$. The between hardware and biological conductances is 22.7. Therefore, as $C_{mem\_ASIC} = 5$ nF, and considering that $C_{mem\_bio} = 1\ \mu F/cm^2$, we simulate a neuron with a membrane area of 22.10^{-5} cm². The resulting parameters values for the FS biological neuron model are summarized in Table 1.

To compare the hardware and software simulation, we plotted V_{mem} for different values of a constant stimulation current (I_{STIM}). Figure 5.A plots the membrane voltage for both simulations when the FS neuron spikes at 44.3 Hz. Figure 5.B plots the simulated neurons spiking frequency depending on I_{STIM}. This plot is characteristic of the FS neuron. We can observe that the hardware and software neurons characteristics are similar.

V. CONCLUSIONS

The biophysics parameters extraction from an analog neuromimetic IC is possible with the voltage-clamp technique. It is possible to apply on the chip *Pamina* , that was designed with an adapted architecture. The parameters obtained by the voltage-clamp technique are the exact neuron parameters computed by the circuit, as shown by comparing with software simulations. This method can be used for adjusting models on neuromimetics ICs where parameters are stored on-chip or can be controlled. This approach provides is also an interesting feedback for the IC designers, between the low-level electrical simulations (time- and power consuming) and the neuron membrane voltage measurement (fast but not precise).

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TABLE I. EXTRACTED MODEL PARAMETERS (FS NEURON)

Variable			Value
Membrane		C_{mem}	**1 µF/cm²**
		Surface	**22.10^{-5} cm²**
Leak channel		g_{Leak}	**107.4 µS/cm²**
		E_{Leak}	**-125.2 mV**
Sodium channel		g_{Na}	**16.74 mS/cm²**
		E_{Na}	**38.6 mV**
	activation	τ_m	**0.037 ms**
		V_{offset_m}	**-42.4 mV**
		V_{slope_m}	**5.9 mV**
	inactivation	τ_h	**0.42 ms**
		V_{offset_h}	**-46.3 mV**
		V_{slope_h}	**3.8 mV**
Potassium channel		g_K	**21.44 mS/cm²**
		E_K	**-98.6 mV**
	activation	τ_n	**2,5 ms**
		V_{offset_n}	**-37.3 mV**
		V_{slope_n}	**11.3 mV**

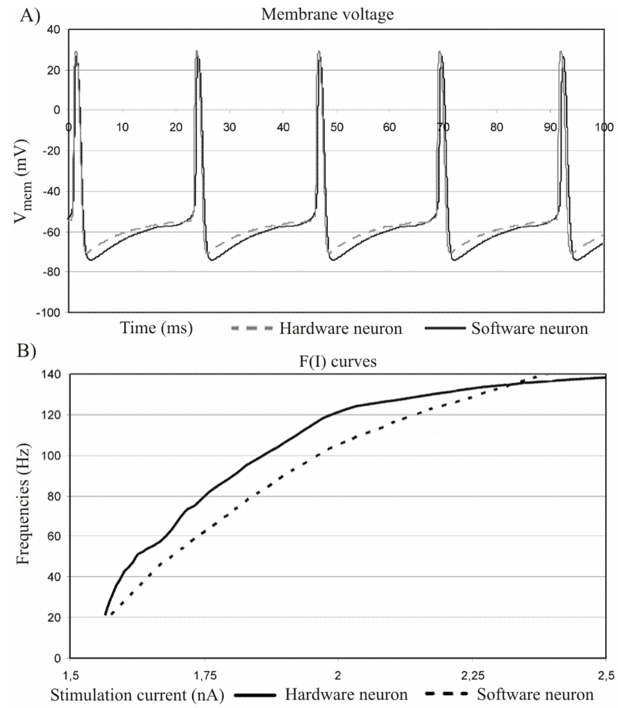

Figure 5: A) Hardware and software membrane voltages when neurons spiking at 44.3 Hz. B) Frequencies versus stimulation current curves from hardware and software simulations.

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