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Long-term Alleviation of Parkinsonian Resting Tremor Using Wireless Optogenetic Nanonetworks

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***Abstract*—Resting tremor is one of the major symptoms of Parkinson's disease, which causes havoc in motor functions of the body, has its genesis in communication impairments in the subthalamic nucleus of the basal ganglia. The modern sophisticated surgical treatments, including electrical deep brain stimulation do not yield satisfactory results due to their inability to provide long-term cure and minimize side effects, such as discomfort and increased infection rates. In this work, we propose a novel system based on the emerging communication technology of *wireless optogenetic networks of neural dusts* to provide a long-term solution for the alleviation of resting tremor. Interfaced with neural dusts, each of the subthalamic nucleus neurons can be controlled and stimulated by the ultrasonic waves which are transmitted from a single/multiple subdural transducer(s) that are placed in the dura mater of the brain. Moreover, in order to address the challenging tasks of charging and addressing each of the neural dusts, we propose a protocol, named as Single Time Instant addressing Protocol, which outperforms the state-of-the-art *parallel charging* protocol. The basic idea of our protocol is that it selects most frequently occurring spike patterns in a single time instant and assigns the pattern with an ultrasonic frequency. With the improved efficiency of Single Time Instant addressing Protocol validated with empirical datasets, the proposed system is expected to revolutionize the way of treatment of parkinsonian resting tremor.**

***Index Terms*—Parkinsonian resting tremor, eDBS, STN, wireless optogenetic nanonetworks, Parkinson's disease, neural dusts, sinle neuron stimulation.**

I. Introduction

A. Motivation

PARKINSON'S disease is a complex neurodegenerative disorder that adversely affects the motor functions of the body. The number of patients suffering from Parkinson's disease in around the world is expected to rise from five million in 2005 to nine million by 2030 [1]. The major symptoms of the disease are rigidity, akinesia and tremor in the limbs. Furthermore, speech and cognitive impairment, depression and sleep disorders are some of the non-motor symptoms, observed in the Parkinson's disease. As a result, the disorder degrades the quality of life of patients. One of the key causes of the disorder is the depletion of dopaminergic neurons (referred to as depigmentation) in the substantia nigra pars compacta (SNc) of the basal ganglia in the brain [2].

Limbic tremor, which symbolizes Parkinson's disease, is manifested in various forms, such as essential, recurrent and normal tremor. However, tremor-at-rest or resting tremor is the most prominent and is observed in 70-80% of Parkinson's patients [3]. Modern treatments for the disorder include: (a) Levodopa (L-DOPA) administration – L-DOPA, a precursor of dopamine, when used as a medication, regenerates the depleted dopaminergic pathways in the basal ganglia; (b) lesioning – which involves the elimination of neuron clusters (known as heat induced elimination) via placement of electrodes in the thallamus (known as thalamotomy) and regions of the basal ganglia, particularly the globus pallidus (known as palidotomy). However, the greater degree of invasiveness involved with the process and the irreversibility of the procedure make it less preferable for most of the cases; and (c) Electrical deep brain stimulation (eDBS) – which involves the electrical stimulation of the basal ganglia structures via the insertion of implantable electrodes in certain strategic places of the basal ganglia, remedies many of the major adverse motor symptoms [4]. The subthalamic nucleus (STN) owing to its location in the basal ganglia and key role in the generation of tremor, has been identified as the preferred target for eDBS [5] [6]. Typically in an eDBS system, an implantable pulse generator, which generates programmed electrical pulses is surgically implanted beneath the skin in the chest cavity of the patient, and is connected to the implanted electrodes via wires. The replacement of the batteries of the pulse generator (usually every 4-5 years) necessitates surgical intervention which is a major drawback of this approach. eDBS also has other crucial limitations: firstly, it leads to post-operative side effects due to the surgical implantation of chronic electrodes; secondly, the eDBS system is ineffective in single neuron stimulation due to the larger surface area of the electrodes as compared to the size of a neuron [7].

The treatments for Parkinson's disease are neither able to provide a long-term cure for the disorder nor are they free from causing other side-effects (as seen in eDBS). As a result, the need for minimally invasive treatment procedures with relatively lower side effects for remedying the symptoms of Parkinson's disorder is felt across the discipline, which is followed by the emergence of novel ideas and technologies such as wireless optogenetic neural devices [8].

Optogenetic stimulation presents a promising opportunity for single neuron targeting. Moreover the stimulation via light may reduce post-operative side effects. Optogenetics involves the deposition of opsins on the neuron membranes, causing the opsins to act as channel gates for the transport of ions across the membrane. Hence, the process modulates the membrane potential of the neuron. The membranes of neurons become sensitive to optical light of specific wavelength and may express excitatory (Channelrhodopsin) or inhibitory (Halorhodopsin) effects [9]. The conventional techniques for the stimulation of light sensitive neurons focus on the insertion of optical micro-fibres tethered to an external light source, which generates stimulating light pulses [10]. In this work, we

propose a system for optogenetic stimulation of STN neurons, thereby leading to alleviate the problem of resting tremor. The system consists of wireless neural dust devices deployed to each of the target STN neurons, and subdural transducer(s) deployed in the dura mater which charge and activate the devices. Subsequently, we develop an efficient charging as well as addressing protocol which yields the minimal number of ultrasonic frequencies to activate neural dusts based on given spike times. The major contributions of this study are as follows:

- Propose an improved device architecture (of frequency filter switches) for the wireless neural dusts to alleviate resting tremor in Parkinson's disease;
- Develop a charging and addressing protocol to stimulate neurons to improve the stimulation efficiency and charging power, compared to legacy protocols;
- Propose an online version of the charging-addressing protocol to facilitate on-the-go alleviation of parkinsonian tremor;
- Analyze the performance of the charging and addressing protocol when the system uses multiple subdural transducers.

The paper is organized as follows: Section II presents the review of related literature. Section III and IV present the system model of parkinsonian resting tremor, followed by the design specifications of wireless optogenetic neural dust. Section V presents the Single Time Instant addressing Protocol (STIP). Section VI presents the performance evaluation of STIP when compared to existing protocol. Section VII presents the online version of STIP. Section VIII summarizes the discussions on STIP and its online version of and concludes the paper.

II. Related Works

Considerable work has been carried out specifically to study Parkinson's disorder [11] [12]. Duval *et al.* [13] presented a model explaining the generation of parkinsonian tremor, due to the abnormal bursting activity in the basal ganglia. Dirkx *et al.* [14] established the correlation between depletion of dopaminergic pathways and generation of tremor. Furthermore, Poewe *et al.* [4] summarized the diagnosis and current treatment approaches, such as L-DOPA administration and lesioning. Benabid *et. al.* [15] presented the methods, procedures and technology involved in eDBS supported with post-operative review of reduction in Parkinsonian symptoms.

The concept of neural dusts for the purpose of brain machine interfacing was proposed by Maharbiz *et. al.* [16], describing the basic device and network architecture of neural dust. Recently, Haddock *et al.* [17] proposed an automated DBS method using a smart watch and a computer interface in order to alleviate tremor for Parkinson's disease. Wirdatmadja *et. al.* [8] proposed the network architecture of neural dust for optogenetic stimulation of damaged neurons in cortical layers, and developed charging protocols to stimulate the neurons in the cortical layers.Compared to their work, our study proposes the use of wireless optogenetic devices for the stimulation of STN neurons specifically reduce Pariknonian symptoms. The study also presents the bifurcation of charging-addressing schemes along with appropriate modifications in device architecture. The use of multiple transducers as a means to improve system performance has been unexplored in previous works; we investigated this in our study.

III. System Model

A. Parkinsonian tremor model

Resting tremor manifests itself as a low frequency (3-8 Hz, henceforth referred to as tremor frequency band) rhythmic tremor which emerges in the absence of motion in limbs. The commonly accepted hypothesis is that the appearance of an synchronized biological oscillator in the basal ganglia causes the tremor [18]. The strengthening of the *basal ganglia-thalamo-cortical* feedback pathway plays a vital role in generation, amplification and propagation of the tremor throughout the central nervous system (CNS). Microelectrode recordings from various regions of the basal ganglia strongly show the presence of neurons exhibiting oscillatory bursting activity in the tremor frequency band (TFB). The cells exhibiting tremor referred to as tremor cells, have oscillatory bursting spikes, which are highly correlated with the physically estimated tremors [19]. Furthermore the data of the microelectrode recordings of the basal ganglia indicate the presence of such tremor cells in the STN, which may potentially serve as the source for tremor genesis [20]. The STN is a primary input to the basal ganglia, has efferents from the cortex and is responsible for modulation of motor functions. It is reported that electrical stimulation of the STN decreases tremor-like activities, hence targeting tremor cells in the STN is crucial in alleviating resting tremor effectively [21].

B. STN stimulation model

The localization and subsequent targeting of the tremor cells in the STN is an effective and reliable approach for the alleviation of tremor [22]. The stimulation of tremor generating cells is a less invasive approach, which reduces oscillations in the TFB and induces a progressive improvement of the synaptic connections of the network that otherwise regulate the generation of tremor.

C. Model of system architecture

We primarily focus on the stimulation of genetically modified target tremor cells via wireless neural dust devices. The system architecture used is described as follows:

- Wireless optogenetic neural dust device (WiOptND): Neural dust motes are deployed in the STN and placed in close proximity to tremor cells (approximately 300 μm) [4]. Each of the dust motes are approximately 0.5-1 mm apart from one another and are equipped with a light source, i.e., light emitting diode (LED) which radiates optical light of wavelength specific to the activation of the opsin present on target cells. The WiOptND harvests energy from ultrasonic acoustic waves via its piezoelectric nanowires. The device is also equipped with voice operated (VOX) frequency filter switch network designed

for the addressing of the dust motes and capacitor for the storage of energy required for optical stimulation.

- Subdural transducer: It is implanted beneath the cranium, in the dura mater and is approximately 100 mm away from the STN where WiOptND devices are deployed [5]. The subdural transducer has dual functions: a) charging the neural dust motes via transmission of ultrasonic acoustic waves and b) addressing the WiOptNDs for the stimulation of the tremor cell based on spike times information.
- External transducer: Implanted exterior to the cranium, the external transducer communicates and powers the subdural transducer by using radio frequency communication. Additionally, it may be coupled with body sensor networks (if it exists) to detect the changes in state of rest/motion and appropriately communicate such information to the subdural transducer(s).

Fig. 1 illustrates the schematic of the proposed system for the optical stimulation of the tremor cells.[1]

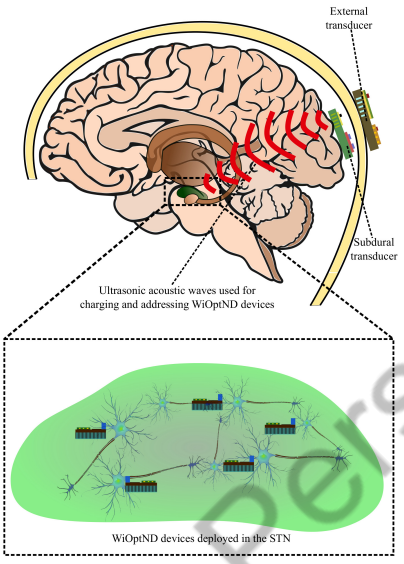

Fig. 1. Schematic representing the system of WiOptNDs and transducers implanted in the brain in order to stimulate the tremor cells. WiOptNDs stimulate target tremor cells in the STN. The subdural transducer(s) charges and addresses the WiOptNDs via ultrasonic acoustic waves. External transducer communicates and provides power to the subdural transducer(s).

IV. Design Specifications of WiOptNDs

A. WiOptND energy harvester design and VOX network

The piezoelectric energy harvester is modelled as a non-ideal voltage source $V(t)$ with current $i(t)$ through circuit as shown in Fig. 1. The electrical power generated by the harvester when an ultrasonic charging signal is transmitted, depends on the intensity of ultrasonic signal, the attenuation due to brain tissues and the efficiency of electromechanical conversion. A rectifier circuit converts the *alternating source* voltage to *direct* source voltage, which is fed to a supercapacitor. The direct current $i_{DC}(t)$ charges the supercapacitor till the energy stored in the capacitor attains its maximum value E_{max}. The PMOS transistor prevents further charging of the capacitor once maximum energy has been stored. The WiOptND is equipped with network of VOX switch in order for the WiOptND to respond to multiple ultrasonic frequencies. Each VOX switch in the network operates at a specific resonant frequency. It is noted that each WiOptND may respond to more than one addressing frequency based on the mapping generated from the addressing protocol. The LEDs interfaced with the tremor cells radiate optical light on the passage of current. Based on the spike times in the raster matrix (a table of ordered spike times of the tremor cells), when a subdural transducer transmits a specific addressing frequency, the VOX switches with corresponding resonant frequencies get activated and the capacitor discharges current, which turns the LEDs on for a predetermined duration.

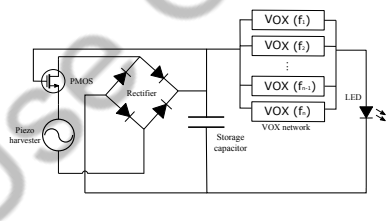

Fig. 2. The circuit diagram of a piezoelectric energy harvester and the layout of the VOX frequency filter switch network of a WiOptND.

B. Estimation of harvested energy

The piezoelectric nanowire harvester of the WiOptND converts the mechanical vibrations which is generated due to incident ultrasonic waves, to electrical current and voltage [23] which is used to drive the LEDs. The light radiated from the LED should have intensity as much as the threshold value required to activate opsin. Hence, the ultrasonic signals (which undergo attenuation in the brain tissues) are required to have sufficient intensity to stimulate the target cells. In the following, we provide an estimation of the energy which is harvested by a WiOptND's based on the deployment of the WiOptNDs in the STN.

- WiOptNDs are assumed to be deployed at a distance of around 300 μm from the tremor cells which are genetically engineered to be stimulated by the light of wavelength 460 nm and intensity 8-12 mW/mm^2 [10] [24]. Using the *Modified Beer Lambert Law* [8] for the scattering and absorption of light in the brain, (where absorption coefficient μ_a=0.07 mm^{-1} and reduced scattering coefficient μ_s=1.404 mm^{-1}), the required intensity of light radiated from the LED (termed as I_o) such that the intensity at 300 μm distance is 12 mW/mm^2 (required for the stimulation of opsin channel), is computed as much as I_o= 13.33 mW/mm^2. For the radiation of light of such intensity, the power required by the LED can be found using its area (e.g., A_{LED}= 20900 μm^2). Therefore the power required by the LED is given by, P_R = $I_o.A_{LED}$ = 0.27 mW.

[1]A schematic of the system organization is provided in the supplementary material.

- The ultrasonic waves undergo attenuation that varies exponentially with the frequencies of ultrasonic waves and the depth of penetration. The resulting intensity of ultrasonic wave at the depth d is given by

$$I = I_s \cdot 10^{-\frac{\alpha f d}{10}} \tag{1}$$

where I_s represents the intensity of the ultrasonic wave at the source, f is the frequency of the ultrasonic wave and α is the attenuation coefficient for brain tissue (reported value 0.435 $dB/(cm.MHz)$) [25]. The maximum permissible value of the ultrasonic source intensity I_s, is limited by 720 mW/cm^2 as per Food and Drug Administration (FDA) safety regulation [8]. The power harvested by the piezo harvester is given by

$$P = I \cdot A_{EH} \cdot \eta \tag{2}$$

where A_{EH} is the area of the energy harvester and η is the efficiency of elctromechanical conversion for the piezoelectric nanowires. Taking the values of I_s= 720 mW/cm^2, f= 500 kHz, d= 10 cm, A_{EH}= $10^{-6}m^2$ and η= 0.5, the power harvested by the piezo harvesters, P_{EH}= 3.42 mW.

V. Charging and addressing protocols

The optical stimulation rate (the rate at which the WiOptNDs stimulate the target tremor cells) to stimulate each tremor cell for preventing tremor generation is be distinct. The values of optical stimulation rates are obtained from the neural spike times information, which is used to alleviate resting tremor. The neural spike times information may be obtained using neural spike recordings via the insertion of microelectrodes in the STN and the observation of changes in spike patterns due to the oscillation generated by the tremor cells. Consequently, the subdural transducer is required to transmit ultrasonic frequencies to charge and address the the WiOptNDs such that they stimulate the tremor cells as per their spiking times, which are provided in the neural spike raster matrix.

A. Single Time Instant addressing Protocol (*STIP*)

The subdural transducer addresses and activates the WiOptNDs according to the STIP, which is based on the neural spike times of the tremor cells [2]. The STIP outputs the minimal number of ultrasonic frequencies required for executing the raster matrix. For the sake of ease of understanding how the protocol works, we consider that the number of the tremor cells and WiOptNDs is same and is n. According to the protocol, at each time instant in the raster matrix the number of neurons and associated WiOptNDs to be stimulated are observed, which is basically a column sequence of $1's$ and $0's$ of the matrix. Since we consider n devices, at each time instant one of the 2^n-1 possible column sequences exists (the column sequence of all $0's$ is excluded). Let S = {s_1, s_2, s_3,..., s_{2^n-1}} represents the set of all such possible column sequences and P = {p_1, p_2, p_3,..., p_{2^n-1}} represents the number of time instants in the raster matrix where each of the 2^n-1 column sequences occurs, the column sequence s_i occurs p_i times in the raster plot. The vector P is rearranged in decreasing order, and a certain number, say, r of the most frequently occurring column sequences in the raster matrix are selected. The selection of column sequences is done in a way that the quantity α (which plays significant role in the estimation of stimulation efficiency)

$$\alpha = \frac{\sum_{k=1}^{r} p_k}{m} \tag{3}$$

has its maximum value, given $r \ll 2^n - 1$.[3]

The STIP indicates that each WiOptND responds to more than one ultrasonic addressing frequency, based on the device-frequency mapping generated by the protocol. The device-frequency mapping, which represents a one-to-many relationship (a device needs to be tuned with multiple frequencies) is realized using the frequency filter VOX switch network.

B. Analysis of STIP for stochastic variations in raster matrix

Practically, the raster matrix based on which the WiOptNDs need to be activated via the STIP is non-static and undergoes stochastic variations. Modelling and incorporating the stochastic behaviour in the protocol and assessing the performance of the modified protocol is necessary to show the efficiency of the protocol in alleviating tremor generation. The stochastic properties of STN neurons may be modelled using the Ornstein-Uhlenbeck process as proposed in [26]. The interspike interval (ISI) is the time duration between consecutive spike times and is inversely related to optical stimulation rate, which is modelled as a *first passage time* problem of the Ornstein-Uhlenbeck process.

Theorem 1: The efficiency of stimulating tremor cells using STIP protocol taking into account the stochastic variations in raster matrix is given by $\eta = 100 \times \left(1 - \frac{\sum_{i=1}^{z} k_i}{\sum_{j=1}^{n}\sum_{j=1}^{z} u_j(l)}\right)$, where $z = m - \sum_{i=1}^{r} p'_i$ and k_i is number of misfires.[4]

Theorem 1 provides us a measure of evaluating the efficiency of stimulating tremor cells by using STIP protocol. The efficiency of the stimulation process is an important metric that may be used to analyze the performance of various charging and addressing protocols. It is a direct measure of the number of misfires occurring in the execution of the raster matrix by using charging and addressing protocol. Increase in misfires in stimulation adversely affects the alleviation of the tremor generation in the STN cells.

C. Multiple subdural transducer for stimulating WiOptNDs

We consider the use of multiple subdural transducers for charging and addressing WiOptNDs. The use of multiple subdural transducers facilitates the transmission of multiple ultrasonic addressing frequencies at the same time instant. The multiple column sequences of the raster matrix may be addressed using the combination of distinct ultrasonic frequencies transmitted from each of the subdural transducer(s). Fig. 3 shows the reduction in total number of ultrasonic addressing

[2]An example of the raster matrix is provided in the supplementary material

[3]The STIP algorithm is described in supplementary material.

[4]Proof provided in supplementary material

frequencies as a result of using multiple subdural transducers.[5] The above exercise may be done conversely, i.e., given a

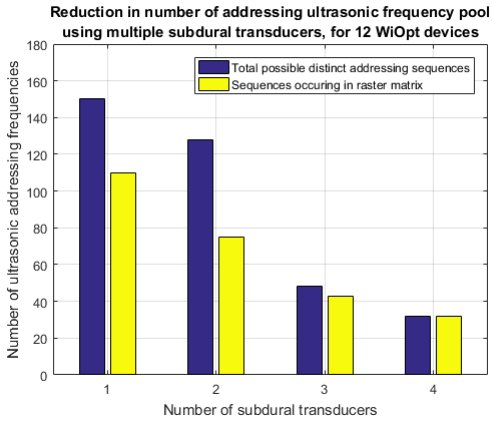

Fig. 3. Reduction in the size of ultrasonic frequency needed for stimulation. The total number of possible addressing sequences and the sequences that occur in the raster matrix indicate the number of ultrasonic frequencies required.

constraint on the number of ultrasonic addressing frequencies (which may arise due to factors such as the limitation on ultrasonic bandwidth) an algorithm can be devised to output the optimal number of subdural transducers, which is required to realize the raster matrix. The reduction in ultrasonic addressing frequencies by using multiple transducers as observed in Fig. 4, may be theorized as follows: let there are t transducers for addressing, and i^{th} transducer addresses n_i number of WiOptND, which implies that n_i rows of raster matrix are addressed by the transducer t_i, where n_1+n_2+...+$n_t = n$, i.e., the total number of devices. The task of addressing WiOptNDs is now divided among multiple transducers. Associated with each transducer there may exist $2^{n_i} - 1$ $(< 2^n - 1)$ possible column sequences. The STIP protocol is applied to each i^{th} transducer to select r_i number of frequently occurring column sequences out of $2^{n_i} - 1$ possible column sequences. The total number of addressing frequencies required is $\sum_{i=1}^{t} r_i$, which is less than the r number of frequencies required for a single transducer. Therefore, with increase in number of transducers, the total number of addressing frequencies decreases.

VI. Performance Evaluation

A. Simulation setup

The performance of the STIP protocol was evaluated using MATLAB-based simulation. We constructed spiking times matrix of tremor cells based on the empirical data obtained from the microelectrode recordings of the STN [23], which is provided to the STIP as the input. Particularly, the spike raster matrix was generated using ISI distribution data (distributed as an OUP) from the microelectrode recordings. Each of the WiOptND has a distinct optical stimulation rate which itself varies with time, and is dictated by the neural spiking raster matrix. On the other hand, the number of WiOptNDs to be deployed and interfaced with the tremor cells is assumed a variable parameter, as it is subject to the clinical diagnosis indicating the severity/progression of Parkinson's disease resting tremor. To evaluate the efficiency of STIP, the protocol is compared with existing parallel charging sliding window protocol [8] with respect to the following performance metrics: (a) stimulation efficiency, (b) total number of frequencies required for stimulation, and (c) average power utilized for charging the WiOptNDs. The parameters and their values used in simulation are listed in Table II.

[5]The algorithm for optimal number of addressing frequencies is presented in the supplementary material.

TABLE I
Simulation Parameters

Parameter	Value [Unit]
Stimulation rate	50-150 [Hz]
Number of devices	5-10
Number of instants	1000
Duration of single time instant	1 [msec]
Raster plot period	1 [s]

B. Size of the pool of ultrasonic addressing frequency

The addressing protocol, which uses less number of addressing frequencies is preferable when a higher number of WiOptNDs are required to be deployed in the STN. As evident from Fig. 4, STIP uses considerably lesser number of frequencies for the stimulation for a given number of devices, when compared to the existing protocol, in which the number of frequencies required for stimulation increases at a much faster rate with the increase of WiOptNDs.

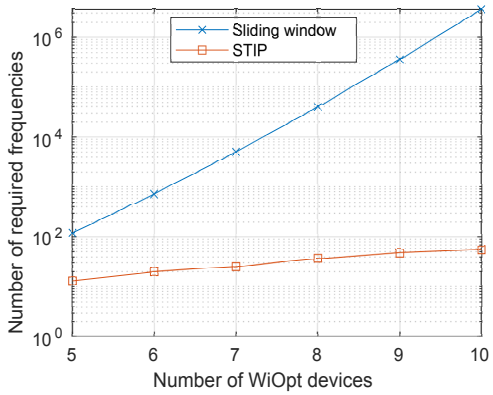

Fig. 4. Comparison of STIP and parallel charging protocols with reference to number of ultrasonic addressing frequencies required for execution of raster matrix by subdural transducer.

C. Stimulation efficiency

The efficiency of stimulation of tremor cells based on the raster matrix of tremor alleviation is the metric to analyze the number of misfires occurring during the stimulation process. The following equations were used for calculating the stimulation efficiency of respective protocols:

- **Parallel charging sliding window protocol**

$$n_{mis} = \sum_{t=1}^{T} \left[\sum_{y=1}^{n} \sum_{k=1}^{n} [min(s(y,t), s(k,t))] \right] \quad (4)$$

$$\eta = 100 \times \left(1 - \frac{n_{mis}}{\sum_{t=1}^{T}\sum_{y=1}^{n} s(y,t)}\right) \quad (5)$$

where n_{mis}, n are the number of misfires and the number of devices, T is the number of time instants and η is efficiency of stimulation. $s(y,t) \in (0,1)$ is the state of y^{th} device at the time instant t.

- **STIP protocol**

$$\eta = 100 \times \left(1 - \frac{\sum_{i=1}^{z} k_i}{\sum_{j=1}^{n}\sum_{j=1}^{z} u_j(l)}\right) \quad (6)$$

where $z = m - \sum_{i=1}^{r} p'_i$ and k_i is number of misfires.

As shown in Fig. 5 the stimulation efficiency of STIP protocol is higher than the existing parallel charging protocol, indicating the superiority of the STIP protocol. Moreover, the decrease in the value of efficiency with increase in the number of devices is steeper in parallel charging protocol is due to the fact that, with the increase in optical stimulation rate the required raster matrix becomes denser. Since the parallel charging protocol employs predetermined patterns in a selected time window for stimulation, the event of misfiring occurs at time instants where more than one WiOptND is required to be stimulated simultaneously. This issue of simultaneous stimulation of WiOptNDs is taken care of by the STIP protocol as it stimulates multiple devices in each time instant based on the appearance of column sequences in a raster matrix.

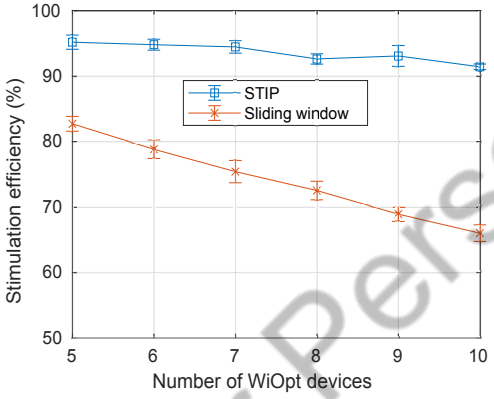

Fig. 5. Comparison of STIP and parallel charging protocols with reference to stimulation efficiency (related to number of misfire events).

D. Average charging power

The average power is the expected value of the power transmitted by the subdural transducer(s) for charging the WiOptNDs calculated over the time window of the raster matrix. The total power utilized is averaged over the number of time instants in the raster matrix where charging and subsequent addressing patterns are provided. The following equations were used for calculation of average charging power for both the protocols.

- **Parallel charging sliding window protocol.** The average power is given as follows:

$$P_{avg} = \frac{\sum_{i=1}^{T} n_i}{m} \cdot P_r \quad (7)$$

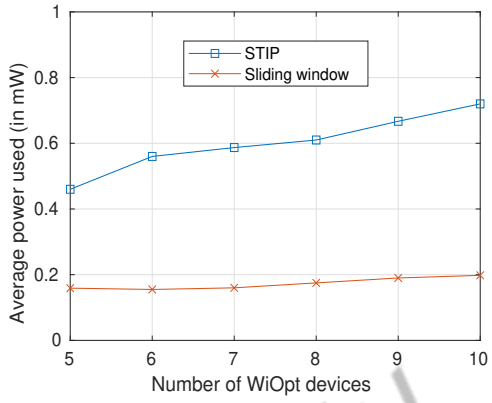

Fig. 6. Comparison of STIP and parallel charging protocols with reference to average power consumed by subdural transducer for charging and addressing devices according to raster matrix.

where n_i is the number of stimulation spikes in the raster matrix in each time window and T is the number of charging time windows.

- **STIP protocol.** The average power is given as follows:

$$P_{avg} = \frac{\sum_{i=1}^{r} n_i \times p_i}{\sum_{i=1}^{r} p_i} \cdot P_r \quad (8)$$

where n_i represents number of stimulation spikes in frequently occurring column sequences and P_r is the power required for stimulating a single WiOptND.

The average charging power consumed in the STIP protocol is higher as compared with existing protocol. This can be attributed to the fact that the STIP protocol charges multiple WiOptNDs at the same time instant to reduce misfiring events whereas existing protocol charges single devices based on the predicted pattern for a time window.

VII. Online version of STIP for tremor alleviation

While having the knowledge of whole raster matrix, the STIP protocol yields the optimal number of ultrasonic frequencies for addressing WiOptNDs. However, in some cases partial knowledge of the raster matrix is available. Hence, we design an online version of the algorithm, which takes a part of the raster matrix as input, and outputs the number of addressing frequencies required for activation of WiOptNDs in the corresponding time instants. The size of the part of the raster matrix or the time window is a design parameter which is subject to how fast the partial raster matrix is formed and patient's response to the partial stimulation. The performance of the online version of the STIP protocol [6] was evaluated for 10 WiOptNDs, and varying the length of time windows of the raster matrix with respect to the following metrics: stimulation efficiency and average consumption (described in Section VI). The results in Fig. 7 show that the online version has lower stimulation efficiency and higher average power consumption when compared with its offline version due to the cumulative effect of misfires in each time window.

[6]Provided in supplementary material

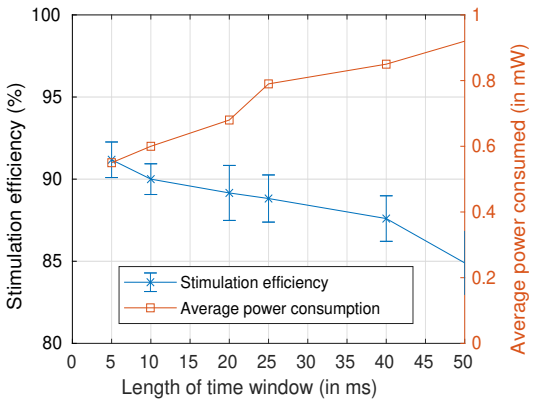

Fig. 7. Stimulation efficiency and average power consumed by the online version of STIP protocol

VIII. Conclusion

In this work, we proposed that a WiOptND-based system provides long-term alleviation of Parkinsonian resting tremor by optical stimulation of the tremor cells. The analysis and evaluation indicate the efficiency of the protocol used as a charging and addressing scheme of the WiOptNDs for the stimulation of STN tremor neurons. The performance of the STIP protocol suggests that it involves lesser misfiring events. However the improvement in the STIP protocol is achieved at the cost of higher power consumption by the subdural transducer. The analysis of the use of multiple subdural transducers for charging and addressing the WiOptNDs indicates that the STIP protocol, implemented on multiple transducers reduces the pool of required ultrasonic frequencies. As a future work, we would carry out the analysis of the implantation of multiple transducers and the subsequent communication and

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