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A Fuzzy Inference System for Resting Tremor Detection in Parkinson's Disease

Carmen Camara · Kevin Warwick · Ricardo Bruña · Tipu Aziz · Francisco del Pozo · Fernando Maestú

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Abstract Parkinson is a neurodegenerative disease whose principal symptomatology includes several symptoms. The treatment entails oral medication or deep brain stimulation. The former decreases its beneficial effects while increases the adverse effects with the time of use. On the other hand, deep brain stimulation depends on a device implanted into the brain that performs a continuous stimulation on the damaged area and whose battery needs to be replaced after few years.

Local field potentials were recorded in the subthalamic nucleus of 10 Parkinsonian patients, who were diagnosed with tremor-dominant PD and underwent surgery for the implantation of a neurostimulator.

In this work we design a tool that learns to recognize the principal symptom of this disease, tremor. The goal of the designed system is to be able to detect when the patient is suffering a tremor episode. A demand driven stimulation would perform a more intelligent use of the device, stimulating only when it is necessary.

Measured LFP signals were preprocessed by means of down sampling, filtering, normalization, rectification and windowing. Then, two synchronization measures are implemented and evaluated on our dataset. These measures inform us about the synchronization level between the subthalamic and the muscular activity. The results of evaluating the indexes on each windows represent the inputs to the designed system. Finally, a fuzzy inference system is applied for tremor detection. Results are favourable, reaching accuracies higher than 98.7% in the 70% of the patients.

Keywords Parkinson's Disease · Deep Brain Stimulation · Fuzzy Logic · Bicoherence · Mutual Information

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1 Introduction

Nowadays, technology is all around us. We use it for a multitude of purposes, such as to communicate from different locations, to access the network and get any information we desire in just seconds by clicking a mouse, predict the weather and make plans accordingly, live in domestic houses that learn from our preferences. More recently it is being used to study the development of Smart Cities or Intelligent Transportation Systems. All these examples of technology are aimed at the same goals, to put technology at the service of people to make our lives easier and more enjoyable.

However, this high technological development arrives to the market before health system applications. It often seems paradoxical that it is possible to fix a malfunction in our computers, but not in ourselves, for example our brains. It is however true that the domain is much more complex. It is also true that we are not the designers of the brain and we do not by any means understand completely the way on which it works, so that repairing a malfunction is not trivial. However, this gap in the application of technology sometimes seems, in many cases, senseless.

We experience tragic diseases, that in a very short time completely disrupt our health and, as a direct consequence, our lifestyle. Such is the case with neurodegenerative diseases. Our capabilities are lessened drastically and often rapidly and to be aware of it makes us feel helpless. If technology exists – or can be developed – that, when integrated in our body, can improve the performance of damaged biological circuits, then it should be so employed. The goal is to put technology at the service of our physiological and neurological needs, so that it can repair us when needed. But, how can technology be enabled to achieve that goal when we do not know the reason of some diseases? A possible solution is the use of learning through examples. By employing machine learning techniques we can design a machine to learn what it is normal and what is pathological, and then ask the system to take decisions.

This study focuses on Parkinson's Disease (PD). In this work we design a tool that learns to recognize the principal symptom of this disease, tremor. The goal of the designed system is to be able to recognize when the patient is suffering a tremor episode. The working environment is a computer, but the idea of demand driven stimulation is embedded in the system in a real neurostimulator [18, 1]. Thus, an intelligent systems that learns from the patient pathology, can improve the treatment provided, and therefore the patients daily life.

1.1 Parkinson's Disease

Motor function is a balance carefully regulated by a number of neurotransmitters in the basal ganglia circuits. When one of the neurotransmitters involved is not released correctly the information between brain cores is inefficient and derivates in diseases of the motor system. In the case of Parkinson's Disease, the main cause is the death of dopamine-secreting neurons. While the reasons for this death are unknown, the effects that this provokes are well known. The principal symptomatology includes tremor, rigidity and bradykinesia [7, 16]. The best known of these is the tremor and it is this aspect that is studied in this paper. There are different types of tremor in Parkinson's disease depending on the circumstances in which it appears. The most common is the so-called resting tremor (RT). RT is a rhythmic movement, which appears in a relaxed and supported limb, disappearing or decreasing when the patient begins a voluntary movement. It occurs at a frequency between 3 and 5 Hz and is very debilitating for the patient.

The treatment of Parkinson's disease is not an easy task. The first choice is an oral treatment, consisting on the provision of levodopa, a precursor of the dopamine. The use of this treatment began to be used at the mid-sixties and it continues being the most used one. It relieves the main symptomatology of PD. However this is not a treatment that adjusts to the evolution of the disease. After a few years of use (around 5 years), the patients typically begin to experience motor fluctuations. This is the so-called ON-OFF effect, wherein episodes in which the medication works (ON), are alternated with periods in which does not (OFF). Furthermore OFF periods increase in duration as the usage time of the treatment increases, thus as time passes so oral medication becomes more inadequate [12, 11].

Furthermore, prolonged use of levodopa can induce dyskinesia (LID), which causes the patient to suffer different types of involuntary movements. Most cases of LID appear when the anti-Parkinson effects of levodopa are at a maximum. It is considered that this is due to an imbalance in the levels of neurotransmitter that are affected by the administration of the medication. This means that setting the best dose for an individual's treatment is a difficult task. Due to these complications many patients have undergone surgery to be treated with Deep Brain Stimulation (DBS). This therapy consists of electrical stimulation applied to specific areas within the brain, most frequently the subthalamic nucleus. This breaks the abnormal activity and imposes a normal brain rhythm [14].

Although neurostimulators are called brain-pacemakers, these implants do not work in the same way. Once the device is implanted and running, it stimulates uninterruptedly. As a result DBS requires that the battery must be changed in a maximum time of 9 years [8].

In this work we propose a real-time resting tremor detection system, which could be a first step towards demand driven stimulation, thereby providing more intelligent healthcare. The rest of the paper is organized as follows. In Section 2, the pre-processing techniques are explained and then we introduce the synchronization measures used in our experimentation. The fuzzy-system is presented in Section 3 and each of its components is explained. Section 4 shows the global results and the results per patient. Finally, In Section 5 we draw some conclusions.

2 Materials and Methods

The dataset used in this study is composed of files from ten patients who were diagnosed with tremor-dominant PD, and who all underwent surgery for the implantation of a neurostimulator (DBS treatment) at the John Radcliffe Hospital in Oxford, UK. The local research ethics committee of the Oxfordshire Health Authority approved the recordings and informed consent was obtained from each patient.

Recordings were performed during a postoperative observation period in which the depth electrodes were already implanted but not stimulating. As a result data was accessible for recording.

Each record consists of two channels, recorded simultaneously. The first one is the Local Field Potential (LFP), collected through the electrodes in the basal ganglia, specifically in the subthalamic area.

The second channel is the associated electromyography (EMG) signal indicting movement (tremor) time sequenced to synchronize with the LFP recording. The EMG records were taken from the extensor in the arm contralateral to the LFP implantation.

2.1 Data Preprocessing

Before dealing with the data it was necessary to carry out a series of preprocessing techniques to eliminate noise, filter the bands and highlight events of interest. In this section the techniques used and the reasons for their need is presented.

2.1.1 Normalization

The files of our dataset vary in amplitude between patients. This is due to the idiosyncrasies of the signal and the symptomatology of the disease.

It is therefore necessary to perform normalization of the data, such that the posterior processing and obtained results are comparable among different patients.

Therefore we normalized all channels separately, so that all of them maintain their oscillatory properties but the mean and the variance were normalized to 0 and 1, respectively.

2.1.2 Resampling

The sampling rate varies between 250-1000 Hz throughout our patient dataset. A re-sampling is realized in order to make the posterior processing the same for all the data and so that the results are comparable. We resampled all the files to 250 Hz, which was the minimum sampling frequency present in all the files.

2.1.3 Filtering

Due to the different characteristics and nature of the LFP and EMG signals, the filtering pipeline was also different.

For LFP we performed a band-pass filtering between 2 and 45 Hz with a 500 order FIR filter designed using a hamming window. LFP signals contain movement artefacts around 1 Hz, so we set the low cut-off frequency at 2 Hz. On the other hand, by fixing the upper cut-off frequency at 45 Hz we excluded the line noise (in Europe 50 Hz) as well.

The EMG signal was filtered in two steps. In a first stage we applied a band-pass order 500 FIR filter between 30 and 125 Hz. This frequency band was selected due to the nature of the EMG signal, consisting in burst starting at 30 Hz. The upper edge of the filter is the maximum allowed frequency of the signal, due to the Nyquist theorem. This signal was then rectified to obtain a baseband signal describing the muscular activity.

Rectification is a nonlinear processing that modifies the signal spectrum. When dealing with EMG this method intensifies the signal power at low frequencies

[19].We calculated the Hilbert transform of the filtered EMG signal and constructed the analytic signal, $A(x)$, which can be expressed as:

$$A(x) = x + iH(x)$$

where x is the original signal, H(x) is the Hilbert transform of x and i is the imaginary unit. From this analytic signal we calculated the envelope, which represent the instanteneous oscillatory energy of the EMG signal. This envelope is often used as an indicator of muscular activity.[10]

Finally, this envelope was filtered with the same filter applied to LFP in order to be able to compare both signals.

2.1.4 Windowing

Tremor episodes experienced by patients in our dataset are not isolated in files of one nature. Therefore in our dataset there are files that contain both tremor and rest episodes due to the patient experiencing both states during the recording period.

We split the data obtained into 2 seconds contiguous windows without overlapping. The window size is based on achieving a trade-off between temporal resolution and the number of available samples. The use of 2 seconds windows provides an adequate temporal resolution (with a frequency step of 1/2 Hz), whilst counting on a significant number of windows an average of 42 per patient. The signal sampling frequency was set to 250 Hz, so each 2 seconds window contained 500 samples.

2.2 Synchronization measures as features

To understand more how the brain works, it is useful to observe it working naturally. We can do that by means of several techniques based on imaging (such as functional magnetic resonance imaging or positron emitting tomography) or based on the electrical or magnetic signals generated in the brain (such as Electroencephalography or Magnetoencephalography). In our case we count with two simultaneous signals: local field potentials and electromyography.

LFP measures the aggregate presynaptic and postsynaptic activity of a population of neurons, meanwhile EMG measures the electrical activity realized due to skeletal muscle contraction.

The analysis of synchronized activity is a new observation window on the functioning of the brain. Analyzing the level of coupling between signals can determine which brain areas share information among them. It is therefore very useful to reveal the covariance between areas or as in this work, between a brain area and the effects which its activity provokes.

The EMG signal is more reliable regarding tremor detection as opposed than raw LFP signal, since the first one measures directly the muscular activity, which is higher under tremor episodes. Moreover, some indexes reflect an increase of synchronization levels under tremor episodes, in comparison with rest states. We consider here two synchronization measures as inputs to a fuzzy controller, mutual information and bicoherence.

The selection of the indexes was based on performance. We tested several synchronization indexes, including correlation, coherence [15] and phase locking value [6]. The selected ones are those which better distinguish between the tremor and resting states.

2.2.1 Mutual Information

Mutual information is an index that defined the amount of information shared by two variables, defining information in the information theory framework. The entropy of a random variable is defined in this framework as the amount of information it holds. It can be defined also as the measure of its uncertainty. The higher the uncertainty, the larger is the entropy.

Given a random signal X, which has a probability distribution $p(x) = P\{X = x\}, x \in X$, entropy is defined as:

$$H(x) = -\sum_{x \in X} p(x) \log p(x) \tag{1}$$

If now we have a pair of random variables, we defined the mutual information between then as:

$$MI = \sum_{x \in X} \sum_{y \in Y} p(x,y) \log \frac{p(x,y)}{p(x)p(y)} \tag{2}$$

Where $p(x,y)$ is the joint probability. If MI(X,Y) = 0, then the variables are independent, they do not share any information. Else if MI(X,Y) > 0, exists an association between X and Y, that is, the knowledge of one variable, would give us some knowledge about the other one [13].

2.2.2 Bicoherence

Power spectrum analysis is usually performed via a Fourier Transform (FT), of the second order statistic of the signal. But, unfortunately, this measure loses information about the phase relationships between frequency components, a fact that has been linked with impaired functions in the brain [17].

The bispectrum is a two dimensional version of the FT based on the third order cumulant of the signal. It is defined as:

$$B(f_1, f_2) = \sum_{m=-\infty}^{\infty} \sum_{n=-\infty}^{\infty} R(m,n) e^{-j2\pi f_1 m} e^{-j2\pi f_2 n} \tag{3}$$

Where R(m,n) is the third order cumulant as a function for the lags m and n and f_1 and f_2 are the frequencies in study.

The bispectrum explores if the signals at f_1, f_2 and $f_1 + f_2$ are synchronized, which would mean that the oscillation at $f_1 + f_2$ is due the nonlinear relation between both signals. Bicoherence can be calculated as a normalized version of the bispectrum [9].

$$BICOH(f_1, f_2) = \frac{B(f_1 f_2)}{\sqrt{P(f_1)P(f_2)P(f_1 + f_2)}} \tag{4}$$

where $P(f)$ is the power spectrum at frequency f . For incoherent signals this measure tends to zero.

3 Fuzzy System

Traditionally the field of predicate logic works by dividing the output space into disjoint sets. Thus, any predicate P applied to a collection U, is associated to a precise set denoted as $P \subset U$. This can be described through the membership function P whose value is determined by the belonging to P of the different elements $u \in U$ which is defined by:

$$\mu_P(u) = \begin{cases} 1 \text{ if } u \in P \\ 0 \text{ otherwise} \end{cases} \tag{5}$$

So if $\mu_p(u)$ is 1, the predicate is true. Whereas if it is zero the predicate will be false.

Designing systems employing classical logic has the problem that they are too rigid. This rigidity is a limitaton in the sense that it is difficult to model systems based on precise rules when the domain is not determined by precise inputs and/or outputs.

Therefore classical logic turns out to be insufficient to solve some problems. From this need, the definition of fuzzy sets and fuzzy logic has appeared. It builds models that are particularly useful to work with uncertainty in a more natural way.

A fuzzy predicate, evaluated on a collection U , is associated to a fuzzy set $V \subset U$, which is defined by the function $\mu_v(u)$ This function determines the membership function of the elements of V to U, as a matter of degree.

$$u_v\colon U \to [0, 1]$$

Thus, a fuzzy set is one in which the elements do not belong completely to only one set, but do belong to that sets to a certain extent. As a result, to work with fuzzy sets we define the degrees of membership of the different elements to each set.

We have decided to use a fuzzy control system for detection of resting tremor motivated by two main reasons which are:

- The impreciseness can be a source of uncertainty. EMG and LFP time series, despite having been meticulously collected by the medical team, may have certain levels of impreciseness because of the noise. This may be due, for example, to differences in skin impedance. As a result this could alter the values of electromyography. Fuzzy methods are able to manage the imprecision present in the data.
- It allows for variability in the data. As a preliminary study, we have explored how the different synchronization index works on each patient. Although generally the trend remains the same for all patients, there is not a threshold that determines from which value of the index we can consider that the patient is experiencing a tremor episode. So there is a short range of values on which the output cannot be easily determined and these can be either a tremor or rest

episode. We know that if the system output is in the range zero to 0.2, the input was a resting episode. Similarly, if the output is greater than 0.4, the input was almost surely a tremor episode. But, what happens when the output is within the approximate interval [0.2-0.4]?

Taking into consideration both situations in the design of the detection system,for the problem addressed in this work it can be beneficial when we attempt to minimize the number of false negatives. A false negative would mean that our system has detected an input as a resting episode, when in fact it is a tremor one. In these situations the resultant controller would not provide stimulation to the patient when it is actually needed. Because of that, we are aiming to diminish the number of false negatives. Indeed this is the most critical situation.

False positives, on the other hand, are not so much of a problem. In such instances an input would be detected as a tremor episode when in fact it was actually a normal resting period. In this case the controller would provide unnecessary stimulation. The negative of this is that useful power is being used up by the device for no reason. In the limit, with lots of such cases, the controller would tend to the present case of continual stimulation. But although this is not a desirable situation it is not critical as current system works in this mode with the patient not suffering any backside.

3.1 Defining the System

The specific components of a fuzzy controller are shown in figure 1. MI (mutual information) and BICOH (bicoherence) are the inputs to the system. These inputs are the results of evaluating the synchronization measures to each window of the preprocessed raw data obtained as described in the previous section.

In Figure. 1 the central block represents the fuzzy system itself. It is composed of three modules on the design of a Mamdani fuzzy inference system: Fuzzification, Rule inference and Defuzzification [2].

- Fuzzification of the input variables. This step evaluates the conditions of the rules and turns the inputs to membership degrees for each set.
- Rule Inference. This step comprises rule evaluation and the aggregation of the generated outputs.
- Defuzzification. Finally it is necessary to carry out defuzzification. This process transforms the aggregate fuzzy output set to a single number. Doing this we translate the result obtained to one that has sense in our domain.

Based on the obtained output the system evaluates if the input corresponds or not to a tremor episode. When the onset of a tremor episode is detected the neurostimulator would give the order to stimulate. In fact, it is also possible to predict such onset and hence apply stimulation to stop the tremor actually occurring in the first place [4].

3.1.1 Fuzzification

This step evaluates the conditions of the rules and turns the inputs to membership degrees for each set.

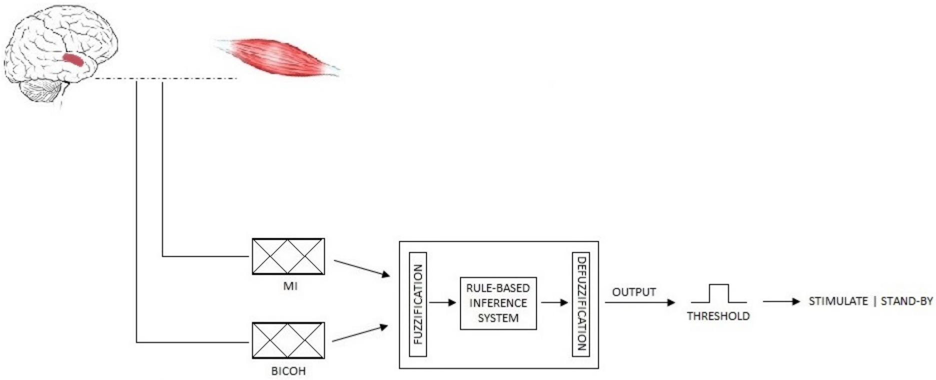

Fig. 1 System operation scheme

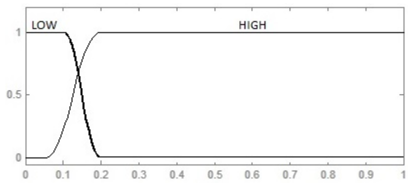

Fig. 2 Membership for Mutual Information Input

The membership function defines the fuzzy sets. Its determination is a matter of design and tends to be subjective. It must be designed with full knowledge of the domain and the nature of the inputs which are provided to the fuzzy control system. Therefore we have taken certain aspects into account: [5]

– The sets are sufficiently wide to allow noise in the measurement.
– A certain amount of overlap is desirable; otherwise the controller may run into poorly defined states, where it does not return a well defined output.

The selection of the membership function for each set is based on knowledge of the dataset. In that sense, we have chosen spline-based functions for the NO-TREMOR input set, given by:

$$f(input) = \begin{cases} 1 & \text{if } input <= 1 \\ 1 - 2(\frac{input-0.1}{0.1-0.2})^2 & \text{if } 0.1 <= input <= \frac{0.1+0.2}{2} \\ 1 - 2(\frac{input-0.2}{0.2-0.1})^2 & \text{if } \frac{0.1+0.2}{2} <= input <= 0.2 \\ 0 & \text{if } input >= 0.2 \end{cases} \quad (6)$$

In the same way we define spline-based curves for the TREMOR input, given by:

$$f(input) = \begin{cases} 0 & \text{if } input <= 0.05 \\ 2(\frac{input-0.05}{0.2-0.05})^2 & \text{if } 0.05 <= input <= \frac{0.05+0.2}{2} \\ 1 - 2(\frac{input-0.2}{0.2-0.1})^2 & \text{if } \frac{0.1+0.2}{2} <= input <= 0.2 \\ 0 & \text{if } input >= 0.2 \end{cases} \quad (7)$$

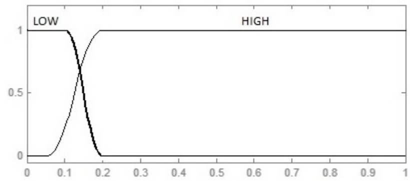

Fig. 3 Membership for Bicoherence Input

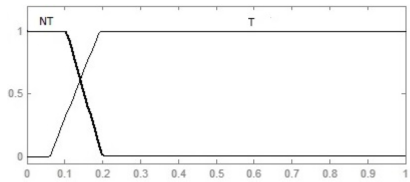

Fig. 4 Systems Output Membership

The output represents the state of the neurostimulator. Depending of the tremor state of the patient, the stimulator can be either stimulating or kept waiting, just listening (We denominate this state as *stand-by* henceforth). To model this, we opted for trapezoidal-shaped membership functions, defined by:

$$f(output) = \begin{cases} 0 & \text{if } output <= 0 \\ 1 & \text{if } 0 <= output <= 0.1 \\ \frac{0.2-output}{0.2-0.1} & \text{if } 0.1 <= output <= 0.2 \\ 0 & \text{if } 0.2 <= output \end{cases} \tag{8}$$

$$f(output) = \begin{cases} 0 & \text{if } output <= 0.05 \\ \frac{output-0.05}{0.2-0.05} & \text{if } 0.05 <= output <= 0.2 \\ 1 & \text{if } 0.2 <= output <= 1 \\ \frac{1-output}{1.01-1} & \text{if } 1 <= output <= 1.01 \\ 0 & \text{if } 1 <= output \end{cases} \tag{9}$$

3.1.2 Rule Evaluation

This step comprises rule evaluation and aggregation of the generated outputs. Evaluation of the rules uses fuzzy operators, which are applied over the inputs to calculate the trigger force of the rules. The result is a fuzzified value for each of the rules.

Fuzzy Operators

Fuzzy logic is a superset of classical logic. Classical logic uses absolute operators to calculate the output of a given input, that is, only Boolean values for the output are contemplated. Meanwhile fuzzy logic employs fuzzy operators which contain the values 0 and 1 as extremes, but also takes into account all the intermediate values, thereby allowing for uncertainty. We use the *AND* operator, which in our case works with the minimum method.

Rule Number	MI	BICOH	DECISION
1	LOW	LOW	STAND-BY
2	HIGH	LOW	STIMULATE
3	LOW	HIGH	STIMULATE
4	HIGH	HIGH	STIMULATE

Table 1 Systems Rules

Definition of the rules

The rule set defines how the inputs are related to the outputs. Fuzzy rules differ from classical rules in that the antecedent of a classical rule must be 100% true in order that the consequent can be evaluated. However in fuzzy rules, the antecedent can be partially true, which does not in itself enable or prevent the trigger of the rule, simply that the consequent is partially true.

During the design stage, the definition process of the fuzzy rules usually requires an adjustment process to optimize the performance of the system. The defined rules are shown in Table 1, where each row represents a rule. As described in previous section, the synchronization indexes can take the fuzzy value of low or high. Meanwhile the overall/final output is either Stimulate or Standby.

Evaluation and Aggregation

Once rules have been evaluated we have one physical output for each rule. But having different output sets does not provide any directly meaningful information, thus it is necessary to perform an aggregation of the outputs. This step performs a unification combining the membership functions of all the rule consequents. In our case we have chosen the maximum method to perform the aggregation.

3.1.3 Defuzzification and Thresholding

Finally it is necessary to carry out a defuzzification. This process transform the aggregated fuzzy output set to a single number. Doing this we turn the result obtained into one that has sense in our domain. In this step we have opted for the *centroid* method, which calculates the centre of area of the obtained fuzzy set.

The output of the system represents the degree of synchronization between LFP and EMG. This value does not however itself determine the level of stimulation from the device. Therefore, a thresholding module is added. This module compares the output to a preset threshold, in this way:

$$device - decision = \begin{cases} stimulate \ \text{ if } output >= threshold \\ stand - by \ otherwhise \end{cases} \tag{10}$$

As will be seen in the next section, this threshold can be the same for all of the patients involved or it can be adjusted individually. This last option can be of interest as it can improve the tremor detection. It has been previously shown that there appear to be different types of Parkinson's Disease [3]. It may well be therefore that the threshold is linked to the disease classification.

<table>
<tr><th>Interval</th><th>Number of NT Instances (red dots)</th><th>Number of T Instances (green dots)</th><th>FP</th><th>FN</th><th>GLOBAL ACCURACY</th><th>TREMOR ACCURACY</th><th>NO-TREMOR ACCURACY</th></tr>
<tr><td>[0-0.2)</td><td>29</td><td>1</td><td rowspan="3">42 (12.2%)</td><td rowspan="3">–</td><td rowspan="3">87.8%</td><td rowspan="5">88.2%</td><td rowspan="5">82%</td></tr>
<tr><td>[0.2-0.3)</td><td>78</td><td>6</td></tr>
<tr><td>[0.3-0.4)</td><td>195</td><td>35</td></tr>
<tr><td>[0.4-1]</td><td>66</td><td>314</td><td>–</td><td>66 (17.4%)</td><td>82.6%</td></tr>
<tr><td>[0-1]</td><td colspan="4">Global Accuracy</td><td>85.1%</td></tr>
</table>

Table 2 Global Results

4 Results

In this section we present the obtained results. By considering the range of the outputs, we can define four ranges: [0-0.2), [0.2-0.3), [0.3-0.4) and [0.4-1]. We evaluate the number of false positives, false negatives, tremor accuracy, no-tremor accuracy and global accuracy for each range.

A false positive occurs when the system determines that the input was a tremor instance, whilst in really it was a no-tremor instance. Analogously, false negatives are the cases in which the system considers the input corresponds with a no-tremor episode but in fact the patient was trembling.

As previously mentioned, the final determination as to whether the system provides stimulation or not, depends on whether the output is greater than a fixed threshold or not. The operation of the indexes, although very similar, is not exactly the same across the patients. Therefore, threshold determination is critical for the accuracy of the system.

With this in mind, we studied here how the system works by determining the threshold in two different ways: 1) globally, fixing a global threshold for all the patients (so we take all the patient dataset into account together) and 2) Individually for each patient, taking the instances of each patient separately.

4.1 Global Results

By defining the system taking into account all the patients together, through experimentation we found that the best value for the threshold was 0.4. This value minimized the number of false positives below the threshold and the number of false negatives above it. This can be observed in Figure 2, where the output of the fuzzy system for each input is depicted. The numerical results are presented in Table 2.

The accuracy of tremor detection (named as tremor accuracy in the table) can be improved by lowering the threshold, getting then lower no-tremor accuracy. But, as have been mentioned before, for the patients comfort it is preferable to ensure that any time there is a tremor episode the neurostimulator is working.

4.2 Results per patient

In this section we perform the analysis by running the system for each patient individually. As for the global results, we show the numeric values in Table 3. This

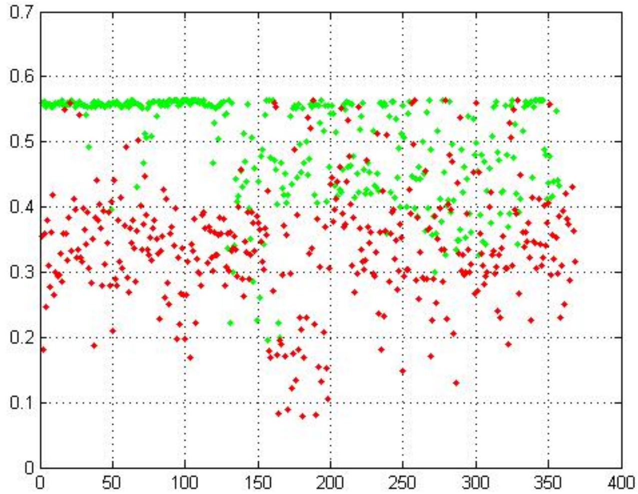

Fig. 5 System operation scheme

Patient	Threshold	Interval	NT (red)	T (green)	FP	FN	Accuracy	Global Accuracy	T Accuracy	NT Accuracy
Patient 1	0.5	[0 - 0.5)	69	0	-	0	100%	95.8%	100%	94.5%
		(0.5 - 1]	4	22	4	-	84.6%			
Patient 2	0.4	[0 - 0.4)	-	1	-	1	0%	98.95%	98.95%	-
		[0.4 - 1]	-	95	0	-	100%			
Patient 3	0.4	[0 - 0.4)	36	4	-	4	90%	90.31%	83.33%	94.73%
		[0.4 - 1]	2	20	2	-	90.9%			
Patient 4	0.4	[0 - 0.4)	6	9	-	9	60%	80%	62.5%	100%
		[0.4 - 1]	0	15	0	-	100%			
Patient 5	0.4	[0 - 0.4)	27	0	-	0	100%	96.96%	100%	96.42%
		[0.4 - 1]	1	5	1	-	83.3%			
Patient 6	0.4	[0 - 0.4)	39	0	-	0	100%	80.75%	100%	79.59%
		[0.4 - 1]	10	3	10	-	23%			
Patient 7	0.4	[0 - 0.4)	83	0	-	0	100%	79.82%	100%	78.30%
		[0.4 - 1]	23	8	23	-	25.8%			
Patient 8	0.4	[0 - 0.4)	6	1	-	1	85.71%	98.82%	98.73%	100%
		[0.4 - 1]	0	78	0	-	100%			
Patient 9	0.3	[0 - 0.3)	27	1	-	1	96.42%	82.93%	98.76%	56.25%
		[0.3 - 1]	21	80	21	-	79.2%			
Patient 10	0.4	[0 - 0.4)	4	3	-	3	57.14%	55.16%	80%	28.57%
		[0.4 - 1]	10	12	10	-	54.54%			

Table 3 Results per patient

time, we include the column *threshold*, which indicates from which output value the system decides to apply stimulation. The graphical results are illustrated in Figure 3.

5 Discussion

The system is able to reach an accuracy of 100% in tremor detection for 4 out of 10 of the patients. For other 3 out of 10 of the patients the number is almost 99%.

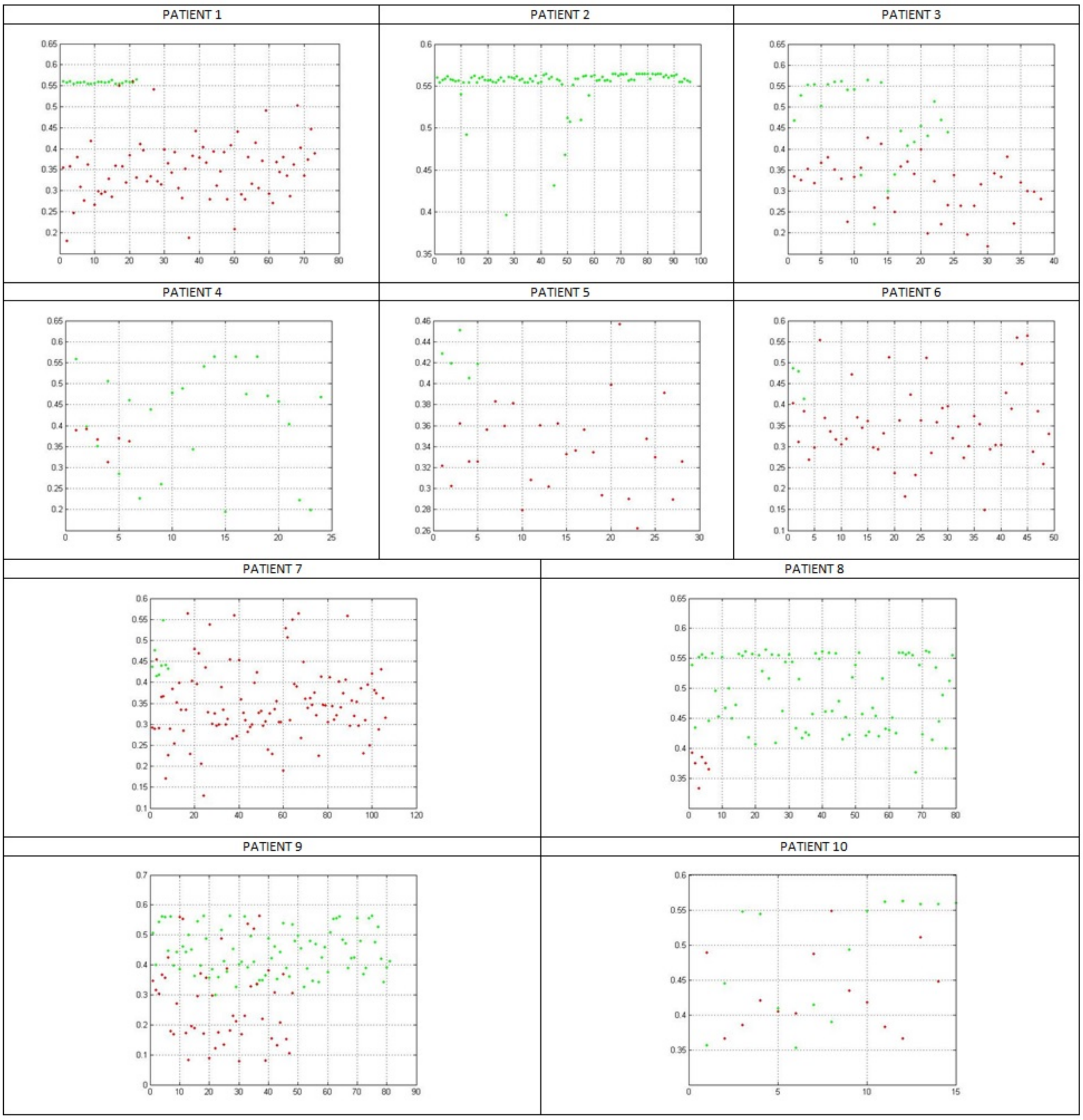

Fig. 6 System operation scheme

For 2 out of 10 of the patients the accuracy reaches 80%. Unfortunately in the case of one patient the system was only able to automatically detect 62% of the tremor episodes.

Moreover, the system is also able to reach high levels of accuracy for no-tremor episodes, as shown in the last column of Tables 2 and 3. This implies an improvement of 82% (for the global evaluation) in comparison with the neurostimulators used nowadays. This improvement is even higher when we evaluate the system for each patient, reaching the 100% in some cases.

The accuracy differences among patients are due to the fact, as can also be observed in the figures, that there is a clear separation between episodes of tremor and rest in some patients, whilst this segregation is not so clear in others. The physiological cause of this is unknown at present, and could be due to a misplacing in the electrode positioning. However, showing such differences clearly points to areas of further study.

With patient number 4 an accuracy of tremor detection of only 62.5% was achieved, however for this patient an accuracy of 100% was achieved for no-tremor detection. Therefore a solution to improve the performance in these situations could be to lower the threshold. This would though slightly increase the false positives but increase the tremor detection accuracy, which is the priority. As we previously pointed out, an increase in the false positive detection rate would not be harmful for the patient. So, despite this, the performance of the system would be superior to the one offered by the solutions currently used.

6 Conclusions

In this work we have proposed a real-time resting tremor detection system which could be a first step towards demand driven stimulation, providing more intelligent healthcare for patients who suffer from Parkinson's Disease.

The results are favourable, in the sense that 100% accuracy in tremor detection can be achieved in almost half of the cases. In fact only 3 out of the 10 cases we obtained an accuracy lower than 98.7%. Moreover, even in those cases, the system allowed a gain adjustment which increased the accuracy. For all the patients, a system such as the one proposed in this paper would improve the stimulation performance compared to the current stimulation systems, which basically consist of continuous stimulation.

In this study we used synchronization measures as features for tremor detection. We have selected the two measures which are most effective for tremor detection. It would be desirable to carry out an in depth study on the level of synchronization between basal ganglia and muscle effectors in order to unveil why in some patients the coupling between signals is not so clear. This knowledge would help in the development of demand driven stimulation device, enabling it to be more stable across the patient spectrum.

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Conflict of Interest The author declares that they have no conflict of interest.

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