Sparse representation of MER signals for localizing the Subthalamic Nucleus in Parkinson's disease surgery

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***Abstract*— Deep brain stimulation (DBS) of Subthalamic Nucleus (STN) is the best method for treating advanced Parkinson's disease (PD), leading to striking improvements in motor function and quality of life of PD patients. During DBS, online analysis of microelectrode recording (MER) signals is a powerful tool to locate the STN. Therapeutic outcomes depend of a precise positioning of a stimulator device in the target area. In this paper, we show how a sparse representation of MER signals allows to extract discriminant features, improving the accuracy in identification of STN. We apply three techniques for over-complete representation of signals: Method of Frames (MOF), Best Orthogonal Basis (BOB) and Basis Pursuit (BP). All the techniques are compared to classical methods for signal processing like Wavelet Transform (WT), and a more sophisticated method known as adaptive Wavelet with lifting schemes (AW-LS). We apply each processing method in two real databases and we evaluate its performance with simple supervised classifiers. Classification outcomes for MOF, BOB and BP clearly outperform WT and AW-LF in all classifiers for both databases, reaching accuracy values over 98%.**

I. Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by symptoms caused by a loss of dopamine, predominantly from the basal ganglia of the brain. Loss of dopamine causes bradykinesia (slowness of movement), tremor, muscular rigidity, shuffling gait and flexed posture [1]. During the last years deep brain stimulation (DBS) has become a routine method for the treatment of advanced Parkinson's disease, leading to striking improvements in motor function and quality of life of PD patients [2]. DBS is a stereotactic guided neurosurgery where a stimulating electrode is inserted into specific nuclei. In most cases, the target structure is Subthalamic Nucleus (STN). In the operating room, a team of specialists acquires and analyzes physiological signals that represent the nonlinear electrical activity generated by neurons. These signals are called microelectrode recordings (MER). MER signals analysis has proved to be a powerful tool to locate basal ganglia, specially the STN [3], [4]. Therapeutic outcomes depend of a precise positioning of a stimulator device in the target area.

MER exhibit a strong non-stationary behavior. For this reason, such signals require advanced methods for processing and feature extraction. The Wavelet transform (WT) is widely used to represent non-stationary signals, including MER [5], [6]. In this approach, the recordings are transformed to a time-scale space using some basis function (mother wavelet). Then, one can obtain statistical descriptors (i.e, mean, variance, etc) from either approximation or detail coefficients. However, this analysis still leaves a significant gap to identify STN and others structures relevant in DBS: Thalamus (Thal), Zone Incerta (ZI) and Substantia Nigra pars reticulata (SNr). The problem with WT is that analysis depends on having correlation between the selected basis function and MER signals. This is not easy to achieve, due to the highly oscillatory nature of neuronal background noise of MER data.

A recent method for adaptive wavelet based on lifting schemes (AW-LS) showed better results than WT [7]. Although AW-LS is able to identify the STN with good accuracy, it is possible to get more discriminant features through sparse coding of MER. Sparse coding is a set of unsupervised methods with over-complete basis which represent data efficiently. Here, we define sparsity as having few non-zero components or having few components not close to zero. The idea behind sparse coding methods is to represent signals using a redundant set of vectors called *atoms* [8]. These atoms are obtained using a larger set of basis functions, called *dictionary* [9]. There is a great number of available dictionaries: Wavelets, steerable wavelets, segmented wavelets, Gabor dictionaries, multiscale Gabor dictionaries, wavelet packet, cosine packets, chirplets and warplets [10]. An intuitive advantage of sparse coding is that this approach collects the relevant information of the signals into a compact set of coefficients. Therefore, it is easier to extract discriminant features to identify the STN during DBS. Another interesting ability of sparse coding methods is the merging of two or more dictionaries. This is very useful, because a representation with only a dictionary may omit intrinsic properties from MER signals.

In this paper, we show that sparse coding of MER signals obtains a significant improvement in identification of STN during DBS applied in Parkinson's disease patients. We apply three different methods to represent MER signals, namely, Method of Frames (MOF), Best Orthogonal Basis (BOB) and Basis Pursuit (BP). Inside of each method, we merge two dictionaries: Wavelet Packet and Cosine Packet. We compare the techniques proposed here, with classical methods for signal processing like Wavelet Transform (WT) and adaptive Wavelet with lifting schemes (AW-LS). We apply each processing method in two real databases with two classes (STN and Non-STN), and we evaluate its performance with simple supervised classifiers. Classification outcomes for MOF, BOB and BP clearly outperform to WT and AW-LF in all classifiers for both databases, reaching accuracy values over 98%.

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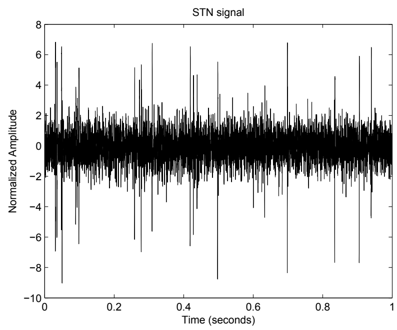

Fig. 1. Example of a MER signal from Subthalamic Nucleus (STN). This recording belongs to DB-UTP and it is sampled at 25 kHz

II. Materials and Methods

A. Databases

The first MER database comes from Universidad Tecnológica de Pereira (DB-UTP) and includes recordings of surgical procedures in patients with Parkinson's disease, whose ages are between 55 ± 6 (four men, and two women). All the patients signed an informed consent form. Microelectrode recordings were obtained using the ISIS MER system (Inomed Medical GmbH). MER signals were labeled by neurophysiology and neurosurgery specialists from the Institute of Epilepsy and Parkinson of the Eje Cafetero, located in the city of Pereira, Colombia. In total, there are 600 neural recordings divided in two classes: 300 signals from Subthalamic Nucleus (STN), and 300 signals from other brain structures (Thalamus-Thal, Zone Incerta-ZI, Substantia Nigra reticulata-SNr). Each record lasted a second with sampling frequency of 25 kHz and 16-bit of resolution. Figure 1 shows an example of a MER signal from Subthalamic Nucleus (STN).

The second database belongs to Universidad Politécnica de Valencia (DB-UPV). DBS signals were obtained in the General University Hospital of Valencia, Spain, and labeled by specialists in neurophysiology and electrophysiology. The medical equipment used for data acquisition was the LeadPointTM Medtronic (Medtronics Functional Diagnostics). Each signal is a second long, sampled at 24 kHz. In total, there are 240 recordings coming from four patients: 120 recordings belong to STN and 120 recordings come from other brain regions.

B. Sparse representation with over-complete dictionaries

The aim of sparse coding is to find a set of basis vectors (atoms) ϕ_i such that, a signal $\mathbf{s}$ can be represented as a linear combination of these atoms. The full set of waveforms $\{\phi_\mathbf{i}\}_{i=1}^{n}$ is called the dictionary Φ. Given a dictionary Φ and a set of coefficients α_i, we can construct a decomposition of the signal $\mathbf{s}$ as [10]:

$$\mathbf{s} = \sum_{i=1}^{n} \alpha_i \phi_i \tag{1}$$

Since the decomposition given by equation (1) is non-unique, this representation allows adaptivity, sparsity and merging of dictionaries. Sparsity is achieved when the number of necessary atoms n is minimized over all possible representations [9]. Several methods have been proposed in the state of the art for signal decomposition using over-complete dictionaries. We apply three approaches: Method of Frames (MOF) [11], Basis Pursuit (BP) [12] and Best Orthogonal Basis (BOB) [13]. In each method, we merge the wavelet packet dictionary and the cosine packet dictionary to represent the MER signals. We select these dictionaries using cross-validation.

C. Method of Frames (MOF)

The MOF [11] selects a solution where coefficients α_i minimize the l^2 norm:

$$min \left\| \boldsymbol{\alpha} \right\|_2, \quad s.t \quad \Phi\boldsymbol{\alpha} = \mathbf{s} \tag{2}$$

The above formulation corresponds to a quadratic programming (QP) problem, which has an unique solution. It is denoted like $\boldsymbol{\alpha}^\dagger$. MOF generates low sparsity, because each atom that has nonzero inner product with the signal is a member of the solution. The method finds the coefficients α_i closest to the origin of a subspace $\mathbf{E}^p$ formed by all feasible solutions of equation (2). The optimal coefficients $\boldsymbol{\alpha}^\dagger$ can be calculated using a system of linear equations:

$$\boldsymbol{\alpha}^\dagger = \Phi^\dagger \mathbf{s},$$

where matrix $\Phi^\dagger$ is the generalized inverse of Φ:

$$\Phi^\dagger = \Phi^\top \left(\Phi\Phi^\top \right)^{-1}$$

D. Basis Pursuit (BP)

Basis Pursuit finds the coefficients α_i that minimize the l^1 norm [12]:

$$min \left\| \boldsymbol{\alpha} \right\|_1, \quad s.t \quad \Phi\boldsymbol{\alpha} = \mathbf{s} \tag{3}$$

Unlike MOF, BP is a method that preserves a high degree of sparsity in the representation. Minimization of l^1 norm implies a considerable number of zero coefficients. We can associate the optimization problem established in equation (3) with a linear programming (LP) problem. The standard form of a LP problem is given by:

$$min \quad \mathbf{c}^\top \mathbf{x}, \quad s.t \quad A\mathbf{x} = \mathbf{b}, \quad \mathbf{x} \geq \mathbf{0} \tag{4}$$

Using (4), we can reformulate the optimization problem of (3) in standard LP form, making the following assignments:

$$\begin{aligned} A &\leftrightarrow [\Phi, -\Phi] \\ \mathbf{b} &\leftrightarrow \mathbf{s} \\ \mathbf{c} &\leftrightarrow [1, ..., 1]^\top \\ \mathbf{x} &\leftrightarrow \boldsymbol{\alpha} \end{aligned}$$

The problem proposed in (3) is solved with convex optimization. BP-Simplex and BP-Interior are the most common algorithms for BP [10].

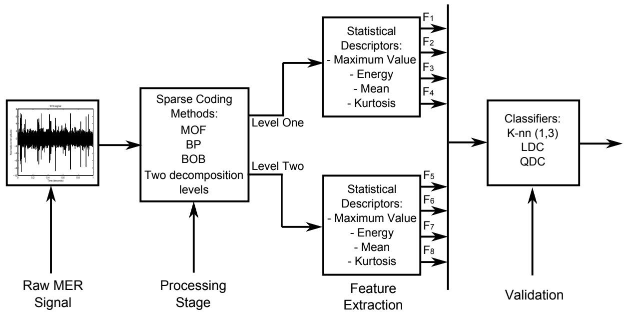

Fig. 2. Methodological framework: we process the MER signals with sparse coding methods to obtain two decomposition levels. Then, we extract eight features applying statistical descriptors over both representation sets. Finally, we validate the proposed methods through basic classifiers.

E. Best Orthogonal Basis (BOB)

Some dictionaries Φ (i.e Wavelet packet and Cosine packet) have special properties that allow the construction of orthogonal bases. In [13] the authors propose a non-linear transformation with orthogonal adaptive bases. This method is robust to noise and selects the *best basis B* among several potential orthogonal bases. BOB finds the best basis, minimizing the entropy $\mathscr{E}$ of B:

$$min\{\mathscr{E}(B) : B \subset \Phi\} \quad (5)$$

BOB has sparsity, when the signal has a sparse representation in the subspace formed by the orthogonal bases.

F. Feature Extraction

Methodological framework is illustrated in figure 2. We apply MOF, BP and BOB to MER signals. Then, we calculate 4 statistical descriptors (maximum value, energy, mean and kurtosis) from two representation sets $\alpha_{i,p}$, $(p = 1,2)$. For each MER signal, we obtain a feature vector $\mathbf{x} \in \mathbb{R}^{1\times 8}$.

G. Learning algorithms and Validation

We test the proposed methods for MER signals representation with standard supervised classifiers: a Naive Bayes classifier with shared and different covariance matrix per class (LDC,QDC); and a K-nearest neighbors (KNN) algorithm with K = 1 and K = 3 (KNN1, KNN3). The reader can find the full theory of both learning algorithms in [14]. For both databases, we evaluate the accuracy in the identification of STN and a measurement of true positive rate (TPR) using the area under the curve (AUC) with ROC analysis. We perform two experiments. First, we use the 50% of each database (300 signals from DB-UTP and 120 signals from DB-UPV) for training the learning algorithms and we test the generalization capability using the remaining 50% of the data. Second, we mix DB-UTP and DB-UPV in a single database and we follow the same procedure of the first experiment. The experiments for each method and each classifier are performed 100 times, taking random sets for training and validation. To select the best model, we compare average performances between MOF, BP and BOB with a Kruskal-Wallis test [15].

TABLE I

COMPARISON OF ACCURACY (% IN STN IDENTIFICATION) FOR DIFFERENT METHODS PROPOSED

Method	Classifier	DB-UTP	DB-UPV	UTP+UPV
WT	LDC	80.5 ± 1.3	90.3 ± 1.4	73.9 ± 1.1
WT	QDC	89.7 ± 1.0	90.4 ± 1.4	79.4 ± 1.1
WT	KNN-1	93.5 ± 0.9	93.8 ± 0.7	90.5 ± 0.5
WT	KNN-3	93.0 ± 1.0	93.1 ± 1.5	92.0 ± 0.6
AW-LS	LDC	88.1 ± 1.1	90.8 ± 1.4	80.3 ± 0.8
AW-LS	QDC	91.1 ± 1.3	89.5 ± 1.4	83.2 ± 1.2
AW-LS	KNN-1	94.6 ± 0.8	93.3 ± 1.3	92.6 ± 0.5
AW-LS	KNN-3	95.1 ± 0.6	91.7 ± 1.7	93.1 ± 0.7
MOF	LDC	89.3 ± 0.8	92.3 ± 1.2	75.3 ± 0.9
MOF	QDC	95.1 ± 0.6	94.1 ± 1.1	88.0 ± 1.0
MOF	KNN-1	$\mathbf{98.1 \pm 0.3}$	96.0 ± 1.0	95.0 ± 0.4
MOF	KNN-3	97.5 ± 0.5	92.7 ± 1.2	94.2 ± 0.5
BP	LDC	91.0 ± 0.9	91.2 ± 1.1	88.4 ± 0.7
BP	QDC	92.5 ± 0.8	91.1 ± 1.4	89.6 ± 0.6
BP	KNN-1	97.4 ± 0.6	96.1 ± 1.1	$\mathbf{96.3 \pm 0.6}$
BP	KNN-3	97.2 ± 0.5	95.0 ± 1.0	95.5 ± 0.4
BOB	LDC	90.9 ± 0.7	94.6 ± 1.0	77.5 ± 0.7
BOB	QDC	93.9 ± 0.6	93.6 ± 1.0	87.0 ± 1.1
BOB	KNN-1	97.5 ± 0.4	$\mathbf{98.8 \pm 0.6}$	95.4 ± 0.5
BOB	KNN-3	96.9 ± 0.6	97.1 ± 1.3	94.2 ± 0.7

TABLE II

MEASUREMENT OF TRUE POSITIVE RATE (TPR) USING ROC ANALYSIS

Method	Classifier	DB-UTP	DB-UPV	UTP+UPV
WT	LDC	0.834 ± 0.020	0.919 ± 0.019	0.762 ± 0.022
WT	QDC	0.911 ± 0.020	0.911 ± 0.027	0.800 ± 0.033
WT	KNN-1	0.982 ± 0.005	0.971 ± 0.006	0.963 ± 0.006
WT	KNN-3	0.934 ± 0.020	0.952 ± 0.026	0.907 ± 0.017
AW-LS	LDC	0.920 ± 0.013	0.909 ± 0.023	0.848 ± 0.013
AW-LS	QDC	0.929 ± 0.016	0.905 ± 0.023	0.870 ± 0.017
AW-LS	KNN-1	0.984 ± 0.005	0.974 ± 0.010	0.969 ± 0.006
AW-LS	KNN-3	0.949 ± 0.017	0.917 ± 0.031	0.920 ± 0.018
MOF	LDC	0.908 ± 0.013	0.898 ± 0.026	0.752 ± 0.023
MOF	QDC	0.961 ± 0.010	0.928 ± 0.022	0.859 ± 0.044
MOF	KNN-1	$\mathbf{0.996 \pm 0.002}$	0.984 ± 0.012	0.978 ± 0.006
MOF	KNN-3	0.974 ± 0.013	0.921 ± 0.040	0.941 ± 0.015
BP	LDC	0.905 ± 0.014	0.903 ± 0.019	0.898 ± 0.012
BP	QDC	0.935 ± 0.013	0.915 ± 0.022	0.910 ± 0.013
BP	KNN-1	0.994 ± 0.003	0.987 ± 0.008	$\mathbf{0.991 \pm 0.004}$
BP	KNN-3	0.971 ± 0.014	0.941 ± 0.031	0.955 ± 0.013
BOB	LDC	0.923 ± 0.011	0.935 ± 0.020	0.772 ± 0.023
BOB	QDC	0.964 ± 0.009	0.924 ± 0.023	0.873 ± 0.032
BOB	KNN-1	0.994 ± 0.003	$\mathbf{0.992 \pm 0.005}$	0.985 ± 0.005
BOB	KNN-3	0.964 ± 0.015	0.960 ± 0.025	0.948 ± 0.016

III. RESULTS AND DISCUSSION

We compare the proposed methods (see subsections II-C, II-D and II-E) to the classical Wavelet Transform (WT) and a more advanced method called Adaptive Wavelet with Lifting Schemes (AW-LS). We show the accuracy in positive identification of STN for both databases in Table I and true positive rate (TPR) results in Table II.

We synthesize the most remarkable aspects of the results in the following paragraphs:

1) It can be noticed that the sparse coding of MER signals allows the extraction of more discriminative features. Global outcomes in Tables I and II show a better performance for the methods proposed in this paper. We compare MOF, BP and BOB with classical methods for signal processing in the state of the art,

like WT or AW-LS. If we look at both databases and all experiments, the sparse coding methods always improve the results of WT and AW-LS.

2) The best accuracy result in UTP-DB is 98.1% with MOF+KNN-1 and 98.8% in UPV-DB with BOB+KNN-1. These results are satisfactory, because we are only using simple classifiers, meaning that the strength of the methodology relies on the sparse coding of MER signals. We are currently looking at implementing these methods in on-line systems applied to Parkinson's disease surgery.
3) Notice that when we mix the databases (UTP+UPV), there is a considerable reduction in performance of all classifiers. The reduced performance is explained due to UTP-DB is sampled at 25 kHz and UPV-DB is sampled at 24 kHz. However, the method BP is not seriously affected by this issue and its performance in Tables (I, II) is still very high.
4) The best result for the TPR is 0.996 (MOF+KNN-1) for UTP-DB and 0.992 (BOB+KNN-1) for UPV-DB. It means that the proposed methods have less than 0.1% of false alarms in STN identification. By contrast, the best TPR of WT is 0.982 and the best TPR of AW-LS is 0.984 (less than 0.2% of false alarms). Clinical significance of results in table II is remarkable. Because a high TPR is a necessary attribute for an automated system applied in DBS. False alarms could be critical for the correct implantation of the stimulation device in the STN. Therefore, therapeutic outcomes generated by DBS could be suboptimal and patients could suffer side effects.
5) According to the statistical analysis with the Kruskal-Wallis test, there are not significant differences between the methods proposed here. So, we can not establish the best model. An alternative way to evaluate sparse coding is related to the average of sparsity level. Recall that sparsity is the quantity of zeros (or near to zero) coefficients needed for a successful representation. A sparse coding method seeks to represent a signal with the fewest number of coefficients. MOF has 1.5% of sparsity, BP has 2.7% and BOB has 66.7%. That is, BOB only requires the 33.7% of the coefficients to represent MER signals.

IV. Conclusions and Future Work

We presented in this paper the application of several sparse coding to MER signals for identification of subthalamic nucleus (STN) during deep brain stimulation (DBS) in PD patients. This approach seeks to represent the signals with the fewest number of coefficients needed to construct an overcomplete space. We tested three sparse coding techniques, namely, Method of Frames (MOF), Basis Pursuit (BP) and Best Orthogonal Basis (BOB) and we merged two classical dictionaries: Wavelet Packet and cosine Packet. This processing methodology allows identification of STN with an accuracy over 98% in two real datasets and improves the results obtained by traditional methods like the wavelet transform and advanced methods like adaptive wavelets. However, it is important to note that we employed very simple machine learning algorithms as Naive Bayes classifier and K-nearest Neighbor. We even obtained similar results than other works where it is applied more powerful methods for pattern recognition as Support Vector Machines [16] or Gaussian processes [3].

Preliminary results are highly satisfactory, we would like to implement these methods in a software system for clinical support during DBS.

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References

[1] S. Fahn, *Description of Parkinson's Disease as a Clinical Syndrome*. N. York. Acad. Sci, 991, pp 1–14, 2003.
[2] S. Breit, J.B. Schulz and A-L. Benabid,, *Deep Brain Stimulation*. Cell Tissue Res (2004) 318, pp. 275–288, 2004.
[3] H.D. Vargas, A.A. Orozco and M.A. Álvarez, *Multi-patient learning increases accuracy for Subthalamic nucleus identification in deep brain stimulation*. In proc. of the IEEE-EMBC 2012, pp. 4341-4344, 2012.
[4] P. Novak, S. Daniluk, S. Elias, and J. Nazzaro, *Detection of the subthalamic nucleus in microelectrographic recordings in Parkinson disease using the high frequency (500 hz) neuronal background*. Neurosurgery, vol. 106, p. 175–179, 2007.
[5] P. Gemmar, O. Gronz, T. Henrichs and F. Hertel, *Advanced methods for target navigation using microelectrode recordings in stereotactic neurosurgery for deep brain stimulation*, in Proc. of the CBMS 2008, pp. 99-104, 2008.
[6] W. Gang, W. Zhizhong, C. Weiting, and Z. Jun, *Classification of surface emg signals using optimal wavelet packet method based on davies-bouldin criterion*, Journal Medical and Biological Engineering and Computing, vol. 44, no. 10, pp. 865–872, 2006.
[7] E. Giraldo, G. Castellanos and A.A. Orozco, *Feature Extraction for MER Signals Using Adaptive Filter Banks*, in Electronics, Robotics and Automotive Mechanics Conference, pp. 582-585, 2008.
[8] L. Ørtoft Endelt and A. La cour-Harbo, *Comparison of Methods for Sparse Representation of Musical Signals*, in ICASSP 2005. pp. 13-16, 2005.
[9] P.S. Huggins, and S.W. Zucker, *Greedy Basis Pursuit*, IEEE TRANSACTIONS ON SIGNAL PROCESSING, VOL. 55, NO. 7, pp.3760-3772, 2007.
[10] S.S. Chen, D.L. Donoho and M.A. Saunders, *Atomic Decomposition by Basis Pursuit*, Society for Industrial and Applied Mathematics, SIAM REVIEW, Vol. 43, No. 1, pp. 129–159, 2001.
[11] I. Daubechies, *Time-frequency localization operators: A geometric phase space approach*, IEEE Trans. Inform. Theory, 34, pp. 605–612, 1998.
[12] S. Chen and D. Donoho, *Basis pursuit*, in Proc. 28th Asilomar Conf. Signals, Syst. Comput, pp. 41–44, 1994.
[13] R. R. Coifman and M. V. Wickerhauser, *Entropy-based algorithms for best-basis selection*, IEEE Trans. Inform. Theory, 38, pp. 713–718, 1992.
[14] C. Bishop, *Pattern Recognition and Machine Learning*, Springer, 2006.
[15] J. Pizarro, E. Guerrero and P. L. Galindo, *Multiple comparison procedures applied to model selection*, Neurocomputing, 48: 155-173, 2002.
[16] JP. Guillen, F. Martinez, R. Sanchez, M. Argaez, and L. Velasquez, *Characterization of subcortical structures during deep brain stimulation utilizing support vector machines*, In proc. of the IEEE-EMBC 2011, pp. 7949-7952, 2011.