

Particle Swarm Optimization Algorithm to Optimize the Activity Patterns of Internal Globus Pallidus in Parkinson Disease



Shri Dhar, Sanjay Yadav, Jyotsna Singh, AK Yadav, Phool Singh

Abstract: Parkinson disease, one of the widely known brain disorders, affects the movement of body parts due to dopamine reduction in the basal ganglia. In this paper, a model of internal globus pallidus is taken into consideration for a primate suffering from Parkinson disease. The discharge patterns generated for a primate suffering from Parkinson disease are compared with the discharge patterns of a healthy primate. The lags in the discharge patterns of primate with Parkinson disease due to slow movement are shown in the result section of the paper. On the basis of analysis of the model, four parameters have been optimized to remove these lags; which are membrane potential from GPe to GPi (denoted by V_{gg}), membrane potential from STN to GPi (denoted by V_{sg}), synaptic conductance from GPe to GPi (denoted by g_{gg}) and synaptic conductance from STN to GPi (denoted by g_{sg}) as the model is most sensitive to these four parameters among all the parameters taken into consideration. Optimization of these parameters has been carried out using particle swarm optimization algorithm over a time span of 300 msec. A qualitative comparison has been made using correlation coefficient computed between the discharge patterns for a healthy primate and primate with Parkinson disease. The value of correlation coefficient turns out to be 0.9994 showing very high degree of overlap between the two discharge patterns, and validates the high degree of accuracy of the results obtained by particle swarm optimization algorithm.

Keywords: Activity pattern, Internal globus pallidus, Parkinson disease, particle swarm optimization algorithm.

I. INTRODUCTION

Brain disorders are one of the major challenges of the present time for the people of scientific society [1]–[2]. Parkinson disease (PD) is one of the well-known brain disorders which effect the movement of the primate who is suffering from this disease. Due to this reason, it is also known as movement

disorder. This disease was recognized by James Parkinson in 1817. The neurons present in substantia nigra pars compacta (which is a part of the brain) are affected the most in Parkinson disease [3]–[4]. These neurons present in substantia nigra pars compacta are responsible for the production of dopamine which manages the signals and messages involved in the movement process. This dopamine depletion results in many dysfunctions. Once the symptoms of Parkinson disease are visible, then treatments for this disease are available [5]–[7]. As basal ganglia are responsible for the smooth movement of the body parts, so in movement disorders it cannot be ignored that the basal ganglia got affected [8]–[10]. Basal ganglia is made up of four major nuclei which are a).striatum b).globus pallidus (external notated by GPe and internal notated by GPi), c).subthalamic nucleus (STN), d).substantia nigra (pars compacta denoted by SNc and pars reticulata denoted by SNr). Many researchers devoted their time to find the actual cause of the origin of Parkinson disease [11]–[16] but a specific cause of the origin of Parkinson disease is still unknown. However, based on the above studies, many conclusions have been drawn by the researchers regarding the oscillations, tremor and bursting of the motor function in the model of basal ganglia [17]–[20]. The role of subthalamic nucleus (STN) in the tremor and bursting is also discussed. Other researchers discussed the role of globus pallidus in the motor function of basal ganglia. When the dopamine production reduces in Parkinson primate, uninterrupted hyperactivities take place in globus pallidus due to extended glutamatergic input from STN. Also, the role of globus pallidus is important in deep brain stimulation [21] which is very much required on routine basis for a PD primate. Researchers also suggested [22] that the applied current ($I_{app\ GPi}$) has inhibitory impact which results in the reduction of the activity of internal globus pallidus. The factors responsible for these inhibitory impacts are discussed in [23]–[24].

All these results and hypothesis motivated many researchers to study the discharge patterns of basal ganglia nuclei for the primates of Parkinson disease, and to analyse the behaviour of these patterns under various ionic currents. Feng *et al.* [25] in 2007, analysed the patterns of subthalamic nucleus and optimized the deep brain stimulation by using genetic algorithm (GA). In a recent study, Singh *et al.* [26] made the sensitivity analysis of the patterns of subthalamic nucleus for a Parkinson disease primate and suggested that the various membrane potentials affect the activity pattern but the effect of calcium membrane potential (V_{Ca}) is the maximum.

Manuscript published on January 30, 2020.

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These two studies motivated us to analyse the sensitivity of discharge patterns of a PD primate for a model of internal globus pallidus instead of subthalamic nucleus followed by the optimization of the parameters to which the discharge patterns are highly sensitive.

The optimization of the currents has been carried out by using particle swarm optimization algorithm by considering all the parameters simultaneously. After the analysis, it was found that membrane potential from GPe to GPi (denoted by V_{gg}), membrane potential from STN to GPi (denoted by V_{sg}), synaptic conductance from GPe to GPi (denoted by g_{gg}) and synaptic conductance from STN to GPi (denoted by g_{sg}) have high impact on the discharge patterns of the PD primate among all the parameters. All these four parameters are optimized simultaneously using particle swarm optimization algorithm in the present study. An attempt is made to identify the factors which are responsible for tremor and bursting. For this purpose, a model shown in Fig. 1 is taken into consideration.

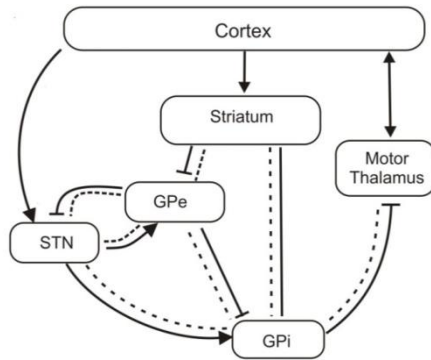


Fig. 1 Modified basal ganglia-thalamo-cortical circuit[26].

Dotted lines in the above figure represent inhibitory synapse while the excitatory synapses are represented by arrows. Bold lines are used for healthy while dotted lines are used for the Parkinson disease primate. During 1970s, back propagation (BP) was a majorly used algorithm to optimize any model, having linear or non-linear functions. While using this algorithm, it was a major challenge for the researchers to choose the initial set of values wisely, otherwise the calculations leads to fluctuation or overflow instead of optimum value(s). In 1995, a technique for optimization known as particle swarm optimization (PSO) was proposed by Eberhart and Kennedy[27] in which all the variables were considered simultaneously to get the optimized solution. The basic approach used in this technique is taken from a flock of birds that are moving to get their food. They are learning through communication and managing their positions as per the best position searched by any of the bird in the flock. They are reaching to their destination by repeating this process again and again. In last two decades, PSO algorithm is successfully implemented over the variety of models to compare the performance of this technique over the other algorithms [28], to optimize non-linear problems [29], to optimize the diameter errors in boring machine [30]. Other than the above mentioned models where this algorithm has been successfully implemented, we have several models

where PSO has been implemented with a great accuracy and better performance as compared to the previous algorithms, out of which few notable ones are [31], [32], [33], [34].

This paper consists of 5 sections which are organized as: Section 2 consists of the description of the model of basal ganglia. Section 3 explains the implementation of particle swarm optimization algorithm followed by results and discussion section. Finally, the conclusions of the study are given in the Section 5.

II. MODEL OF BASAL GANGLIA

We have considered a single-compartment conductance based model[26] as shown in Fig. 1. The various inhibitory and excitatory currents for a healthy primate as well as for a PD primate are shown in the model by bold and dotted lines respectively. Our focus is to study the effect of various currents in internal globus pallidus (GPi) and then optimize those parameters which are affecting the discharge patterns for a PD primate significantly. Also, we have taken conductance and time scale to analyse the discharge patterns in internal globus pallidus model for a healthy and a PD primate. Simulation and analysis is performed with the help of MATLAB 7.16 (over 4 GB RAM Machine and i7 Intel processor) with ODE45. The simulated results are run for a time span of 300 msec.

In this model of internal globus pallidus, membrane potential (V_{GPi}) includes sodium ($I_{Na_{GPi}}$), fast spike producing potassium current ($I_{K_{GPi}}$), high-threshold Ca^{2+} currents ($I_{Ca_{GPi}}$), low threshold T-type current ($I_{T_{GPi}}$), leak current ($I_{l_{GPi}}$), Ca^{2+} activated voltage independent after-hyperpolarization K^+ current ($I_{AHP_{GPi}}$), synaptic current ($I_{syn_{GPi}}$) and internal globus pallidus current (I_{GPi}). The equation of membrane potential (V_{GPi}) is given by:

$$C_m \frac{d(V_{GPi})}{dt} = -I_{Na_{GPi}} - I_{K_{GPi}} - I_{Ca_{GPi}} - I_{T_{GPi}} - I_{l_{GPi}} - I_{AHP_{GPi}} - I_{syn_{GPi}} + I_{GPi} \quad (1)$$

where C_m represents the capacitance of the membrane. The following currents which are used in equation (1) can be written in terms of membrane potential (V_{GPi}) as:

$$I_{Na_{GPi}} = g_{Na} m_{\infty}^3(V_{GPi}) h_{\infty} [V_{GPi} - V_{Na_{GPi}}] \quad (2)$$

$$I_{K_{GPi}} = g_k n^4 [V_{GPi} - V_{k_{GPi}}] \quad (3)$$

$$I_{Ca_{GPi}} = g_{Ca} s_{\infty}^3(V_{GPi}) h_{\infty} [V_{GPi} - V_{Ca_{GPi}}] \quad (4)$$

$$I_{T_{GPi}} = g_T a_{\infty}^3(V_{GPi}) r_{\infty} [V_{GPi} - V_{Ca_{GPi}}] \quad (5)$$

$$I_{l_{GPi}} = g_l [V_{GPi} - V_{l_{GPi}}] \quad (6)$$

$$I_{AHP_{GPi}} = g_{AHP} \frac{[Ca]}{[Ca] + k_{GPi}} [V_{GPi} - V_{Ca_{GPi}}] \quad (7)$$

where k_{GPi} represents the disassociation constant of after-hyperpolarization K^+ current ($I_{AHP_{GPi}}$) whose value is 30 taken from [35].

The value of $[Ca]$ in equation (7) is the solution of the following differential equation

$$\frac{d[Ca]}{dt} = \epsilon_{GPI} [-I_{Ca_{GPI}} - I_{T_{GPI}} - k_{Ca_{GPI}} [Ca]] \quad (8)$$

ϵ_{GPI} in equation (8) represents calcium flux whose value is $1 \times 10^{-4} m/sec$, $k_{Ca_{GPI}}$ is the calcium pump rate taken to be 20 as in[35]. The following differential equation can be used to find the values of n, h, r :

$$\frac{dx}{dt} = \frac{\varphi_x [x_{\infty}(V_{GPI}) - x]}{\tau_x(V_{GPI})} \quad (9)$$

where x can be n, h, r ; φ_x represents a constant for the gating variables and τ_x , is a function of V_{GPI} , represents time constant function that can be calculated from the following equation:

$$\tau_x(V_{GPI}) = \tau_x^0 + \frac{\tau_x^1}{\left[1 + \exp\left[-\frac{V_{GPI} - \theta_x^r}{\sigma_x^r}\right]\right]} \quad (10)$$

The values of τ_x^0 and τ_x^1 are taken from [35] for n, h, r respectively. $x_{\infty}(V_{GPI})$ (steady-state voltage dependence) will be obtained by the equation:

$$x_{\infty}(V_{GPI}) = \frac{\tau_x^1}{\left[1 + \exp\left[-\frac{V_{GPI} - \theta_x}{\sigma_x}\right]\right]} \quad (11)$$

The values of θ_x (half activation or inactivation voltage) and σ_x (slope factor) are also taken from [35]. Finally, the synaptic current ($I_{syn_{GPI}}$) is considered as the sum of synaptic current from GPe to GPi and synaptic current from STN to GPi represented as follows:

$$I_{syn} = g_{gg} \cdot s_{gg} \cdot [V_{GPI} - V_{gg}] + g_{sg} \cdot s_{sg} [V_{GPI} - V_{sg}] \quad (12)$$

where g_{gg} and g_{sg} represent the synaptic conductance from GPe to GPi cell and STN to GPi respectively and the values of these parameters are taken from[35]. s_{gg} and s_{sg} are the two synaptic variables that manage the strength of synaptic input currents. Membrane potentials from GPe to GPi cell and STN to GPi cell are taken from [35].

The synaptic variables can be obtained as the solution of the differential equation:

$$\frac{ds_i}{dt} = \alpha \cdot H_{\infty}(V_{GPI}) (V_{presyn} - \theta_g) \cdot [1 - s_i] - \beta s_i$$

for $i = gg, sg$

(13)

where the sigmoid function $H_{\infty}(V_{GPI})$ is given by:

$$H_{\infty}(V_{GPI}) = \frac{1}{\left[1 + e^{\left[-\frac{V_{GPI} - \theta_g^H}{\sigma_g^H}\right]}\right]} \quad (14)$$

The values θ_g^H and σ_g^H are also taken from [35].

III. PARTICLE SWARM OPTIMIZATION

Particle swarm optimization algorithm (PSO)[36] is a commonly known technique successfully implemented to optimize the linear and non-linear models. In 1995, Kennedy

and Eberhart proposed this approach which was based on the idea of personal best to global best. The idea of particle swarm optimization algorithm is derived from a flock of birds searching for food. They were learning through the communication while moving and approaching their destination. A particle refers to a single solution in case of particle swarm optimization algorithm while a swarm refers to a collection of all the solutions. In this algorithm, three important parameters are: the velocity of the particle; personal best configuration (pBest) achieved by the particle and the position the particle which is at the best location with reference to the destination (called gBest). The whole swarm adjust their velocities after each generation by keeping the point in mind that the new position achieved by them should be close to gBest as well as pBest. The governing equations for the positions and velocity are given by:

$$x_{i,j}(t+1) = x_{i,j}(t) + v_{i,j}(t+1)$$

$$v_{i,j}(t+1) = w \times v_{i,j}(t) + c_p \times r_p \times (P_{i,j} - x_{i,j}(t)) + c_g \times r_g \times ((P_g)_j - x_{i,j}(t))$$

where $x_{i,j}$ and $v_{i,j}$ are the positions and velocities of i^{th} particle which is moving in j^{th} direction, w is the momentum, c_p and c_g are constants, r_p and r_g are random variables that can take values from the interval [0, 1].

In the present study, we have four particles under consideration which are: membrane potential from GPe to GPi (denoted by V_{gg}), membrane potential from STN to GPi (denoted by V_{sg}), synaptic conductance from GPe to GPi (denoted by g_{gg}) and synaptic conductance from STN to GPi (denoted by g_{sg}). Our aim is to find the optimum values of these particles by taking them simultaneously. The search space given to find the optimum solution is as follows:

V_{gg} has given the search space from $-120mV$ to $-40mV$, V_{sg} has given a search space from $-1mV$ to $5mV$, g_{gg} and g_{sg} has given search spaces from $0 nS/\mu m^2$ to $5 nS/\mu m^2$.

IV. RESULTS AND DISCUSSION

To optimize the discharge patterns obtained for a primate suffering from PD, we generated the discharge patterns for PD primate and compared the discharge patterns with the discharge patterns of a healthy primate for a time span of 250 msec.

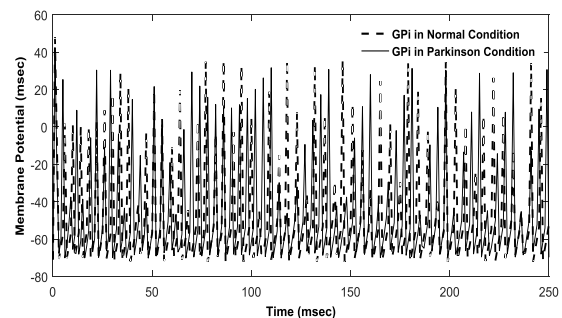


Fig. 2 Discharge Patterns for internal globus pallidus in normal and Parkinson condition primate.

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The time span is considered for 250 msec due to machine and processor constraints. The larger time span can be considered to analyze the parameters in the future research. In Fig. 2, lag in the discharge patterns for a PD primate is clearly visible when compared to that of a healthy primate. After the analysis, it was revealed that the model of internal globus pallidus is significantly sensitive to the four parameters among all the parameters used in the model. These parameters are: membrane potential from GPe to GPi (denoted by V_{gg}), membrane potential from STN to GPi (denoted by V_{sg}), synaptic conductance from GPe to GPi (denoted by g_{gg}) and synaptic conductance from STN to GPi (denoted by g_{sg}). These parameters have been optimized simultaneously using particle swarm optimization algorithm. The optimality of these parameters has been validated by taking correlation coefficient (CC) between the discharge patterns of the two primates taken into consideration. Correlation coefficient generally describes the likeness of the two patterns. If the value of correlation coefficient is close to 1, the two patterns compared are overlapping each other with a very high degree of similarity. The value of correlation coefficient obtained in this case is 0.9993 which is very close to 1 computed over different time spans up to 300 msec. The results obtained after simulations are as follows:

a) For a time span of 100 msec

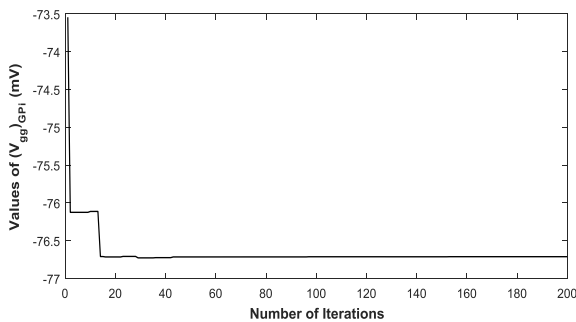


Fig. 3(a) Variation in the values of V_{gg} for 200 iterations of PSO algorithm for 100 msec.

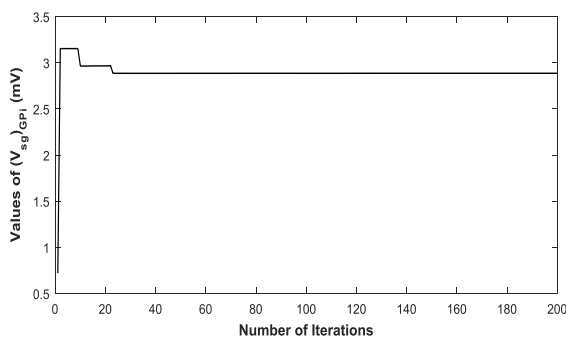


Fig. 3(b) Variation in the values of V_{sg} for 200 iterations of PSO algorithm for 100 msec.

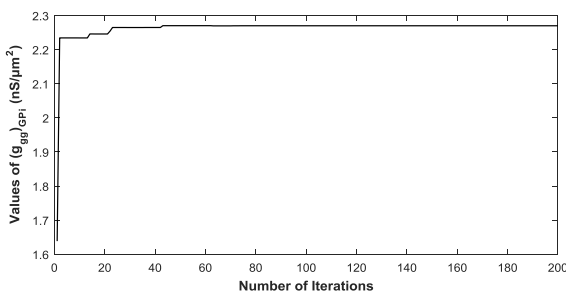


Fig. 3(c) Variation in the values of g_{gg} for 200 iterations of PSO algorithm for 100 msec.

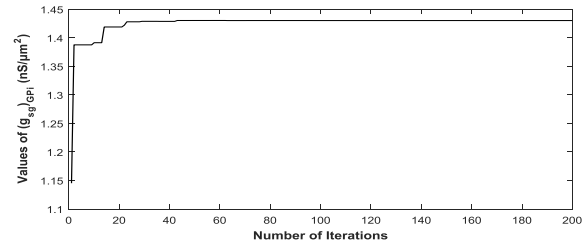


Fig. 3(d) Variation in the values of g_{sg} for 200 iterations of PSO algorithm for 100 msec.

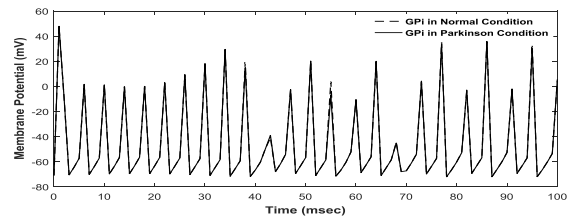


Fig. 3(e) Discharge pattern for 100 msec for optimized values of V_{gg} , V_{sg} , g_{gg} and g_{sg} .

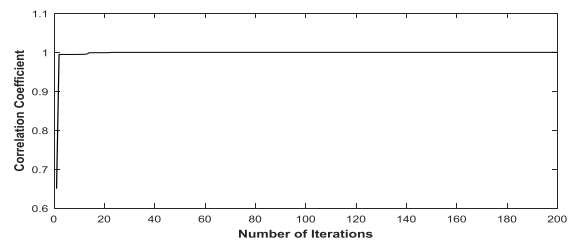


Fig. 3(f) Correlation coefficient for 200 iterations of PSO algorithm for 100 msec.

The optimized values obtained for $(V_{gg})_{GPi}$, $(V_{sg})_{GPi}$, $(g_{gg})_{GPi}$ and $(g_{sg})_{GPi}$ are -76.7110 mV, 2.8857 mV, 2.2700 nS/ μm^2 and 1.4303 nS/ μm^2 respectively. We have considered 200 generation/ iterations and variation of these parameter in these 200 iterations are depicted in Fig.3(a)-3(d). These optimum values when substituted in the model of internal globus pallidus of a PD primate to generate the discharge patterns, which give highly overlap pattern with a healthy primate as shown in Fig.3(e). Also, Correlation coefficient between the two discharge patterns is calculated generation wise as shown in Fig.3(f). Value of Correlation coefficient is reaching to 0.9999 after 25 iteration.

b) For a time span of 200 msec

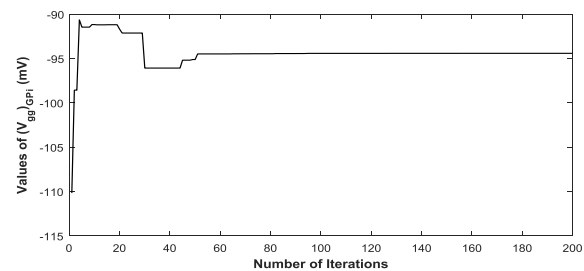


Fig. 4(a) Variation in the values of V_{gg} for 200 iterations of PSO algorithm for 200 msec

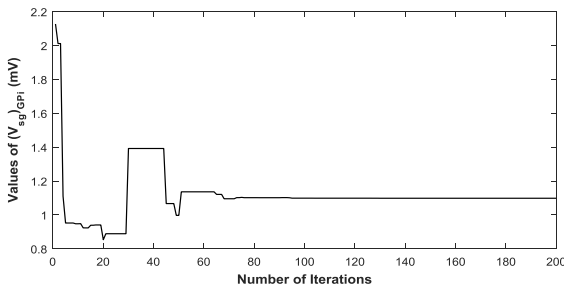


Fig. 4(b) Variation in the values of V_{sg} for 200 iterations of PSOalgorithm for 200 msec

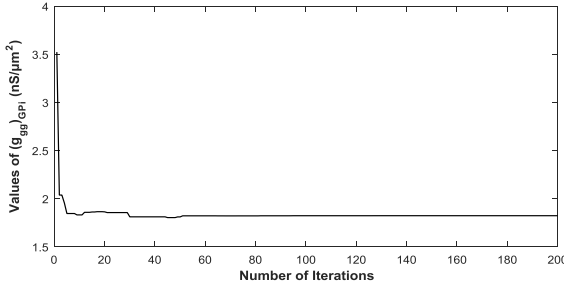


Fig. 4(c) Variation in the values of g_{gg} for 200 iterations of PSOalgorithm for 200 msec

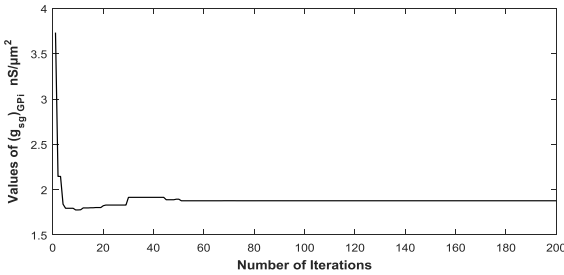


Fig. 4(d) Variation in the values of g_{sg} for 200 iterations of PSOalgorithm for 200 msec

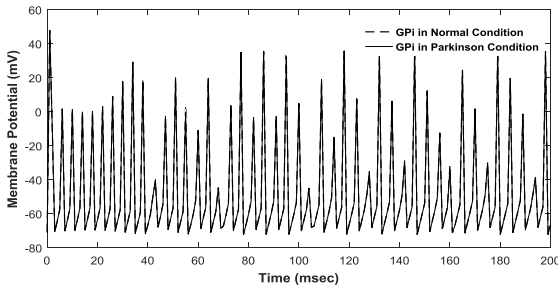


Fig. 4(e) Discharge pattern for 200 msec for optimized values of V_{gg} , V_{sg} , g_{gg} and g_{sg}

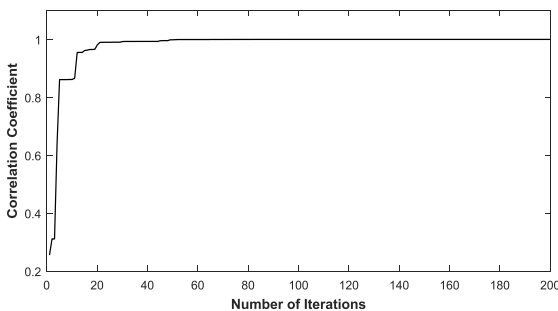


Fig. 4(f) Correlation coefficient for 200 iterations of PSO algorithm for 200 msec.

From the Fig. 4(a)-4(d), the optimum value of membrane potential from GPe to GPi (denoted by V_{gg}) is -94.4065 mV, for membrane potential from STN to GPi (denoted by

V_{sg}) is 1.0984 mV, for synaptic conductance from GPe to GPi (denoted by g_{gg}) is 1.8225 nS/ μm^2 and for synaptic conductance from STN to GPi (denoted by g_{sg}) is 1.8774 nS/ μm^2 . Figure 4(e) is validating the accuracy of optimum values of parameters as the two discharge patterns are showing a very high degree of overlap and Fig. 3(f) is showing that correlation coefficient is attaining a value 0.99999 after 45 generation.

c) For a time span of 300 msec

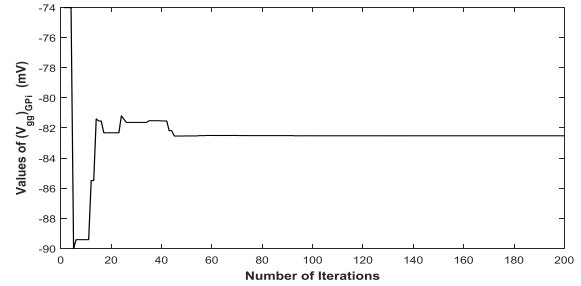


Fig. 5(a) Variation in the values of V_{gg} for 200 iterations of PSOalgorithm for 300 msec

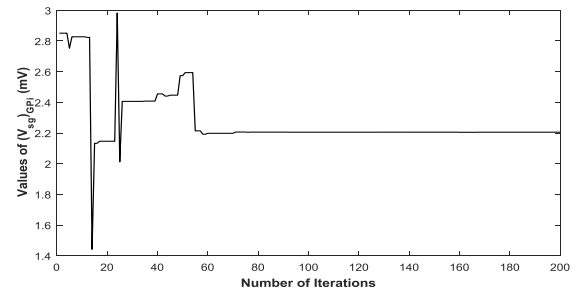


Fig. 5(b) Variation in the values of V_{sg} for 200 iterations of PSOalgorithm for 300 msec

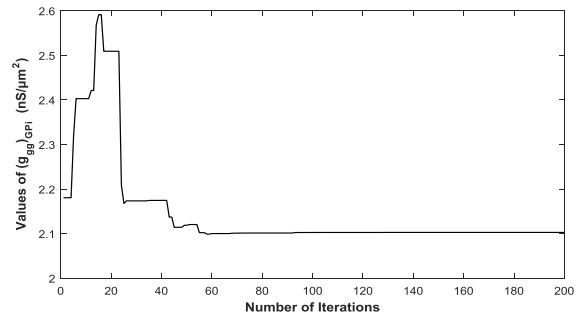


Fig. 5(c) Variation in the values of g_{gg} for 200 iterations of PSOalgorithm for 300 msec

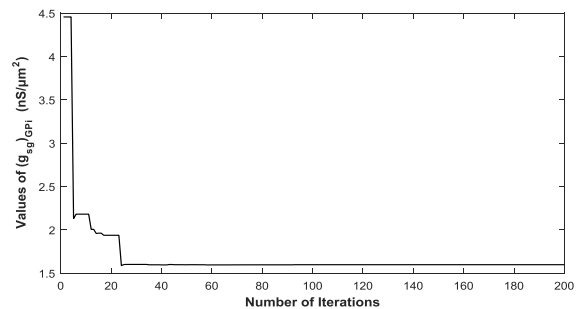


Fig. 5(d) Variation in the values of g_{sg} for 200 iterations of PSOalgorithm for 300 msec

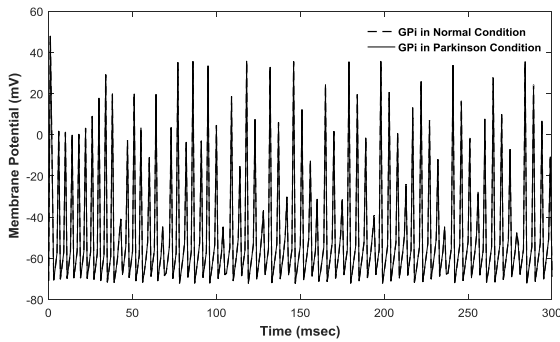


Fig. 5(e) Discharge pattern for 300 msec for optimized values of V_{gg} , V_{sg} , g_{gg} and g_{sg}

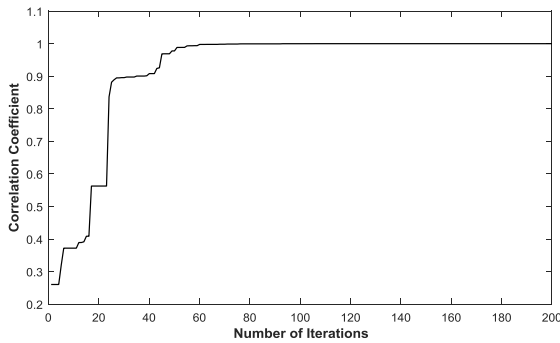


Fig. 5(f) Correlation coefficient for 200 iterations of PSO algorithm for 300 msec

From the Fig. 5(a)-5(d), the optimum value of membrane potential from GPe to GPi (denoted by V_{gg}) is -82.5222 mV, for membrane potential from STN to GPi (denoted by V_{sg}) is 2.1026 mV, for synaptic conductance from GPe to GPi (denoted by g_{gg}) is 2.1026 nS/ μm^2 and for synaptic conductance from STN to GPi (denoted by g_{sg}) is 1.5972 nS/ μm^2 . Figure 4(e) is validating the accuracy of optimum values of parameters as the two patterns are overlapping to a very high degree and figure 3(f) is showing that correlation coefficient is attaining a value 0.99998. The simulation can be done for the larger time span but due to the lab constraints of machine and processor, only time span up to 300 msec has been considered. Results show that the PSO algorithm optimizes the parameters in PD primates discharge pattern and mimic them to discharge pattern of a healthy primate. These results may be utilized in developing medicine for Parkinson disease.

V. CONCLUSIONS

In this study, particle swarm optimization algorithm has been implemented to get the optimized values of four parameters of internal globus pallidus model of basal ganglia to which the discharge patterns are considerably sensitive for a primate suffering with Parkinson disease. PSO algorithm has been used for the first time to optimize the parameters in such a model and for discharge patterns of a Parkinson disease primate. The optimized values of the parameters have been validated by using correlation coefficient between the discharge patterns of a healthy primate and a primate suffering from Parkinson disease for a time span of 300 msec. Results obtained by this approach show a significant improvement over the results reported in a recent study by Singh *et al.* [26] taken over the time span of 250 msec where

the value of correlation coefficient obtained was 0.92 as compared to 0.9999 in our study for a time span of 300 msec. With the availability of high speed computational power, this algorithm can provide the optimized values of parameters over a larger time span of 1000 msec or more. That may be a possible interest for researchers to identify the parameters from the model and optimize them for a large time span to get improved discharge patterns for PD primate.

APPENDIX

In this section, we define all the parameters used in the paper along with their units as follows:

$g_l = 0.1$ nS/ μm^2	$g_k = 45$ nS/ μm^2	$g_{sg} = 2$ nS/ μm^2 (for healthy primate)
$g_T = 1.7$ nS/ μm^2	$g_{Ca} = 0.15$ nS/ μm^2	$g_{APH} = 30$ nS/ μm^2
$g_{gg} = 0.9$ nS/ μm^2 (for healthy primate)	$V_l = -55$ mV	$V_k = -80$ mV
$V_{Na} = 55$ mV	$V_{Ca} = 120$ mV	$V_{gg} = -100$ mV
$V_{sg} = 0$ mV	$\tau_n^1 = 0.27$ msec	$\tau_h^1 = 0.27$ msec
$\tau_r^1 = 17.5$ msec	$\tau_n^0 = 0.05$ msec	$\tau_h^0 = 0.05$ msec
$\tau_r^0 = 40$ msec	$\phi_n = 0.1$	$\phi_h = 0.05$
$\phi_r = 1$	$k_{Ca} = 20$	$k_1 = 30$
$\theta_n = -50$	$\theta_m = -37$	$\theta_h = -58$
$\theta_r = -70$	$\theta_a = -57$	$\theta_b = 0$
$\theta_s = -35$	$\theta_n^\tau = -40$	$\theta_h^\tau = -41$
$\theta_r^\tau = -84$	$\theta_g^H = -57$	$\theta_g = 20$
$\sigma_n = 14$	$\sigma_m = 10$	$\sigma_h = -12$
$\sigma_r = -2$	$\sigma_a = 2$	$\sigma_b = -0.1$
$\sigma_s = 2$	$\sigma_n^\tau = -12$	$\sigma_h^\tau = -4$
$\sigma_r^\tau = -2.2$	$\sigma_g^H = 8$	$\epsilon = 1$ $\times 10^{-4}$ m/sec
$\alpha = 2$ m/sec	$\beta = 0.08$ m/sec	$w = 0.8$
$C_m = 1$	$c_p = 1.4$	$c_g = 2$

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Particle Swarm Optimization Algorithm to Optimize the Activity Patterns of Internal Globus Pallidus in Parkinson Disease



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