Neural signal analysis and artifact removal in single and multichannel in-vivo deep brain recordings

Ivan Gligorijevic[1], Marleen Welkenhuysen[2], Dimiter Prodanov[3], Silke Musa[4], Bart Nuttin[5], Wolfgang Eberle[6], Carmen Bartic[7], Sabine Van Huffel[8]

[1,8] ESAT/SCD, Dept. of Electrical Engineering, Katholieke Universiteit Leuven, Belgium

[2,3,4,6,7] Bioelectronics Systems group at IMEC, Belgium

[5] Division of Experimental Neurosurgery and Neuroanatomy, Katholieke Universiteit Leuven, Belgium

Abstract

Single-channel neural signal recordings were obtained from deep brain region in normal rats and rats conditioned as an animal model for human obsessive-compulsive disorder (OCD), both in anesthetized condition. Artifact noise of consistent 70Hz repetition frequency and its harmonics was observed and found to significantly distort recorded data inducing spike-like shapes. A multichannel probe developed in IMEC was later introduced and the FastICA algorithm was successfully applied to eliminate the artifact noise. Wave_clus algorithm served as a verification tool and showed that detection and clustering performance was largely enhanced on FastICA preprocessed signals. Multichannel microprobes combined with advanced signal post-processing show a great promise for observation of neural activity.

1 Introduction

In prospect of the development of neuromodulatory clinical applications, proper recording and analysis of neural spike trains is necessary. Deep brain stimulation (DBS) is already in use for treating Parkinson disease and it has also recently been approved for treatment-resistant patients with obsessive-compulsive disorder (OCD) [1].

Neuronal extracellular activity potentials, so-called spikes, can reveal specific local properties of the neural network communication in the brain region in which they are located. These properties are embedded in the statistics of their interspike intervals. Analysis of these statistics is a necessary prerequisite for a meaningful stimulation.

Comparison and analysis is dependent on the recording and processing of a large number of neurons.

Detecting spikes and grouping them according to the ``firing'' neuron is called neural spike clustering and is a crucial precondition for spike train analysis.

First, we wanted to explore additional brain regions (apart from clinically used ones) as potential target for deep brain stimulation therapy. We performed a series of experiments to characterize the firing pattern of neurons, using a commercial electrode, in both normal rats and rats subjected to schedule-induced polydipsia, a condition which is considered to be a validated animal model for the human OCD.

After this experiment was finished, we introduced IMEC's multichannel planar recording probes [2] in a trial set of measurements similar to the ones mentioned, to evaluate what would be the possible benefit of using these in similar experiments and whether multichannel blind-source separation techniques used as a preprocessing tool can induce some improvement.

The objective of this work is to present problems and possible solutions for future recordings and analysis of spike trains. Emphasis is put on the use of Independent Component Analysis (ICA) [3] as a preprocessing tool for multichannel neural recordings to remove artifacts and improve the signal for subsequent analysis.

2 Methods

All recordings were performed by the medical partners with rat subjects under anesthetized conditions.

The recording depth was varied inside the target region itself, resulting into 5-minute recordings for each depth. Filtering was adjusted to spike detection (500Hz-5kHz), with 24kHz digitization frequency. A Medtronic LeadPoint device and a commercial FHC electrode were used.

In the trial set of measurements mentioned, IMEC's multichannel electrode array was used and several ICA algorithms were applied as a signal

conditioning tool for cleaning the signal from artifacts.

The Wave_clus algorithm [4] based on superparamagnetic clustering [5] was applied in all the cases to identify spikes and cluster according to a neuron that fires them. The template matching Osort algorithm [6] was also considered but Wave_clus was chosen due to the fact that superparamagnetic clustering relies on comparing "closest neighbors", which makes it possible to properly assign sometimes different spike shapes (for instance different amplitudes) to the same cluster, in cases where it is justified. This is particularly the case when having a longer recording (as in the OCD experiment) where shape differences could be induced for example by occasional electrode drift. Contrary to that, Osort, although itself a very widely used and successful algorithm, relies on template matching, where a template is being extracted from most recent spike shapes assigned to a certain cluster. While this can improve overall mean spike shape, it is also less robust to sudden changes, like for instance, the aforementioned and expected electrode drift.

The output (formed spike clusters and corresponding timestamps) was combined with indigenously written Matlab code to enable statistical analysis.

The goal was to classify neurons as good as possible according to their firing properties: firing rates, variability of interspike timings [7], representing the ratio of the standard deviation of interspike intervals (ISIs) to the mean ISI, and randomness as described in [7] which is a quantity corresponding to number of possible values of observed interspike intervals, somewhat similar to entropy ([7]) and burst activity (fast neural consecutive firing). Then, the procedure examines comparable neurons (like tonic, which fire regularly or bursting, etc.) and uses them to evaluate if there is a "global" change.

After originally planned OCD experiment was done, a multichannel recording probe of the new generation was introduced on a trial basis, to test possible improvements in similar experiments to be done in future. Usage of multichannel probes, with closely spaced electrodes, allows observation of a larger set of neurons per trial, thereby making the analysis more relevant. Measurements obtained using them, were preprocessed with several ICA algorithms (SOBE [8], InfoMax [9] and FastICA, [10]) mostly to reduce both biological and appearing artifact noise (to be discussed below). InfoMax and FastICA were found to perform best for detection of spike-like shapes (which was also the shape of artifacts we wanted to exclude) but FastICA was selected due to its computational efficiency which is important when coping with large amount of data (high sampling frequency of 24kHz). Preprocessing was done by applying FastICA to four recording channels from closely spaced electrodes, so that signals were somewhat correlated which is a necessary condition for effective use of ICA algorithms. Among the independent components extracted by FastICA, one was identified as being artifact noise and excluded in the signal reconstruction. The reconstructed preprocessed signals were then analyzed according to the above-mentioned analysis (clustering and statistics).

3 Results

Obtained signal-to-noise ratio (SNR) in the first part (OCD experiment) was rather low (1.3-2.5 in most of the cases). We compared Wave_clus and Osort in several cases, before finally deciding to proceed with the first algorithm.

The use of the Wave_clus algorithm made it possible to still work below 2.0 SNR level. Although Osort was found to have better detection in some cases, it also exhibited lower discrimination as signal-to-noise ratio drops, which is shown in Figure 1. Same color in the picture represents spikes recognized by the algorithm as belonging to the same cluster.

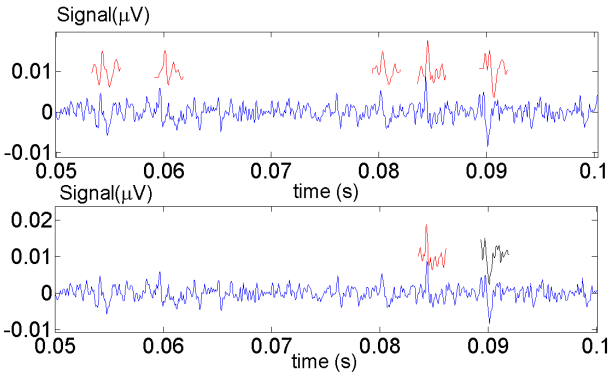


Figure 1: Comparison in performance of Osort and Wave_clus with low SNR. a) (upper trace) spikes detected and clustered with Osort. b) Wave_clus classification

A group analysis of over 400 recorded 5 minute duration signals was successfully performed.

We found that, so far unexplained artifact noise of 70Hz and its harmonics is present and greatly reduces the accuracy of detection, in some cases completely masking the spikes of interest.

When we later introduced the multichannel array probe, several channels were severely corrupted by the artifact noise also present in the

single channel recordings of the OCD experiment. One of these is shown in Figure 2; the upper trace zooms into a segment of lower trace. Red shapes shown are artifacts induced as a transient process of this noise.

Figure 3 shows Fourier spectra of the signal before and after cleaning with FastICA: strong artifact components of 70Hz and its aliased frequencies before and after removal are shown.

Figure 4 zooms into a signal from one of the electrodes, and illustrates the performance of the Wave_clus algorithm before and after cleaning. It shows artifact induced spikes (upper trace, pointed to by red arrows) having been removed (lower trace) in the time domain, also revealing additional spike shapes.

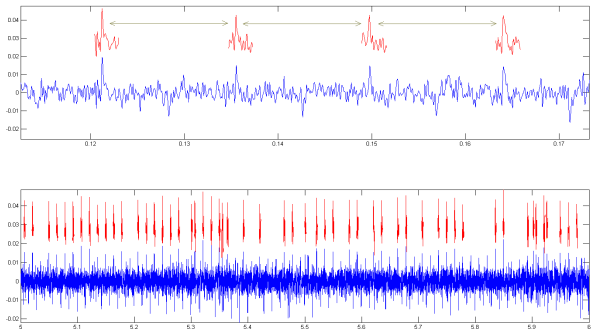


Figure 2: Artifact noise in time domain: upper trace is a zoomed part of a trace below

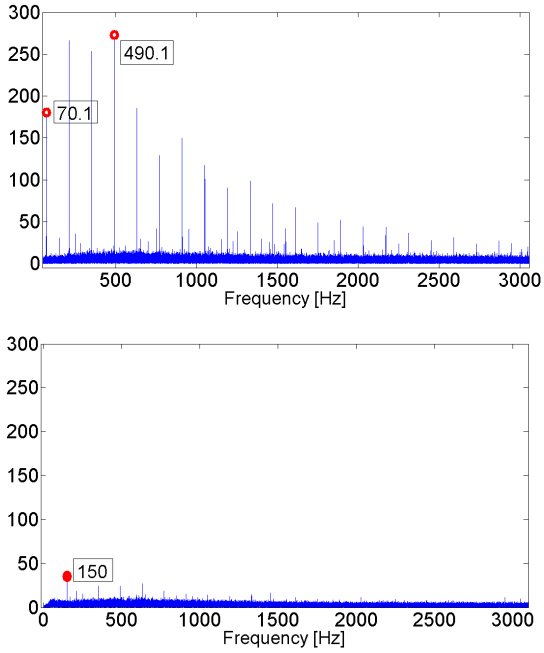


Figure 3: Fourier spectra of the original signal (up) showing strong 70Hz and its harmonics (70Hz and 490Hz components were indicated), and after (down) the removal of artifacts (weak 150 Hz component indicated).

Figure 5 reveals sharp peaks in the interspike interval histogram (left) of the detected artifact cluster (right) wrongly identified as a neural spike cluster.

Signal quality of each individual microelectrode proved to be comparable to that of a commercial single channel electrode.

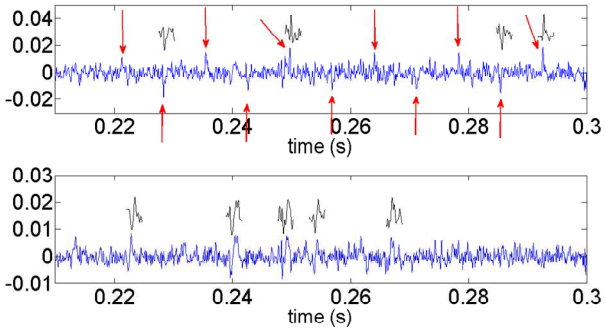


Figure 4: Time domain signal before (up) and after (down) removal of artifact. Red arrows point to a noise trace. After artifact removal, additional spikes were revealed (down)

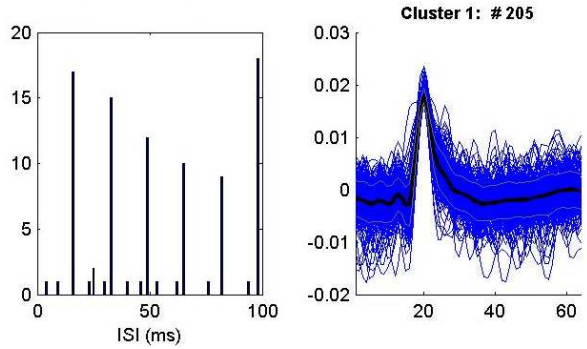


Figure 5: Interspike interval histogram (left) for the detected shapes (right)

4 Discussion

We used the Wave_clus algorithm successfully for detection and clustering of spikes. Its performance proved to be satisfactory for most of the cases, taking into account that below a certain SNR level (in our experience 1.7) signals had to be discarded, even if spikes were detected, due to the low reliability of their classification. Wave_clus algorithm, combined with our code, enabled spike train analysis in the OCD experiment.

When observed in single channel recordings, reported artifact noise posed a big obstacle, since we were unable to remove it successfully without significant distortion of the signal of interest. That's why, filtering was rejected in this case and the signal left as it was. If, for example, a comb filter was applied, the artifact could be removed but at the

expense of a great loss of valuable information in the frequency range of interest (500Hz-5kHz).

We compared Osort and Wave_clus algorithms. Although sometimes more spikes were detected by Osort, an error was also introduced (Figure 1 upper trace, all shapes are assigned to the same cluster although for example the last spike obviously differs from the others, as well as the first three shapes which are smaller and probably represent firing of a different neuron). When Wave_clus was used, "smaller" spikes were sometimes not detected but more accurate assignment is observed (in Figure 1 lower trace, two indicated shapes put in different clusters represented by red and black color).

Artifact 70Hz frequency and its strong harmonics actually posed a double threat: one being the general signal corruption, and the second one, even more important, that the transient process of this frequency appearance induces shapes strongly resembling spikes (red shapes in Figure 2), often overlapping with neuronal spikes or being wrongly detected by the program as being spikes themselves. These artifact "spikes" are also spread around the same frequency spectra as the real ones, making the classical filtering approach unsuitable. It is visible that shapes wrongly identified as spikes are actually artifacts, located equidistantly with a 14ms appearance interval, which corresponds to 70 Hz.

Artifacts reported could be successfully removed without distorting existing spikes when using a multichannel recording system. View of the spectra (Figure 3 up and down) shows that the signal of interest was not affected while removing the strong artifacts, leaving only weaker aliases of 50Hz power line which didn't affect the signal greatly.

Preprocessing largely improved the performance of the detection and clustering algorithms. Not only artifacts were suppressed but in addition, new spikes, which were originally suppressed, emerged and could be successfully detected by the Wave_clus algorithm, as seen in Figure 4.

Figure 5 depicts the histogram (left) of detected artifact cluster (right) wrongly identified as a real neural spike cluster. If it was really a spike process, it would mean that spikes are appearing in perfectly exact intervals which is not a biological property of process of neural firing. After cleaning, the whole cluster was removed.

5 Conclusion

Using multichannel microelectrodes combined with powerful emerging multichannel processing techniques indicates promising future for long-term reliable observation of neuronal activity. FastICA showed great performance in the preprocessing phase, helping remove reported noise, which we couldn't filter out in the single channel case. Possibilities offered don't end there. Improvements in the quality of proper neural detection and classification, as well as rising potential to observe a larger number of neurons, make multichannel techniques a preferable choice for further exploration.

Acknowledgements

Research supported by Research council KUL: GOA MANET, CoE EF/05/006, by DWTC: IUAP P6/04 (DYSCO); by EU: Neuromath (COST-M0601), IMEC SLT PhD scholarship

References

[1] http://www.fda.gov/NewsEvents/Newsroom/

PressAnnouncements/ucm149529.htm

[2] Silke Musa et. Al. Planar 2D-Array Neural Probe for Deep Brain Stimulation and Recording (DBSR) IFMBE Proceedings 2009

[3] A. Hyvärinen and E. Oja. Independent component analysis: algorithms and applications, Neural Networks Volume 13, Issues 4-5, June 2000, Pages 411-430

[4] R. Quian Quiroga, Z. Nadasdy and Y. Ben-Shaul

Unsupervised spike detection and sorting with wavelets and superparamagnetic clustering. Neural Computation 16, 1661-1687; 2004.

[5] Blatt, M., Wiseman, S., & Domany, E. (1996). Superparamagnetic clustering of data. *Phys. Rev. Lett., 76*, 3251–3254.

[6] U. Rutishauser, E. M. Schuman, A.N. Mamelak Online detection and sorting of extracellularly recorded action potentials in human medial temporal lobe recordings, in vivo. *Journal of Neuroscience Methods*, 2006, 154:204-224, 2006

[7] L. Kostal, P. Lansky. Randomness of Spontaneous Activity and Information Transfer in Neurons. Physiol. Res. 57 (Suppl. 3): S133-S138, 2008

[8] A. Belouchrani, K. Abed-Meraim, J.-F. Cardoso, and E. Moulines. A blind source separation technique using second order statistics. *IEEE Trans. Signal Processing*, 45:434–444, 1997.

[9] Bell, A. and Sejnowski, T. (1995). An information-maximization approach to blind separation and blind deconvolution. *Neural Computation*, 7:1129–1159.

[10] A. Hyvaarinen and E. Oja, A Fast Fixed-Point Algorithm for Independent Component Analysis. Neural Computation, 9(7):1483-1492