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Resting tremor classification and detection in Parkinson's disease patients

Carmen Camara[a,b,*], Pedro Isasi[b], Kevin Warwick[c], Virginie Ruiz[c], Tipu Aziz[d], John Stein[e], Eduard Bakštein[f]

[a] Center for Biomedical Technology, Technical University of Madrid, Spain
[b] Dept. of Computer Science, Carlos III University of Madrid, Spain
[c] Dept. of Cybernetics, University of Reading, UK
[d] Dept. of Surgery, John Radcliffe Hospital, Oxford, UK
[e] University Laboratory of Physiology, University of Oxford, UK
[f] Dept. of Cybernetics FEE, Czech Technical University, Czech Republic

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ABSTRACT

Parkinson is a neurodegenerative disease, in which tremor is the main symptom. This paper investigates the use of different classification methods to identify tremors experienced by Parkinsonian patients. Some previous research has focussed tremor analysis on external body signals (e.g., electromyography, accelerometer signals, etc.). Our advantage is that we have access to sub-cortical data, which facilitates the applicability of the obtained results into real medical devices since we are dealing with brain signals directly.

Local field potentials (LFP) were recorded in the subthalamic nucleus of 7 Parkinsonian patients through the implanted electrodes of a deep brain stimulation (DBS) device prior to its internalization. Measured LFP signals were preprocessed by means of splinting, down sampling, filtering, normalization and rectification. Then, feature extraction was conducted through a multi-level decomposition via a wavelet transform. Finally, artificial intelligence techniques were applied to feature selection, clustering of tremor types, and tremor detection.

The key contribution of this paper is to present initial results which indicate, to a high degree of certainty, that there appear to be two distinct subgroups of patients within the group-1 of patients according to the Consensus Statement of the Movement Disorder Society on Tremor. Such results may well lead to different resultant treatments for the patients involved, depending on how their tremor has been classified.

Moreover, we propose a new approach for demand driven stimulation, in which tremor detection is also based on the subtype of tremor the patient has. Applying this knowledge to the tremor detection problem, it can be concluded that the results improve when patient clustering is applied prior to detection.

1. Introduction

1.1. Background

Different parts of the brain perform distinct tasks. There are areas devoted to control vision, memory, movement, and so on. The synchronization process between neurons is crucial. A well-coordinated synchrony between neuronal populations results in a decisive mechanism for neural signaling and information processing [1–3]. Some degree of de-synchronization however is the key-point to the proper functioning of neurons [4]. If neurons that do not work properly are in the circuits of the motor functions, this implies a dysfunction of the motor system, which results in conditions such as Parkinson's Disease (PD) [5,6]. In PD the neurons start firing themselves collectively in a periodic manner due to the loss of dopamine secretion [7], and this is the cause of the resting tremor (RT), being characteristic of PD in 70% of patients [8–10].

In this study we have dealt with signals captured through surgical intervention from the Subtalamic Nucleus (STN), the affected

* Corresponding author at: Center for Biomedical Technology, Technical University of Madrid (UPM), Montegancedo Campus, 28223 Pozuelo de Alarcón, Madrid, Spain.
E-mail address: carmen.camara@ctb.upm.es (C. Camara).

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region in all of the analysed patients. In the following sections we refer to this area of the brain when we mention the collected signal. Moreover, the subthalamic nucleus is the preferred target for deep brain stimulation in patients with advanced PD [11].

Parkinson is a neurodegenerative disease, in which patients suffer different symptoms: resting tremor, akinesia and rigidity [12–14]. Some existing patients may have a very severe disabling tremor, while others may not have any tremor at all. In this way, different studies refer to patient classification between tremor-dominant and non-tremor-dominant [15–18]. PD affects approximately 1% of the population over 55 years of age, although it can occur in younger subjects [19], it being the second most common neurodegenerative disease after Alzheimer's disease [20].

There is no recognized cure for PD, although there is treatment for the symptoms [21]. The main drug is L-dopa (L-3,4-dihydroxyphenylalanine – levodopa), the principal metabolic precursor of dopamine. However, the continued use of levodopa, in advanced stages of the disease, entails the so-called ON-OFF effect in patients. The patient goes through OFF periods, in which, despite receiving medication, a worsening of the symptoms appears involving increased rigidity, resting tremor and bradykinesia, in a severe, abrupt and unpredictable way. Moreover, OFF periods alter with ON periods, in which the effect of medication leads to dyskinesia episodes (levodopa-induced dyskinesia (LID)) into patients [22,23].

Several previous works have studied diverse methods to detect and quantify PD tremors [24–26]. Most of them focus the analysis on external body signals such as accelerometry, electromyography (EMG) and/or electroencephalography (EEG) – not exploring what exactly is happening in the areas of interest inside the brain but conversely dealing with the question as a black-box problem. Fortunately, the advantage of our experimentation is that we have access to sub-cortical data, which facilitates the applicability of the obtained results into real medical devices since we are directly dealing with brain signals.

1.1.1. Deep brain stimulation

Applying real-time medical imaging techniques, neurologists can recognize the optimal stimulatory target based on diagnosis for each patient. Electrical stimulation using electrodes implanted into this area then allows significant suppression of PD symptoms. This procedure is called deep brain stimulation (DBS) and is employed in patients who no longer respond properly to their medication [27–29].

The positioning and fine tuning of deep brain stimulation has become very accurate. Nowadays, surgeons can place electrodes in numerous areas of the brain, to turn-on or turn-off, stimulate or inhibit neuronal populations, in order to correct the malfunction of the regions in which the electrodes are implanted [28,30–32]. This technique is not only used in PD, but also in various neurological conditions such as dystonia, epilepsy, depression, or obsessive compulsive disorder.

This therapy is carried out with the use of an implanted medical device called a neurostimulator. Neurostimulators transmit continually high frequency electrical signals (typically 150–180 Hz) through one or more electrodes to various parts of the brain, stimulating or suppressing abnormal neuronal activity. Regarding PD, this treatment restores the natural frequencies of neurons, giving back their asynchronous functioning [27,28,33].

Numerous studies conclude that DBS is as effective as ablative therapies [28,30,32]. Furthermore, it has the noticeable advantage of being a reversible therapy and the treatment can be adjusted for each patient – modulating the stimulation supplied by the device.

Implantable medical devices are equipped with an integrated battery. The battery energizes the implant for treatment, monitoring and wireless communication tasks. Once implanted, it can last for up to 8 years, in the case of neurostimulators [34], to 10 in the case of other implants such as pacemakers [35]. Battery consumption has a direct impact on the device lifetime. Once empty, it has to be replaced, which requires further surgery and may entail some risks [36]. Alternatively a battery can be recharged externally by using magnetic fields, but this option it is not available in most stimulators.

Demand driven stimulation (DDS) has already been proposed in previous works [37,38]. The main goal of DDS is to achieve a more intelligent way of stimulation, such that it is only administered when it is necessary. Under this approach, it allows for the brain structures, in which the electrodes are implanted, to perform normally during non-tremor activity instead of being stimulated all the time. This would be beneficial, not only in the case of Parkinson Disease, but also for other movement disorders such as Essential Tremor, in which the patients have a lower degree of tremor. Moreover, the battery would be used in a more efficient way, independently of the way of charging it or the use of more advanced batteries.

Making the neurostimulator into a smart device is also interesting for other approaches. For instance, the processing and analysis of electrophysiological activity by the demand driven stimulation (DDS) device could provide clinically relevant information, such as duration of ON/OFF episodes, tremor frequency, etc.

In this paper we propose a new approach for DDS, in which the detection of tremor is also based on the tremor subtype the patient suffers.

1.2. Tremor

Tremor is a rhythmic and involuntary movement that appears in one or more parts of the body [39]. There are different kinds of tremor, depending on: (1) the circumstances in which it appears: at rest, during maintenance of certain positions or while performing voluntary actions; (2) the affected body area: hands, arms and other body parts; and (3) the frequency at which the tremor manifests itself: low (<4 Hz), medium (4–7 Hz) or high (>7 Hz) frequency bands. According to these three factors, tremor can be classified within a movement disorder pathology.

The Consensus Statement of the Movement Disorder Society on Tremor [40] categorizes subtypes of tremor for this condition into 3 distinctly separate groups:

1. Resting tremor (RT), which is the most characteristic of PD tremors, occurs at a frequency band between 4 and 6 Hz [41] and disappears when a voluntary movement is performed. Its presence is a good criterion for the diagnosis of PD, since this sort of tremor is usually not associated with other pathologies. On the other hand, for the vast majority of PD patients, the resting tremor emerges along with postural and/or kinetic tremors at the same frequency. Therefore many studies simply assume that it is a continuation of the resting tremor under postural, kinetic conditions or vice versa [42–48].

   Postural tremor takes place when the patient suffers a tremor episode maintaining a position against gravity, for instance keeping the arms 90° horizontally relative to the trunk. Meanwhile kinetic tremor occurs when the subject performs any voluntary movement.
2. The second group is made up of PD patients who have episodes of RT together with postural/kinetic tremor episodes at higher frequencies than the resting tremor, referred to as Essential Tremor (ET). Many research studies justify this since ET episodes can co-exist together with RT episodes in PD [33].
3. The last group includes patients who do not have resting tremor episodes. This subgroup of patients is only affected by kinetic and postural tremor episodes [49].