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A neural simulation system based on biologically realistic electronic neurons

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Abstract

This paper describes an original neural simulation platform designed as a tool for computational neuroscience. The system, based on artificial electronic neurons implemented in specific integrated circuits, computes in real-time and emulates in analogue mode the electrical activity of single neurons or small neural networks. Neurons are modelled using a biologically realistic description of membrane excitability and synaptic connectivity. The characteristics of the simulator are discussed and simulation examples are presented, including the implementation of "hybrid networks", where living neurons and artificial one are interacting in real-time in a mixed neural network.

Keywords: Neural networks; Simulation; Silicon neurons; Analogue ASICs; Hybrid neural networks

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1. Introduction

Understand how neurons and networks can process information through their electrical activity is one of the major goal of computational neuroscience.

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Theoretical approaches have made successful use of neural simulation software packages dedicated to biologically realistic simulations. However, there are still difficult compromises to be done between the precision of the models and the computing speed that limit the model's complexity, at the single-neuron level as well as at the network level.

We describe here an original neural simulation platform, based on artificial electronic neurons implemented in specific integrated circuits. These circuits simulate analogically and in real-time the neural networks electrical activity, using biologically realistic models of neural excitability and connectivity. The characteristics of the simulation set-up are discussed, and demonstrated in different experiments, including construction of "hybrid systems", i.e. mixed living–artificial neural networks.

2. Simulations with analogue devices

Neural simulators aiming to address the resolution of a biological relevant problems involving neural networks have to take into account very different levels of mechanisms [1], from the sub-cellular structure (cell morphology, intracellular calcium dynamics), to ionic channels (voltage and chemically dependent) and synapses, and up to massively connected large networks.

We are here interested in the field of "single-neuron modelling", which allows exploration of a single neurons or small networks, using their precise and realistic biophysical properties. The time variation of the membrane voltage V_{mem}, which is the potential difference between the inside of the membrane and the outside, is the main parameter related to the neuron activity. The cell membrane acts like a capacitor, while the electrical charge carriers (ionic species such as Na^+, K^+, Cl^-, Ca^{2+}) pass through ionic channels in the membrane.

The currents flowing in parallel through those channels are well characterized by a set of non-linear equations depending on V_{mem} and time. These equations were originally described by Hodgkin and Huxley [2,3], and lead to one of the most successful set of models used in neurobiology. Using the Hodgkin–Huxley formalism, the neuron membrane potential is due to a combination of different biophysical currents passing through ionic channels and applied on a membrane capacitance (Fig. 1). While simple neural activity (action potentials) can be described with only three types of ionic currents, more complex models integrate up to 6 ionic currents, with eventual interdependencies [1]. The generic equations for the Hodgkin–Huxley formalism are collected in Table 1.

When looking at that description for a neuron electrical activity, it is easy to notice how close it is to an electrical equivalent circuit, where ionic currents act as electronic currents. This observation is the origin of the idea of implementing biophysical neuron models on electronic integrated circuits [4–6]. The

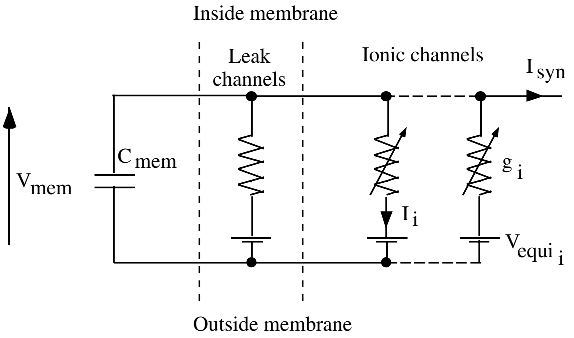

Fig. 1. Electrical equivalent circuit of excitable membrane. Each branch is representative of an ionic current; all currents, including synaptic or stimulation external ones, are summed on the neuron membrane capacitance.

circuits form the core of the neuron simulator, while the chips internal currents and voltages represent the models variables; primitives of computation arise from the physics of devices (transistors, resistors, capacitors). These devices are organized in a circuit which current–voltage relations follow the neurons model equations; equations time-dependencies are then reproduced in real-time by the circuit, which finally provides, in continuous time, continuous variables representing the neuron activity [7].

Our analogue simulation platform includes integrated circuits (ICs) of artificial neurons, which present an electrical activity identical to the one of real neurons, and the electronics environment to support the ICs and interface it with a user-software. This software is supported by graphics and dialogs, and drives the neural network parameters and data storage.

The analogue computation mode can be compared to digital computation, which typically means computation in discrete time with discrete variables. Digital computation can be implemented on programmable logic devices (PLA, FPGA) to optimize computation speed, but runs more classically on standard microprocessors. We can quote for that latter configuration neural simulation software packages, such as *Neuron* or *Genesis* [8,9], dedicated to the exploration of single neurons or small networks. Neurons are modelled at their biophysical level, which corresponds to the analogue neurons description level, and is specially favoured by neurophysiologists that intend to combine experimentation and modelling.

Let us point out pros and cons of the analogue computing mode

Cons

- The development time and costs are much larger when choosing the analogue solution: the artificial neurons are full custom ICs, specifically

Table 1

Generic equations of the Hodgkin–Huxley formalism: time and voltage dependencies of ionic conductances for neural internal and synaptic currents

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Membrane voltage time-dependence

$$C_{\text{mem}} \frac{\mathrm{d}V_{\text{mem}}}{\mathrm{d}t} = -\sum_i I_i - I_{\text{syn}} \tag{1}$$

V_{mem}: membrane voltage; C_{mem}: membrane capacitance; I_i: ith ionic current;
I_{syn}: synaptic current

ith ionic specie current

$$I_i = g_{\max\_i} \cdot m^p \cdot h^q \cdot (V_{\text{mem}} - V_{\text{equi\_}i}) \tag{2}$$

$g_{\max\_i}$: maximal conductance; m, h: membrane permeability state variables (see Eq. (3));
p, q: integers; $V_{\text{equi\_}i}$: resting potential

State variable time-dependence

$$\tau_s(V_{\text{mem}}) \cdot \frac{\mathrm{d}s}{\mathrm{d}t} = s_{\inf}(V_{\text{mem}}) - s \tag{3}$$

τ_s: voltage-dependent time constants; $S_{\inf}$: voltage-dependent static value (see Eq. (4))

Static value voltage dependence

$$s_{\inf} = \frac{1}{1 + \exp\left(\pm \frac{V_{\text{mem}} - V_{\text{offset}}}{V_{\text{slope}}}\right)} \tag{4}$$

V_{offset}, V_{slope}: voltage parameters of the sigmoidal function

Synaptic current

$$I_{\text{syn}} = g(V_{\text{pre}}) \cdot (V_{\text{post}} - V_{\text{equi\_syn}})$$

$g(V_{\text{pre}})$: synaptic conductance depending on time and on presynaptic membrane potential;
V_{post}: postsynaptic membrane potential; $V_{\text{equi\_syn}}$: synaptic resting potential

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fabricated for our platform. The digital solution offers various and cheap solutions, with a fast design flow: software development, programmable logic circuits (FPGA)...

- Computation is offset and noise sensitive: offset comes from mismatches in the parameters of the physical devices, and noise from temperature fluctuations in the physical devices or from external sources. These phenomena increase when cascading analogue stages: complex systems with many stages are difficult to build. In digital systems, signals are restored to 0 and 1 at each stage, and noise is only due to round-off error, which is generally not very significant.

Pros

- Analogue processing can be much more efficient than digital: primitive operations may necessitate much less devices (an addition of 2 n-bits words in analogue mode is a simple wire, whereas is takes almost 2^n transistors in a standard CMOS technology), with an immediate gain on the equivalent silicon area and power consumption. A crucial result is the fact that an analogue artificial neural network will always run in real-time, whatever its complexity. Thus, more than a simulation, integrated circuits provide a neural emulation. The topic of computational speed will be detailed in paragraph 4. However, the real-time property is a key element for the use of the analogue artificial neurons as equivalent neural elements in neurophysiology experiments: examples of such applications will be developed later in this paper.
- The noise sensitivity of ICs can be exploited as an advantage for realistic neural simulation, as the neural activity has a similar type of sensitivity. In the same manner, the discrepancies due to the fabrication process can be compared as the natural disparity in biology. The mathematical model of a type of neuron corresponds more to the average activity of a population, and isolated neurons activities are distributed around an average behaviour.

From this point-to-point comparison, we conclude that analogue emulation is an interesting alternative to digital computing for close-to-biology modelling and for computational applications close to experiments. On-chip analogue computation is not very commonly developed, and is dedicated to specific applications. Mixed analogue–digital architectures intending to exploit best of both worlds may be interesting solutions for large networks where there is no absolute necessity for real-time simulation [10,11].

3. The neural simulation system

The analogue simulation platform, “Vortex”, comprises two main parts: the neural computation core and the user interface. The computing system is composed of a set of electronics boards, each supporting artificial neurons on specifically designed ICs (ASICs), and an adapted hardware control interface. ASICs are integrated in a 0.8 μm BiCMOS technology. The neurons model equations are computed using the transistor voltage–current transfer functions. Each ionic conductance, source of an associated ionic current, and described by a set of non-linear equations (Table 1, Eqs. (2)–(4)), is computed by a specific circuitry of transistors, resistors, and capacitors, following the structure shown in Fig. 2. A current-mode design approach has been chosen, to optimize the use of bipolar transistors and minimize the chip area [12].

Each ASIC computes up to four ionic conductances blocks using 500 transistors on a 4 mm^2 silicon area. A microphotograph of a chip is presented in Fig. 3. Control software allows the user to freely set the artificial neurons parameters and connectivity, to form the desired neural network. According to Table 1, up to eight parameters are handled for each ionic conductance, as well as for synaptic conductances for which we use the same formalism. The whole system calculates in real-time each neuron membrane voltage and synaptic currents are available as analogue outputs of the set-up, and can be displayed on an oscilloscope or redirected to specific instrumentation amplifiers to create artificial-living hybrid networks (see paragraph 6). In addition to the

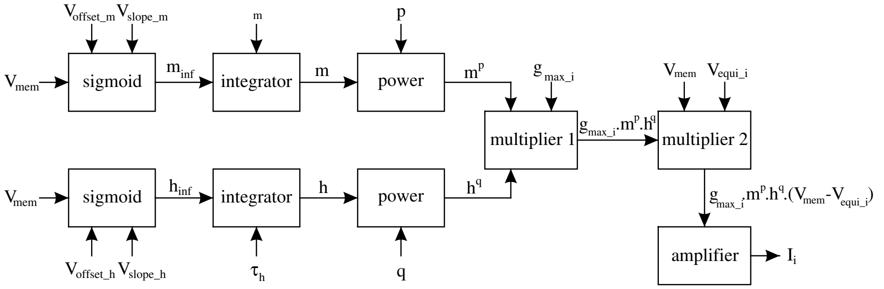

Fig. 2. Architecture of an ionic current generator (output I_i). The chained sub-circuits have been specifically developed, each effecting a specific mathematical operation. The model parameters are input of the sub-circuits, V_{mem} is shared by all the ionic currents of the neuron.

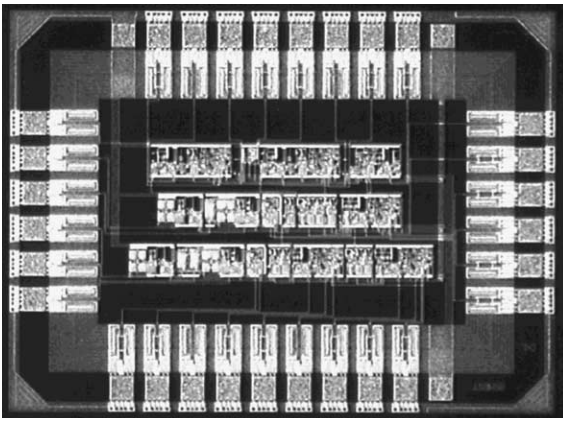

Fig. 3. Microphotograph of an analogue artificial neuron. This prototype includes four ionic current generators in a BiCMOS 0.8 μm technology, in an area with pads of 4 mm^2.

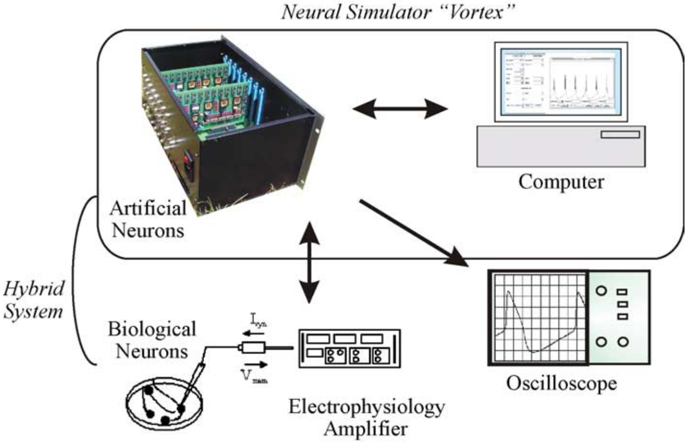

Fig. 4. The Vortex simulation platform with peripherals. The system is organized around a rack containing the artificial neurons chips. The control software runs on a PC. To run hybrid networks experiments, artificial neurons are connected to biological neurons via an electrophysiology amplifier.

parameters setting, the control software running on a standard personal computer provides data storage and basic processing tools. Scripts can also be defined to automatically run simulations with an automatic screening of neurons models parameters.

The Vortex system provides real-time and analogue synaptic outputs and inputs for bi-directional connections with biological living cells in an in vitro preparation, to form a hybrid living–artificial neural network. The Vortex output synaptic currents are then injected in the living neurons through a glass microelectrode and a specialized amplifier (Fig. 4), while synaptic output currents from the living cells are applied to the artificial neurons. A closed and real-time loop between the neurons is then constructed, to offer a systematic evaluation of the network activity. A hybrid network application example is presented in paragraph 6.

4. Increasing computing speed

Real-time computing of artificial neurons is necessary for hybrid network experiments. Aside from this specific application, it may be interesting to consider the advantage of IC computational speed. In the case of a simple neuron, where the integrated circuits follow the equations given in Table 1, the computation speed is directly linked to the time-dependence and kinetics of dynamical variables in the equations. By dividing all time-dependencies by an identical factor α, one "speeds up" the neural activity, and therefore the computation speed by the same α factor. This is mathematically equivalent to modify C_{mem} and τ_m in Eqs. (1) and (3) for all ionic currents.

Thus, changing these model parameters will increase the computation speed, when referenced to real-time. The limit of the increase factor will only be due to the electronics neurons frequency bandwidth.

Tests on the computation speed have been realised on the Vortex. The reference is a simple spiking artificial neuron modelled by 2 voltage and time-dependent ionic currents (sodium and potassium) and a voltage-dependent leak current. The neuron presents regular and spontaneous action potentials, at 30 Hz when using the real-time parameters. If we consider the neuron's activity over time, increasing the computation speed will correspond to shrink the time axis, i.e. to increase the spiking frequency by the α factor.

Fig. 5 illustrates the test results when we divide the model kinetic parameters (C_{mem} and τ_m) by a factor α, as indicated above. Fig. 5A plots the measured membrane voltage (V_{mem}), when α varies in the range $[0.01; 300]$, with the associated spiking frequency in 5B. We also look at the shape of the action

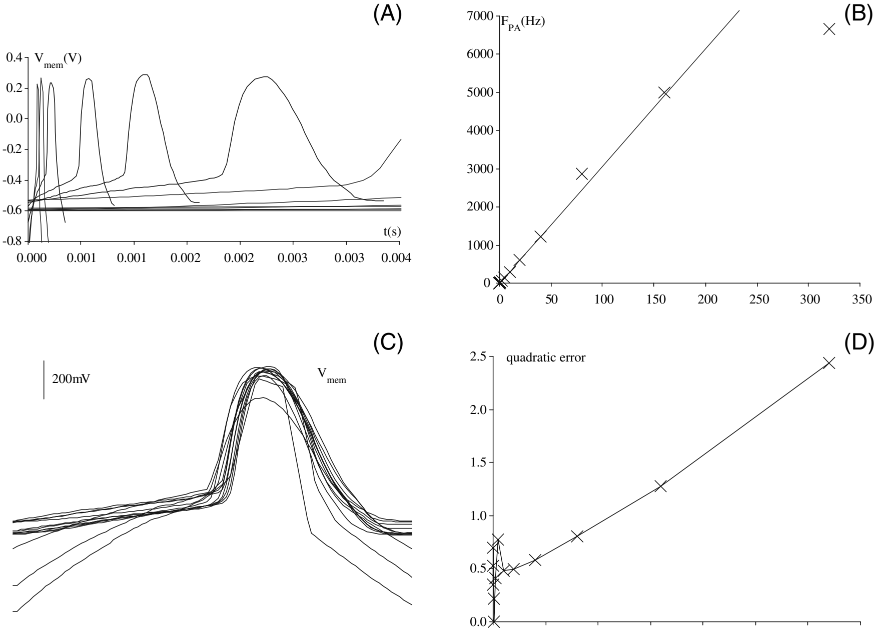

Fig. 5. Computation speed measurements. A: Time variation of the membrane voltage V_{mem} for different α values. B: V_{mem} frequency variations with α (plain line: theoretical curve; crosses: experimental measurements). C: V_{mem} signal shape for different α values (on a unit period). D: Quadratic error on a single oscillation with α (crosses: experimental points).

potentials signal: Fig. 5D plots the quadratic error of the signal shape on a single action potential (normalized on a unit period, see 5C), compared to the reference signal for $\alpha = 1$.

We observe a gradual change in the shape and in the oscillation frequency as α increases. The limit ($\alpha > 100$) corresponds to kinetic values in the model when getting close to the standard time constants of parasitic capacitance in the integrated circuit. To improve these frequency values, the circuits should be specifically designed for a high frequency range, which implies a more complex and expensive process.

We can however deduce from these results that the computation speed of the system can be notably increased without degrading its precision. This feature is of considerable importance for computational applications that requires a large number of simulations (optimization algorithms, parameters screening, learning, ...).

5. Simulation of the thalamic network

The programmability of this simulator allows the same circuits to model different types of biological neuron and network. We applied it to the study of the thalamus filtering properties. The thalamus is major relay structure of the brain where all the sensory inputs (visual, somato-sensory, auditive...) transit before reaching the cerebral cortex [13]. This position allows the thalamus to filter or faithfully transmit this sensory information depending on the various state of arousal (sleep, awake). When thalamic circuitry is in the 'sleep' mode, sensory information is blocked and when the network is in the "awake" mode, the same information is forwarded to the higher structure (cortex) for further cognitive processing. To study how this sensory gating is performed, we have investigated the interaction between two cell types, the thalamo-cortical neurons (TC) that receive sensory inputs from the sensory organs (retina, cutaneous receptor, ears, ...) and project to the cortex, and local inhibitory interneurons (nRt). These two cells populations are reciprocally connected by an excitatory (TC to nRt) and inhibitory (nRt to TC) loop. Fig. 6A shows an analogue model of a TC neuron responding to an inhibitory pulse by a rebound burst of action potentials. As a comparison, Fig. 6B is a real TC recorded in guinea pig slice in vitro. Using the Vortex system, we are also able to reproduce the synaptic interactions from TC to nRt and nRt to TC (Fig. 6C and D). In this case, the reciprocal connection leads to sustained oscillations known as "spindle waves", a landmark of early stage of sleep in animals and humans. This modelled network, running in real-time despite its complexity, has been used to study the role of spindling in information transfer in the visual thalamus. It appeared in the simulation that changes in the synaptic gains did affect the temporal correlation between nRt spikes and TC spikes, thus offering

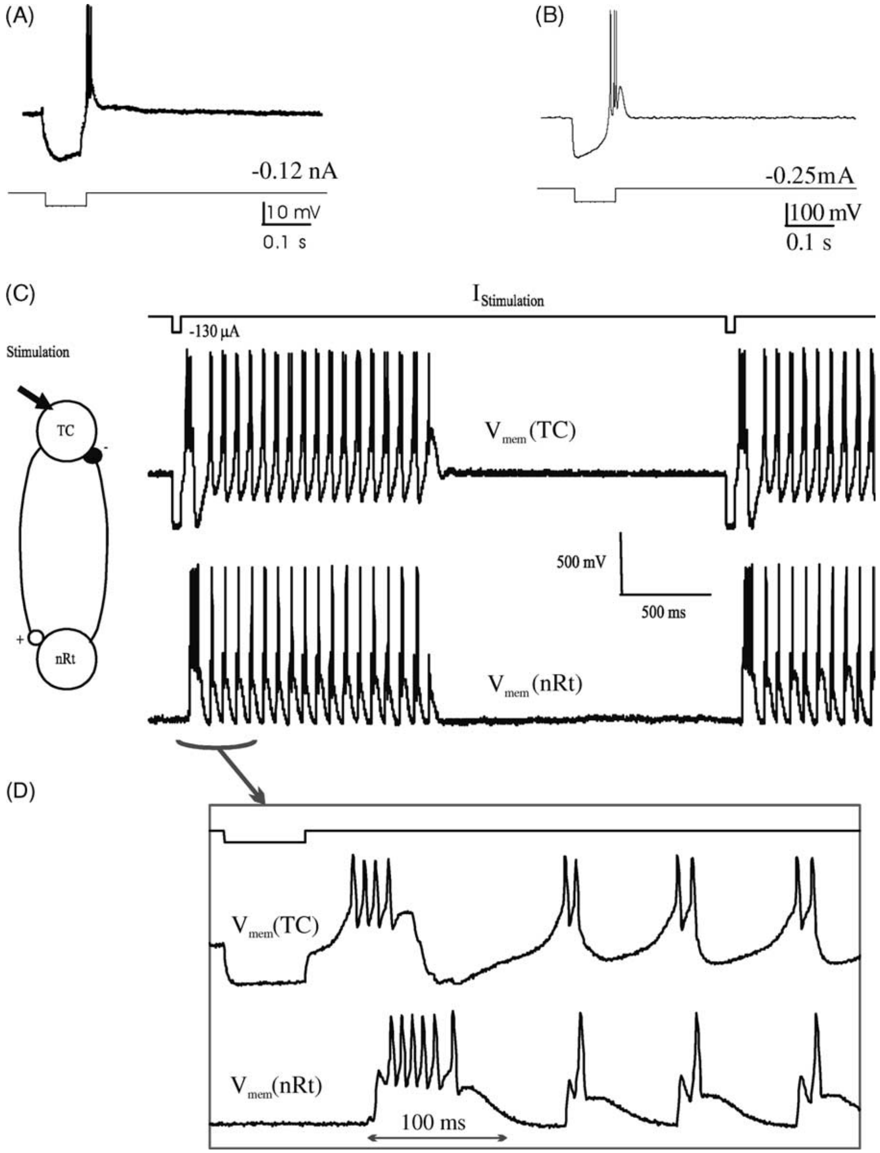

Fig. 6. Realistic simulation of thalamo-cortical neuron and intrathalamic network. A: When a negative current pulse is injected into a TC biological neuron the characteristic response is a rebound burst of action potential. B: The analogue model neuron reproduces the same behaviour. C: When two neurons are synaptically coupled (a TC and an inhibitory interneuron) the same inhibitory pulse generates a sustained oscillation. D: Zoom of graphic C.

a mechanism for spike transfer control. The validity of that hypothesis was lately proven by the run of hybrid experiments on the TC–nRt network [14].

6. Hybrid networks

This technique was originally developed as a tool to study small networks interaction and dynamics. A hybrid network is formed of both living and artificial neurons, reciprocally interconnected by artificial integrated synapses. The contact is made using an intracellular recording electrode, which injects in the biological cells a precomputed synaptic current, and measures its membrane voltage, used to compute the reciprocal synaptic current. This procedure requires as many intracellular electrodes as artificial synapses, which is a clear limitation. It however provides a way to connect in a realistic way a biological neuron recorded in vivo or in vitro with a model cell or network. This method lies between pure computational modelling and experiments, associating the strength of direct experiments and the analytical power of computational methods. Experimentalists can attain a level of evaluation of networks dynamics that is not possible with current methods used in electrophysiology. Hybrid networks provide in-depth and real-time control of membrane, synaptic conductance and network structure in order to assess their role in the activity of cells and networks.

An example of hybrid network if showed in Fig. 7A. The living neuron is a PD cell (Pyloric Dilator) of the STG (Stomato-Gastric Ganglion) of the lobster, the artificial neuron a 3-conductances spiking neuron (SP). Reciprocal inhibitory synapses connect the two cells, and generate a 2-phases activity

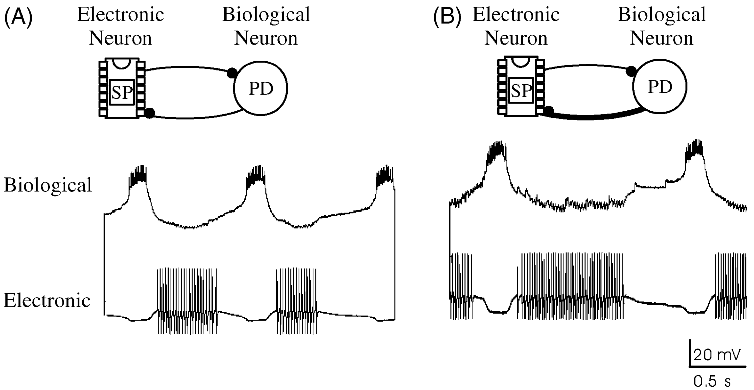

Fig. 7. Hybrid network. A: Hybrid network gathering bursting (PD) neuron and a spiking (SP) artificial neuron, with reciprocal inhibitory synapses. B: When the SP to PD synaptic conductance is increased, the pattern frequency goes lower, proving the synaptic efficiency.

pattern. Changing the PD → SP synaptic strength (Fig. 7B) effectively modifies the pattern frequency, slowing down the network rhythm. Individual inhibition associated to single action potential clearly appears in this case. Such hybrid networks have been used to validate the models proposed by neurophysiologists for the STG neurons, and study the interaction process between pairs of cells in rhythmic pattern generators [15].

7. Conclusion

We have presented a neural simulation set-up, using electronics artificial neurons to compute in a biologically realistic mode the activity of single neurons or small networks. The artificial neurons are designed to compute in analogue mode (continuous values, continuous time), which is for some applications an attractive alternative to digital computation. Although it is designed for real-time processing, the system also offers interesting possibilities for accelerated processing, using neuron model which kinetics are raised up to the technological limits of the integrated circuits. We present several applications to demonstrate the system capabilities, neural simulation or hybrid network simulation. The Vortex system, which has been designed as a tool for computational neuroscience, will evolve according to neuroscientist needs: we are currently adding an optimization tool that will automatically run simulations to extract the model parameters of an unidentified biological neuron, for which only the global electrical activity is known.

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