

# On the Impact of Pathological Tremor Intensity on Noninvasive Characterization of Motor Unit Discharge Properties

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**Keywords:** Surface Electromyograms, Decomposition, Motor Units, Pathological Tremor, Motor Unit Discharge Patterns.

**Abstract:** The impact of severity of pathological tremor on surface EMG decomposition was systematically assessed on eight essential tremor patients. The inertial data and surface EMG signals were concurrently recorded from wrist extensor and flexor muscles of both patients' arms. The inertial recordings were segmented into different tremor cycles and the tremor amplitude was assessed in each tremor cycle. Surface EMG was decomposed by Convolution Kernel Compensation (CKC) technique in order to yield individual motor unit discharge patterns in each tremor cycle. Accuracy of EMG decomposition was assessed for each identified motor unit and was largely uncorrelated with tremor amplitude. In all the patients, the percentage of EMG energy identified by decomposition and the number of identified motor units were found to be positively correlated with tremor amplitude, though the correlation was relatively weak and not always significant. The results demonstrate that the CKC decomposition not only copes with moderate and severe tremor but also improves its performance with tremor intensity.

## 1 INTRODUCTION

Pathological tremor is one of the most common movement disorders, affecting up to 15% of population aged between 50 and 89 years (Benito-León et al., 2006). Although not life-threatening, tremor causes serious difficulties in activities of daily living and greatly reduces the quality of life of affected person.

Among pathological tremors, essential (ET) and Parkinsonian (PD) tremors are the most common. None of them is completely understood and their origin is largely unknown. It has been previously demonstrated that in both tremors peripheral (PNS) and central nervous system (CNS) interact with each other (Halliday et al., 1995) to produce rhythmic, involuntary oscillatory movements of various body parts.

Involvement of CNS into the tremor genesis is typically assessed by neuroimaging techniques, such as Dynamic imaging of Coherent Sources (Gross et al., 2001) and Renormalized partial directed

coherence (Scheltera et al., 2009) that offer an important insight into the connectivity and tremorogenic activity of central networks, such as primary sensor motor cortex, thalamus and basal ganglia. For example, it has been demonstrated that in PD patients basic tremor frequency and its higher harmonics could have different cortical origins (Muthuraman et al., 2012). The same differences have been also observed in ET patients, but to much lesser extent than in PD (Muthuraman et al., 2012).

On the other hand the tremorogenic activity of PNS is measured by the inertial and EMG sensors. Inertial recordings are easy to collect and, thus, very appealing candidates for the tremor quantification, diagnosis and/or tracking (Deuschl et al., 1995); (Muthuraman et al., 2011); (Saunders-Pullman et al., 2008); (Groznič et al., 2013). However, although agreeing on the diagnostic power of the inertial recordings, the current studies offer limited insight into the origin of mechanic oscillations. The latter can be better assessed by the EMG measurements. However, practically all published studies focus on a

very simple surface EMG metrics, such as EMG rectification, to estimate the neural drive to tremorogenic muscles (Gross et al., 2001); (Scheltera et al., 2009); (Raethjen et al., 2009). Moreover, surface EMG acquisition is typically limited to bipolar recording systems that offer no insight into discharges of individual motor units (MUs). This is a problematic step as surface EMG amplitude is known to reflect many anatomical properties of investigated muscles that interfere with the central control component (voluntary and tremorogenic neural drive) from spinal and supraspinal neural circuits (Farina et al.; 2008, 2010).

A very few studies of individual MU discharge characteristics in pathological tremor exist. They focus mostly on PD patients (Das Gupta, 1963); (Dietz et al., 1974); (Dengler et al., 1986); (Christakos et al., 2009), whereas the studies of MUs in ET patients are close to absent. Moreover, all these studies rely on invasive indwelling EMG recordings that limit the number of concurrently identified MU to a very few and hinder their long-term tracking.

Recently, advanced surface EMG decomposition technique has been demonstrated to identify the discharge patterns of up to several tens individual motor units in wrist flexors and extensors of tremor patients (Holobar et al., 2012). The work presented herein extends the one in (Holobar et al., 2012) by systematically assessing the relationship between the identified MU discharge patterns and the severity of pathological tremor. This study focuses on ET patients, whereas PD patients will be addressed in the future work.

## 2 PROCEDURE

Eight ET patients (3 females, 5 males, age of  $68 \pm 8$  years), with mild (4 patients), moderate (2 patients) and severe (2 patients) tremor according to the Fahn-Tolosa-Marin scale participated to the experiment. Six patients had family history of essential tremor. Three patients (patient B, C and D) were taking medications for the treatment of ET syndromes. Detailed description of the patients is presented in Table 1.

The experiments were conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of the 12 de Octubre University Hospital, Madrid, Spain. The patients received a detailed explanation of the study and gave written informed consent prior to participation.

Table 1: Description of patients involved in the study.

Patient	Gender	Age	Family history	Age at tremor onset	Tremor severity
A	F	69	yes	48	severe
B	F	63	yes	56	moderate
C	M	76	no	74	moderate
D	M	67	yes	46	mild
E	M	75	yes	32	mild
F	M	69	yes	59	mild
G	F	51	no	41	mild
H	M	73	yes	50	severe

### 2.1 Experimental Protocol

The patients were equipped with surface EMG sensors and inertial measuring units (IMUs) mounted bilaterally over both upper extremities. Inertial sensors with 3D accelerometer, gyroscope and magnetometer (Technaid Motion Capture System) have been mounted to the third metacarpal, edge of the forearm (dorsal side), olecranon process and distal part (dorsal side) of each arm. The inertial signals were sampled at 200 samples/s and recorded concurrently with surface EMG.

Matrices of  $12 \times 5$  surface electrodes (OT Bioelettronica and LISiN, Italy) were centred over the bellies of the left and right flexor carpi radialis and extensor carpi ulnaris. Before mounting the matrices, the skin has been lightly abraded by using the abrasive paste (Meditec-Every, Parma, Italy) and cleansed afterward. Electrical conductivity was ensured by filling the electrode grids with conductive gel (Meditec-Every, Parma, Italy). The signals were amplified, band-pass filtered (3 dB, 10-500 Hz) and sampled at 2048 samples/s (EMG-USB2 amplifier, OT Bioelettronica).

Patient performed three repetitions of the following tremor-triggering tasks, each in duration of at least 30 s:

1. Arms outstretched against gravity (AO): after 5 seconds of rest, the patient outstretched his/her arms and maintained the posture against gravity.
2. Arms outstretched against gravity with weights (WO): the same as AO task with additional weight load of  $\sim 1$ kg applied to both hands.
3. Arms supported + postural tremor elicited (PO): patient was sitting relaxed, with arms supported in elbow and with wrists hold extended against the gravity.

## 2.2 Data Analysis

The acquired surface EMG signals were decomposed by Convolution Kernel Compensation (CKC) technique (Holobar et al., 2012), which is fully automatic and provides so called Pulse-to-Noise ratio (PNR) which has been demonstrated to reliably assess the decomposition accuracy for every identified motor unit (Holobar et al., 2013). Only MUs, with PNR > 26 dB and, thus, sensitivity in identification of discharges > 80 % and false alarm rates < 5 % (Holobar et al., 2013) were kept for further analysis. All the remaining motor units were discarded.

The surface EMG signals were reconstructed using the MU action potential (MUAP) shapes estimated by spike-triggered averaging of surface EMG (Holobar et al., 2010) and the discharge times estimated from the surface EMG decomposition. The surface EMG reconstructed in this way was compared with the original signal by the following signal-to-interference ratio (SIR):

$$SIR(i) = \left( 1 - \frac{E \left[ (x_i(n) - \sum_j z_{ij}(n))^2 \right]}{E[x_i^2(n)]} \right) \cdot 100\% \quad (1)$$

where  $x_i(n)$  denotes the  $i$ -th surface EMG channel and  $z_{ij}(n)$  stands for the MUAP train of the  $j$ -th MU as reconstructed from the  $i$ -th surface EMG signal.

In addition to decomposition, surface EMG was also band-pass filtered (50-200 Hz) and full-wave rectified (Halliday et al., 1995). Relative power ( $RP_{BF}$ ) of basic tremor frequency was then calculated for each EMG channel as the ratio between the peak in the power spectrum of rectified EMG and its total power.

The recorded IMU data has been upsampled to 2048 samples/s, synchronized with EMG signals and processed by Ensemble Empirical Mode Decomposition (Wu et al. 2009) in order to extract tremor component from voluntary movement (Rocon et al., 2006). The extracted tremor component and the MU discharge patterns have been segmented into different tremor cycles (Figure 5). The following metrics have been calculated for each identified tremor cycle: the mean tremor amplitude and power as assessed from inertial data, the number of active MUs as assessed from surface EMG decomposition, the total number of MU discharges and standard deviation (SD) of their discharge times within the tremor cycle.

All extracted features were statistically analysed in RStudio software. The Wilcoxon matched pairs signed rank test was used to compare the extracted

features between extensors and flexors muscles and Spearman correlation coefficient was used to evaluate the relationship between the  $RP_{BF}$  and SIR and inertial tremor measurements and MU discharge characteristics, respectively. Statistical significance was set to  $P < 0.05$ . The results are presented as mean  $\pm$  SD.

## 3 RESULTS

From 2 to 30 ( $19.2 \pm 8.8$ ) MUs were identified in extensors muscles and from 0 to 32 MUs ( $18.9 \pm 11.1$ ) in flexor muscles in all the patients and all the tasks. All the cases with zero identified MUs coincided with the lack of muscle activity as measured by surface EMG. PNR was not significantly correlated with  $RP_{BF}$ , except in patient H, where a positive correlation of 0.48 and 0.61 was observed in the extensor and flexor muscles of dominant tremor arm, respectively.

Figures 1 and 2 depict the distribution of the maximal  $RP_{BF}$  (maximum calculated across all EMG channels per matrix) and the SIR, as defined in Eq. (1), calculated on the channel with maximal  $RP_{BF}$  ( $SIR^*$ ). Across the patients, the maximal  $RP_{BF}$  varied from 0.04 to 0.72 ( $0.24 \pm 0.17$ ) on extensor and from 0.05 to 0.65 ( $0.24 \pm 0.17$ ) on flexor muscles (Figure 1).

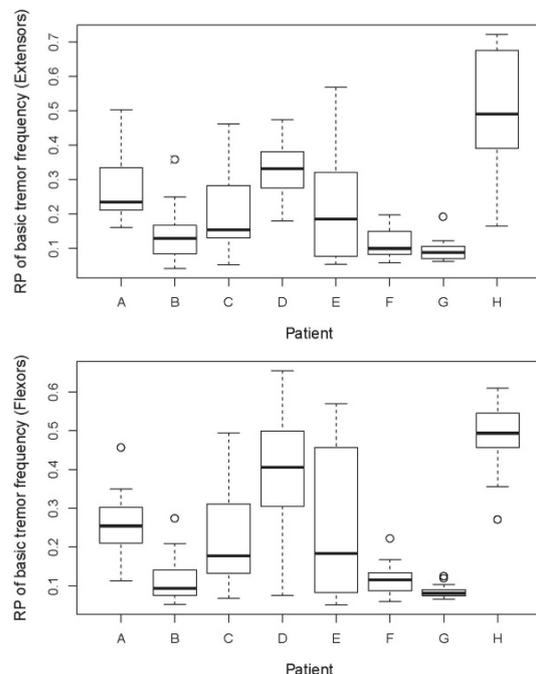


Figure 1: Distribution of the maximal  $RP_{BF}$  across all the tasks of individual patients.

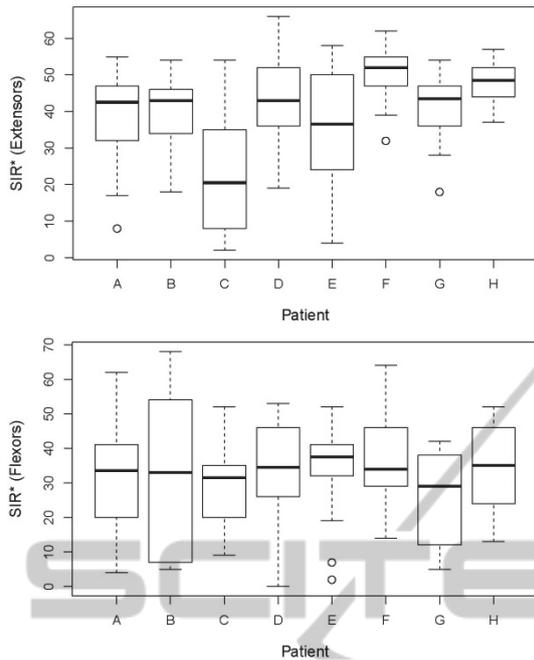


Figure 2: Distribution of SIR\* across all the task repetitions of individual patient. In each task repetition, the SIR\* was calculated on the EMG channel with maximal RP<sub>BF</sub>.

Wilcoxon matched pairs signed rank test indicated no significant differences in maximal RP<sub>BF</sub> of extensors and flexors muscles, except in patient B where maximal RP<sub>BF</sub> was significantly higher in extensors ( $z = -2.72$ ). In EMG channel with maximal RP<sub>BF</sub>, the SIR\* varied from 2 to 66% ( $39.6 \pm 14.2$ ) on extensor and from 0 to 68% ( $31.9 \pm 15.2$ ) on flexors muscles. Wilcoxon matched pairs signed rank test indicated significant difference between SIR of extensor and flexor muscles in 4 out of 8 patients (Patient A, F, G and H in Figure 2).

The relation between the maximal RP<sub>BF</sub> and the corresponding SIR in each task repetition is depicted in Figures 3 and 4 and summarized in Table 2. Practically all the patients exhibited a positive correlation between the RP<sub>BF</sub> and the SIR\* in at least one out of extensor and flexor muscles. In six out of eight patients, the correlation was statistically significant ( $P < 0.05$ ). In patients G and H the correlation was not statistically significant. In patient H correlation was negative but SIR\* was extremely high over all measurements on wrist extensors (Figure 4) and flexor muscles (results not shown). In patient G, the tremor amplitude was always low (Figure 1).

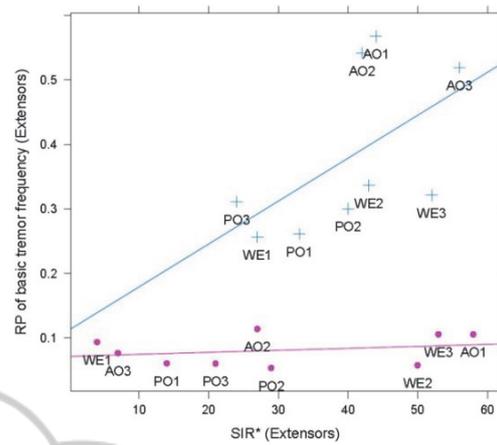


Figure 3: The relationship between the RP<sub>BF</sub> of wrist extensor muscle and the SIR\* (patient E). Blue pluses depict results on dominant hand, the pink dots represent a non-dominant hand.

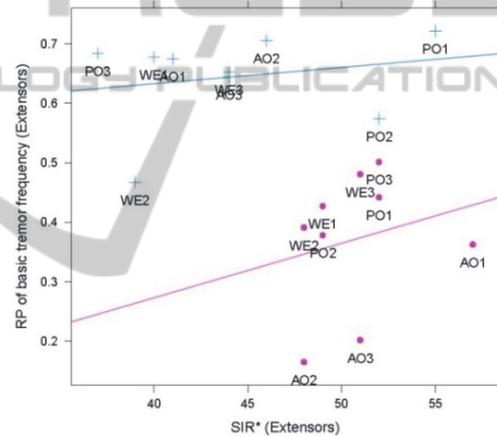


Figure 4: The relationship between the RP<sub>BF</sub> of wrist extensor muscle and the SIR\* in patient H. Blue pluses depict results on dominant hand, the pink dots represent a non-dominant hand.

Table 2: Correlation coefficients between the maximum RP<sub>BF</sub> and SIR\* in both arms. ▲ statistically significant correlation, Spearman Correlation test ( $P < 0.05$ ).

Patient	Extensors RP <sub>BF</sub> & SIR*	Flexors RP <sub>BF</sub> & SIR*	Extensors No. MU <sub>s</sub> & SIR	Flexors No. MU <sub>s</sub> & SIR
A	0.49 <sup>▲</sup>	0.16	0.79 <sup>▲</sup>	0.57 <sup>▲</sup>
B	0.51 <sup>▲</sup>	0.42	0.76 <sup>▲</sup>	0.87 <sup>▲</sup>
C	0.62 <sup>▲</sup>	0.19 <sup>▲</sup>	0.71 <sup>▲</sup>	0.29
D	0.30	0.80 <sup>▲</sup>	0.93 <sup>▲</sup>	0.80 <sup>▲</sup>
E	0.41	0.74 <sup>▲</sup>	0.71 <sup>▲</sup>	0.56 <sup>▲</sup>
F	-0.25	0.54 <sup>▲</sup>	0.36	0.35
G	0.13	0.05	0.37	0.73 <sup>▲</sup>
H	-0.33	0.36	0.00	0.89 <sup>▲</sup>

In dominant tremor arm alone a significant correlation between the RP<sub>BF</sub> and the SIR\* was

observed in the wrist flexor or extensor muscles in 4 patients only. The reduction in sample size (3 AO, 3 PO and 3 WE tasks) is the most likely reason. In the nondominant tremor arm the correlation was frequently not significant, likely because of relatively low tremor amplitude values, especially in patients with unilateral tremor (Figure 3).

The discharge patterns of individual MUs as identified by surface EMG decomposition of extensor and flexor muscles of dominant tremor hand in patient H are depicted in Figure 5, along with the tremor component as recorded by inertial sensor placed at the patient’s wrist. Out-of-phase flexor-extensor activity is clearly visible. The MU discharge patterns in the same patient but during the period of low tremor amplitude are depicted in Figure 6. The difference in MU discharge patterns between the periods with high and low tremor amplitudes are clearly visible.

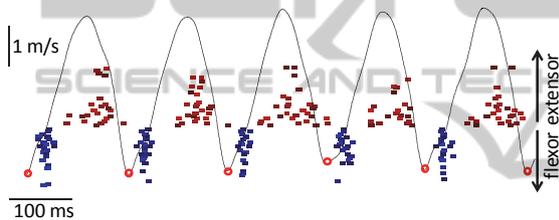


Figure 5: discharge patterns of individual MUs identified by surface EMG decomposition of extensor and flexor muscles of dominant tremor arm in patient E during the period of high tremor amplitude. Each filled rectangle denotes one MU firing. Thin black line depicts the tremor component as measured by the inertial sensor. Circles denote the segmentation of inertial tremor recording into the tremor cycles.

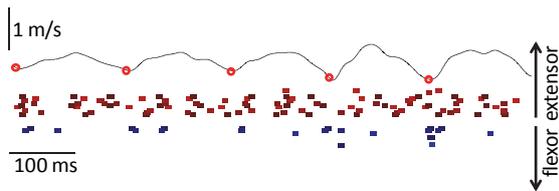


Figure 6: discharge patterns of individual MUs identified by surface EMG decomposition of extensor and flexor muscles of dominant tremor hand in patient E during the period of low tremor amplitude.

The global relationship between the tremor amplitude as assessed by inertial measurements and the identified MU discharge characteristics in each tremor cycle are exemplified in Figure 7 and summarized in Table 3. In the tremor dominant arm, all the patients exhibited relatively weak but statistically significant positive correlation between

the tremor amplitude and the number of MUs discharges per tremor cycle in at least one of measured muscles (wrist extensors and flexors). The same applies for the number of active MUs (Table 3).

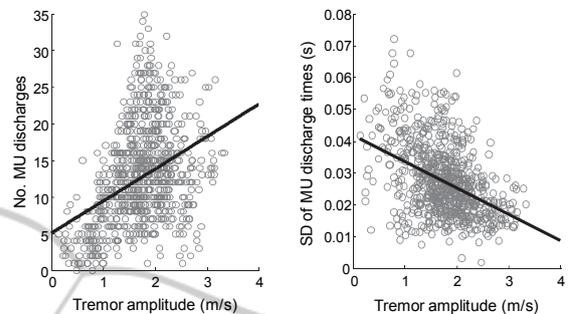


Figure 7: The number of MUs discharges per tremor cycle as identified from the left wrist extensor of patient H (left) and the dispersion of their discharge times (right) vs. tremor amplitude in each tremor cycle. Results are accumulated over three repetitions of AO, WE and PO tasks.

Table 3: Correlation coefficients between the number of MUs (No. MUs), the number of their discharges (No. MUs disch.), and their dispersion (SD MUs) in individual tremor cycle and the tremor amplitude as measured by inertial sensor placed at dominant wrist; n.s. - not significant.

Patient	Flexors			Extensors		
	No. MUs.	No. MUs disch.	SD MUs	No. MUs.	No. MUs disch.	SD MUs
A	n.s.	n.s.	-0.25	0.24	0.24	<b>-0.48</b>
B	0.19	0.21	n.s.	n.s.	n.s.	-0.20
C	<b>0.47</b>	0.25	n.s.	0.19	0.16	-0.26
D	<b>0.47</b>	<b>0.46</b>	-0.18	n.s.	n.s.	-0.14
E	0.26	0.29	n.s.	<b>0.42</b>	0.32	<b>-0.43</b>
F	n.s.	0.20	n.s.	0.25	0.31	n.s.
G	0.11	0.12	n.s.	0.20	0.18	-0.25
H	<b>0.53</b>	<b>0.52</b>	n.s.	0.37	<b>0.45</b>	<b>-0.44</b>

Dispersion of MU discharges within the tremor cycles, as measured by SD of MU discharge times was inversely related to tremor amplitude, though also in this case the correlation coefficients were relatively small.

It is noteworthy that the strongest correlations between the tremor amplitude and investigated MU discharge characteristics were observed in patients with strongest tremor (A, C, D, E and H), whereas they were much weaker or even not significant in the

patients B, F and G with relatively mild tremor. The strongest correlations were observed in patient with the most severe tremor (patient H).

Also interesting, there were frequently different trends in MU behaviour with increasing tremor amplitude. Patient A, for example, increased the number of active MUs in extensors and synchronized their discharges. The same MU synchronization was also observed in flexor muscle, though to much less extent. Patient D, on the other hand, mostly increased the number of active MUs and their discharges in the flexor muscle.

## 4 CONCLUSIONS

In this study, the CKC-based decomposition of multichannel surface EMG was tested on eight ET patients with different tremor severity. Two different measures of decomposition performance have been applied. First, the PNR measure of decomposition accuracy (Holobar et al., 2013) was found to be largely uncorrelated with tremor severity, except in patient H where correlation was positive for both extensor and flexor muscles. Note that the higher the PNR, the more accurate the decomposition and that MUs with  $\text{PNR} > 30$  dB typically exhibit sensitivity in the identification of their discharges greater than 90% (Holobar et al., 2013).

The second measure of decomposition performance was SIR as defined in Eq. (1). SIR measures the relative proportion of signal energy that is accounted for by identified MUs and typically ranges between 20 % and 50 % in healthy subjects (Holobar et al., 2010). The values measured in ET patients are in perfect agreement with these values. No negative impact of pathological tremor on SIR was observed. On the contrary, as demonstrated by results in Figures 3 and 4 and Table 2, the SIR was mostly positively correlated with the tremor intensity as measured by  $\text{RP}_{\text{BF}}$  i.e. the relative power of rectified surface EMG at basic tremor frequency. Not surprisingly, the SIR was also positively correlated with the number of identified MUs (Table 2).

Detailed analysis of MU discharge patterns in each tremor cycle revealed weak but consistent positive correlations between the number of MUs discharges and MU synchronisation and tremor amplitudes as measured by inertial sensors. The observed weakness of correlation can be contributed to many different factors. First, the inertial sensors measure the net mechanical oscillations contributed by many different muscles. In our case, not all the

muscles of wrist were measured, hindering the full interpretation of the mechanical oscillations with the introduced electrophysiological variables. Second, relatively simple and crude metrics of MU synchronization and neural drive to the muscle were used in this study, preferring, for example, the time resolution over the accurate estimation of MU synchronization. Third, we did not quantify the extent of out-of-phase flexor-extensor activity depicted in Figure 5. All this factors likely contributed to conservative estimation of relation between the observed MU discharge properties and kinetic tremor properties and need to be addressed in the future work.

In conclusion, the impact of tremor severity on surface EMG decomposition has been systematically assessed on eight ET patients. As demonstrated by the results, the CKC decomposition not only fully copes with severe tremor but also improves its performance in sense of percentage of identified signal energy and the number of identified motor units. This makes it an appealing novel tool for non-invasive and long-term tracking and physiological interpretation of pathological tremor.

## ACKNOWLEDGEMENTS

This study was supported by the Commission of the European Union, within Framework 7, under Grant Agreement number ICT-2011.5.1-287739 "NeuroTREMOR: A novel concept for support to diagnosis and remote management of tremor".

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