Recording and simulation of hippocampal neural networks

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In order to simulate the spiking activity of in-vitro neuron networks recorded by MEA, the engine SIMONE (Statistical sIMulation Of Neuronal networks Engine) has been updated and used. SIMONE has been originally designed to produce realistic extracellular signals used as input data for the validation of spike detection and sorting algorithms. The aim of this study is to compare simulated with measured spikes trains. We present different simulations based on the architecture of a real network composed by 14 neurons grown around one electrode. The comparison between real and simulated data is quantitatively performed using different spike detection tools based on thresholding or wavelet analysis. A careful adjustment of SIMONE parameters allows to reproduce the spontaneous bursting pattern of this real network while further investigations emphasize the role of synaptic noise in network activity.

1 Methods

For experimental measurements, neurons from mice embryo hippocampus are grown on a MEA covered by polylysine and observed 24 days after plating.

The code SIMONE [1] simulates the spiking activity of a neuronal network measured by a MEA. It is built using the R environment, an open source version of the well-known S language [2]. SIMONE's dynamic model is based on two coupled stages : (i) each neuron is represented by the leaky integrate-and-fire (LIF) model [3], with spike waveforms generated from templates, (ii) the extracellular detection is modeled via an electrode gain while the neural signal attenuation versus the distance to the electrode is described by a pseudo-monopole of current in the extracellular medium.

The user can define different distributions, functions and parameters to describe the desired neural network and the associated electrodes (an unique electrode in our case, with a distribution of surrounding cells similar to the real case). Three types of currents are taken into account here to feed the LIF model: synaptic current, noise current and self-induced current. The last one models the recovery dynamics, not included in the classical LIF model, and shape the bursting regime [4]. The overall model may be fully parametrized using stochastic functions.

2 Results

Real and simulated networks are shown in Fig. 1. The so-called simulated network 1 is made from random connections while network 4 is built from unidirectional connections. The small population (6%) of inhibitory compared to excitatory neurons in the hippocampus [5] yields the presence of only one inhibitory neuron in the center of network 1. Three neurons are within the detection range of the electrode while the remaining eleven cells compose the surrounding network.

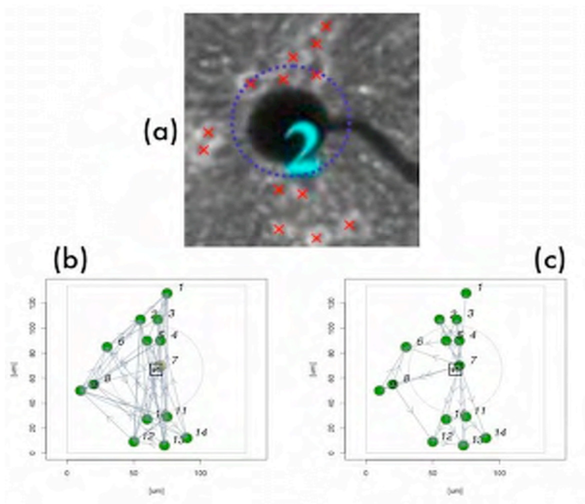

Fig. 1. (a) real network geometry; (b) simulated network 1; (c) simulated network 4. The centre of the electrode is represented by the square label "e1". Green (yellow) spots represent excitatory (inhibitory) neurons. The blue circle in a) and the grey circles in b) and c) represent the range of electrode detection (70 m). They enclose three neurons actually detected by this particular electrode "e1".

Activity of these networks with a I_{noise} contributing to only 8% of the total current is given in Fig.2. I_{noise} variations control both the amount of spike and the

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delay between the start of the simulation and the beginning of the spiking activity, showing an oscillating behaviour (Fig.3). The mean spiking rate is typically multiplied by a factor of 3.5 between the values 5% and 15% of I_{noise} (network 4).

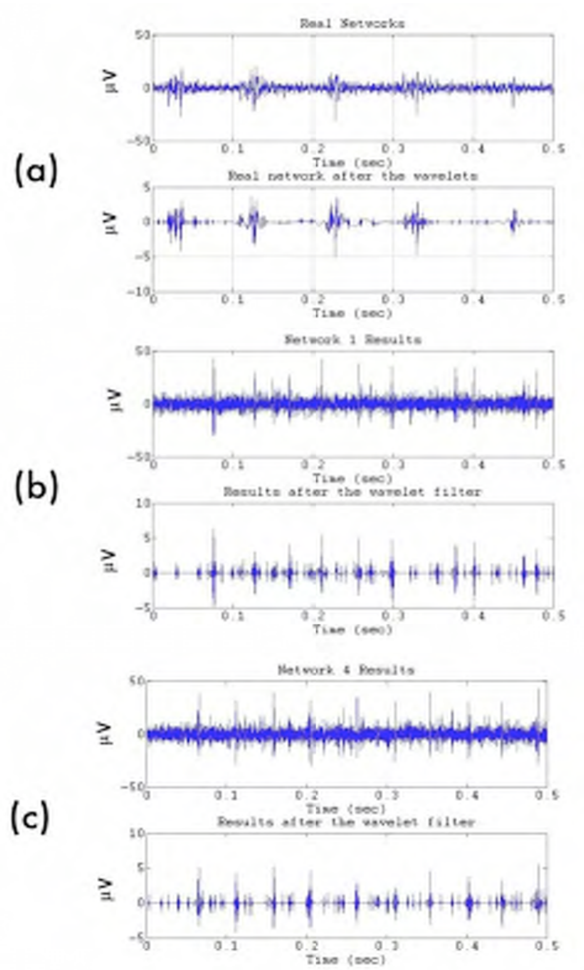

Fig. 2. Signals before and after a wavelet filtering are shown with I_{noise}=8% of the synaptic current and I_{self}=0. (a) Real network; (b) network 1; (c) network 4.

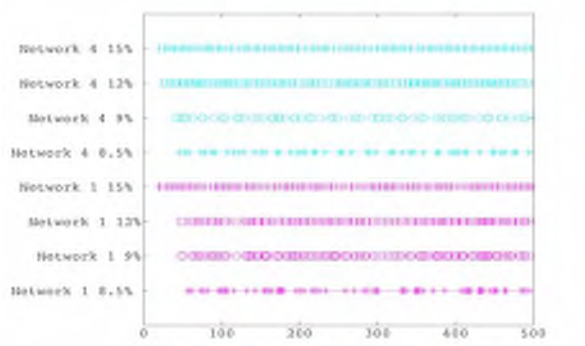

Fig. 3. Spiking activity of networks 1 and 4 with different I_{noise} during 50 ms (500 samples).

Tuning Iself and adjusting Inoise yields a remarkable similarity between the simulated and the real networks (Fig.4).

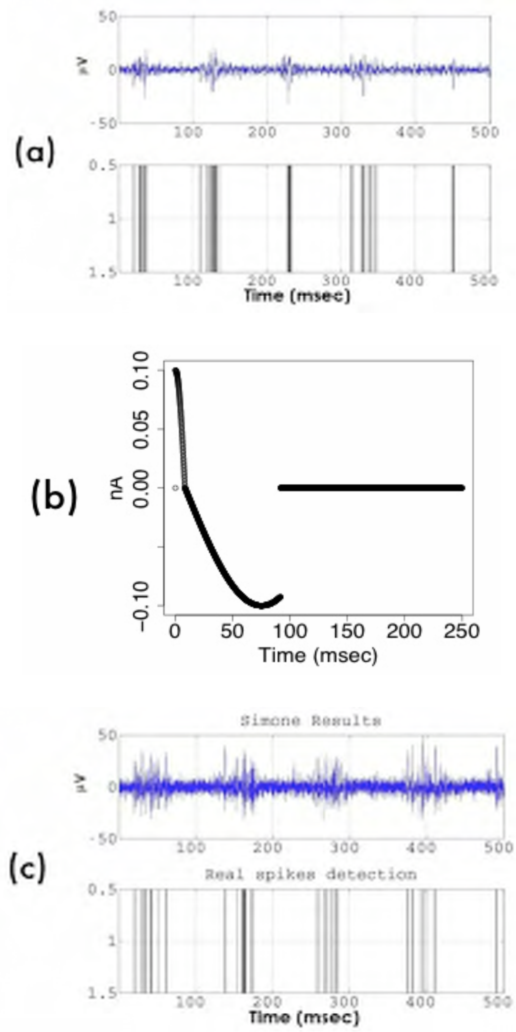

Fig. 4. (a) Real signal with the spike detection. Many burst can be noticed; (b) I_{self} used for the simulation of the real signal (a); (c) Results of the simulation on network 4 with I_{noise} =15 %.

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