Informatik-Bericht Nr. 2008-8

Schriftenreihe Fachbereich Informatik, Fachhochschule Trier

Fuzzy classifier for microelectrode recording-based target navigation in deep brain stimulation

P. Gemmar[1], M.E. Tercero[1], T. Henrichs[1], Y. Thesen[1], O. Gronz[1], F. Hertel[2]

[1] University of Applied Sciences (FH) Trier, Institute for Innovative Informatics Applications (i3A), Trier, Germany
[2] Klinikum Idar-Oberstein GmbH, Idar-Oberstein, Germany

contact person: p.gemmar@fh-trier.de

Abstract:

This study describes novel methods for supporting navigation and placement of electrodes during surgeries for deep brain stimulation (DBS). Critical to these procedures in neurosurgery is the localization and identification of different target structures along the electrode's trajectory in the brain such as the subthalamic nucleus (STN), and finding the best position for the stimulating electrode.

Typically, neurosurgeons use microelectrode recordings (MER) of local neural activity for detecting the target region intra-operatively. We developed specific methods using wavelet transformation for feature extraction from MER signals and generated a fuzzy inference system for automatic classification between STN and non-STN signals. The classifier will support the surgeon and make the decision process for the final electrode position more reliable and less time consuming. It can be adapted easily for the classification of other functional neural areas than the STN also.

Key words: Fuzzy classifier, wavelet transformation, microelectrode recordings (MER), target navigation, deep brain stimulation (DBS), stereotactic neurosurgery, Dystonia, Parkinson's Disease

1 Problem

Deep brain stimulation (DBS) of specific structures in the basal ganglia has become a promising treatment option for different kinds of neurological diseases such as Parkinson's disease (PD), Dystonia, different kinds of tremors, or chronic pain also [1]. In the treatment of advanced PD and Dystonia, the subthalamic nucleus (STN) is considered the most promising target. DBS surgery is preceded by a planning phase for the determination of the 3D-position of the STN and the selection of secure trajectories for sliding the electrodes through the brain. Automatic procedures evaluating CT- and T1-MR-imagery are available for this process [2]. In the surgery phase, a stereotactic frame is used for pushing the stimulating electrodes – one per each hemisphere – along the planned trajectory towards the target position. However, MRI distortions, limited mechanical precision, and shifting of the brain within the cranium prevent from reaching the real target structure with the electrode's stimulation poles precisely.

Therefore, in the surgery phase very often up to five electrodes are inserted on parallel trajectories for finding the best hit with the target structure [3]. Most surgeons use microelectrode recordings (MER) to recognize the target structure while sliding the electrodes towards the target. MER signals measure the local activity within a small area proximal to the tip of the electrode as it is moved stepwise through the brain. The MER of different brain structures can be distinguished based on commonly known features such as background activity, spike or burst rates [4,5].

Classification of the MER signals is sometimes ambiguous and often time consuming even for experienced neurosurgeons. There are different approaches for automatic analysis and classification of MER signals using statistical features or digital spike trains [6,7]. We developed a new method for MER classification based on soft de-noising and multi-level decomposition of the MER signals using wavelet transformation. The method extracts features for a Fuzzy classifier, which comes up with a self-adapting decision structure for discerning MER signals coming from different local brain areas and from different patients.

2 Materials and Methods

MERs for development and testing of the classifier were recorded at two Hospitals in Germany. The sampling rate for the MERs was 24kHz at the first hospital and 25kHz at the second hospital, respectively. The MER signals were meas-

ured in 1 mm (0.5 mm in target proximity) intervals along the electrode's trajectory. We always considered signals of 10s length per each depth step.

Within the last decade, the main characteristics of STN signals and useful methods for their identification have been examined and described thoroughly (e.g. [4]). In principle, the most useful criteria considered for recognition of STN signals are the distribution of spikes and bursts and an increased background noise (see Figure 1 left). Nevertheless, the quantitative data specifying the most important features – spike rate and spike distribution – differ considerably, which seems to be natural, as these values differ from patient to patient.

Feature extraction

Based on the results we obtained from investigations of statistical features in the time domain and of spectral power features in the frequency domain, we concentrated our feature extraction for MER signals on two aspects. Firstly, we examine the background activity of MER signals. Potential neural active signals show higher background activity and higher cell activity (Figure 1). We measure the grade of background activity by specific quantiles of the signal's amplitude distribution. Let vector s represent a discrete MER signal, then *quantile(s,α)* calculates an *α-quantile* of s. We calculate the distribution of the *α-quantile* of all MER signals s_i collected along the trajectory of one electrode. From this distribution, we use a *β-quantile* to extract a patient specific threshold θ_m discerning the MER signals s_i coming from neural or non-neural brain areas. We do this latter comparison ($c_1(i,j) = quantile(s_{ij},α)- \theta_m$) with respect to sub-signals s_{ij} obtained from subdividing each signal s_i into a series of intervals.

In addition, we calculate the standard deviation *std(s_i)* of signals s_i and a threshold θ_s from their distribution in the same manner we achieved θ_m. Again, we compare the local standard deviation of sub-signals s_{ij} with θ_s: $c_2(i,j) = std(s_{ij})- \theta_s$. Now, we linearly combine these two comparisons $c_1(i,j)$, $c_2(i,j)$ and get feature $f_1(i)$ describing the background activity.
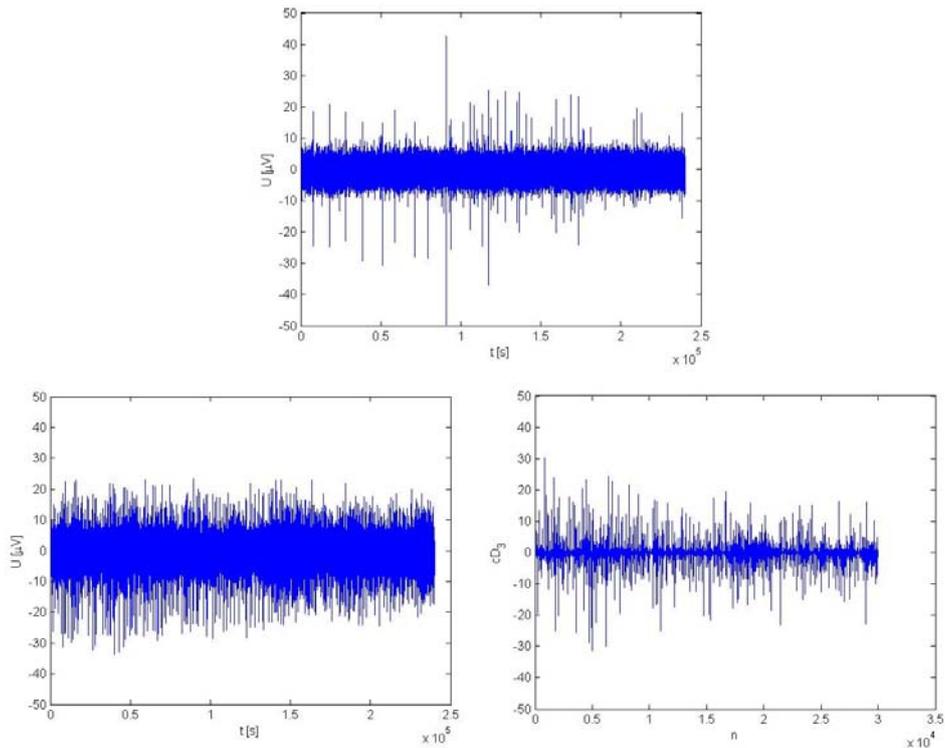

Figure 1: Typical MER signals (upper: no neural activity, below left: STN area, right: cD_3 of STN signal)

In the second aspect, the signals are inspected with respect to irregular bursting patterns of the STN. We can assume that two different sources are responsible for the background activity: first the activity of a large set of neurons in different distances to the electrode and second noise produced by the recording system itself, which is present for signals outside STN, too. Concentrating on the first source, signal s_i, respectively each sample s_{ij} is a sum of strong single cell activity of spontaneously active neurons close to the electrode, which produces the so-called spikes, and activity of a large set of neurons firing independently and in random manner. Thus, the signals s_i can be approximated as a sum of single cell activity S_i and independent and identically distributed standard Gaussian random variables z_i. The noise produced by the recording system can be described equally. To remove this kind of noise or to estimate the unknown signal S_i "Denoising by Soft-Thresholding" [8] is an effective tool. The estimator comes nearly as close in mean square error to S_i as any measurable estimator can come to (according to [8]).

We use wavelet transformation to de-noise the signals. Signal s_i is transformed into the wavelet domain resulting in a finite set of coefficients c_k. A threshold τ is determined and the set is transformed by a simple decision function using this soft threshold. Finally, the modified coefficients C_k are transformed back to time domain, resulting in the estimation of S_i. The background activity contained in the original signal (Figure 1) is nearly completely removed and only the spikes remain.

We use the de-noised signals and analyze only specific frequency ranges by multi-level wavelet decomposition. In each level of the wavelet decomposition process, the signal is split into two parts. One part we get from convolving signal s_i with a high-pass φ_{high} followed by dyadic decimation (down sampling) resulting in the detail coefficients cD_1 of level 1. Then, we convolve signal s_i with a low-pass φ_{low} followed by dyadic decimation resulting in the approximation coefficients cA_1 of level 1, which give us the other part. The latter one is used as input for level 2, resulting again in detail coefficients cD_2 respectively in approximation coefficients cA_2 that are used for the next level etc. Here, detail coefficients cD_3 of level 3 are considered for feature extraction (Figure 1right). First we subdivide the detail coefficients in intervals cD_{3ij} and calculate their standard deviation. We examine the standard deviations of the set of intervals $\{std(cD_{3ij})\}$ and calculate feature $f_2(i)$ as γ-*quantile* of their distribution.

Fuzzy classifier

Having these two features – background $f_1(i)$ and burst activity $f_2(i)$ – we use a Fuzzy classifier for assigning the signals s_i to one of two classes: STN or non-STN. The mapping from the input feature space to the output class space is performed by means of a rule-based inference mechanism. We use fuzzy variables for the antecedent part of rules R_i: IF $x_1=A_{1k}$ AND $x_2=A_{2l}$ THEN $y_i = p_{i0} + p_{i1}x_1 + p_{i2}x_2$. Here, the fuzzy terms are defined over the input variables features f_1 and f_2, respectively. The consequent parts of the rules deliver crisp outputs y_i and the final result y is accumulated from the outputs of the rules weighted by their firing strength μ_i: $y = \Sigma\mu_i y_i/\Sigma\mu_i$ (Takagi-Sugeno [9]).

The structure of the Fuzzy classifier – fuzzy sets A_{1k}, A_{2l} ($k,l=1,...$) and the rule base – is created automatically. A training set $T = \{X=(f_1(i),f_2(i)),Y=(y_i)\}$ with feature vectors and desired outputs from a representative selection of MER signals s_i is used for supervised learning. Firstly, we use subtractive clustering to determine the antecedent membership functions (Figure 2, left). Each cluster C_r creates one fuzzy term A_{jr} for each fuzzy variable x_j by projecting the cluster center (x_{1r},x_{2r}) towards the axis of the according input variable x_j ($j=1,2$). Membership functions are defined as 1D-Gauss-Functions $N_{\mu\sigma}$ with mean μ specified by the value of the according cluster center's coordinate x_{jr} and the variance is determined by the cluster's range of influence with respect to this coordinate. The combination of all Fuzzy sets of both input variables in the rule antecedent delivers the rule base. Then, the parameters $P = (p_{ij})$ of the linear consequent equations of each rule are determined. The feature vectors X and the desired outputs Y from the training set are used to create an over-determined linear equation system with the consequent equations: $Y = XP$. This system can be solved by known methods (e.g. least squares) yielding the unknown parameters of the rule's consequent equations in an optimized manner: $P' = (X^TX)^{-1}X^TY$. Now, the classifier's output indicates the degree [0,1] to which a signal is STN or non-STN.

3   Results

We developed a prototype of the Fuzzy classifier with Matlab™. In a first step, we established its structure and tested it with MER data from nine patients from one hospital. The classifier was trained with MER data from one electrode of one patient and afterwards tested with the remaining data. In total, we had 1504 MERs of 73 electrodes for verification. The binary output of the classifier was congruent with the decision of a specialist in 97% of the cases. In a second step, we tested the classifier with MER data from another 48 electrodes originating from a second hospital. We trained the classifier with MER data from 5 electrodes and tested it with data from another 43 electrodes. In 96% of the cases the classifier's output was correct compared to surgery records. Figure 2 right shows classification results for one electrode. The processing time with the Matlab-Prototype was approximately 2s per MER signal on a standard PC (1.7 GHz Intel-Centrino©, 2 GB main memory).

4   Discussion

The structure of the classifier, its parameter settings for patient specific feature extraction and its decision surface are established by supervised learning without any manual intervention. In both test situations, the classifier worked very well when it was trained with a representative set of MER data. Since it adjusts its decision parameters dynamically with every new sequence of MER data, the sequence should show a reasonable distribution of MER signals from neural and non-neural areas. Most deviations from surgery records occur for signals on the passage between neural and non neural areas. In these cases the signals don't show clear STN or non-STN features and it remains often a subjective decision whether a signal is already STN or is still non-STN. The analog output of the classifier mostly responds to this

situation but the binary output can't. The classifier fails, if there are solely STN or non-STN signals in a series of MER signals from one electrode. This problem can be solved by restricting the parameter adaption to situations showing signals from both classes and working with static parameter sets from booting in other cases.
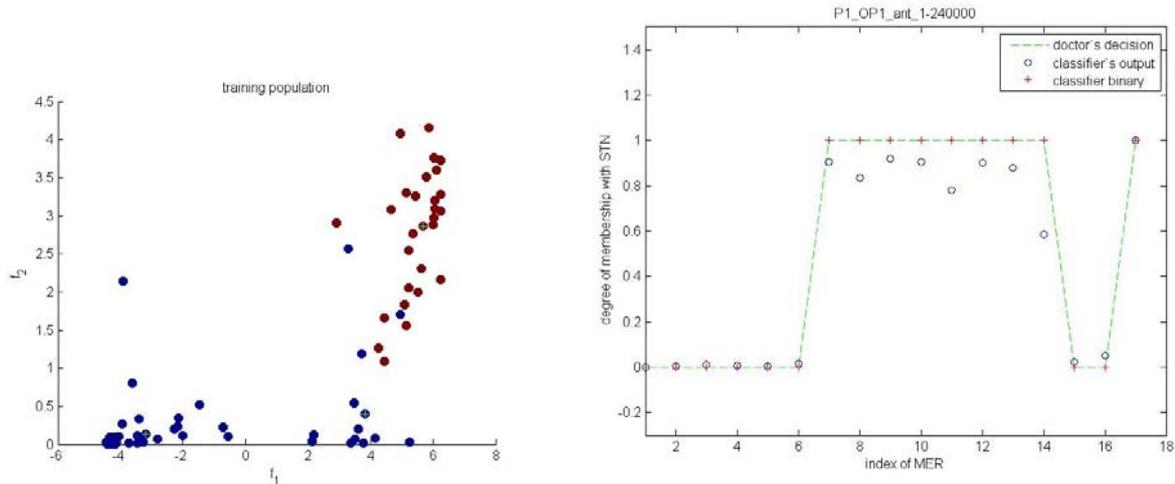

Figure 2: MER classification (left: clustering of training population, right: STN classification)

5   Outlook

At present, the classifier produces binary decisions STN or not-STN. Actually, we investigate its usage for other target structures like e.g. globus pallidus (GPi). Extending the classifier to handle various signal classes also seems to be a promising field. In addition, the classifier can be used to build up a 3D-electrode model for matching it with a geometric model of the target structure. This would enable creating a 2.5D-visualization of the target region and intersecting electrodes intra-operatively. Consequently, this would facilitate a better navigation and support the surgeon to get an objective and high quality decision about the final position of the stimulating electrode.

6   References

[1]   J.K. Krauss, J. Jankovic, and R.G. Grossman, Surgery for Parkinson's Disease and Movement Disorders, Lippincott Williams and Wilkins, Philadelphia, 2001.

[2]   P. Gemmar, F. Hertel, O. Gronz, K. Fisch, P. Mrosek, Automated Target Locating and Trajectory Selection for Deep Brain Stimulation, Analysis of Biomedical Signals and Images, Biosignal 2008 Proceedings, Brno (CzR), ISSN 1211-412X, 1-7, ISBN 978-80-214-3612-1, 25, 2008.

[3]   P. Gemmar, O. Gronz, T. Henrichs, F. Hertel, Advanced Methods for Target Navigation using Microelectrode Recordings in Stereotactic Neurosurgery for Deep Brain Stimulation, Proceedings 21th IEEE International Symposium on Computer-Based Medical Systems, IEEE Computer Society, 99-104, 2008.

[4]   A. Benazzouz, S. Breit, A. Koudsie, P. Pollak, P. Krack, and Alim-Louis Benabid, Intraoperative microrecordings of the subthalamic nucleus in parkinson's disease, Movement disorders, 17:145-149, 2002.

[5]   W.D. Hutchinson, R.J. Allan, H. Opitz, R. Levy, J.O. Dostrovsky, A.E. Lang, and A.M. Lozano, Neurophysiological identification of the subthalamic nucleus in surgery for parkinson's disease, Annals of neurology, 44:622-628, 1998.

[6]   J.H. Falkenberg, J. McNames, J. Favre, and K.J. Burchiel, Automatic analysis and data visualization of microelectrode recording trajectories to the subthalamic nucleus: Preliminary results, Stereotactic and Functional Neurosurgery, 84(1):35-45, 2006.

[7]   J. McNames, Microelectrode signal analysis techniques for improved localization, in Z. Israel and K.J.Burchiel, editors, Microelectrode Recordings in Movement Disorder Surgery, pages 119-129, Thieme, New York, 2004.

[8]   D. L. Donoho, De-noising by soft-thresholding. IEEE Transactions on Information Theory, 41(3):613–627, 1995.

[9]   T. Takagi, M. Sugeno, Fuzzy identification of systems and its applications to modeling and Control, IEEE Transactions on Systems, Man, Cybernetics, 15:116-132, 1985.