Parkinson's Resting Tremors: A NetLogo-Based Neural Simulation of Dopamine and DBS

Pragya Goyal

pragyathehuman@gmail.com

***Abstract*—This paper visualises the neural activity during resting tremors and the effects of different treatments using a custom-built agent-based simulation in NetLogo to model a simplified neural resting oscillator.**
Among other symptoms of Parkinson's Disease, this study focuses on Parkinsonian Resting Tremors and investigates two treatments namely Deep Brain Stimulator and an Automatic Dopamine Dosage. Among other compounds effecting tremors, this study looks at dopamine levels as a primary factor for the frequency of tremors. It analyses the effects of treatments when various parameters are changed to observe the efficiency of both the treatments.
The simulation demonstrates that Deep Brain Stimulation (DBS) is significantly more effective at suppressing Parkinsonian tremors when applied to the thalamic region compared to the cortical region. It also shows that increasing disease severity demands higher dopamine dosage frequency and quantity, with diminishing effectiveness at later stages.*

***Keywords*—Parkinson's Disease, Resting Tremors, Deep Brain Stimulation (DBS), Dopamine Therapy, Neural Oscillations**

I. Introduction

Parkinson's Disease is a neurodegenerative disease, which affects the motor activities due to the degeneration of dopamine-producing neurons. The symptoms for this disease can be noted as Bradykinesia, rigidity and resting tremors. These motor symptoms are linked to dysfunction in the basal ganglia—a group of subcortical nuclei responsible for initiating and regulating voluntary movement. Low dopamine levels in the body cause resting tremors in patients. These tremors range between 4-6Hz in frequency. Currently, two of the treatments that temporarily improve the health of patients are Dopamine Dosages and Deep Brain Stimulator.

Dopamine dosage increases synaptic dopamine levels, which helps restore balance in the motor circuits and reduces abnormal neural oscillations. This results in temporary suppression of tremors and improved motor control. **Deep Brain Stimulation (DBS)**, on the other hand, involves the surgical implantation of electrodes into deep brain regions such as the **subthalamic nucleus** or **globus pallidus internus**. These electrodes deliver high-frequency electrical impulses, usually ranging from 130-180Hz, that modulate abnormal neuronal activity and stabilize motor output.

While both therapies offer symptomatic relief, they do not reverse the disease. Additionally, their effectiveness is not constant throughout all conditions. This research aims to model Parkinsonian tremors and investigate the differential effectiveness of dopamine therapy and DBS in disrupting the underlying oscillatory circuits responsible for these tremors.

II. Neural circuit background

A. Neurons

Neurons in each group have a specific resting potential threshold which is between the range of -70mV to -60mV. The neurons fire an action potential if and only if the sum of the voltages of the inputs is greater than the threshold. If the sum of the input voltages is greater than the threshold, the neuron can either send an excitatory signal or an inhibitory signal. Excitatory signals increase the likelihood of the receiving neuron firing by depolarizing the neuron's membrane potential and bringing it closer to the threshold. The neurotransmitter glutamate is the most common excitatory transmitter in the brain. Inhibitory signals, on the other hand, hyperpolarize the membrane potential, making it less likely for the neuron to fire. The primary inhibitory neurotransmitter is GABA (gamma-aminobutyric acid).

B. Motor signalling in healthy brain and Parkinsonian Brain

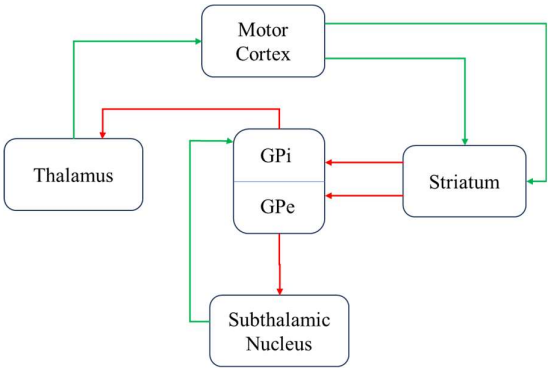


Figure 1: Diagram of the Basal Ganglia

The region of the brain that controls movement functions is collectively known as the Basal Ganglia.

The direct and indirect pathway are the two principal routes through which the basal ganglia influence movement. Both pathways originate from the Striatum, which receives excitatory input from the Motor Cortex and modulatory input from dopaminergic neurons in the Substantia Nigra Pars Compacta (SNr).

The Striatum sends inhibitory signals to the Globus Pallidus Internus (GPi) and the SNr. The GPi and SNr normally inhibit the Thalamus, so when they are themselves inhibited, this disinhibits the Thalamus. The thalamus becomes more active and sends excitatory input back to the motor cortex, promoting movement. This is the direct pathway. Dopamine acts on the direct pathway receptors in the striatum to enhance this pathway making it more likely to facilitate movement.

For the indirect pathway, the Striatum sends inhibitory signals to the globus pallidus externus (GPe). The GPe normally inhibits the subthalamic nucleus (STN). When the GPe is inhibited, the STN becomes disinhibited. The STN sends excitatory input to the GPi and SNr. This increases their inhibitory output to the thalamus. Increased inhibition of the thalamus results in reduced motor cortex stimulator, thereby suppressing movement. Dopamine acts on the indirect pathway in the Striatum to inhibit the indirect pathway, thus reducing its suppressive effect on movement.

In Parkinson's Disease, dopaminergic neurons in the SNc degenerate, leading to reduced dopamine levels in the Striatum. This causes a reduced activation of the direct pathway. It further leads to an increased activity of the indirect pathway. The net result is excessive inhibition of the thalamus.

For this paper, it has been simplified to the Motor Cortex, Thalamus and Dopaminergic Neuron (not shown in the model).

In a health brain, the Motor cortex sends inhibitory signals to the Thalamus. The Dopaminergic Neuron simultaneously sends inhibitory signals to the Thalamus as well. This inhibition signal inhibits the previous signal. Since no inhibition signal is being sent to the Thalamus, the thalamus is excited. It then sends excitatory signals to the Motor Cortex which further excites muscles. In the case of a Parkinsonian patient, the dopaminergic neuron dysfunctions resulting in excessing inhibition of the Thalamus and thus restricting motor signals and impairing movement.

III. Methodology

In this study, the severity of the disease is measure by the rate at which the dopamine decreases. Additionally, the dopamine level is relative to the dopamine level present in a healthy brain. The dopamine level in a healthy brain, in this model, is taken to be 100.

A. Agents

The turtles, the moving components, of this study are deep brain stimulator electrodes. Although, by concept they are turtles, it should be noted that they are merely a switch and not the central agents of the model The patches, non-moving components, of this study are the neurons and muscles. The model includes the thalamic neuron (Neuron 5), 4 cortical neuron (Neuron 1 – 4) and an α neuron (Neuron 0).

B. Parameters

Disease-Severity: A slider which changes the severity of the disease.
Dosage-Size: A slider which changes the size of dosage of dopamine given
Automatic-dopamine-dosage: A switch which switches the dopamine dosage treatment on and off
Dopamine-freq: A slider which changes the frequency at which the dopamine dosages are given

DBS-thalamic: A switch which injects the electrode in the thalamic neuron at frequencies determined through the DBS-freq when switched on

DBS-cortical: A switch which injects the electrode in a cortical neuron at frequencies determined through the DBS-freq when switched on

DBS-freq: A slider which changes the frequency at which the stimulator electrodes are injected

C. Our Model

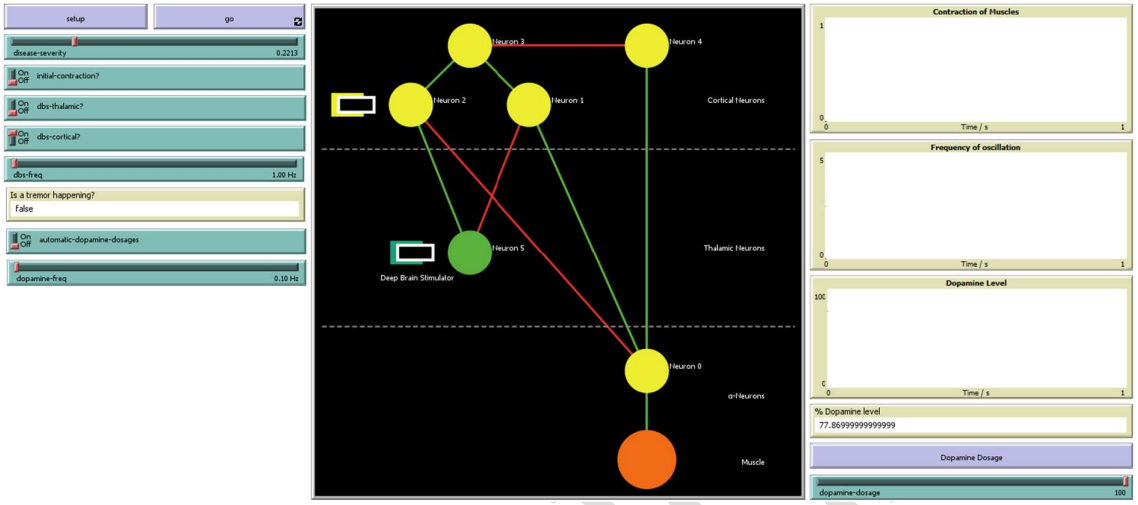


Figure 2: Initial NetLogo setup window of the model

This model offers an illustrative simulation of Parkinson's disease (PD), using an oscillatory neural network to represent the characteristic resting tremors observed in patients. It highlights how interventions such as dopamine supplementation and deep brain stimulation (DBS) can reduce tremor frequency by stabilizing neural activity in the motor cortex.

The cortical neurons, represented in yellow, activate in a rhythmic sequence, each influencing the next in a loop. Within this network, two units behave in a mutually exclusive manner, acting like a toggle switch between competing outputs. This reciprocal pattern produces a self-sustained oscillation, generating tremor-like activity, even in the absence of dopamine or external inputs.

The thalamic neuron, shown in green, plays an inhibitory role. When dopamine levels are sufficient, it actively suppresses cortical oscillations, preventing excessive or involuntary movement. In conditions where dopamine is deficient, as seen in Parkinson's disease, the thalamic neuron fails to fire effectively, which allows the cortical circuit to oscillate freely and produce tremor-like activity.

This model supports interactive experimentation with dopamine dosage, which boosts thalamic inhibition, and the DBS, which can override or modulate neural firing

The cortical neurons along with alpha neuron oscillate due to mutual excitation and inhibition, allowing a balanced circuit. Neurons 0 to 4 form a loop that generates rhythmic activity. Neuron 0 fires when it receives input from neuron 4, which becomes active when neuron 3 is inactive. Neuron 3 receives input from both neuron 1 and neuron 2, and becomes active if either of them is firing. Neurons 1 and 2 act like a switch. Their activity depends on the earlier firing of neuron 0 and on whether the thalamic neuron, neuron 5, is active. This switching behaviour creates an alternating pattern that drives the circuit.

The thalamic neuron (neuron 5) becomes active when dopamine levels are sufficiently high. Once active, it decreases the input to neuron 1 while increasing the input to neuron 2. This change alters the balance between the two neurons, interfering with their usual alternation. Since this alternating pattern is crucial for sustaining the rhythmic activity of the cortical loop formed by neurons 0 to 4, the thalamic influence effectively disrupts the oscillation and helps stabilize the system.

When the dopamine levels fall below 95% there is a chance that the oscillations start. The thalamic neuron receives excess inhibition at this stage causing oscillation which is visualised through a pulsing muscle agent. As the dopamine levels drop, the frequency of the oscillations increases. When the dopamine levels are below 55%, the oscillations are continuous.

Dopamine can be added using a button (Indicated by the DOPAMINE-LEVEL) that increases the input voltage to the thalamic neuron, making it more likely to fire. The combined effect of the added dopamine and a random noise term helps the thalamic neuron reach the firing threshold.

Deep Brain Stimulation (DBS) can drive the thalamic neuron to fire at a frequency set by DBS-FREQ, regardless of dopamine levels, thereby suppressing the oscillatory activity that produces tremors. Additionally, DBS can directly stimulate neuron 2 within the cortical circuit. This direct activation disrupts the normal switching pattern between neurons 1 and 2, tipping the balance of the oscillator and further reducing the tremor-like rhythmic activity.

Dopamine is added to the system (indicated by the dopamine level at the synaptic scale or DOPAMINE-LEVEL) when automatic-dopamine-dosages is activated at a certain frequency (DOPAMINE-FREQ) by a certain amount (DOSAGE-SIZE).

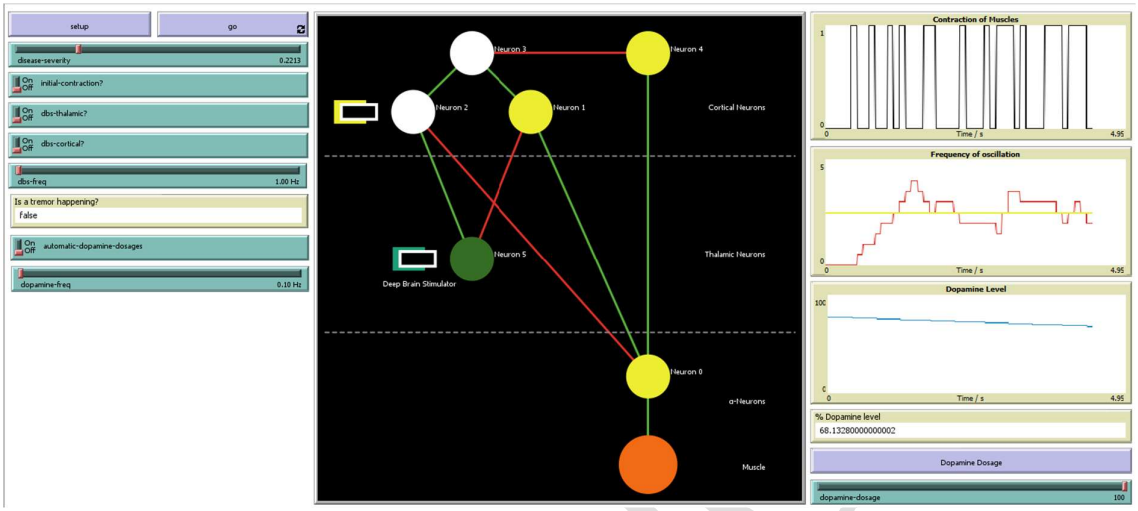


Figure 3: NetLogo window after the model has been run

The muscle contraction plot displays a periodic oscillating curve, representing tremors through the continuous contraction and relaxation of the muscle in response to neural activity. Another plot shows the frequency of oscillations, which increases as dopamine levels decrease, and decreases as dopamine is replenished. A yellow reference line, parallel to the x-axis, marks the threshold for normal oscillatory frequency. Oscillations above this line are classified as Parkinsonian tremors.

D. Relevant Extracts from the Netlogo Code

```
 ;calculating frequency
set muscle-contraction-list (list 0 0 0 0 0 0 0 0 0 0) ;; 1 if the muscle is contracting in this cycle, 0 otherwise
set muscle-osc-list (list 0 0 0 0 0 0 0 0 0 0) ;; 0.5 if the muscle has changed state from contracted to relaxed, 0 otherwise
set cycles 0 ;; 1 cycle = 8 ticks, 1 second = 10 cycles
set frequency 0 ;; sum of the values in the muscle-osc-list
 ;calculating frequency ends
reset-ticks
label-neurons
```

```
;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;
;;; asking each neuron to receive inputs from the neurons they're connected to and fire if the sum is greater than the threshold ;;;
;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;
ask neuron 1 [
  set current-voltage (4 * [firing-number] of neuron 0) + (4 * (1 - [firing-number] of neuron 5))
  ifelse current-voltage > 7 [fire][set firing-number 0 set color yellow]
]
update-tick
ask neuron 2 [
  set current-voltage (4 * (1 - [firing-number] of neuron 0)) + (4 * [firing-number] of neuron 5)
  ifelse current-voltage > 7 [fire][set firing-number 0 set color yellow]
]
update-tick
ask neuron 3 [
  set current-voltage (4 * [firing-number] of neuron 1) + (4 * [firing-number] of neuron 2)
  ifelse current-voltage > 3 [fire][set firing-number 0 set color yellow]
]
update-tick
ask neuron 4 [
  set current-voltage 8 * (1 - [firing-number] of neuron 3)
  ifelse current-voltage > 7 [fire][set firing-number 0 set color yellow]
]
update-tick
update-tick
update-tick
update-tick
if dopamine-level - disease-severity >= 0 [set dopamine-level dopamine-level - disease-severity] ;; decreasing the dopamine level based on the disease severity
set frequency sum muscle-osc-list
ask neuron 5 [
  set current-voltage (dopamine-level / 5) - 4 + (random 8000) / 1000
  ifelse current-voltage >= 15 [set firing-number 1][set firing-number 0]
   ;;firing the DBS if it is activated and time to fire
   ifelse dbs-thalamic? and (cycles mod dbs-time-period) < 0.0001 [set firing-number 1 ask patch -8 0 [set pcolor yellow]][ask patch -8 0 [set pcolor black]]
   ifelse firing-number = 1 [set color green + 2][set color green - 2]
]
ask neuron 0 [
  set current-voltage 8 * [firing-number] of neuron 4
   ifelse current-voltage > 7 [fire ask turtle 6 [set size 2]][set firing-number 0 set color yellow ask turtle 6 [set size 4]]
]

to fire ;;turtle procedure
 set color white ;;visuals
 set firing-number 1
end

to update-tick ;;tick updating procedure
  tick
  ask neurons [set current-voltage current-voltage - 1]
  set cycles ticks / 8
  ;; firing the DBS in each brain region
  ifelse dbs-thalamic? and precision (cycles mod dbs-time-period) 5 < dbs-time-period / 8 [
    ask neuron 5 [set firing-number 1]
    ask patch -8 0 [set pcolor yellow]
  ][
    ask patch -8 0 [set pcolor black]
  ]
  ifelse dbs-cortical? and precision ((cycles - 0.25) mod dbs-time-period) 5 < dbs-time-period / 8 [
    ask neuron 2 [fire]
    ask patch -12 10 [set pcolor yellow]
  ][
    ask patch -12 10 [set pcolor black]
  ]
  ;; Adding dopamine to the brain if automatic-dopamine-dosages is activated and it is time to add dopamine.
  if automatic-dopamine-dosages and precision (cycles mod dopamine-time-period) 5 < 0.0125 [add-dopamine]
end

to add-dopamine
  ifelse dopamine-level <= 100 - dopamine-dosage [set dopamine-level dopamine-level + dopamine-dosage][set dopamine-level 100]
end
```

IV. Experiments and Observations

A. Which region of the brain when connected to the deep brain stimulator will be most effective?

Two electrodes were placed, each in a different location. One was connected to the thalamic neuron and the other connected to the cortical neuron. Each electrode was activated one at a time. 17 frequencies of oscillation were extracted and the effects of the stimulators were observed. It was observed that out of the 17 data points, 15 frequencies were subdued more effectively when they were connected to the thalamic neuron.

B. How does the severity of the disease affect the minimum frequency at which a DBS should run to control tremors?

The severity of the disease was changed with intervals of 0.1 from 0 to 1, 0 being a low severity and 1 being the highest severity. The minimum frequency at which the stimulator should run to subdue the tremors was observed to be 5Hz, which remained constant throughout all the severity of diseases.

C. How does the severity of the disease affect the minimum frequency at which an automatic dopamine dispenser should run to control tremors?

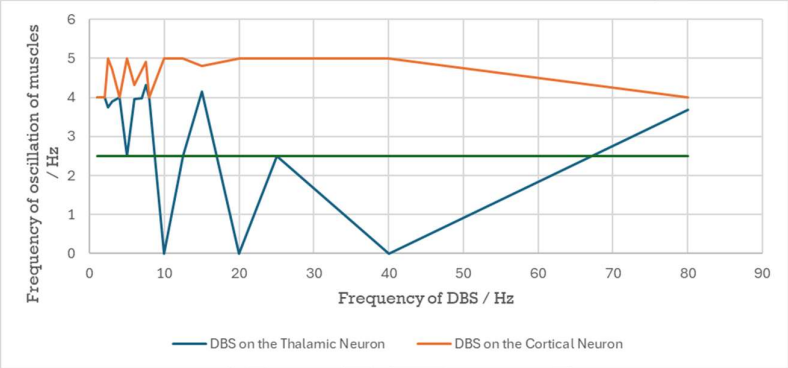
The severity of the disease was changed with intervals of 0.1 from 0 to 1, 0 being a low severity and 1 being the highest severity. The minimum frequency at which the dosages should be given to subdue the tremors was observed to have a positive correlation with the severity of the disease. For this experiment, the size of the dosage was kept constant at 20 units.

D. Given a certain frequency of the automatic dopamine dispenser, how does the severity of the disease affect the minimum required size of a dopamine dosage to control tremors?

The severity of the disease was changed with intervals of 0.1 from 0 to 1, 0 being a low severity and 1 being the highest severity. The minimum dosage size required for the dopamine dosage to subdue the tremors was observed to have a positive correlation with the severity of the disease until some point. For this experiment, the frequency of the dosage was kept constant at 0.1Hz.

V. Results

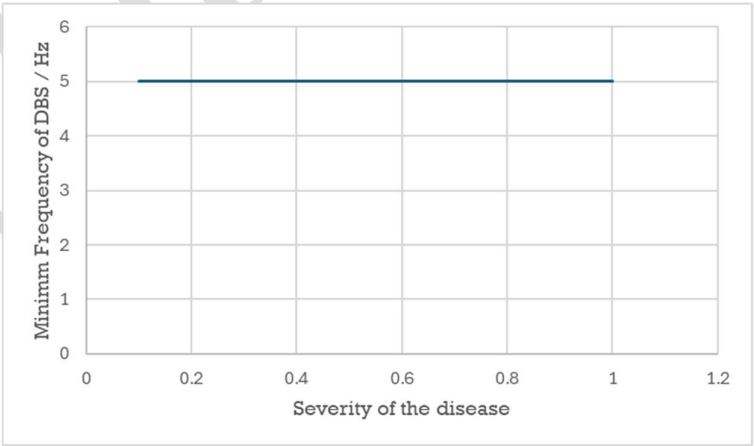
A. Which region of the brain when connected to the deep brain stimulator will be most effective?



Graph 1: Effect of Deep Brain Stimulator, connected in different regions of the brain, on oscillations

The frequency of the oscillations after the electrode is connected should be as low as possible or close to the green line which is the frequency of the oscillation which is considered normal. For most of the points, the line for the DBS on the Thalamic Neuron was below the green line indicating that the Parkinsonian tremors were subdued. The line for the DBS on the Cortical Neuron, on the other hand, remained above the green line all throughout. This indicates that the tremors were not subdued.

B. How does the severity of the disease affect the minimum frequency at which a DBS should run to control tremors?

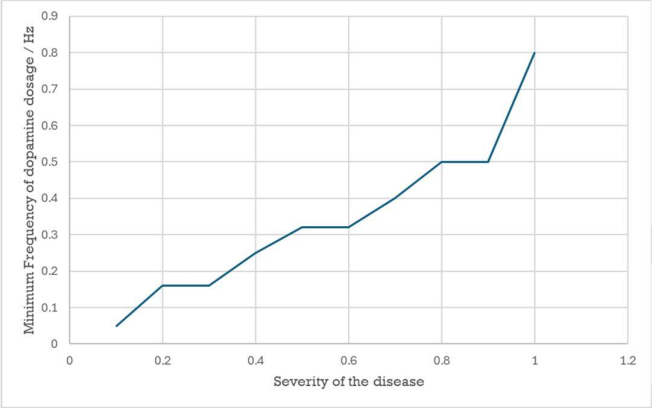


Graph 2: Minimum frequency of Deep Brain Stimulator Required for varying disease severity

The minimum frequency of the stimulator required to subdue the oscillations remained constant regardless of the severity of the disease.

The minimum required frequency of stimulation was consistently 5Hz, which aligns with the characteristic frequency of Parkinsonian tremors.

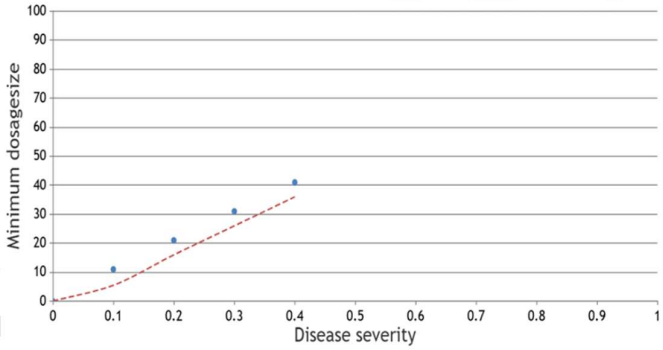
C. How does the severity of the disease affect the minimum frequency at which an automatic dopamine dispenser should run to control tremors?



Graph 3: Minimum frequency of dopamine dosage required for varying disease severity

The minimum frequency of dosages required increased as the severity of the disease increased depicting a positive correlation between the two.

D. Given a certain frequency of the automatic dopamine dispenser, how does the severity of the disease affect the minimum required size of a dopamine dosage to control tremors?



Graph 4: Minimum dopamine dosage size required for varying disease severity

The minimum dosage size continuously increases as the disease severity increases. However, it becomes completely ineffective after the severity of the disease has reached a certain point which for this study is 0.4.

VI. Discussion

A. Which region of the brain when connected to the deep brain stimulator will be most effective?

For the deep brain stimulator to work effectively, it must be connected deep into the brain where the abnormal neural activities are originating from. The stimulator would only be effective when connected to the thalamic region and not when it is connected to an outer region such as the cortex. Thalamic stimulation disrupts the oscillatory circuit more effectively because it directly targets the thalamic neuron, a central node in the feedback loop. By altering its firing behavior, the stimulation breaks the rhythm of alternating activity between the thalamus and cortex, effectively stopping tremor-like output. In contrast, cortical DBS targets only a single neuron, resulting in a comparatively weaker dampening effect. Additionally, connecting it to the cortical neuron is not interrupting the abnormal oscillatory loops that originate deeper inside the brain and thus when it is connected, the abnormal pattern has already been performed.

B. How does the severity of the disease affect the minimum frequency at which a DBS should run to control tremors?

The disease severity has little to no effect on the minimum frequency required at which the stimulator can control the oscillations. A patient suffering from a higher severity may respond to the same frequency of the stimulator in a similar manner as would a patient suffering from a lower severity of the disease.

C. How does the severity of the disease affect the minimum frequency at which an automatic dopamine dispenser should run to control tremors?

In this study, the severity of the disease is defined by the rate of depletion of dopamine levels. To maintain the dopamine levels, the automatic dopamine dispenser must also increase in frequency. For it to have an effect on the tremors, the frequency of the dosages must be more that the rate at which the dopamine levels are depleting. In the real-world, high severity of the disease causes the neurons to continuously degenerate and the ability of the brain to store and regulate dopamine declines. This leads to faster drops in the dopamine levels and consequently patients need more frequent dopamine dosages.

D. Given a certain frequency of the automatic dopamine dispenser, how does the severity of the disease affect the minimum required size of a dopamine dosage to control tremors?

In early to intermediate stages of Parkinson's Disease, the frequency of the automatic dopamine dosage requirements increases as the severity of the disease increase. However, in advanced stages of Parkinson's Disease, dopamine dosages become less effective regardless of dosage size. This occurs because the degeneration of dopaminergic neurons reaches a critical point where the brain can no longer store, regulate, or respond adequately to exogenous dopamine.

VII. Limitation of the Model

It is to be noted that in the simulation, the muscle patch receives signals only when the dopamine is below 95% and starts pulsating visualising tremors. This is not the case in the real world. Low dopamine levels disrupt the basal ganglia-thalamocortical circuitry, resulting in abnormal rhythmic signals that cause involuntary tremors. When the dopamine levels are adequate, the oscillations are suppressed and the muscle ceases involuntary tremors. Unlike the model however, the signals sent to the muscle do not stop. The muscle still receives commands for voluntary movements.

The resting potential thresholds and the weights given to each neuron are purely arbitrary which may lead to a few technical inaccuracies concerning neuron firing.

VIII. Extensions & Future Work

A. Adding Circadian Rhythm for Treatments

Both dopamine therapy and Deep Brain Stimulation show variations in effectiveness across the circadian cycle. Addition of the circadian cycle can improve the understanding of when the treatments are most effective or alternatively, which treatment is more effective at a certain time of the day.

B. Adding Voluntary Movements

We previously discussed how unlike what is shown in our model, when the dopamine levels in the body are adequate, the muscles still receive signals for voluntary movements. Our model does not include voluntary movements. Adding it would not only make it scientifically more accurate but also help in understanding the other effects Parkinson's Disease has on movement such as Bradykinesia which is related to voluntary movements.

C. Elasticity of the Muscle

Rigidity is another prominent symptom of Parkinson's Disease. It can also significantly influence the amplitude of tremors. In highly rigid muscles, the resistance to oscillatory movement may decrease the visible amplitude of tremors, even though the underlying neural oscillations persist. This interaction suggests that tremor expression is not solely a function of neural activity but can also be affected by the properties of the muscle.

D. Simulating Death of Neuron

In cases of high severity of the disease, some neurons start to die. This has not been included in our model. Simulating neuron death allows the model to reflect the progressive and irreversible nature of Parkinson's Disease. Unlike temporary dopamine depletion, neuronal death leads to a structural loss of function, limiting the effectiveness of treatments over time.

E. *Adding α – synucleate*

In this study, dopamine levels are taken as a sole cause of the disease and its severity. Another compound which actively causes Parkinson's Disease is the α – synucleate. The accumulation and aggregation of this protein are strongly associated with dopaminergic neuron death. Modelling its progressive buildup will allow for a more detailed representation of disease progression.

F. *Thresholds and Weights*

An important extension that could be made to this model to make it more accurate would be taking realistic resting potential thresholds and weights for each neuron

IX. Conclusion

This study presents a simplified agent-based model to simulate the neural mechanisms behind Parkinsonian resting tremors and analyse the relative effectiveness of two common treatments: dopamine therapy and Deep Brain Stimulation (DBS). By visualizing how oscillatory circuits in the motor cortex behave under varying dopamine levels and external stimuli, the model demonstrates how pathological rhythmic activity emerges in Parkinson's Disease due to dopaminergic neuron dysfunction.

The results from the simulation clearly show that DBS is significantly more effective when targeted at the thalamic region, a central node in the feedback loop responsible for oscillatory activity. Cortical DBS, in contrast, fails to interrupt the circuit effectively due to its peripheral position in the neural loop. Additionally, dopamine therapy requires progressively higher frequency and dosage size as disease severity increases, up to a point beyond which dopamine becomes ineffective — mimicking real-world treatment resistance in advanced stages of Parkinson's.

The model also allows us to observe the effect of disease severity on treatment dynamics, offering insights into dosage tuning, target selection, and the limitations of current therapies. Although the model simplifies many aspects of Parkinson's pathology, including neuron thresholds, voluntary movement, and the effects of rigidity, it serves as a useful platform to explore neural behavior and treatment outcomes.

This work lays the foundation for future extensions that can incorporate circadian rhythm, neuron degeneration, α-synuclein aggregation, muscle rigidity, and more biologically accurate parameters. By refining and expanding the model, researchers can continue to bridge the gap between theoretical neuroscience and real-world treatment optimization for Parkinson's Disease.

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