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 by 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 us 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 obtain a measure of the quality and usability of ICA for solving the neural cocktail party problem. The results are promising.

Key words: Independent Component Analysis, Spike Detection, Spike Sorting, Biological Realistic Network Simulation, 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 within dynamically changing networks. So far, their corresponding peaks in extracellular voltage are measured most easily using low-traumatizing microelectrodes that are inserted into the neuropil with as little damage as possible to the cells.

Unfortunately, an electrode 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 famous 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 [1].

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 measured signals to extract sources from these incoming mixtures, ICA tries to find not only a decorrelated but statistically independent decomposition of these mixtures. 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. In the following, we used the fastICA matlab

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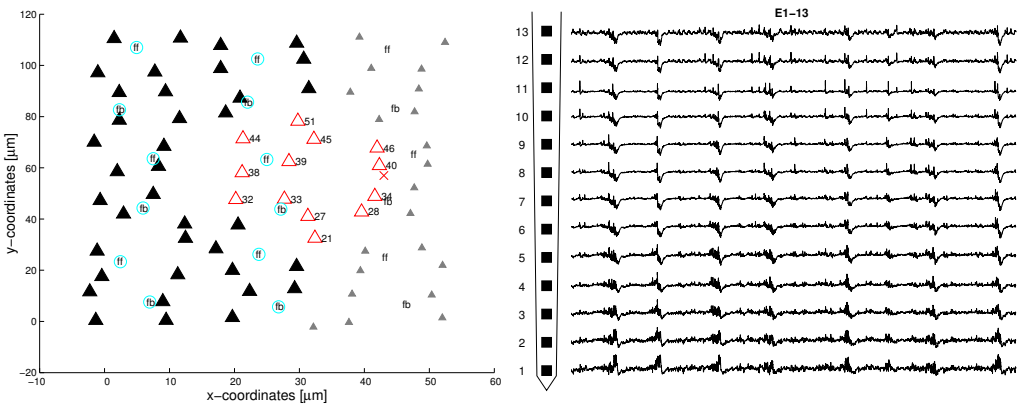
package from Hyvärinen et al. [1], which is one of the most frequently used methods due to its high robustness and fast convergence.

Brown et al. [2] already used ICA for spike sorting on 448-channel photodetector signals from the seaslug, *Tritonia diomedea*. In this experiment, neurons were stimulated to perform time dependent activity bursts, which were then used to evaluate the performance of the ICA. However, a 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 the subjective judgment of an expert [3].

This fundamental problem may be bypassed using biologically realistic simulations, e.g. with GENESIS [4]. This simulation software was originally developed to simulate single neurons. The simulation of an ensemble of such neurons can mimic extracellular recordings as if achieved with real multielectrodes. The difference in this case is that 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 have revealed that the reliability of the commonly used detection methods is not very high. Menne et al. [5,6] 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 reasons 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. Interneurons are denoted by *ff* and *fb*, respectively. The probe is located perpendicular to the cross. Contributing cells are shown as large triangles, 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 [5]. Figure 1a shows this setup. The pyramidal cell clones are arranged in a 6×12 array. 9 feed-forward and 9 feed-backward interneurons are distributed among the pyramidal cells. The z-coordinate of all cells is randomly altered in a range of $\pm 50 \mu m$, and pyramidal cell clones are rotated randomly around the z-axis to provide for more morphological variability. Compartment models according to Traub et al. are used for the pyramidal cells [7] as well as for the interneurons [8]. Here, a single multielectrode probe equipped with 13 linearly arranged microelectrodes is simulated. These electrodes are arranged with a step width of $12.5 \mu m$, mimicking their fixation on one side of an insulating carrier. Without the z-offset, all cells initially have a z-position between the fifth and sixth electrode. At $15 \mu m$ cell-electrode distance, positive spike

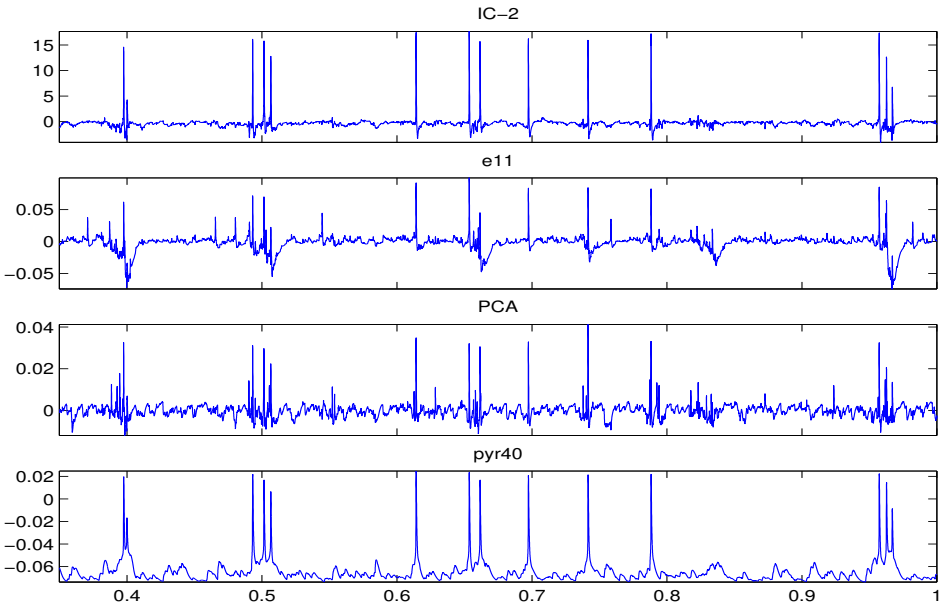


Fig. 2. The top plot shows an IC with a sufficiently high normalized scalar product with at least one of the electrode signals. The second plot shows the electrode signal best matching with this IC. The third plot shows the best matching principal component, and the last plot shows the best matching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

amplitudes lose more than 2/3 of their height [5].

Due to this signal attenuation as well as to the recording directionality of the simulated electrodes, only certain 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.

Assuming a linear mixture of statistically independent sources measured with 13 electrodes, we can separate the signals of at most 13 cells. Since only 13 pyramidal cells and 2 interneurons contribute spikes above the noise level, the number of channels is in a reasonable range.

ICA solves the sorting task *before* the detection task. Figure 2 shows an IC and,

as determined by the normalized scalar product, its best matching electrode. The third plot shows the best matching principal component (PC), and the last plot shows the best matching intracellular neuronal signal. This particular cell is recorded very well by the electrode shown. Still, it can be seen that some spikes get weaker or disappear completely, while other spikes are recorded from other cells. The IC visually matches an original cell signal, while the PC has problems to separate the signal from the background signal.

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 large scalar product indicates that an IC correlates well with a certain subset of spikes found on one of the electrodes. In this way, we constrain our results to cells that are already visible on the raw data. On the other hand, our method is based only on extracellular data. Hence, exactly the same framework can be used on real signals. Furthermore, as we will see later, with the product between IC and electrode signal, it is possible to estimate the position of the corresponding neuron relative to all electrodes. Using our prior knowledge of the extracellular simulation, we derived two receiver operating characteristic (ROC) curves, one for detection and one for sorting. Detection results are superior to the quality level of common approaches, as far as evaluated on simulated data [5]. Here, spike detection means that we combine the spikes of all ICs and compare them to the spikes of their best matching cells. Spikes in those ICs are then detected with a positive threshold, as these ICs are assumed to represent the potentials of single neurons. To determine the spike detection performance, results are compared with the overall spike train of all cells represented by these ICs.

The performance of spike sorting is defined by the ability to extract the spikes of each neuron individually. Therefore, for all significant ICs, we determined

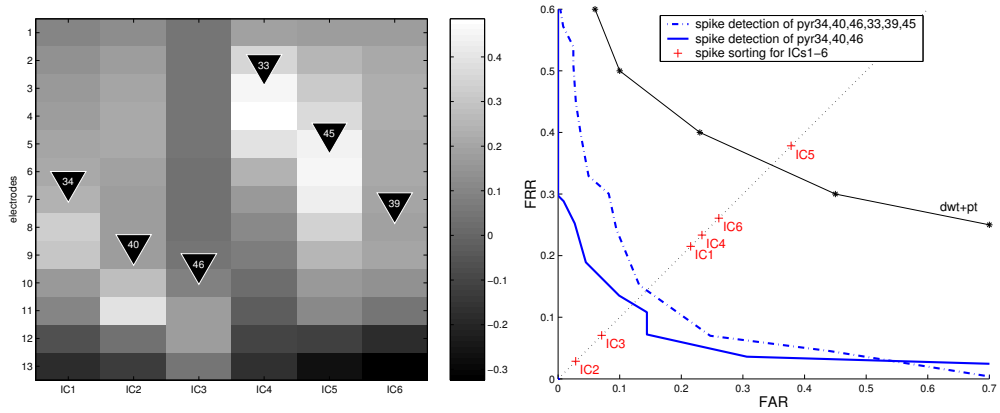
the equal error rate between each IC and its best matching intracellular cell potentials.

3 Results

We used a 1.5 second simulation of the described 13 channel multielectrode recording to extract 13 independent components. Calculating the scalar product between the electrode signals and the independent components, we extracted six ICs that matched well enough onto the electrode signals to be taken as representing neuronal signals. At this point, we completely discarded the remaining seven ICs. In future work they might be taken into account as well. The scalar product matrix for these "top 6" 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.

Figure 3b shows the ROC curves for the spike detection performance. So far, the best result for spike detection performance has been obtained for a combined discrete wavelet and positive threshold (pt) method [5]. 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 case (EER=12%), however, even for all six cells we still reach an EER of remarkable 14%.

Next we evaluated sorting performance. For this purpose, we generated a ROC curve for each of the six ICs. So not to clutter Figure 3b, we only show the equal error rate (FAR=FRR) of each ROC curve. Sorting is harder than the



(a) **(b)**

Fig. 3. **(a)** The gray values show the normalized scalar product of ICs and electrode signals, white for a best 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 [5]. 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 truth. The crosses mark the EER for the spike sorting task for each IC with its best matching cell signal (see triangles in Figure 3a).

overall detection of spikes. For example, a false positive sorted spike of one IC might become a correctly detected one if we look at the set of all ICs (as we do for detection). In spite of this, for some of the cells we reach an impressive EER of below 10% for spike sorting. This means that, 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 an 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 the ICs from both, the 5s and the 1.5s window. This was done for different 1.5s windows. In all cases, 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

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 matched six pyramidal cells in the surroundings of the multielectrode. We were able to estimate the position of these cells up to a certain offset. Not only did we reach a superior result for spike detection, we even obtained 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 electrodes along the z-axis without any induced ensemble activity. Using a parallel version of GENESIS, we will be able to simulate much larger networks with individually grown cell models with several thousand compartments. Then, it might be possible not only to design different site layouts for optimal use with ICA, allowing us to generate 3D maps of detected neurons, but also to examine the capabilities and restrictions of using ICA on the analysis of synchronous activity of neuron ensembles.

ICA can be performed on-the-fly. Once the transformation that decomposes the mixed signals into their independent sources has been learned, a time series of electrode data can be decomposed on-line. Hence, 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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