Tremor Suppression Using Functional Electrical Stimulation

Zahra Habibollahi, *Student Member, IEEE*, Yue Zhou, *Member, IEEE*, Mary E. Jenkins, S. Jayne Garland, Evan Friedman, Michael D. Naish, *Member, IEEE*, and Ana Luisa Trejos, *Senior Member, IEEE*

***Abstract*— Parkinson's disease (PD) and essential tremor are two major causes of pathological tremor among people over 60 years old. Due to the side effects and complications of traditional tremor management methods such as medication and deep brain surgery, non invasive tremor suppression methods have become more popular in recent years. Functional electrical stimulation (FES) is one of the methods used to reduce tremor in several studies. However, the effect of different FES parameters on tremor suppression and discomfort level, including amplitude, the number of pulses in each stimulation burst, frequency, and pulse width is yet to be studied for longer stimulation durations. Therefore, in this work, experiments were performed on 14 participants with PD to evaluate the effect of thirty seconds of out-of-phase electrical stimulation on wrist tremor at rest. Trials were conducted by varying the stimulation amplitude and the number of pulses while keeping the frequency and pulse width constant. Each test was repeated three times for each participant. The results showed an overall tremor suppression for 11 out of 14 participants and no average positive effects for three participants. It is concluded that despite the effectiveness of FES in tremor suppression, each set of FES parameters showed different suppression levels among participants due to the variability of tremor over time. Thus, for this method to be effective, an adaptive control system would be required to tune FES parameters in real time according to changes in tremor during extended stimulation periods.**

***Index Terms*— Functional electrical stimulation, Parkinson disease.**

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Zahra Habibollahi is with the Department of Electrical and Computer Engineering (ECE), Western University, London, ON N6A 5B9, Canada (e-mail: zhabibol@uwo.ca).

Yue Zhou was with the School of Biomedical Engineering (BME), Western University, London, ON N6A 5B9, Canada. He is now with Trudell Medical International, London, ON N5V 5G4, Canada (e-mail: yzhou426@uwo.ca).

Mary E. Jenkins is with the Movement Disorders Program, Clinical Neurological Sciences, Western University, London, ON N6A 5B9, Canada (e-mail: Mary.Jenkins@lhsc.on.ca).

S. Jayne Garland is with the Faculty of Health Sciences, Western University, London, ON N6A 5B9, Canada (e-mail: jgarland@uwo.ca).

Evan Friedman is with Intronix Technologies Corporation, Bolton, ON L7E 1E6, Canada (e-mail: drevan@intronixtech.com).

Michael D. Naish is with the Department of Mechanical and Materials Engineering, ECE, and BME, Western University, London, ON N6A 5B9, Canada (e-mail: mnaish@uwo.ca).

Ana Luisa Trejos is with ECE and BME, Western University, London, ON N6A 5B9, Canada (e-mail: atrejos@uwo.ca).

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I. Introduction

TREMOR is one the most common motor symptoms of Parkinson's Disease (PD) and Essential Tremor (ET), and it can significantly affect the quality of life of people with PD or ET [1], [2]. Tremor is characterized by high amplitude oscillations at frequencies ranging from 3 Hz and above. It can affect different body parts such as the hands, arms, legs, and face. Most participants experience arm tremor, which can affect their activities of daily living (ADLs) [3], [4]. Surgical interventions [5], [6] or pharmaceutical treatments [7] are often used for tremor management. However, medications often lose effectiveness over time and some patients may experience side effects [7]. Brain surgery, as the second alternative, is costly and may not be suitable for all patients.

Alternatively, external tremor suppression using electrical stimulation [8], [9], [10], [11], [12], [13], [14] has been proposed and studied. Functional electrical stimulation (FES) stimulates the muscles of the target joint to suppress tremor. FES contracts the flexor and extensor muscles simultaneously (co-contraction method) [11], [13], or in an alternating way to counteract tremor (out-of-phase) [8], [9], [10], [12], [14]. FES parameters that can be varied include pulse width, current intensity, frequency, and the number of pulses. Even though the results of existing studies have shown FES to be a promising solution for tremor suppression, most studies have only experimented with a limited number of stimulation parameters.

Although longer stimulation durations below motor threshold have been studied in the past [15], [16], [17], stimulation above motor threshold has only been applied for 10 seconds or less in the literature. Applying electrical stimulation during extended periods might show highly variable results because of changes in the tremor patterns and the participant's reaction to the stimulation. In other words, it might not be feasible to specify a single set of parameters for an individual to suppress

their tremor, as they might result in a decrease or increase in tremor, depending on the situation.

Lastly, as has been mentioned in [18], further studies are needed in this field, since it has been challenging to draw conclusions about the effectiveness of using FES for tremor suppression. Results to date have been limited by the combination of ET and PD groups in many studies in the literature, the use of various stimulation parameters in different studies, the lack of a standard method for changing these parameters, and by some studies only reporting the highest reduction in tremor. The objective of this study is to focus on these gaps by designing and implementing a protocol to address the lack of a consistent and standard method for systematically applying different stimulation parameters only to individuals with Parkinson's disease. Since different participants have different tolerance levels for stimulation, as well as different levels of tremor, the protocol initially establishes a baseline for motor threshold and sensory threshold for each participant, and follows a general rule for assigning parameter settings afterward. Using different levels of stimulation for each individual permits analysis to understand the effectiveness of different stimulation levels on different tremor intensity levels in various individuals. Each combination has been repeated three times to increase the accuracy. In other words, an approach that considered the effect of cognitive co-activation and muscle fatigue, repeated each combination three times, compared the results with the baseline, and averaged the results was implemented to allow more explicit conclusions to be made about the effectiveness of the method. This approach was designed to address the lack of consistency in previously published results, such as studies that only have reported the maximum tremor suppression.

II. Methods

To evaluate the effect of FES on tremor suppression as described above, an experiment was conducted on participants with PD, using a custom-developed experimental setup. Details of the experiment are explained in the subsections below.

A. Participants

The research protocol (114632) for this study was approved by the University of Western Ontario's Human Research Ethics Board before starting the trials. A total of 14 participants (three females, eleven males) with PD volunteered for this study; all were diagnosed and recruited by a movement disorders neurologist. Since the focus of this study is tremor suppression of the wrist, all of the participants were chosen by the neurologist to have relatively high tremor in their hands and arms. The study was completed with a small percentage of female participants despite efforts to include more women in the study. Part of the difference comes from PD being more prevalent in a male population; however, this only explains a portion of the imbalance. Unfortunately, recruitment was limited to the patient population at the clinic at the time of the study. On average, participants have been diagnosed with PD for 5 years, with a maximum duration of 10 years and

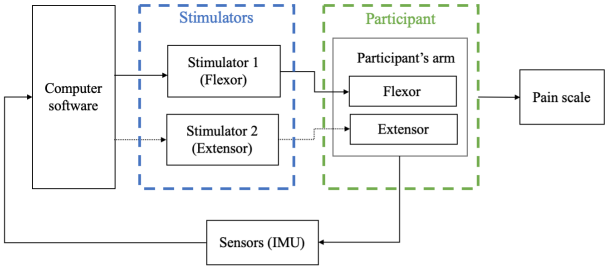

Fig. 1. A summary of interactions between the software, hardware, and the participant.

a minimum of 6 months at the time of the experiment. The Unified Parkinson's Disease Rating Scale (MDS-UPDRS) of the resting tremor for the most affected side was evaluated on a scale of 1 to 4, with 1 indicating slight tremor and 4 severe tremor. In three of the 14 participants, tremor was at Level 1. It was Level 2 for three other participants, Level 4 for one participant, and Level 3 for the remaining seven participants. The most affected hand was the right hand for all but four participants. An explanation of the experiment, including the procedure, risks, and objectives, was given to each participant, and all participants signed a written informed consent before starting the trials.

B. Experimental Setup

Figure 1 shows the interactions between the participant and the hardware and software used in the experimental setup. The computer software block in Fig. 1 is custom software for online configuration of the system and to control tremor suppression. The software was developed in Visual C# (Visual Studio, Update 5, Microsoft®, 2013). The software presents a user-friendly interface for the different steps of the study, as well as the recording of the tremor data, generating stimulation combinations (as will be explained in Section II-C), and generating commands to activate the stimulators in an opposite direction to the tremor motion. The software uses a central controller that orchestrates all of the components and associated controllers required during all of the experiment steps. These components are the IMU sensors, the stimulators, and the pain scale keyboard, and they are connected to the PC using microcontrollers and a serial to USB adapter.

The stimulators block in Fig. 1 consists of two constant current electrical stimulators (DS7A, DS7AH, Digitimer) that were used to apply electrical stimulation to the flexor and extensor muscles. The stimulators were controlled by an external trigger connected to the software to stimulate the antagonistic muscle to the tremor motion. The frequency of the monophasic pulses was set to 120 Hz, and an external trigger controlled the number of pulses at the desired stimulation current intensity. Two pairs of self-adhesive electrodes (square, 2" × 2") placed over the flexor and extensor muscle bellies to deliver the stimulation pulses. Tremor motion was collected using a motion-sensing system, including five IMUs (LSM9DS1, ±2000°/s angular rate scale, 16-bit resolution, STMicroelectronics ®, Geneva, Switzerland) in the format of angular velocity. Gyroscope data, collected at a sampling rate

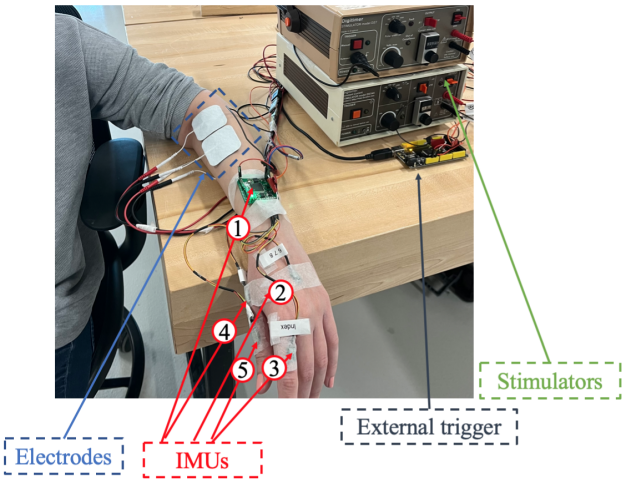

Fig. 2. The experimental setup, including two stimulators, five IMU sensors, two pairs of electrodes, and an external trigger that activates the stimulators when determined by the software.

of 50 Hz, using a microcontroller through the I^2C protocol, were sent to the PC using a serial to USB adapter. Figure 2 shows the experimental setup that was used in this study. IMU sensors were placed proximal to the wrist joint (IMU 1, Fig. 2), on the metacarpals of the hand (IMU 2, Fig. 2), on the proximal phalanx of the index finger (IMU 3, Fig. 2), on the thumb metacarpals (IMU 4, Fig. 2), and on the thumb proximal phalanx (IMU 5, Fig. 2). All sensors were placed on the dorsal side of the hand and on the majorly affected arm of the participant. IMUs 1 and 2 were used to measure the wrist tremor by subtracting the values in real time. The absolute values were used to measure the tremor amplitude, and the signs after subtraction were used to measure the direction of the wrist tremor. Pitch was used in these real-time measurements. The participant's arm was placed in a neutral orientation and was monitored during the experiment to make sure that the orientation was not changing. This information was used in real time using a multi-threaded software calculation to perform out-of-phase stimulations. IMUs 2 and 3 were used to measure the tremor on the MCP joint of the index finger, and IMUs 4 and 5 were used to measure thumb MCP joint tremor. The collected data and the calculated tremor frequency were used to estimate tremor direction and apply stimulation to the target muscles at the time of directional changes.

C. Experimental Protocol

After obtaining consent, the severity of PD was assessed by a movement disorders neurologist using the MDS-UPDRS score. The participants were seated comfortably in a chair next to a desk. The most affected arm was selected for the experiment, and was placed on the desk. The skin overlying the wrist flexor and extensor muscles was cleaned using an alcohol swab, and stimulating electrodes were placed on the belly of the flexor and extensor muscles of the wrist. A set of IMUs was placed on the skin on either side of the thumb, index finger, and wrist joints using medical tape to collect the motion data.

As has been mentioned in [19], cognitive co-activation can affect tremor intensity and variability in different ways. To avoid this effect on participants during data collection and later on when they receive the stimulation, and in order to bring out the tremor in a consistent fashion during the experiment, participants were asked a variety of simple questions (such as travel memories or counting downward) to invoke the tremor. As not all participants respond the same to mental arithmetic, engaging them in other conversations was more effective.

The experiment started by recording the tremor motion for 30 seconds. This recording represents the baseline tremor, and it was used to calculate the dominant frequency of the tremor during the trial and for further offline analysis.

In the next step, the sensory (ST) and motor threshold (MT) [20], as well as the maximum tolerable current (MAX), were determined for each muscle group. At first, the sensory threshold was determined by starting from a low-level stimulation intensity (e.g., 8 mA), a level at which all the participants could feel the stimulation without pain or side effects. The current intensity was then decreased in fixed steps (1 mA) until the participants could not feel the stimulation anymore. The step right before the stimulation could no longer be felt was denoted as the sensory threshold.

After determining the sensory threshold, the motor threshold for each muscle was determined by stimulating the muscle at increasing levels of current intensity, in steps of 1 mA. The current intensity when the proctor could observe the muscle twitch was denoted as the motor threshold.

From this point, the current was increased in fixed steps (1 mA), and the participant was asked to rate their comfort level. This process was repeated until the participant reached a comfort rating of three out of 10 using a graphical pain scale [21]. On this pain scale, three is considered tolerable, minor pain that does not interfere with most daily activities, and patients can adapt to the pain psychologically, while ten is unimaginable, unspeakable, severe pain that disables the patients from performing normal activities. This current value was recorded as the maximum current intensity (MAX). The process of measuring the sensory threshold, the motor threshold, and the maximum current intensity was repeated three times for each muscle using trains of two, four, and six pulses. After these measurements, a set of combinations that varied the amplitude and number of pulses was generated with a fixed frequency and pulse width to test the experimental procedure, as explained below. The study started with a pilot trial with four participants. In this pilot trial, stimulations were applied to the target muscles with high variability in the parameters for one repetition per combination and for only five seconds. It was observed that regardless of the ongoing conversations with the participants aimed at distracting them, they reacted differently to the new sensation of stimulation. Since this reaction could affect the results, to reduce the transient effect on the final results and considering the total time of the stimulation and individual exhaustion, the final protocol was adjusted to apply only nine stimulation combinations for an extended period of time (30 seconds). Table I shows the parameter sets for each stimulator parameter. It should be

TABLE I
PARAMETER SETS FOR EACH OF THE FOUR STIMULATOR PARAMETERS

Stimulator Parameters	Parameter Values
Current Intensity (mA)	max (50% MT, ST) min (MT +50% MT, MAX) MT
Pulse Width (μs)	200
Frequency (Hz)	120
Number of Pulses	2, 4, 6

noted that bursts of pulses were applied in this study. Each burst or train of pulses that was delivered to the target muscle contained 2, 4, or 6 pulses, with a frequency of 120 Hz, and each burst had a pulse width of 200 μs. Time off between each burst was equal to the full burst time. From Table I, the value of max (50% MT, ST) for current intensity is the larger of the sensory threshold and half of the motor threshold. Since both of these values are below the motor threshold, this value is referred to as the current intensity below motor threshold (BMT) in this article. On the other hand, the min (MT +50% MT, MAX) value is determined as the smaller of two values–the current intensity that participants labeled as level three out of 10, and a current that is 50% above the motor threshold. This ensures that the stimulation level does not exceed the participant's tolerance level (MAX). As both of these values are above the motor threshold, this value is referred to as the current intensity above motor threshold (AMT) in this article.

After determining the combinations of FES parameters for each participant, the out-of-phase tremor suppression strategy was tested at all parameter combinations. Each combination was repeated three times in random order, with blinded onset, and the stimulation duration was 30 seconds for each combination. Compared to previous studies and observations in our pilot trials, longer stimulation durations were used in this study to account for cognitive co-activation, tolerance, and mental effects during the study. Similarly, the reason for repeating each stimulation 3 times was to consider the effect of muscle fatigue, and cognitive co-activation as highlighted in [19]. It was hypothesized that averaging the overall signal acquired in 30 s and comparing the results of the 3 rounds would balance out the effects mentioned above.

After each stimulation, the participant was given a rest of at least 60 seconds. The tremor frequency was recalculated and compared to the baseline frequency during this period. Participants could stop the experiment anytime during the session if they felt discomfort or had concerns.

D. Data Analysis

As shown in Eq. 1, the power spectrum density (PSD, W/Hz) of the baseline tremor and the PSD of the tremor during the stimulation was used to calculate the tremor power suppression ratio (TPSR) in each experiment. From Eq. 1, when the tremor power during stimulation is lower than the baseline tremor power, the TPSR shows a higher percentage and therefore, greater tremor suppression. On the other hand, if the PSD during stimulation exceeds the baseline PSD, TPSR shows a negative value. A more negative TPSR signifies a larger increase in the tremor and worse results.

$$\mathrm{TPSR} = 1 - \frac{\mathrm{PSD}_{\mathrm{stimulation}}}{\mathrm{PSD}_{\mathrm{baseline}}} \times 100\% \tag{1}$$

It was decided that it was best to compare each stimulation with the baseline recording and not with the recordings during the pre-stimulation window because some studies have suggested that FES might reduce the tremor intensity for a while even after the stimulation is turned off [22]. Also, tremor is highly variable over time, and using the baseline to compare all of the stimulation results is expected to be a more consistent way of comparing different FES parameter combinations.

Due to the variability of pathological tremor over time in a single participant and due to environmental or psychological effects of stimulation, participants showed different reactions to each repetition of any single combination. It was observed that the first round of each combination generally showed a different trend in its effect on the tremor compared to other rounds. For example, the first round had a high tremor suppression in some cases; which could be because the stimulation drew the participant's attention, and they might have intentionally suppressed their tremor regardless of the purposeful distractions during the experiment. On the other hand, sometimes the stimulation caused no tremor suppression, or even an increase in tremor, in the first round, which could be due to the stress and unfamiliarity of the participant with long stimulation periods and its sensation. This appeared to be a psychological reaction to the stimulation when it was a new sensation for the participants. It was hypothesized that participants might get used to the stimulation over time, since it was observed that the results of the second and third rounds were in more similar ranges. Nevertheless, a highly different TPSRs for a single participant using a single combination could be considered an outlier. Therefore, to statistically evaluate the outliers in the dataset, the scaled median absolute deviation method (sMAD) was used to detect and remove outlier data points. The scaled median absolute deviation (sMAD) is defined as

$$\mathrm{sMAD} = c \times \mathrm{median}(|A_i - \mathrm{median}(A)|), \quad i = 1, 2, \ldots, N \tag{2}$$

$$c = \frac{1}{Q(0.75)} \tag{3}$$

where A is a vector of length N, in Eq. 2, and $Q(0.75)$ in Eq. 3 is the 75th percentile of the z-score, which is estimated as $c = 1.4826$ [23]. Using sMAD, a value that was more than three sMAD from the median was labeled as an outlier.

Statistical analyses, including the repeated measures ANOVA (RMA) with a Bonferroni correction and alpha value of 0.05, or the univariate ANOVA, were performed to evaluate the effectiveness of different combinations and stimulation levels in tremor suppression. Since MT and ST differ among participants, stimulation amplitudes were labeled as 0, 1, and

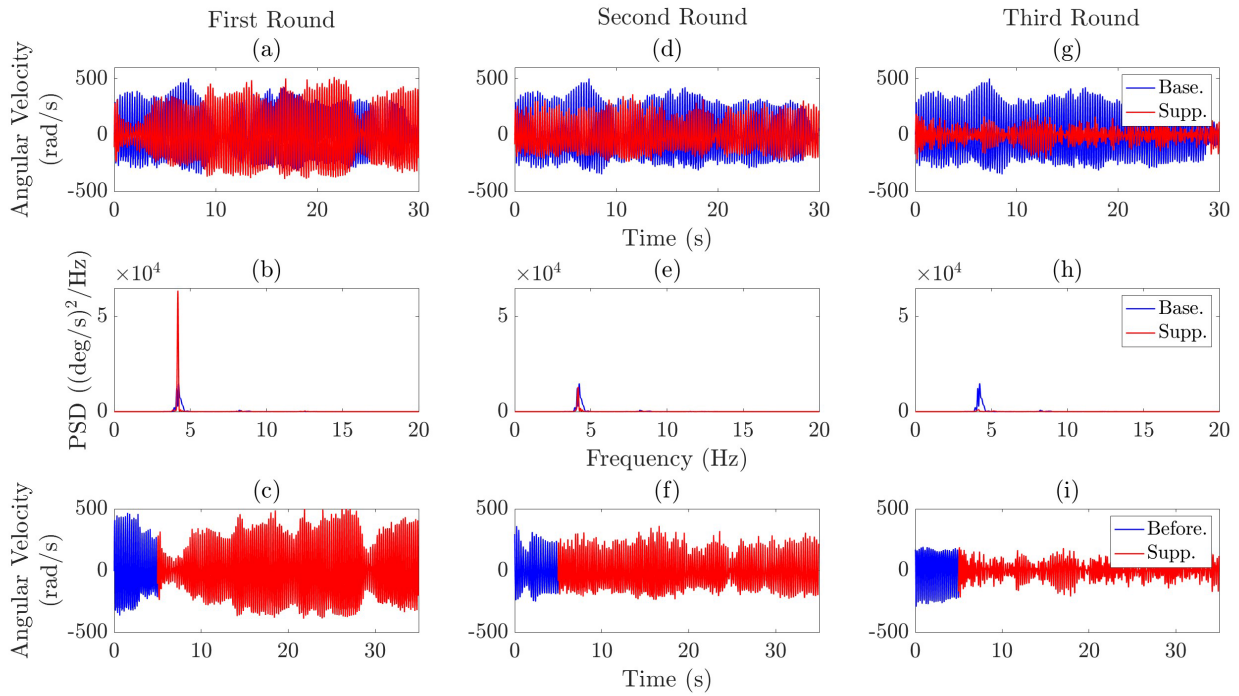

Fig. 3. A sample of collected data from a single participant with identical stimulation combinations in three different repetitions during the experiment. (a), (d), (g) Angular velocity (AV) of the baseline tremor in blue, AV of the tremor during stimulation in red, in the time domain. (b), (e), (h) PSD of the baseline tremor in blue, PSD of the tremor during stimulation in red, in the frequency domain. (c), (f), (i) AV of the tremor during the five seconds before stimulation in blue, and AV of the tremor during stimulation in red, in the time domain. All signals are showing the wrist tremor, collected by subtracting the signals from IMU 1 and 2.

2 for BMT, MT, and AMT levels, respectively. The IBM Statistical Package for Social Sciences (SPSS Statistics v28) software was used to perform all of the statistical analyses. Further details are explained in Section III.

III. Results and Discussion

A. Baseline Tremor and General Effect of Stimulation

Figure 3 shows a sample of the collected data. In Fig. 3, the first and second rows represent the baseline tremor in blue and the tremor during stimulation in red in both the time and frequency domains, respectively. The third row shows five seconds of tremor before stimulation in blue, followed by the tremor during stimulation in red. Each column of this figure represents one round of stimulation with an identical parameter combination (pulse = 2, the amplitude at motor threshold) in a single participant. As shown in Fig. 3 (a), (b), and (c), the first round of stimulation with this particular combination has no positive effect on tremor suppression. Indeed, the stimulation has increased the tremor power, as shown in Fig. 3(b), and has slightly increased the tremor amplitude, compared to both baseline and pre-window tremor, as shown in Fig. 3(a), (c), respectively. On the other hand, the second and third rounds of stimulation have reduced tremor, as shown in Fig 3(d)-(f), and (g)-(i), respectively, with more tremor suppression in the last round.

The TPSR for each participant calculated using Eq. 1 is shown in the second column of Table II. In the third column of Table II, results are shown after applying the sMAD algorithm discussed in Section II. In the analysis, 9.4% of the data points were identified as outliers by the algorithm. These outliers were present in different repetitions of the combinations of P 02, P 08, and P 12-P 14. When an outlier was detected in a repetition, the algorithm removed the entire repetition for all combinations. Consequently, further analyses did not consider P 12-P 14, and the TPSR values for these participants were recorded as "Not Applicable" (NA) in Table II.

From Table II, the overall effect of tremor suppression varied among different participants and had no mean positive

TABLE II
AVERAGE OF TPSR FOR EACH PARTICIPANT OVER ALL STIMULATION TRIALS, BEFORE AND AFTER THE OUTLIER DETECTION ALGORITHM. THE SYMBOL * MEANS THAT THE HIGHLIGHTED PARTICIPANT'S DATA HAD SIGNIFICANT CHANGES AFTER APPLYING THE OUTLIER DETECTION ALGORITHM

Participant ID	Average of TPSR (before outlier detection)	Average of TPSR (after outlier detection)
P 01	76.5	76.5
P 02*	52.1	51.1
P 03	88.3	88.3
P 04	86.1	86.1
P 05	56.9	56.9
P 06	59.3	59.3
P 07	76.3	76.2
P 08*	47.2	61.7
P 09	74.6	74.6
P 10	80.9	80.9
P 11	52.3	52.3
P 12	-37.0	NA
P 13	-11.7	NA
P 14	-25.8	NA

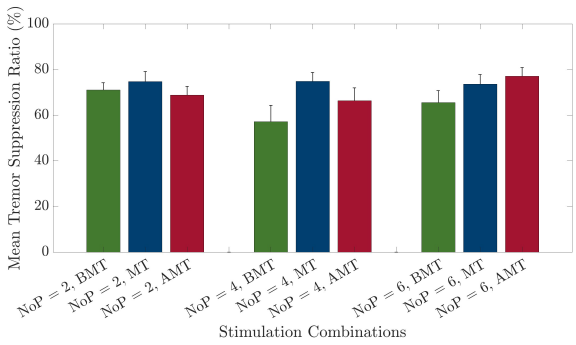

Fig. 4. Mean of TPSR in different stimulation combinations. RMA showed no statistically significant difference among these combinations (pulse × amplitude, $p = 0.254$). NoP represents the number of pulses.

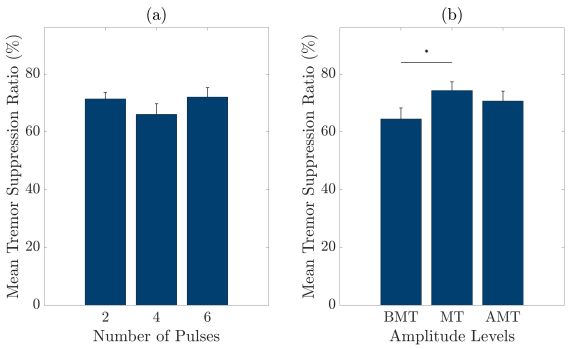

Fig. 5. Effect of different stimulation variables on TPSR. (a) Mean of TPSR for the different number of pulses. (b) Mean of TPSR for different amplitude levels. Whiskers represent the standard error in each data group, and * represents a statistically significant difference between groups.

effect in the last three participants. The difference in results of tremor suppression among participants could be due to several reasons, which will be discussed in Section III-E.

Figure 4 shows the mean and standard error of the TPSR for each combination, using the filtered dataset with the sMAD algorithm. From this figure, stimulation amplitude levels at the motor threshold, shown in blue, have a generally better trend in tremor suppression for almost all pulse numbers compared to stimulation amplitude levels below the motor threshold, shown in green, and stimulation amplitude levels above the motor threshold shown in red. However, there is a slight improvement in the results for stimulation amplitudes above the motor threshold for six pulses. It should be noted that the results of an RMA test showed no statistically significant difference among different stimulation combinations (pulse × amplitude).

Further analysis was performed using an RMA on the filtered dataset with the first 11 participants, in order to evaluate the effectiveness of the different stimulation parameters, including three different numbers of pulses and three amplitude intensity levels (Table I), on the TPSR. The results of these analyses are discussed in Sections III-B and III-C.

B. Effect of Stimulation Pulses

As shown in Fig. 5(a), it was not possible to find a significant difference in the TPSR based on the number of pulses using the filtered dataset ($p = 0.087$). When comparing two, four, and six pulses with the three stimulation intensities combined, the mean ± std are 71.4 ± 2.3, 66.1 ± 3.6, and 72 ± 3.2, respectively. Therefore, changing the number of pulses might not be a valuable control parameter for future stimulation and tremor suppression studies.

C. Effect of Stimulation Intensity

The results show that the amplitude level has a significant effect on the tremor suppression ratio ($p = 0.042$). As shown in Fig. 5(b), there is a significant difference between amplitude levels below and at motor threshold (64.5 ± 3.8 for BMT vs. 74.3 ± 3.0 for MT, $p = 0.032$). However, no significant difference was observed between amplitudes below and above the motor threshold (64.5 ± 3.8 for BMT vs. 70.7 ± 3.4 for AMT, $p = 0.472$), or amplitudes at and above motor threshold (74.3 ± 3.0 for MT vs. 70.7 ± 3.4 for AMT, $p = 0.781$). Therefore, as a general trend, amplitudes at the motor threshold tend to be more effective among most participants in most trials.

Several reasons could explain the above observations. First, amplitude levels below the motor threshold might not be enough to suppress tremors with higher power intensity. On the other hand, amplitude levels above the motor threshold might generate extra torque for tremors with lower power intensity. Furthermore, it was observed that higher amplitudes might cause an effect similar to co-contraction of the muscles, preventing participants from moving their hand comfortably. Second, as will be discussed in Section III-E, unstable experimental situations, such as tremor changes and variable muscle and forearm properties–for example the thickness of the adipose tissue layer under the skin or muscle mass [24], [25]–among participants can highly affect the results.

Although the underlying mechanisms of tremor generation in Parkinson's disease and the suppression of tremor using out-of-phase submotor threshold stimulation is still unclear, studies have shown that this type of stimulation can suppress tremor by up to 88% [12], [22] (4 PD and 1 ET participant in the first study, and all ET participants in the second study). This could be explained by the hypothesis that sensory stimulation can produce reciprocal inhabitation [15], [16] by mimicking the effect of stretch receptors in the muscle. Stretch response happens when an external force is applied to a muscle and stretch receptors within that muscle are activated. Afferent fibers from stretch receptors then project to interneurons in the spinal cord and inhibit the activity of the motor pool of the opposing muscle [26]. Similarly, applying an out-phase stimulation right before the arrival of the tremor burst on the opposing muscle can activate the Ialpha afferents of the target muscle, inhibit the activity of the motor pool, and reduce tremor.

The final set of data to analyze corresponds to the comfort ratings given by the participants. As shown in Fig. 6(a), the comfort rating at amplitudes below the motor threshold is mostly zero, indicating no pain and normal feeling. As the amplitude increases in Fig. 6(b) and Fig. 6(c) to the motor

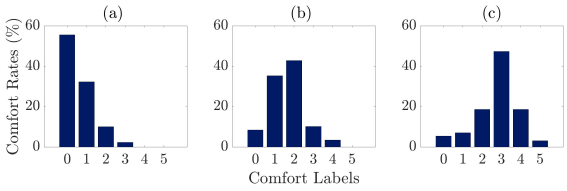

Fig. 6. Effect of different stimulation amplitudes on the sensation of pain and discomfort. (a) Percentage of comfort levels for stimulation intensities below the motor threshold. (b) Percentage of comfort levels for stimulation intensities at the motor threshold. (c) Percentage of comfort levels for stimulation intensities above the motor threshold.

threshold and above the motor threshold, the majority of the pain level ratings increase to two and three, respectively. The variability observed in the ratings of different stimulation intensity levels could be attributed to variations among participants, their perceptual sensitivity, and their ability to tolerate the stimulation. It is worth mentioning that one participant's (P 05) ratings were excluded from the analysis because of their overall misunderstanding of the rating scale.

D. Effect of Tremor Power Intensity

The effect of different stimulation combinations on tremor suppression has been discussed. However, observations suggest that different amplitude levels, even in a single participant, show different results in different situations and times. This observation suggests that tremor is highly variable over time, and higher tremor power intensities might require higher stimulation intensities for a higher suppression ratio.

To analyze this effect, tremor power intensities ((degrees/s)^2/Hz) in the five-second window prior (pre-window) to each stimulation were first extracted from the filtered dataset. Next, the common logarithm of the extracted data was calculated, which lies in the range of 1.84 to 5.89, with a mean value of 4.1, a first quartile of 3.28, a median of 4.38, and a third quartile of 5.01. The dataset, including the common logarithm of pre-window tremor power and TPSR, was then divided into four groups using the quartiles. The data below 3.29 (the first quartile) were categorized into "Group 1," the data within the range of 3.3 and 4.38 (between the first quartile and the median) were categorized into "Group 2," the data between 4.39 and 5.01 (between the median and the third quartile) were categorized into "Group 3," and the data above 5.02 (the third quartile) were categorized as "Group 4." This means that data included in Group 1 corresponded to the lowest intensity tremors, and the data included in Group 4 corresponded to the highest intensity tremors.

Using this categorization, Fig. 7 shows the mean of the TPSR in each tremor level group. It can be seen that Group 1 and Group 2 have a better suppression ratio than Group 3 and Group 4. A univariate ANOVA test was used to study the relationship between the amount of suppressed tremor (TPSR) and the tremor power intensity before stimulation (the pre-window). The test showed a highly statistically significant difference among tremor power groups and TPSR ($p < 0.001$). There is a highly significant difference between

TABLE III
TPSR ACCORDING TO PRE-WINDOW TREMOR POWER INTENSITY AND ANOVA COMPARISON RESULTS

Group	TPSR	p value			
		G1	G2	G3	G4
G1	81.2 ± 2.9	-	$p = 1$	$p < 0.001$	$p < 0.001$
G2	79.0 ± 2.9	$p = 1$	-	$p < 0.001$	$p < 0.001$
G3	59.2 ± 2.9	$p < 0.001$	$p < 0.001$	-	$p = 1$
G4	59.9 ± 2.9	$p < 0.001$	$p < 0.001$	$p = 1$	-

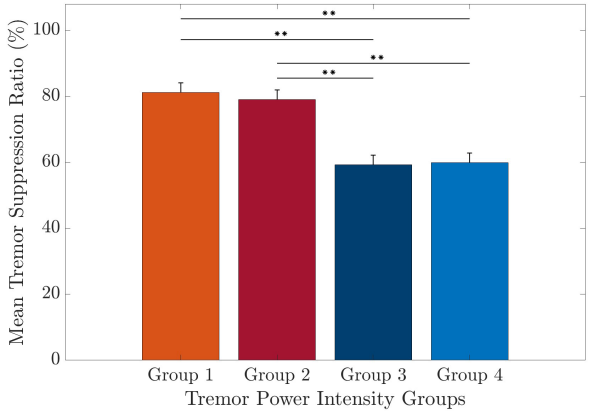

Fig. 7. Mean of the tremor power suppression ratio for different tremor power groups, with statistical analysis. Whiskers represent the standard error in each group, ** shows a highly statistically significant difference between groups.

the Group 1 and Group 3 ($p < 0.001$), a significant difference between Group 1 and Group 4 ($p < 0.001$), but no significant difference between Group 1 and Group 2 ($p = 1$). Also, a highly statistically significant difference was observed between Group 2 and Group 3 ($p < 0.001$), and a highly statistically significant difference between Group 2 and Group 4 ($p < 0.001$) was observed. No statistically significant difference was observed between Group 3 and Group 4 ($p = 1$). Table III summarizes these results.

To explore these results further, Fig. 8 shows the relationship between TPSR and the common logarithm of the power of the tremor in the pre-window. In this figure, the y axis shows the TPSR, and the x axis represents the common logarithm of the tremor power in the pre-window.

Fig. 8(a) categorizes the data based on the stimulation intensity level. Three first-order polynomial fits in this figure demonstrate that regardless of the stimulation intensity, the TPSR decreases with an increase in tremor power. It is noteworthy that the stimulation intensities at the motor threshold (blue line) exhibit a higher trend in TPSR in the overall range of pre-window tremor power. On the other hand, Fig. 8(b) divides the data points based on different pre-window tremor power intensities, as described earlier. The TPSR in this figure is the outcome of all stimulation combinations. It can also be observed from this figure that the TPSR declines as the tremor power increases.

A univariate ANOVA test was performed on the filtered dataset, containing the TPSR as the dependent variable, and the pre-window power groups and the stimulation amplitude

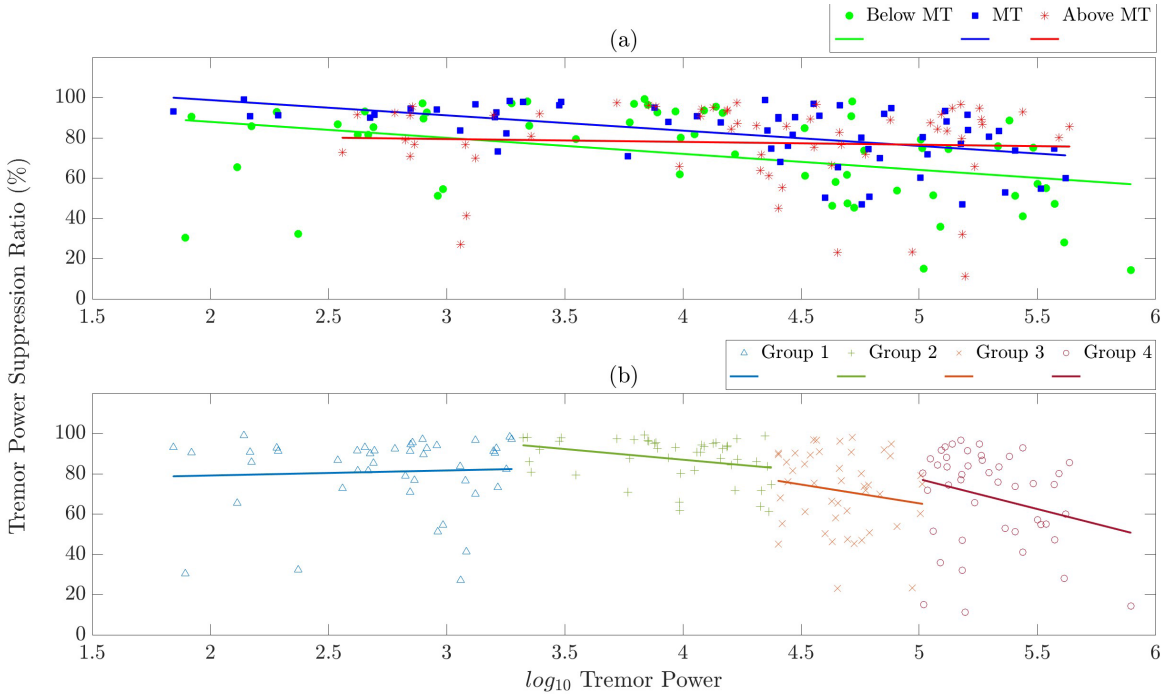

Fig. 8. Relationship between TPSR and the tremor power in the pre-window before stimulation. (a) Data points in green show the TPSR using amplitudes below MT, data points in blue show the TPSR using amplitudes at MT, and data points in red show the TPSR using amplitudes above MT. Green, blue, and red lines show the first-order polynomial fit to the associated data points for below, at, and above motor threshold amplitudes, respectively. (b) Data points in blue, green, orange, and red show the TPSR in Group 1-Group 4 of pre-window tremor power groups. Each line corresponds to a first-order polynomial fit of the data points of the same color.

levels as fixed factors (V_1 and V_2). The results showed a statistically significant difference using various amplitude levels in different tremor power groups ($V_1 \times V_2$, $p = 0.016$). As shown in Fig. 9, there is a statistically significant difference in TPSR using BMT (green) for Groups 1, 3 ($p < 0.001$), Groups 1, 4 ($p < 0.001$), Groups 2, 3 ($p = 0.003$) and Groups 2, 4 ($p = 0.001$). Also, using MT (blue), the results showed a statistically significant difference between Groups 1, 4 ($p = 0.004$). Using AMT (red), there is a statistically significant difference among Groups 1, 3 ($p = 0.043$), and Groups 2, 3 ($p = 0.006$). Lastly, there is a statistically significant difference using BMT and AMT in Group 4 ($p = 0.035$). This figure further emphasizes the results obtained earlier in Fig. 8, which show that tremor suppression is lower at higher tremor intensities. Furthermore, by comparing the effect of stimulation intensity in each group, it can be seen that although there is no statistically significant difference between TPSR in the first three groups when changing amplitude levels, amplitudes above the motor threshold show better performance in the last group compared to amplitudes below the motor threshold.

E. Limitations

The response to Functional Electrical Stimulation (FES) can vary greatly among individuals, and even within the same individual using different combinations of FES, or the same combination at different times. This variability has been observed in relation to tremors, especially parkinsonian tremors, which can vary greatly depending on the time of day and mental state of the individual, including during times of stress and anxiety. A single participant can respond differently to an identical stimulation combination in different time frames. This problem could be addressed by designing and developing a closed loop control system that adapts to the changes in tremor intensity. As shown in [27] and [28], repetitive control and model predictive control can be beneficial in this application. However, experiments and tunings involving participants with pathological tremor are required to evaluate and compare methods effectiveness. Tremor variability is not the only reason for different results among participants. Experimental conditions, such as skin conditions, or changes in the hand or arm orientation can slightly shift the targeted muscle belly, thereby reducing the effectiveness of stimulation from fixed electrodes [29]. Therefore, an electrode array with a control system might also help to improve the stimulation outcomes. Other limitations of this study that can be highlighted are the limited number of participants, the lack of balance between male and female participants, and the absence of a method to measure or estimate muscle fatigue. Simulations at and above the motor threshold might have caused muscle fatigue during the experiment and altered the results in later stimulations compared to the initial rounds. The rest time could have been extended in the study protocol to reduce this effect on the results; however, the total length of the study was kept as short as possible in order to limit the participant's inconvenience. For the same reason, the number of repetitions per stimulation combination was limited to three; however,

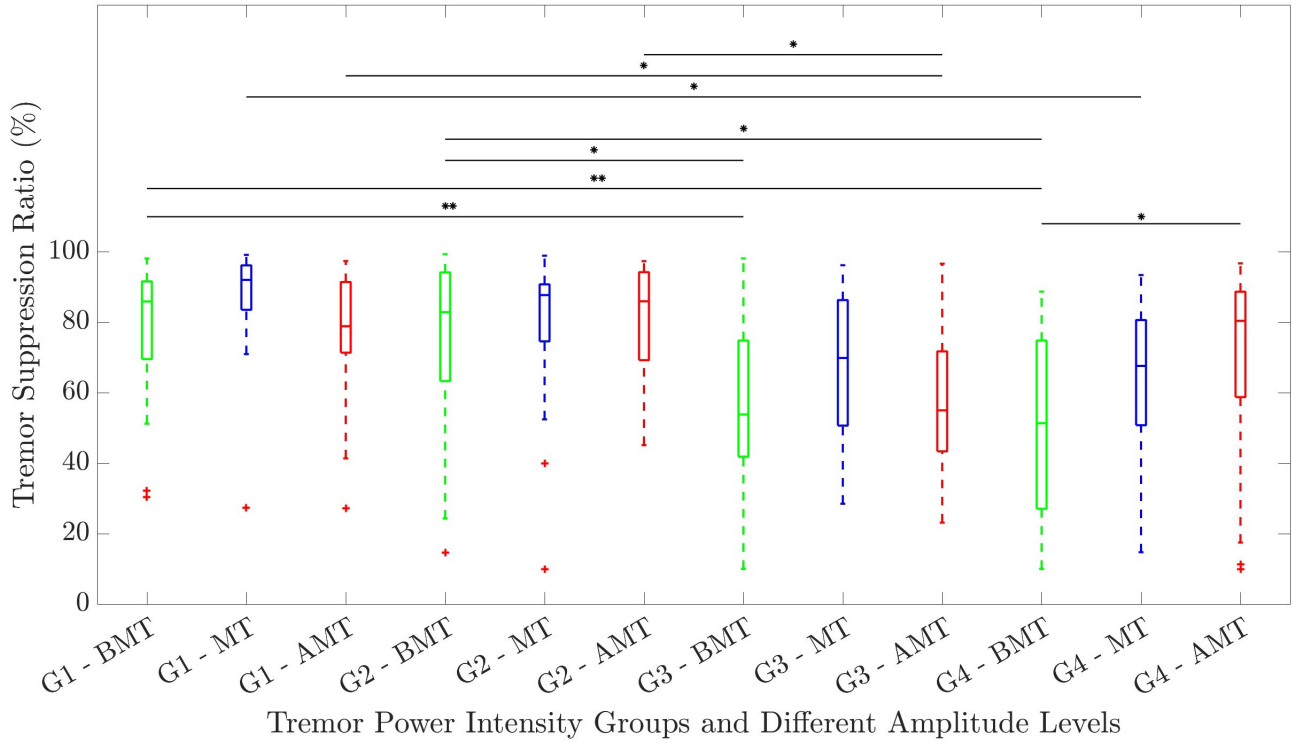

Fig. 9. Effect of different amplitude levels on TPSR, compared in different pre-window tremor power ranges. Red, green, and blue boxes represent the range of TPSR using amplitude levels below (BMT), at (MT), and above motor threshold (AMT), respectively. On each box, the bottom and top edges of the box show the 25th and 75th percentiles, respectively. The central mark shows the median, and whiskers extend to the most extreme points that are not considered as outliers. Outliers are plotted as +. * and ** show a statistically significant difference and a highly statistically significant difference between groups, respectively.

further experiments can be performed in future work to extend the results. Generated muscle fatigue might have reduced the effectiveness of FES in tremor suppression since the torque generated by the fatigued muscles using the same level of stimulation decreases. Therefore, the potential negative effect on the suppression might have caused less tremor suppression in the later rounds of the stimulation. Lastly, further analysis can be conducted on the collected data to study changes in tremor power for different harmonics during suppression, and the effect of suppressed wrist tremor on tremor characteristics at the wrist and distal joints.

IV. Conclusion

The effect of different stimulation parameters in 30 seconds of tremor modulation was studied in this work. Motion data were recorded from 14 participants with PD tremor to investigate the effect of different stimulation parameters, and comparisons were performed over tremor data with and without stimulation. Parameter combinations include a fixed frequency of 120 Hz, a fixed pulse width of 200 μs, a variable number of pulses at 2, 4, or 6, and variable current intensities derived from participant-specific sensory and motor thresholds. Observations and data analysis showed that tremor generally decreased during stimulation intensities close to or slightly above the motor threshold in most cases. Furthermore, different suppression ratios were obtained from different repetitions of each combination for a participant, and generally among different participants. Although stimulation duration was extended in this study to reduce transient response effects on the final results, it was observed that the effect of specific stimulation parameters is highly dependent on the ongoing intensity of the tremor. Therefore, the new method of testing electrical stimulation that was presented in this paper not only shows the highly variable suppression results within one individual, but also highlights the dependency of suppression rate on the existing tremor intensity. This implies that a real-time control approach is required to update the stimulation intensity online according to the tremor intensity for each individual. Lastly, it should be noted that although the focus of this study was the suppression of tremor in Parkinson's disease, and treatments and pathophysiology are different for Parkinson's disease, essential tremor, and other neurological disorders that cause tremor, the results of this study could support the understanding of other types of tremor, and lead to developing suppression technologies using FES.

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