

Frédéric Bourgeois*, Nicola Pambakian, Jérôme Coste, IJsbrand de Lange, Jean-Jacques Lemaire, Erik Schkommodau* and Simone Hemm*

An online movement and tremor identification algorithm for evaluation during deep brain stimulation

<https://doi.org/10.1515/cdbme-2022-1028>

Abstract: INTRODUCTION: Deep brain stimulation (DBS) is widely used to alleviate symptoms of movement disorders. During intraoperative stimulation the influence of active or passive movements on the neuronal activity is often evaluated but the evaluation remains mostly subjective. The objective of this paper is to investigate the potential of a previously developed Weighted-frequency Fourier Linear combiner and Kalman filter-based recursive algorithm to identify tremor phases and types. METHODS: Ten accelerometer recordings from eight patients were acquired during DBS from which 186 phases were manually annotated into: rest, postural and kinetic phase without tremor, and rest, postural and kinetic phase with tremor. The method first estimates the instantaneous tremor frequency and then decomposes the motion signal into voluntary and tremorous parts. The tremorous part is used to quantify tremor and the voluntary part to differentiate rest, postural and kinetic phases. RESULTS: Instantaneous tremor frequency and amplitude are successfully tracked online. The overall accuracy for tremorous phases only is 89.1% and 76.3% when also non-tremorous phases are considered. Two main misclassification cases are identified and further discussed. CONCLUSION: The results demonstrate the potential of the developed algorithm as an online tremorous movement classifier. It would benefit from a more advanced tremor detector but nevertheless the obtained digital biomarkers offer an evidence-based analysis and could optimize the efficacy of DBS treatment.

Keywords: Tremor estimation, Deep Brain Stimulation, Microelectrode Recording, Weighted-frequency Fourier Linear combiner, digital biomarker.

*Corresponding author: **Frédéric Bourgeois:** Institute for Medical Engineering and Medical Informatics, School of Life Sciences, University of Applied Sciences and Arts Northwestern Switzerland, Muttenz, Switzerland, frederic.bourgeois@fhnw.ch
2nd author Nicola Pambakian, 4th author IJsbrand de Lange: STIL B.V., Delft, Netherlands
3rd author Jérôme Coste, 5th author Jean-Jacques Lemaire: Université Clermont Auvergne, Clermont Auvergne INP, CHU Clermont-Ferrand, CNRS, Institut Pascal, F-63000 Clermont-Ferrand, France

1 Introduction

Deep Brain Stimulation (DBS) [1] has become one of the most important neurostimulation therapies for movement disorders such as Parkinson's disease (PD) and essential tremor (ET) to alleviate tremor among other symptoms [2]. Although DBS application under full anaesthesia is currently being researched [3], the majority of interventions are performed with awake patients. During the surgical procedure, electrodes are implanted in the thalamic or subthalamic area depending on the disease and symptoms. The severity of rest, postural or kinetic tremor [4] is evaluated by inspecting the patient's tremor while performing key tasks. It is linked with intraoperative microelectrode recording (MER) of neuronal activity and acute stimulation to achieve precise targeting. After the surgery, tremor is studied during therapeutic stimulation for parameters adjustments and to follow the disease progression. Moreover, symptom assessment is an issue for the new generation of implanted stimulators (Percept™ PC neurostimulator, Medtronic).

Clinical evaluations are usually done semi-quantitatively via clinical rating scales such as the TETRAS [5] or the Unified Parkinson's Disease rating scale [6] with the inherent interrater variability. We [7] and others [8-9] have previously shown that quantitative objective digital tremor biomarkers can support neurosurgeons and neurologists and generate more precise and continuous data. An automatic differentiation between the different arm or body positions, between voluntary and tremor motion and between tremor types (rest, postural, kinetic) could facilitate an online and offline correlation analysis between stimulation settings and changes in neuronal activity, respectively.

The aim of the present paper is to investigate the potential of a previously developed Weighted-frequency Fourier Linear combiner (WFLC) [10] and Kalman filter-based recursive algorithm to identify rest, postural and kinetic (movement) phases and to separate tremor from voluntary movements for the quantification of changes in tremor. The approach is tested with acceleration data intraoperatively acquired in parallel to MER during DBS surgery.

2 Methods

Four ET and four PD patients participated in a clinical study at the University Hospital in Clermont-Ferrand (2011-A00774-37 / AU905) including four males and females each (mean \pm std: age 67.3 ± 10.0 years). Seven subjects exhibited tremor in the upper limb and one in the lower limb.

During DBS surgery, MER recordings were performed along two trajectories per hemisphere at several positions before and behind the target position identified on preoperative images [11]. A three-channel accelerometer placed on the back of the hand (side of the leg) and an additional static video camera recorded the procedure. The subjects were asked to perform motor tasks, such as holding the arm in the air (postural phase), closing/opening one hand (kinetic phase), or leaving the arm at rest (rest phase). Throughout the recording the subjects partially exhibited tremor. The assessment protocol was adapted to the patient's pathology and expected cooperation, e.g., some subjects were not asked to perform any movement phases and other showed only few tremor phases.

In six cases either the video or the accelerometer data were unavailable resulting in a total of ten evaluable recordings each lasting around 10 minutes (with one exception). 186 phases were manually labelled based on the video footage into: rest without (58), rest with tremor (35), postural without (22), postural with tremor (27), movement without (14) and movement with tremor (30).

To retrieve the dominant tremor axis the accelerometer data are reduced to one dimension by performing a principal component analysis (PCA) using an eigenvalue decomposition of the covariance matrix. Note that although this step is done offline, it doesn't affect the online character of the main algorithm presented below. Since the accelerometer signal is not gravity compensated it can be interpreted as a direction information of the gravity vector around an arbitrary axis i.e., it is equivalent to a positional information.

A WFLC [10] applied on the band-pass filtered (Butterworth 4th order, frequency range 3-8 Hz) accelerometer signal (sampled at 100 Hz) is used to first estimate the instantaneous tremor frequency ω based on a least mean squares recursion. Then the unfiltered accelerometer signal is decomposed into tremorous and voluntary parts using a Kalman filter (internal state x , measurement model \tilde{y}), where tremor is modelled as a time-varying sinusoid with its frequency within the bandpass filter range and the voluntary part v as a model with constant first derivative \dot{v} during integration step and a slow adaptation rate (see eq. 1-3, time dependencies omitted for simplicity)

$$x^T = [w_1 \quad w_2 \quad v \quad \dot{v}]^T \quad (1)$$

$$\tilde{y} = \underbrace{w_1 \cdot \sin(\omega \cdot t) + w_2 \cdot \cos(\omega \cdot t)}_{tremor} + \underbrace{v}_{voluntary} \quad (2)$$

$$\frac{d}{dt} v = \dot{v} \quad (3)$$

where $w_{1,2}$ and t stand for the coefficients of the sinusoid and the time, respectively.

Tremor presence is detected by comparing the estimated instantaneous tremor amplitude $A = \sqrt{w_1^2 + w_2^2}$ with a patient independent threshold. A recursive algorithm is used to calculate the moving standard deviation σ of the voluntary part [12]. σ is reduced by a patient independent tremor amplitude factor c to further reject non-filtered tremorous residuals in the voluntary part estimation (see eq. 4). The tremor type detection (rest, postural and kinetic) is then obtained by comparing the reduced standard deviation $\tilde{\sigma}$ with two patient independent thresholds. The movement is considered rest if below, postural if in between and kinetic if above both thresholds, respectively.

$$\tilde{\sigma} = \sigma \cdot (1 - c \cdot A) \quad (4)$$

All used algorithms (except the PCA) are recursive and were selected to comply with the online requirement. Especially the computational requirements for the WFLC are very low due to its simplicity [10].

At every timestep the algorithm classifies the signal according to the thresholds. The performance is evaluated by comparing the manually labelled phases with their estimations, given by the mostly estimated class during this time. For a pure online approach also the phase changes should be detected. As a matter of fact, Bodenham's algorithm [12] was originally developed to detect changes in a signal and can be used for this purpose. The estimation accuracy is given by the number of correctly classified phases divided by the total number of phases.

3 Results

Two representative analyses of partial recordings are shown in Figure 1 including tremor isolation and phase classification. Tremorous movement (Figure 1.a, recording #3), clearly distinguishable with its peaks in the frequency domain, is successfully estimated in the time domain including its frequency and amplitude. The labelled and estimated phases match with one exception, where rest tremor is estimated as postural tremor. A second partial recording in Figure 1.b (recording #6) illustrates the difficulties of the algorithm when no tremor is present. Postural phases without tremor are

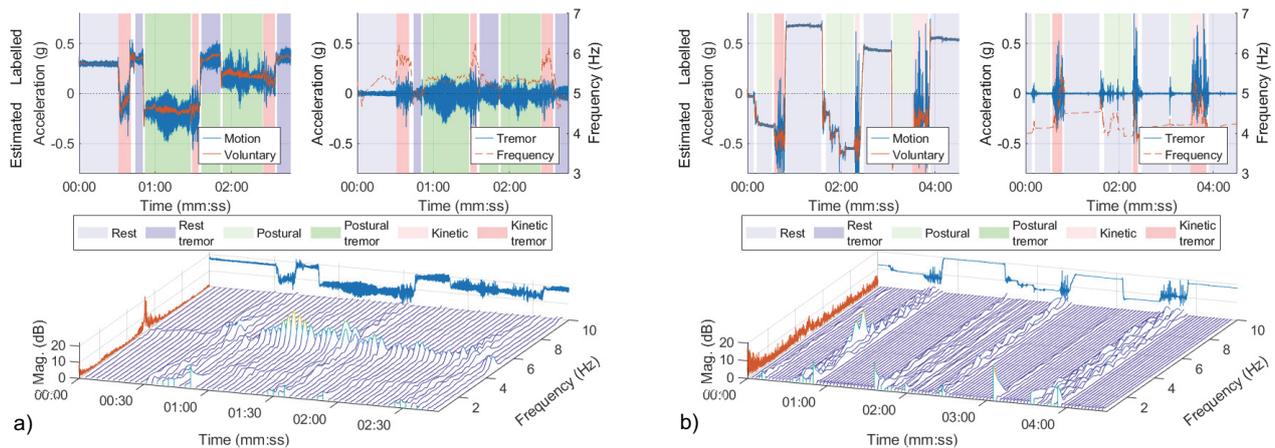


Figure 1: Representative analysis of two partial recordings, one with tremor (a, recording #3) and one mostly without (b, recording #6).

Top plots: Motion signal decomposed into voluntary (left) and tremorous (right) part together with the estimated instantaneous tremor frequency. Phases are colored according to the labelled (top half) and estimated (bottom-half) type of tremor. Bottom plot: Short-time Fourier transform of the motion signal (4s window, 50% overlap) with a scaled signal representation in the back and a scaled overall Fourier transform on the left.

classified as rest without tremor and movement phases without tremor as movement with tremor. It can be observed that voluntary movements cause broad-spectrum artefacts also in the range of tremor (2-8 Hz).

The error matrix for the classification of rest, postural and kinetic motion types where phases with and without tremor are merged has an overall accuracy of 85.5% (see Figure 2). The misclassification of postural phases in rest phases is clearly noticeable. Figure 3 shows a more detailed error matrix also differentiating between tremorous and non-tremorous phases with an accuracy of 76.3%. The misclassification discussed above mainly occurs in cases when tremor is not present (postural) and only to a minor extend when tremor is present (postural tremor). A second inaccurate estimation regards voluntary movement without tremor (kinetic) being estimated

as movement with tremor (kinetic tremor). Table 1 presents the accuracy for every recording individually. The percentage of tremorous phases greatly influences the accuracy of the recordings and show the heterogeneity of the data.

Table 1: Accuracy of every individual recording with classification of all six classes.

Recording #	# Phases	#Tremor Phases	Accuracy
1	18	8	94.5%
2	17	12	82.4%
3	25	22	92.0%
4	31	23	93.5%
5	21	1	52.4%
6	23	1	39.1%
7	5	5	100.0%
8	12	6	91.7%
9	21	12	66.7%
10	13	2	69.2%

Labelled	Rest	90	3	0	97%
	Postural	20	26	3	53%
	Kinetic	0	1	43	98%
		82%	87%	93%	
		Rest	Postural	Kinetic	
		Estimated			

Figure 2: Error matrix for the classification into rest, postural and kinetic phases. Phases with and without tremor are merged. The overall accuracy is 85.5%

4 Discussion

The presented recursive online algorithm successfully characterizes tremor by estimating its instantaneous frequency and amplitude. The isolation of both tremor and voluntary movement can be used to identify different phases in a motion signal. This demonstrates a promising application for the algorithm. Although the focus of this work was on pre-, intra- and postoperative clinical evaluations these indications could

Labelled	Rest	56	2	0	0	0	0	97%
	Rest tremor	0	32	0	3	0	0	91%
	Postural	13	0	4	2	0	3	18%
	Postural tremor	0	7	0	20	0	0	74%
	Kinetic	0	0	0	1	0	13	0%
	Kinetic tremor	0	0	0	0	0	30	100%
		81%	78%	100%	77%	-	65%	
		Rest	Rest tremor	Postural	Postural tremor	Kinetic	Kinetic tremor	
		Estimated						

Figure 3: Error matrix for the classification into rest, postural, kinetic tremor, and rest, postural, kinetic phase without tremor. The overall accuracy is 76.3%.

also be useful for other purposes such as tremor suppression wearables where online information is required.

Distinguishing between non-tremorous rest and non-tremorous postural phases is obviously not feasible without additional information as there is no movement content to differentiate them. In cases where tremor is present the results show that the algorithm can differentiate both. This is explained with the fact that even though the subject tries to maintain a certain position in the air the arm is highly prone to drift which is then reflected in the estimated voluntary part. To further improve the accuracy an additional orientation estimation could be incorporated to help differentiate non-tremorous rest from postural phases.

The nature of the presented algorithm is to find the dominant sinusoid in the input signal. It has good response time regarding the adaptation of the instantaneous tremor frequency and amplitude. For an accurate estimation, artefacts from voluntary movements should have a low magnitude in the frequency range of tremor. In contrary when non-tremorous movements are executed, the algorithm still tries to find a (non-existent) dominant frequency as shown in Figure 1.b. The algorithm in its present form is well suited for the characterization of tremor but is not yet adapted for its detection. More sophisticated approaches, e.g., based on the relative signal power should be investigated, before going into clinical use. Assuming a (perfectly accurate) implemented tremor detector the presented algorithm would only be applied on the tremorous phases which would result in an 89.1% accuracy with the given data.

An individual baseline measurement could provide further patient specific information about the tremor severity and its base frequency. Together with machine learning techniques, a more accurate and robust classifier could be

developed from the acquired digital biomarkers and deliver an evidence-based analysis for neurosurgeons and neurologists.

Author Statement

Research funding: The research was funded by the Eurostars programme (E! 113627). **Conflict of interest:** Authors state no conflict of interest. **Informed consent:** Informed consent has been obtained from all individuals included in this study. **Ethical approval:** The research related to human use complies with all the relevant national regulations, institutional policies and was performed in accordance with the tenets of the Helsinki Declaration and has been approved by the authors' institutional review board or equivalent committee.

References

- [1] Wårdell K, Nordin T, Vogel D, et al. Deep Brain Stimulation: Emerging Tools for Simulation, Data Analysis and Visualization. *Frontiers in Neuroscience*. Published online 2022.
- [2] Holsheimer J, Demeulemeester H, Nuttin B, de Sutter P. Identification of the target neuronal elements in electrical deep brain stimulation. *Eur J Neurosci*. 2000;12(12):4573-4577.
- [3] Chen T, Mirzadeh Z, Ponce FA. "Asleep" Deep Brain Stimulation Surgery: A Critical Review of the Literature. *World Neurosurg*. 2017;105:191-198.
- [4] Deuschl G, Bain P, Brin M. Consensus statement of the Movement Disorder Society on Tremor. Ad Hoc Scientific Committee. *Mov Disord*. 1998;13 Suppl 3:2-23.
- [5] Elble R, Comella C, Fahn S, et al. Reliability of a new scale for essential tremor. *Mov Disord*. 2012;27(12):1567-1569.
- [6] Fahn S, Elton RL. Unified Parkinson's disease rating scale. In: Fahn S, Marsden CD, Goldstein M, eds. *Recent Developments in Parkinson's Disease*. Macmillan; 1987:153-163.
- [7] Shah A, Coste J, Lemaire J-J, et al. Intraoperative acceleration measurements to quantify improvement in tremor during deep brain stimulation surgery. *Med Biol Eng Comput*. 2017;55(5):845-858.
- [8] Gantert C, Honerkamp J, Timmer J. Analyzing the dynamics of hand tremor time series. *Biol Cybern*. 1992;66(6):479-484.
- [9] Patel S, Lorincz K, Hughes R, et al. Monitoring motor fluctuations in patients with Parkinson's disease using wearable sensors. *IEEE Trans Inf Technol Biomed*. 2009;13(6):864-873.
- [10] Riviere CN, Rader RS, Thakor NV. Adaptive cancelling of physiological tremor for improved precision in microsurgery. *IEEE Transactions on Biomedical Engineering*. 1998;45(7):839-846.
- [11] Coste J, Ouchchane L, Sarry L, et al. New electrophysiological mapping combined with MRI in parkinsonian's subthalamic region. *Eur J Neurosci*. 2009;29(8):1627-1633.
- [12] Bodenham D. Adaptive Filtering and Change Detection for Streaming Data. PH.D. Thesis. Imperial College, London, 2012.