Unsupervised spike sorting with ICA and its evaluation using GENESIS simulations

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Abstract

Data acquisition for multisite neuron recordings still requires two main problems to be solved — the reliable detection of spikes and the sorting of these spikes back to their originating neurons. Approaches and solutions for both problems are difficult to evaluate quantitatively, due to a lack of knowledge about the "truth" behind the experimental data. Biologically realistic simulations allow to overcome this fundamental problem and to control all the processes which lead to the measured data. Within this framework the quantitative evaluation of the performance of data analysis methods becomes possible. In this paper the potential of Independent Component Analysis (ICA) for spike sorting and detection is studied. A biologically realistic simulation of hippocampal CA3 is used to get a measure of quality and usability of ICA to solve the neural cocktail party problem. The results are promising.

Key words: Independent Component Analysis, Spike Detection, Spike Sorting, Biological Realistic Network Simulation, GENESIS, Multisite Neuronal Recording

1 Introduction

It is now common knowledge that the processing power of the brain is based on its billions of computing units, called neurons. These cells communicate primarily by an exchange of action potentials among dynamically changing networks. So far, their representing peaks in extracellular voltage are easiest

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measured using low-traumatizing microelectrodes that are inserted into the neuropile with as little damage as possible to the cells.

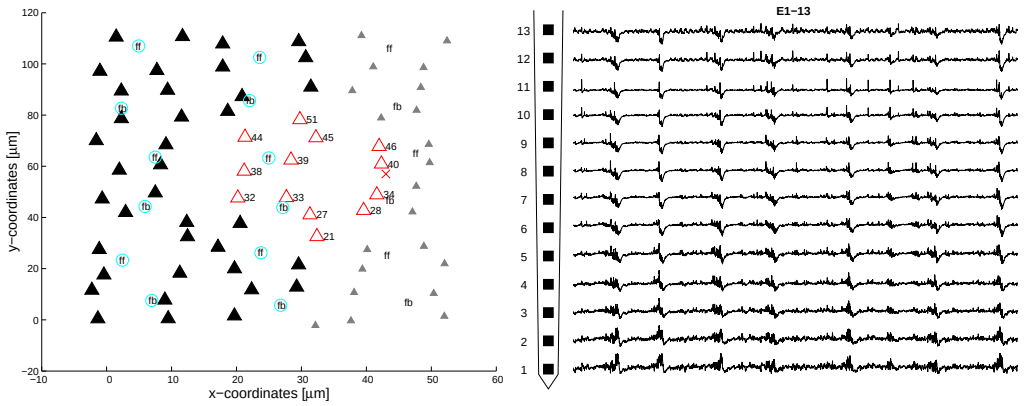
Unfortunately, an electrode's signal is not exclusively the recording of a single neuron but a mixture of all neurons that surround this electrode. As a consequence, the analysis of such a signal, especially the extraction of spikes becomes difficult due to superposition and elimination effects. The problem is similar to the infamous cocktail party problem, which can be solved by using a multiplicity of recording devices and an appropriate signal analysis algorithm, e.g. Independent Component Analysis.

Independent Component Analysis (ICA) is an extension of the widely used Principal Component Analysis (PCA). It assumes that the measured signals are mixtures of statistically independent sources. While PCA decorrelates the measured signals for extracting the sources from these incoming mixtures, ICA not only tries to find a decorrelated but statistically independent decomposition of these mixtures [3]. Here, the statistically independent sources are the neurons. Having extracted the source signals, sorting and detection becomes much easier, as each isolated signal then has the characteristics of the corresponding neuron's intracellular potential.

Brown et al. [2] already used ICA for spike sorting on 448-channel photodetector signals from insects. In this experiment, neurons were stimulated to perform time dependent activity bursts, which then were used to evaluate the performance of ICA. However, the drawback of this kind of evaluation is that the ground truth is not known and can only be crudely estimated, based either on an expected behavior of the system or on an subjective judgment of an expert.

This fundamental problem can be bypassed by biologically realistic simulations, e.g. with GENESIS [1]. This simulation software was originally developed to realistically simulate single neurons. The simulation of an ensemble of such neurons can mimic extracellular recordings as if achieved with real multielectrodes. But this time we know the ground truth, i.e., all the detailed processes behind the measured data.

So far, neural activity has been measured by spikes that were extracted from the raw signal trains. But recent results revealed that the reliability of the commonly used detection methods is not very high. Menne et al. [4,5] evaluated different spike detection algorithms on the proposed GENESIS simulations. All these methods, ranging from simple thresholds to discrete wavelets, showed a rather bad overall detection performance. To reach a false acceptance rate (FAR) of about 10%, most methods end up with a false rejection rate (FRR) of almost 60%. As long as detection results are on this level, the usefulness of sorting algorithms based on these detections is questionable (this might be one of the reason why reference data for the performance of spike sorting approaches can hardly be found).



(a) **(b)**

Fig. 1. **(a)** The GENESIS simulation setup. Pyramids show the position of pyramidal cells and interneurons, denoted by *ff* and *fb*, respectively. The electrode is located at the cross. Contributing cells are large, detectable cells are unfilled. **(b)** An example for a 1.5s multi-channel recording with 13 simulated electrodes.

2 Data and Methods

Menne et al. used GENESIS to mimic the behavior of a tiny part of the CA3 region of a rodent Hippocampus, using a network with 72 pyramidal cells and 18 interneurons. In Figure 1a this setup is shown. The pyramidal cell clones are arranged in a 6×12 array. 9 feed-forward and 9 feed-backward interneurons are distributed among them. The z-coordinate of all cells is randomly altered in a range of $\pm 50 \mu m$, and the clones are rotated randomly around the z-axis to provide for more morphological variability. Compartment models according to Traub et al. for the pyramidal cells [7] as well as for the interneurons [6] are used. Extracellular recordings are taken as if recorded with a single multielectrode probe equipped with 13 microelectrodes, linearly arranged with a stepwidth of $12.5 \mu m$. The multielectrode yields a realistic signal of the transmembrane current, mimicking electrodes fixed on one side of an insulating carrier [4].

Due to the distance energy loss of each cell as well as the estimated opening angle, only some cells have the possibility to contribute to the mixed signal above the noise level. Such cells are marked by unfilled triangles in Figure 1a. Figure 1b shows a typical recording obtained with the proposed setup.

The number of statistical independent sources that ICA can extract is limited by the number of recording channels. In our setup with 13 electrodes we can separate the signals of at most 13 cells. Since only 13 pyramidal cells and 2 interneurons are contributing spikes above the noise level, the number of channels is in a reasonable size.

It should be mentioned again that with ICA we first perform the sorting and then the detection task. This is illustrated in Figure 2. An IC is shown and, determined with the normalized scalar product, its best matching electrode. The third plot shows the best matching principal component (PC), and the

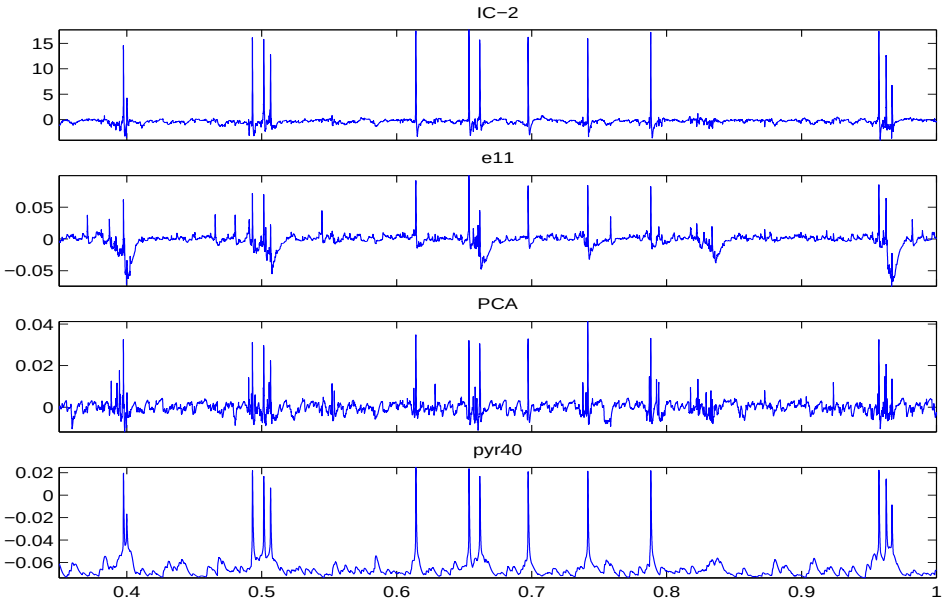


Fig. 2. The top plot shows an IC with a sufficiently high normalized scalar product with at least one of the electrode signals. The second plot shows the electrode signal which is best matching with this IC. The third plot shows the best matching principal component, and the last plot shows the signal of the assigned neuron, in this case the intracellular potential of pyramidal cell 40. The IC represents the signal of its assigned neuron very well.

last plot shows the original neuron signal. This cell is very well recorded by the electrode shown. But still, it can be seen that some spikes get weaker or disappear completely, while other spikes get mixed into the electrode signal from other cells. The IC impressively matches the original cell signal, while the PC has problems to separate the signal from the background noise.

For each IC, we have to decide whether or not it represents a neuron. We used the simple normalized scalar product between the raw electrode signals and the ICs as a measure. A high product indicates that an IC represents a neuron, i.e., a certain subset of spikes are found on one of the electrodes as well. On one hand, this is a drawback of our approach, as we constrain our results to cells that can be seen on the raw data anyway. But on the other hand we only need to use the electrode data for this measure. Hence, exactly the same framework can be used on real data. Furthermore, as we will see later, with the product between IC and electrode it is possible to estimate the position of the represented neuron relative to all electrodes.

Using the knowledge about the original neuron signals, we calculated two receiver operating characteristics curves (ROC curves), one for detection and one for sorting. For the latter, no approaches exist for comparison. It might itself be used as a benchmark in the future. The detection results can be compared to the quality level of classic approaches. For spike detection, we use each IC that was assigned to a neuron and combine the result. The spikes in the ICs can simply be detected with a positive threshold, as these ICs

are assumed to represent the intracellular potentials of single neurons. For determining the spike detection error the result is compared with the overall spike train of all cells that are represented by the ICs.

A measure for the performance of the spike sorting is given by the ability to detect the spikes of a neuron, based on its representing IC. I.e. for each IC that is representing a neuron, we get a ROC curve, this time showing the one-to-one comparison of each IC with its corresponding cell.

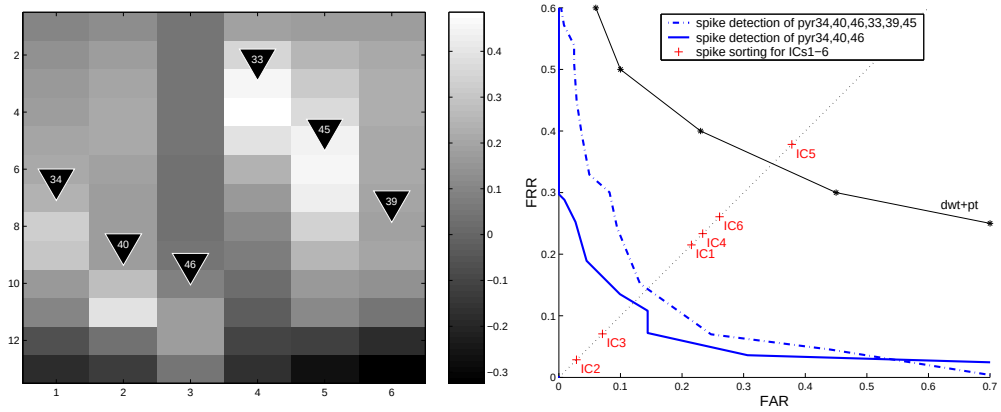
3 Results

We used a 1.5 seconds simulation of the described 13 channel multielectrode recording to extract 13 independent components. Calculating the scalar product between the electrodes and the independent components, we extracted six ICs that matched good enough onto the electrode signals to be assumed to represent neuron signals. At this point we completely discarded the remaining seven ICs. In future work they might be taken into account as well. For the "top 6", the scalar product matrix is shown in Figure 3a. Each column codes the score between an IC and all 13 electrodes. The brightest spot in each column can be used as an estimate for the z-position of the neuron represented by this IC. The "real" positions of the corresponding pyramidal cell somas are shown as well. They all match very well up to a constant offset.

In Figure 3b the ROC curves for the spike detection performance is shown. So far, the best result for spike detection performance has been obtained for a combined discrete wavelet and positive threshold (pt) method [4]. This approach reaches an equal error rate (EER) of only about 35%. We generated two ROC curves for detection, one with all six ICs and one with the three ICs representing the three cells closest to the electrode probe. Of course, the better result is obtained for the latter one (EER=12%), however, also for all six cells we still reach an EER of remarkable 14%.

Then we evaluated the sorting performance. For this purpose we generated a ROC curve for each of the six ICs. Not to overdraw Figure 3b, we only show the equal error rate (FAR=FRR) of each ROC curve. The sorting is harder than the overall detection of spikes. For example, a false positive sorted spike of one IC might be a correctly detected one if looked onto the whole set of ICs (as we do it for detection). In spite of that, for some of the cells we reach an impressive EER of below 10% for spike sorting. That means, for these cells we succeeded in reconstructing more than 90% of all spikes.

We applied the same procedure to a 5 second simulation. To test robustness and time-independence, we performed ICA on the complete 5s and on an arbitrary window of 1.5s length. Then we determined detection and sorting performance on the signals within the 1.5s window with both the ICs from the 5s and the 1.5s window. This was done for different 1.5s windows. All the time the results obtained with the ICs from the 5s interval and the ICs from the respective 1.5s interval were comparable. Thus, ICA on multisite



(a) **(b)**

Fig. 3. **(a)** The normalized scalar product of ICs and electrode signals, white for a 100% match. Black triangles denote the location of the pyramidal cells represented by the ICs. **(b)** The black line with stars shows the ROC curve of a dwt+pt method [4]. The other lines show the ROC curves for spike detection of the top six ICs (slash-dotted) and the top three ICs (solid) with their represented cells as ground The crosses mark the EER for the spike sorting task for each IC, separately.

neuron recordings appears to be a quite time-independent and robust analysis method.

4 Discussion

We have shown that ICA is a promising method for spike sorting. We succeeded in extracting six independent components that represented six cells in the surrounding of the multielectrode. We were able to estimate the position of these cells up to a certain offset. Not only that we reached a competitive result for the spike detection, we even got impressively good results for the spike sorting task within the direct neighborhood of the probe. These results were stable over time.

In the simulation, we used a probe with a very simple linear arrangement of the electrodes along the z-axis. In the future it might be possible to design and test different layouts either for optimal use with ICA or for any other purpose. Then, it might be possible to generate even 3D maps of the recorded neurons and to sort the corresponding spiking activities reliably.

ICA can be performed on-the-fly. Once the transformation which decomposes the mixed signals into their independent sources is learned, a time series of electrode data can be decomposed on-line. This can be extended to the level where ICA multielectrode analysis could lead to a new generation of experimental devices which allow the experimentalist not only to visually inspect the neurons located around the probe but to track the activity of each visible neuron in real-time.

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