Micro-Electric Imaging: Inverse Solution for Localization of Single Neuron Currents Based on Extracellular Potential Measurements

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Abstract

We have introduced the first inverse current source density estimation method directly designed to extracellular action potentials. Based on a priori knowledge of the anatomical and biophysical properties of the cell, a parametric model of the current sources was constructed which is simple enough to estimate the corresponding parameters, but still provides accurate and general description of the system.

Keywords: Micro electrode array; Extracellular potential; Current source density; Inverse solution; Electric Imaging

In spite of the fact that the human brain, when compared with modern computers, consists of relatively slow processing units, the neurons, it shows remarkable performance in many tasks and situations where computers, the existing artificial intelligence solutions or artificial neural networks fail. The most striking difference between a transistor of a computer CPU and a neuron in the mammalian brain is that while a transistor is connected to only two or three other transistors, a typical neuron receives input from 10000 other neurons on average. Thus, we have good reason to assume that the computational power of neuronal circuits relies on the specific input patterns the individual neurons receive and on the sophisticated nonlinear computations they perform on their input. However, our current knowledge about the actual transformations the neurons implement is severely limited by the lack of any experimental technique able to monitor the spatio-temporal distribution of synaptic currents on individual neurons in freely behaving animals. Thus, the breakthrough we have targeted is a new micro-electric imaging technique, which is able to determine the distribution of synaptic currents impinging the dendritic membrane of single neurons and thus provide a crucial insight into how the neuron converts synaptic input into action potential firing [1].

EC potential measurements with chronically implanted micro-electrode systems provide information about spatio-temporal dynamics of cell activities, but this spatial information haven’t been exploited on the single cell level before. Our work challenge the current thinking by aiming the extraction of the spatio-temporal information encrypted in these data about the presynaptic inputs to the individual neurons.

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The EC potential patterns are generated by the membrane currents flowing into the neurons, and this process is well described by the Poisson equation. Thus, extraction of the spatio-temporal information requires an inverse solution of the Poisson equation for reconstructing the current sources, based on the measured EC potentials.

We have introduced the first inverse CSD method directly designed to extracellular action potentials. Based on a priori knowledge of the anatomical and biophysical properties of the cell, a parametric model of the current sources was constructed which is simple enough to estimate the corresponding parameters, but still provides accurate and general description of the system [2]. In order to reconstruct the spatio-temporal distribution of membrane currents of a single neuron we need to make prior assumptions about the shape of its dendritic tree and estimate its distance from the electrodes. Whereas the morphology of the neuron is a parameter of the current source model, the neuron-electrode distance can be directly estimated. This distance estimation method resembles to the auto-focus methods applied in automate photo cameras. There the basic assumption is, that the object has sharp contours. The picture depends on the distance and the lens makes an inverse transformation, which also has a distance parameter, the focus distance. The autofocus system measures the sharpness of the picture and changes the focus until the sharpest picture is reached. Typically it gives only the sharp picture, but it also would be able to estimate the object distance.

First, the new method was tested on simulated data and its performance was compared to the traditional current source density (CSD) estimation method. It was shown, that the our new method was able to reconstruct the original source distribution with much higher accuracy than the traditional method and precisely determinate the cell-electrode distance as well.

Second, our new method was applied to in vivo measured action potentials as well. These spikes were recorded in cat primary auditory cortex with a 16 channel chronically implanted linear probe in vivo. The inter-electrode distance i.e. the spatial resolution of the recordings were 100 microns. Using our new method, the electrode-cell distances were estimated. Our results show, that by using new mathematical source localization methods and high density, chronically implanted micro electrode arrays, previously unobservable details of initiation and spatio-temporal dynamics of neural action potentials can be revealed (Fig. 1).

In perspective, the new micro electric imaging technique raises the possibility to determine the contribution of specific neuronal populations to the local field potential, in order to bridge the gap between the microscopic and the...
macroscopic neuro-electric phenomena. The new method will provide better description of cortical microcircuits and their dynamics, which is essential for the understanding of their computation.

**References**