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NEUROZONE: On-line Recognition of Brain Structures in Stereotactic Surgery - Application to Parkinson's Disease

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Abstract— **The success of stereotactic surgery for Deep Brain Stimulation depends critically on the exact positioning of a microelectrode recording in a target area of the brain. This paper presents the software system NEUROZONE composed of two main applications: first, it allows online recognition of brain structures by the analysis of signals from microelectrode recordings (MER), and second, it processes and analyses off-line databases allowing the inclusion of new trained classifiers for automatic identification. The software serves as a support to the analysis done by a medical specialist during surgery, and seeks to reduce the adverse side effects that may occur because of inadequate identification of the target areas. The software also allows the specialists to label recordings obtained during surgery, in order to generate a new off-line database or increase the amount of records in an already existing off-line database. NEUROZONE has been tested for Deep Brain Stimulation performed at the Institute for Epilepsy and Parkinson of the Eje Cafetero (Colombia), achieving positive identifications of the Subthalamic Nucleus (STN) over to 85% using a naive Bayes classifier.**

I. Introduction

Parkinson's disease (PD) is a group of neurological disorders characterized by hypokinesia, shaking and muscular rigidity. In parkinsonian patients, neurosurgery may be an effective treatment that requires the precise position of target areas for the implantation of stimulating devices. Surgical treatment of Parkinson's disease is based on Deep Brain Stimulation (DBS), especially in the Subthalamic Nucleus (STN) [1], where the procedure to locate the target area and define the trajectory to be followed by the electrodes requires the intervention of a specialized team of neurosurgeons and neurophysiologists [2]. Usually, the use of appropriate imaging techniques like magnetic resonance imaging (MRI) and Computed Tomography (CT) is essential for the surgical planning. However, the MRI and CT are not enough for validating the location of target points and the boarding trajectory, because they do not provide information about the electrical behavior of neurons. At this stage, the interpretation of physiological signals known as Microelectrode Recording signals (MER-signals), becomes crucial [3]. Traditionally, the analysis of such signals has focused on the visual and auditory neural activity recorded. Unfortunately, this information may be insufficient: even an experienced neurophysiologist could take a long time to find specific areas of interest based only on this procedure, given that these records do not correspond to a specific neural discharge, but to the bioelectrical activity of neurons surrounding the microelectrode recording. For this reason, it is important to determine discriminating features that provide information about the functional states of these adjacent neurons, and achieve positive identification of the different brain areas.

Currently, different research groups are developing automated on-line tools for functional localization of targets brain structures for Deep Brain Stimulation [4]. In [5], the authors proposed an automatic pattern recognition system based on Spikes analysis and frequential transform methods, to identify MER signals from specific subcortical structures (i.e. Zone Incerta-ZI, Subthalamic Nucleus-STN, or Substantia Nigra Reticulata-SNR). The classification is based on models constructed from MER data from subcortical structures of several patients, obtaining results with an accuracy of 89 % with the characterization through spikes, and 50 % with the characterization through frequential techniques. Also in [6], an automated feature extraction tool to locate the STN using an unsupervised algorithm was developed. The system uses the neural noise background, the firing rate of the spikes and the power spectral density along the microelectrode trajectory. It then applies a threshold-based method that detects the dorsal and ventral borders of STN. Depending on the combination of measures used for the detection of borders, the algorithm assigns confidence levels for the prediction made (i.e. high, medium and low), achieving a prediction accuracy of 88 %. Finally, despite that in [5] and [6] tools for automatic identification of basal ganglia were developed, they have not been implemented in on-line systems that can be used in surgery.

NEUROZONE is a software system that allows online acquisition of up to 5 simultaneous MER signals for the purposes of displaying, listening, processing and identification of basal ganglia (Thalamus-TAL, Zone Incerta-ZI, Subthalamic Nucleus-STN, Substantia Nigra Reticulata-SNR) during a surgical procedure. The system also includes a tool for processing and analysis of MER signals databases, called Neurotrain. This application has several methods for signal processing such as filters; threshold-based techniques for denoising and smoothing; feature extraction using adaptive wavelets or inter spike interval analysis; and classifiers that include Bayesian LDC, Bayesian QDC, KNN, for the de-

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velopment of the identification stage. The goal is to provide a support for the diagnosis made by the neurosurgeons and reduce the adverse side effects that may occur because of inadequate identification of the target brain areas. Another important aspect of this software is the labeling of acquired records by different specialists. This feature is useful for the construction of databases. The techniques of analysis and processing of MER signals implemented in NEUROZONE, are part of the methodologies developed in previous years by researchers at the Instrumentation and Control Group of the Technological University of Pereira (UTP) [7], [8], [9], [10].

II. Materials and Methods

A. MER Signals Database

The database of the Technological University of Pereira (DB-UTP) include recordings of surgical procedures in patients with Parkinson's disease, whose ages are between 55 ± 56 (3 men, 1 woman). All the patients signed an informed consent form. Microelectrode recordings were obtained using the ISIS MER system (Inomed Medical GmbH) [11]. MER signals were labeled by neurophysiology and neurosurgery specialists from the Institute of Parkinson and Epilepsy of the Eje Cafetero, located in the city of Pereira, Colombia. In total, there are 190 neural recordings divided in four classes: 26 signals from Thalamus (TAL), 71 signals from STN, 80 signals from SNr, and 13 from ZI. This database was used for training the machine learning algorithms for automatic identification of brain structures.

B. ISIS MER

The neurosurgical equipment ISIS MER (Inomed Medical GmbH), is used to collect data for derivation of potentials from the trajectory of microelectrodes in deep brain stimulation applied to Parkinsonian patients. The sampling frequency of the ISIS MER is 25 KHz [11].

C. Software Development

NEUROZONE is composed of a main program and 4 independent modules, which are loaded dynamically during the program initialization. These modules are related by functions and controls defined in the main program. Software modules include:

1) User Interface Module
2) Data Acquisition Module
3) Patient Registration Module
4) Brain Structures Identification Module

1) User Interface Module: NEUROZONE contains different windows, as described in Figure 1:

- Operation Mode: set the initial parameters of NEUROZONE, where you select a new procedure, label a stored recording or start the program in demo mode.
- Patient Information: enter basic data for a patient. It can be a new procedure or it can load an existing patient from a database.

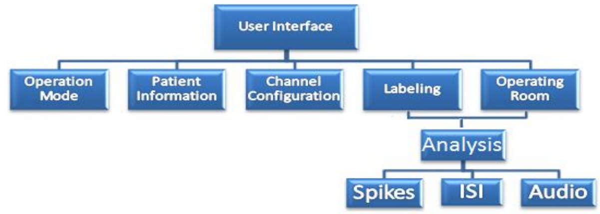

Fig. 1. User Interface Module. It contains the different windows of NEUROZONE for the initial parameters settings, operation mode and selection of analysis methods.

- Channel Configuration: set the channels of electrodes, considering the parameters of side, channel, position and rotation, as well as its initial position with respect to the target point.
- Operating Room: MER signals are acquired during the surgical procedure. The specialists can implement the methods of analysis and classification of NEUROZONE to identify the brain area corresponding to the position of the electrode, also the medical specialist can do his own labeling.
- Labeling: this procedure is done off-line, since the aim is to analyze and label an existing record in the database. It is similar to the operating room module because it has the tools for visualization, analysis and classification. The difference is that it does not require communication with the ISIS MER equipment.

2) Data Acquisition Module: ISIS MER has a 12 bits A / D converter with a 4-8 channels multiplexer. In Table I, the function of each channel is described.

TABLE I
Channels Distribution

Channel	Usage
1-5	Microelectrode Register
6	Depth Sensor
7-8	ECG

3) Patient Registration Module: Patient registration is done as shown in Figure 2.

- Read Data and Create File: the user enters personal information of patients and creates the file that stores this information.
- Store and Display: the basic information of each patient is saved in a text file.
- Update Files: the database is updated when the user enters a new patient.

4) Brain Structures Identification Module: Identification of the brain region corresponding to the signal provided by the microelectrode in the surgical intervention, requires a trained classifier previously generated in the application NeuroTrain, as we will describe in subsection III-A. The algorithms used correspond to a variety of methods developed in previous works by our research group [7], [8], [9], [10]. This module can be seen in Figure 3.

Fig. 2. Patient Registration Module. It acquires basic information of patients and creates the files of each person. The files are stored in a database.

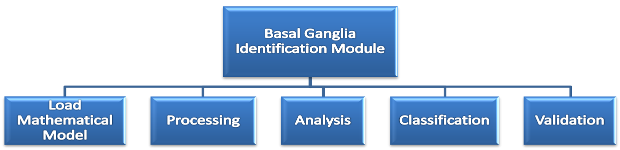

Fig. 3. Brain Structures Identification Module. In this module, the trained classifier obtained from NeuroTrain is applied (See subsection III-A). This classifier is necessary for identify the brain area corresponding to the signal provided by the microelectrode in the surgical intervention.

III. Experimental Results and Discussion

A. NeuroTrain

It is an application where engineers can implement, test and validate algorithms for analysis and processing of MER signals. This application is executed off-line using already created databases. The first part of Neurotrain has optional methods for signal pre-processing such as ordinary filters (Fil); threshold-based techniques for denoising and smoothing (Smo), Normalization (Nor) and Artifacts Remotion (AR). The second part does feature extraction using adaptive wavelets (AW), Wavelet Transform (WT), or Inter Spike Interval (ISI); we can decide if the analysis is done with the complete signal or only with the spikes. The last part of Neurotrain is for classification using a Bayesian Linear Discriminant Classifier (LDC), Bayesian Quadratic Classifier (QDC) or the K-NN (1) Classifier [12].

In this application we develop the trained classifiers models. These models consist of a set of numerical structures that represent the learning algorithms. The model is optimizable and replaceable inside the system. In the table II, outcomes of Neurotrain for the DB-UTP (See subsection II-A) are shown. In the Figure 4, we show the pre-processing interface of NeuroTrain.

TABLE II
Some Outcomes of NeuroTrain for DB-UTP

Type Signal	Pre-Processing Methods	Analysis Method	Classifier	Accuracy (%)
Complete Signal	AR	AW	Bayesian QDC	94.21 ± 1.87
Complete Signal	AR	AW	K-nn (1)	93.44 ± 1.93
Complete Signal	None	AW	Bayesian QDC	92.12 ± 2.73
Complete Signal	AR+Nor	AW	Bayesian LDC	87.00 ± 1.35
Complete Signal	Smo+AR	WT	K-nn	85.12 ± 2.36
Complete Signal	AR+Nor+Smo	WT	Bayesian QDC	82.88 ± 1.94
Only Spikes	AR+Smo	ISI	K-nn	76.97 ± 2.65
Only Spikes	AR+Nor	ISI	Bayesian LDC	71.32 ± 3.32
Only Spikes	AR+Nor+Smo	ISI	Bayesian QDC	70.24 ± 2.53

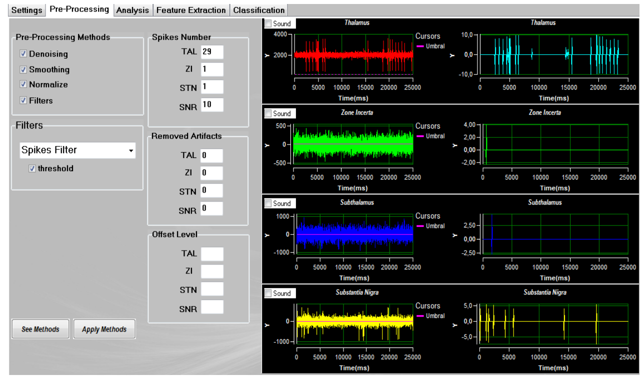

Fig. 4. NeuroTrain: Pre-processing of Databases. The user can choose optional methods: filtering, smoothing, denoising, normalization and artifacts remotion. Samples from original and pre-processed signals belonging to each class are shown in the graphics panel of figure.

B. Results obtained in the operating room

Currently, NEUROZONE has been tested in Deep Brain Stimulation performed at the Institute of Epilepsy and Parkinson of the Eje Cafetero, in Pereira-Colombia, achieving positive identifications of the STN upper to 85%. The Online identification is in real time (immediate) and is done with the best trained classifier obtained from NeuroTrain. To start online operation of NEUROZONE, the user first establishes communication with the ISIS MER, then he configures the information from the surgical planning corresponding to a particular side chosen for the inception of the microelectrode (right-left) and he enters the positions of electrodes, the initial location in millimeters (mm) and the acquisition channels (5 channels max).

Fig. 5. Operating Room. In this window the specialists observe the signals acquired in real time (5 Channel max.). They can analyze the recordings and label them. The applications for Inter Spike Interval analysis and on-line recognition of brain structures are also available.

C. Labeling

The purpose of this application is that neurosurgeons can label recordings obtained during surgical procedures. In this way, the user can build a new dataset or increase the amount of recordings of a database that already exists. The specialists write his own concept in a field of labeling. The classes are labeled like *Thalamus-TAL, Zone Incerta-ZI,* *Subthalamic Nucleus-STN, Substantia Nigra Reticulata-SNR and Unknown*.

D. Discussion

Some important comments about the performance of NEUROZONE are,

1) Outcomes in Table II show that the features extracted with adaptive wavelets (AW) are more discriminant, in comparison to the other analysis methods implemented in NeuroTrain. The AW achieve the best classification accuracy with a quadratic Bayesian classifier. The main advantage of the AW is the excellent representation of the dynamic changes and singularities of MER signals, due to the adaptability of the lifting schemes that represent the wavelets.
2) The classification accuracy of MER signals using only Spikes, reveals that is better to analyze the complete signal without pre-processing. This is because the Inter Spike Interval (ISI) removes the Background Noise (BN) and the BN contains relevant information about the energy and the dynamic behavior of MER signals.
3) Pre-processing: filtering, smoothing and normalization, is not recommended for this signals, because the spectrum of MER signals is very spread. In addition, the normalization changes the amplitudes of the recordings and this may cause a loss of relevant information from either the Background Noise or the high frequency components. As shown in Table 2, the pre-processing affects the classification accuracy. Artifacts Remotion (AR) is the only pre-processing method that improves the original signal.
4) The On-line identification of STN in deep brain stimulation is higher than 85%. This efficiency is lower compared with the best outcome obtained in off-line validation (see table II), where the identification of the STN was 94%. The difference in performance occurs because the impedance of the scanning electrodes is not equal in all cases, then there is a high variation in the amplitudes of the signals and it is necessary to normalize the numerical values of the signals acquired during surgery. This normalization introduces a level of uncertainty that affects the system accuracy.
5) The methods implemented in NEUROZONE could be applied for processing of other biomedical signals, i.e ECG (Electrocardiography), EEG (Electroencephalography) and EMG (Electromyography). Because these algorithms are developed regardless the nature of the signals and diseases. The advantage of NEUROZONE with other similar systems is the flexibility for adding new processing and classification algorithms due to the open architecture of the system.

IV. Conclusions and Future Work

In this paper we have presented the system software NEUROZONE, for automatic on-line identification of brain structures during stereotactic surgery of Parkinson's disease. Also, the system can generate learning algorithms based on MER signals analysis methodologies applied in already existing databases. The main goal was to develop a support tool to the analysis done by specialists in neurosurgery. The software also serves for acquisition, storage and labeling of recordings and for the creation of new databases. NEUROZONE has been tested in surgical procedures performed at the Institute of Epilepsy and Parkinson of the Eje Cafetero in Pereira-Colombia, obtaining positive identification of the STN above 85%.

Although the results are promising, further work is required to optimize the system and to achieve even better accuracy outcomes related to the identification of target areas, especially the STN. In next works, the objective is to include in NEUROZONE more powerful methods for feature extraction and classification.

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