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An analysis pipeline for signaling of human stem cell derived neurons in a microfluidics platform with an embedded microelectrode array

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We developed an analysis pipeline particularly for the human neuronal cells cultured on a microfluidics platform with an embedded microelectrode array (MEA). Our pipeline includes efficient tools for the analysis of spikes (extracellular action potentials), single channel bursts (dense time series of spikes) and network bursts (bursts synchronously occurring in multiple electrodes).

I. Introduction

Microelectrode array (MEA) technology has been used for functional neuronal network studies for decades. Neuronal signal processing and analysis of the collected MEA recordings have vital importance for its right interpretation. Briefly, in MEA measurements, each electrode captures superimposed signals of neurons in its close vicinity, while the contributions of distant cells are considered as distorting noise component of the signal. There is a challenge in the field for the accurate detection of extracellular neuronal activity, i.e., spikes, particularly in human neuronal networks [1]. Dense temporal aggregations of spiking activity called bursts which can be recorded from single or several MEA electrodes and defined as bursts and network bursts respectively.

On-chip neuronal models with microfluidics technology and integrated MEA interface enable to analyze neuronal functionality and network interactions more comparable to *in vivo* counterparts. In conventional open MEA platforms the separation between neuronal populations cannot be identified [2]; thus, network-wide burst analysis is aiming to interpret randomly connected neuronal populations. However, with guided axonal growth, networks are well-defined and the input/ouput relations can be assessed more accurately. Simultaneous occurrence of frequent neuronal activity in specific cell compartments reflects network activity between these compartments. Consequently, such platforms with suitable analysis tools have great potential to study neuronal functionality which makes them more promising for drug validation and disease modeling. Our pipeline is aiming to assess different scales of neuronal activity in such platforms, from single neurons (spikes) to small size- (single channel bursts) and large size-populations (network bursts).

II. Methods

We used MEAs with three microfluidic compartments where axonal growth was guided through microtunnels between the cell compartments [3] (Fig. 1A). The spikes were detected with the combined technique that incorporates traditional amplitude thresholding and stationary wavelet transform based Teager energy operator algorithm (Fig. 1B) [1]. Based on the acquired spike times burst detection was performed with LogISI algorithm [4] (Fig. 1B). The synchronous network activity was assessed with custom algorithm based on former ISIN approach [5] Fig. 1C.

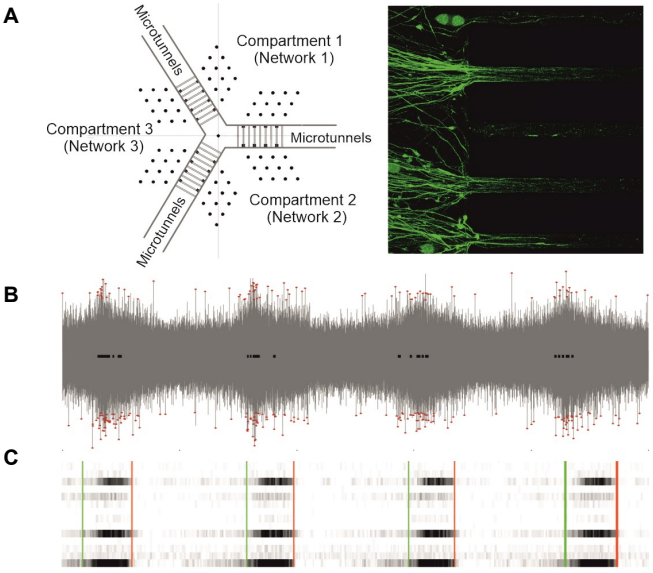

Figure 1. (A) Three-comparmental microfluidics device. Dots are representing the electrodes and lines between comaprtments are representing the microtunnels. (B) Exemplary single channel recording: Detected spikes shown in red circles and single-channel bursts shown in black lines. (C) Examplary network bursts detected among several channels: Green and red lines indicate network burst start and end times respectively.

Our analysis pipeline revealed neuronal functionality in our state-of-the-art models. Consequently, the results of the novel analysis tools will help to discover the mechanisms of epileptic seizures and other types of diseases during their development and spread.

References

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