

Explaining Dopamine Deficiency of Spiking Neurons Based on Quantum Superposition Theory

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ABSTRACT

In all mammalian brain billions of neurons exist and these neurons are working together through synapses and spike responses. Through numerous models presented to describe neuronal response and how the membrane potential would vary due to different tasks, still a big question stand still in the field of neuroscience. Why a neuron can produce different types of spikes under same conditions? Here we build up a new model of spiking neuron based on Izhikevich model which can generate all possible neuronal spikes and we try to answer this question by putting the concept of quantum superposition into account. We showed that unknown and random behavior of neuronal spikes through time can be described by this quantum fact that a neuron can be in many states at a same time, therefore any spike patterns or combination of spike patterns is of interest. Based on neuronal spikes patterns, sometimes we observed an unknown pattern can be explained by this phenomena that a neuron can exist partially in a physical state but when it's response to an stimuli is recorded the result would be only one of the possible states or a linear combination of some states.

Key Words: membrane potential, spiking neuron, stimuli, subthalamic nucleus neurons, quantum superposition

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1. Introduction

The biological phenomena in which the membrane potential of a cell would increase and thus a spike is observed has been studied in various ways in past (Costas *et al.*, 2012; Hramove, 2015). Neuron would produce a response with or without an external stimulus based on some ions velocity in its

membrane such as sodium and potassium (Alivisatos, 2012). These ions acts like currents, resulting a neuron to spike or block a neuron from spiking (Nepas *et al.*, 2012). Under some constraints a neuron would spike patterns that can be related to different tasks and are known as most relevant patterns of neuronal spiking (Conors and Gutnick, 1990). These patterns can be consisted of all bursting patterns such as tonic and phasic bursting, rebound burst and inhibition induced burst through simple responses such as tonic and phasic spikes, spike latency, resonator, integrator, threshold variability and accommodation spikes along with those well-known neuronal spikes called as class 1 and class 2 excitable (Ermentrout

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and Kopell, 1986). With all these really observed spiking patterns, comes some unknown patterns that the nature of its occurrence is still of great interests (Pratte, 2012).

Among mathematical models which tried to describe the process in which a neuron generates an spike some are totally inspired by biological facts in a cell (Lytton, 2002; Hindmarsh and Rose, 1989; Wilson 1999; Lathon *et al.*, 2000) while some more recent models try to address the functionality of a neuron by the actual responses that it produce and comparing these results to the real recordings of a neuron while spiking (Izhikevich, 2003; 2004). Although biologically inspired models obtain more details, their computational cost is higher than those who aims to produce the similar responses to real recordings without considering many chemical factors such as Na or K velocity of a cell (Kaiser, 2011). To investigate those spiking patterns which are not fully described by previous models we proposed a two dimensional ordinary differential equation (ODE) model based on Izhikevich model (Izhikevich, 2003). Due to hyperbolic nature of results of differential equations we built up our model based on a hyperbolic function that can generate all bursting patterns of a neuron along with most of different types of spikes.

We show how our model can also address some issues regarding abnormal neuronal responses via considering the quantum superposition fact. Quantum superposition clarifies a phenomena in which a particle can exist in many states simultaneously but while observing it will be only a particular state (Romero-Isart, 2010; 2011).based on linearity of Schrödinger equation (Muller, 2012) any results that satisfy the equation can be also used in a linear format as a new result. Therefore we can say that abnormal patterns of neuronal spike can be considered as a results of neuron being in a superposition system, hence it can be consisted of all possible spikes as different states at the same time while when we measure the response it will show one of the states or as we call one of the patterns. Due to superposition effect in our model we will discuss two abnormality in neuronal responses: first, in some cases a neuron will respond a well-known pattern and after a while it will switch to another pattern (Gillian, 2011). Secondly, sometimes the recording of a neuron spike shows abnormal pattern which can

be considered as a combination of already exist spikes in a multistate or superposition system (Custellanos and Proal, 2012). The first question can be explained by the fact that in a superposition system many states can exist at the same time so a neuron can produce different patterns as time goes by while for the second phenomena we can emphasize the fact that based on quantum superposition any linear combination of states can be a state or result itself, therefore some abnormal patterns of spiking can be considered as a combination of several patterns.

In section 2 we will review models proposed before to describe the spiking behavior of neurons. In section 3 we propose a new model to use of spiking neurons based on hyperbolic ordinary differential equations and we will show the numerical results of our model and how this model can generate different types of spikes. Also we explain how this model can be used in a superposition system to state the abnormality patterns and in section 4 we explain the significance of this model for further brain disorder description.

2. Neuronal Models

Most of the time we need to motivate a neuron with a stimuli which can be as simple as a dc current. Any changes in membrane potential of a cell to this input stimuli can be considered as a neuronal response. Based on the fact that in presense of ion channels in the cell membrane a spike can be generated, many investigation has been done considering the ion in the membrane of a cell as an important factor in their model. One of the most significant work in this area is the Hodgkin-Huxley model which defines a set of equation based activation and inactivation of Na current with activation of K currents (Lytton, 2002). Some recent models proposed models of spiking neurons witt attemp to reduce the number of parameters and basically by lowering the dimension of equations (Zhao *et al.*, 2014).

Another approach in modeling a neuron is the work done by group of researchers focusing on how their model can adjust to the real recordings of neuron while spiking (Izhikevich, 2003; Hindmarsh and Rose, 1984; Rulkov, 2002). One of the most realistic model that has been



proposed is by Izhikevich which can generate up to 20 of most relevant neuronal spikes with a low computational cost. In his model he used an extra equation responsible for giving a negative feedback to the membrane potential resulting more accurate and realistic spikes (Izhikevich, 2003).

The way brain processes information can be represented by quantum information theory (Accardi *et al.*, 2009; Hameroff, 1998; Khrennikov, 2006). Some works try to signify the decision making problem in brain using quantum information (Asano *et al.*, 2011). Another recently proposed model produces all probabilistic prediction of quantum mechanics based on a classical wave model (Khrennikov, 2009). A neuron in brain sometimes has an abnormal spiking patterns due to various set of disorders. This abnormality can be because of nonlinear complex phenomena in brain which has been described by quantum theory (Melkich, 2013). A significant approach of quantum computing in explaining brain activity is called quantum reduction (Bordonaro and Ogryzko, 2013). This idea can be implemented on mental information processing and further more describe mental issues. The idea of mathematical modeling of quantum information in brain has been proposed by many researchers (Pribran, 2014; Hameroff and Penrose, 1996; Markram, 2006). Mainly they explain an ability in brain by quantum like mental states or a mixture of quantum like mental states. In most of the works done before the main challenge is how a quantum information processing system is able to operate with superposition of states (Asano, 2011). In this paper we proposed a classical spiking neuron model that can generate most of the well known spiking behavior in brain, especially the bursting patterns, in order to use this model as a component in a quantum system. This quantum system investigate the quantum superposition theory to produce abnormal patterns of brain spikes.

3. Proposed Method

Based on the neuronal spiking patterns that have been discovered before, many models has been proposed. Here we model a brain neuron using an

extension over Izhikevich model. In his work, he described neuronal spiking patterns based on two ordinary differential equations that were in form of polynomial. Since most spiking abnormality occurring in brain follows a bursting behavior, we modify Izhikevich formulation to have more realistic bursting patterns. In our work we simply changed the polynomial equation into a hyperbolic function to produce better bursting patterns. Equation 1 shows the relation between potential generated by a neuron through time.

$$\frac{dv}{dt} = \alpha \cosh\left(\frac{v - v_{rest}}{\beta} - 1\right) - \epsilon - H + I \quad (1)$$

$$\frac{dH}{dt} = \tau_H(n_H v - H) \quad (2)$$

Table 1. Parameter set for different spiking patterns.

Neuron Spiking Patterns	Parameters v_{rest}	ϵ	τ_H	n_H
Tonic Burst	-62.5	16	0.02	0.2
Phasic Burst	-61.5	16.6	0.02	0.25
Rebound Burst	-62	16	0.03	0.25
Inhibition Induced Burst	-63	16	0.025	-1
Phasic & Tonic Spikes	-62.5	16.2	0.02	0.2
Frequency Adaptation	-60	16.1	0.01	0.2

The first equation implies the fact that the membrane potential of a cell can be considered as a differential equation related to Na, K and leaky currents. The second equation can determine the rate of spikes along with their resting and peak time. Simply by changing parameters in these equations we can see different types of neuronal firing. As it is showed in figure 1 with selection of $\alpha = 75000$, $\beta = 1000$, $v_{rest} = -62.5$, $\epsilon = 16$, $\tau_H = 0.02$, $n_H = 0.2$ we can see the tonic bursting behavior of neurons spiking. Changing these parameters, we can see all the bursting behavior of neurons that is showed in Figure 1. Note that here the first equation mostly defined the pattern we want to see, while the second equation is responsible for alignment of peak and rest duration. **Table 1** shows parameter set for different types of spiking patterns.



Figure 1 shows various types of neuronal responses that can be generated by this model consisted of *Tonic burst* behavior that mostly happens in neurons related to gamma frequency oscillations in brain in which at any peak we can see a bursting behavior before the spike goes to resting state. *Phasic burst*, these behavior happens while there is a constant stimuli neuron responses only one time and can shows bursting behavior while spiking. *Rebound burst*, based on the anodal break excitation in excitatory membrane, a rebound spike or burst behavior is observed and is more seen in thalamo cortical neurons. *Inhibition induced burst* are also known as a behavior of thalamo cortical cells and when this behavior combines by bursting rhythms, it is considered as a response of neurons while sleeping. *Phasic and tonic spike* is a condition while due to a stimulus neuron starts bursting responses and after a while this behavior would be change to tonic spikes. *Frequency adaptation* this behavior mainly known as reduction in the frequency of spikes which happens mostly in neocortex cells.

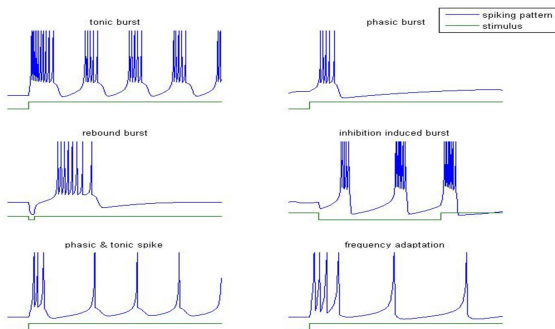


Figure 1. Different bursting patterns generated by our model (blue) under different types of current stimuli (green).

For all bursting patterns showed in figure 1 we set $\alpha = 75000$ and $\beta = 1000$. Appendix section shows how changing parameters from equation 1 and two would provide all different types of bursting patterns. Note that for spike latency and settling time we used the same parameters as (Izhikevich, 2003).

Superposed System

When a neuron does not generate a normal pattern might be in different states because of its previous states. In bursting patterns, under a

pulse stimulus, a neuron would be activated and produce a response and the response might not goes off, even if the stimulus is off. Due to ambiguous nature of neuronal responses in brain we want to investigate a spiking neuron in a quantum system in which all the bursting patterns exist at the same time in our proposed quantum system but when we actually want to see the response of that specific neuron to a stimuli, only one of the predefined states or bursting patterns should be selected. This can be considered as a superposed quantum system that processes all types of bursting patterns at the same time and while measuring the output response it will only choose one of the states.

Quantum superposition defines the quantum mechanics property of a particle to occupy all of its possible states simultaneously (Romero-Isart, 2010). Basically it refers to a condition of Schrödinger equation in which any linear combination of solutions will also be a solution itself. This fact can be considered in our model as well, since any bursting responses a neuron produce, can explain a phenomena in brain, a combination of these bursting responses (states) can also be a response which most likely produce an abnormal response due to real brain disorders.

Many neuronal patterns can be considered as a superposition of a neuron being in different states. Based on superposition principle, if a physical system or let's say a brain cell is in a certain configuration for a specific amount of time and can be in another configuration for another desired time, then the most general state of the system is defined by combination of these individual state. Equation below shows the quantum superposition principal for a multi state system:

$$C_0|0\rangle + C_1|1\rangle + \dots + C_n|n\rangle \quad (3)$$

In which $|0\rangle, |1\rangle \dots |n\rangle$ represent different states of the system and C_0, C_1, \dots, C_n are complex numbers relating to probability of the system to be in that particular state. As shown in Figure 2 if we consider a single cell in brain as a quantum superposed system, we can clearly define how this cell can generate different spiking patterns (quantum states) based on a group of primary patterns already exist in our superposed system.



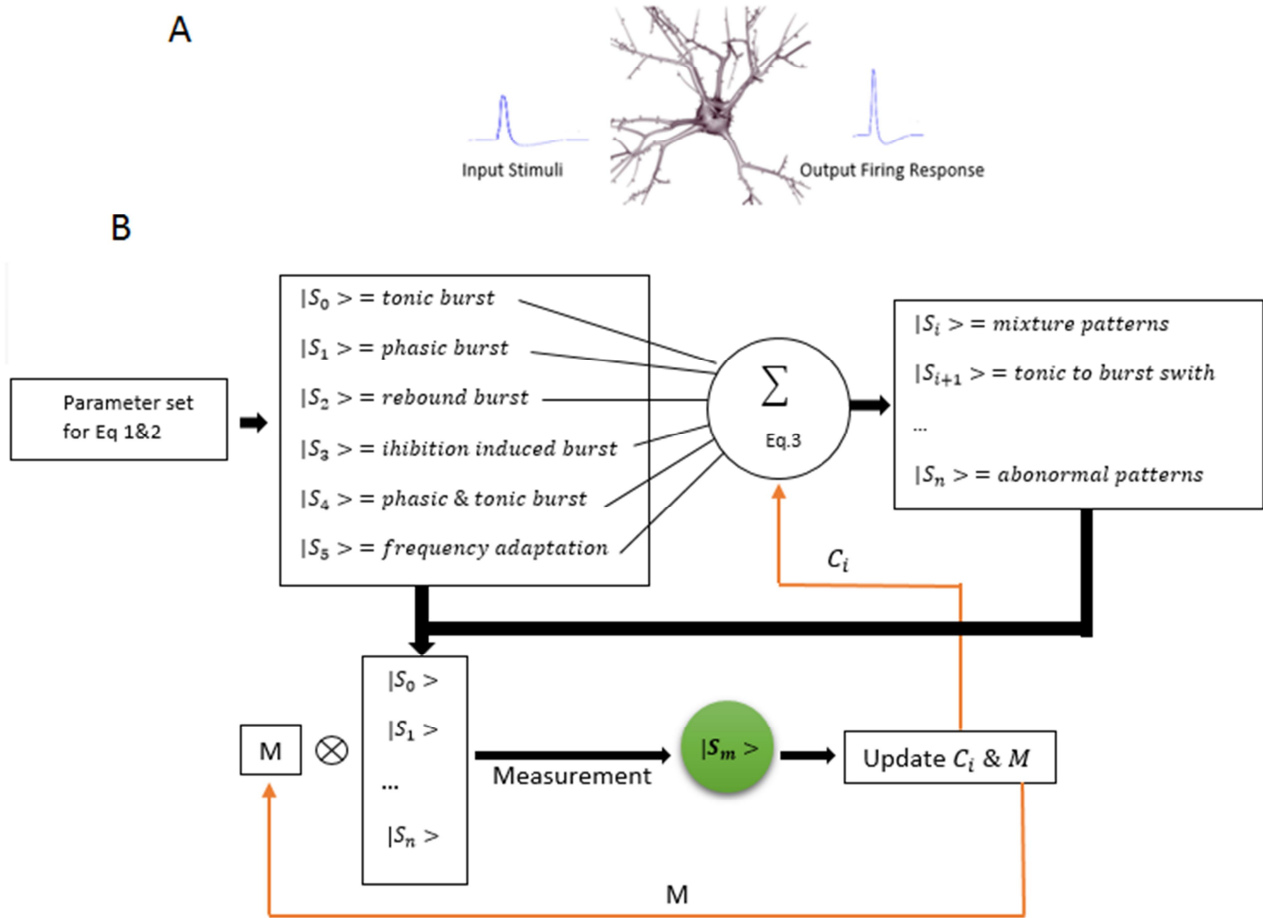


Figure 2A and B. Schematic of a neuron: under input stimuli it will generate a spiking pattern as an output. B. modeling this neuron in a quantum superposed system with the ability of generating unknown and abnormal patterns. Through measurement a state called S_m would be obtainable which is same as our six primary states. Then we should update M and C_i for the next measurement in order to create our desired patterns.

Since for many abnormal patterns in brain cells, it is considered that there is an unknown relation between different patterns a neuron generate, we can fit this to a superposition fact that whenever the system is in one state, it can also be considered to be party in another state as well. Therefore if we say as an example a neuron generate 4 types of spikes such as tonic burst, phasic burst, rebound burst and frequency adaptation, representing 4 different states in our neuron (superposed system), then we can say any combination of two or more of these states is also another state in our system.

As shown in Figure 2 considering 6 well known spiking pattern in a neuron as primary

states of the system, we can combine them and produce different spikes like tonic to burst switching pattern that usually happens in Parkinson's disease due to lack of dopamine in a cell. These new states are also an output for our quantum system of representing a single cell in brain. Note that based on this system we can have a set of n different states but we only see the one that we measure (S_m). More primary states results more patterns as here with 6 primary states we can generate up to n different states in which n is equal to $C(6,2) + C(6,3) + C(6,4) + C(6,5) + C(6,6) + 6$ primary states = 63.

An important issue here is that we should realize, any superposed states in figure 2 should



exist in the system but by the time of measurement, the measured state can be only one of our primary states. So in order to address an abnormal pattern in brain cell, we should consider the measurement process in a timely manner. Let's say for a specific abnormal pattern;

$$|S_i\rangle = C_1 |S_1\rangle + C_2 |S_2\rangle + C_4 |S_4\rangle \quad (4)$$

The measured output is S_1 , so if we consider for abnormal pattern S_i for a certain amount of time of measurement we see S_1 then S_2 and then S_4 and currently the measured output is S_1 we should update our possibilities (C_i). Updating these possibilities means incrementing C_2 so at the next measurement we will see S_2 and after that updating C_4 with the maximum probability would lead to seeing S_4 at the final measurement. In conclusion after each measurement we update C_i in order to reach to the exact sequence of spiking patterns that we aim to model.

As an example in Parkinson's disease Subthalamic Nucleus Neurons (STN), due to Dopamine depletion would generate single spike for a while and then switch to burst firing mode as shown in Figure 3.

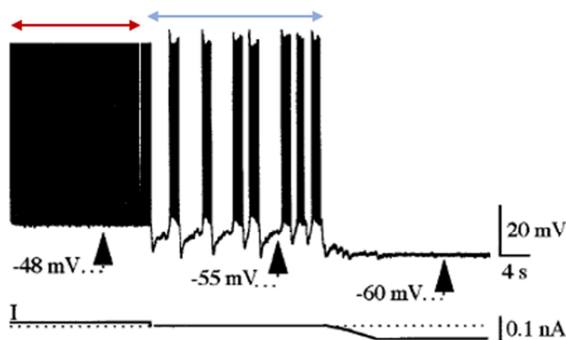


Figure 3. Single spike to burst switching pattern. Single spikes happen in the red area while bursting spikes are shown in blue area (Beurrier *et al.*, 1999).

Suppose we want to create this pattern through our system. Steps below show how this task should be done:

- Generate two different firing patterns based on equation 1 & 2 $|S_0\rangle =$ single spikes and $|S_1\rangle =$ burst spike, which are presenters of our two primary states.
- Based on actual recordings of our desires STN neurons we can create a vector of possibilities $[C_0, C_1]$ which shows in a STN neuron how often we can see single spike or bursting patterns with respect to vector of possibilities (Beurrier *et al.*, 1999).
- Generate the superposed state $|S_2\rangle = C_0|S_0\rangle + C_1|S_1\rangle$
- For a time period T_0 , weight M in order to choose $|S_2\rangle$ (after measurement we will get either state $|S_0\rangle$ or state $|S_1\rangle$ based on the probability of C_0 or C_1).
- Update M and C vector so we can measure state $|S_0\rangle$ or state $|S_1\rangle$ while selecting $|S_2\rangle$ for time period of T_1 .
- Our measurement for time interval T equal to $T_0 + T_1$ gives an abnormal pattern of single spike switching to burst mode of STN neurons in Parkinson's disease.

This procedure can be used for any other types of mixed or abnormal patterns.

4. Results and Discussion

Due to lack of Dopamine in Parkinson's disease, the firing of STN neurons would change to what is shown in Figure 3. Using our proposed system along with parameters and C_i values modification we can generate this abnormal pattern based on Figure 2A and B. Here we implement our method in order to model some types of abnormality in neuronal spiking patterns. Figure 4 shows the result of superposed system in Figure 2 on STN neurons, focusing on getting the single spike into burst switching pattern. Our results obtained via MATLAB software and as it is shown in Figure 4, we can see its compatibility with the actual recording of neurons (Figure 3).



Based our proposed system in Figure 2 we generate the single to burst switching pattern as follows: first of all we set the parameters of our model in equation 1 & 2, in order to get 14 different kinds of spikes consisting of single spike, single burst, phasic spike, phasic burst, rebound spike, rebound burst, inhibition induced spike, inhibition induced burst, phasic and tonic spike, frequency adaptation, spike latency, threshold variability and bi stable spike. We put these spikes as 14 different states of our system named S_0 to S_{13} . Using equation 3 we generated some mixture patterns such as single to burst switching mode and set these new patterns (states) and our 14 primary states in a whole new matrix of states. For any desired pattern we adjust matrix M somehow to select that specific state, which in our case would be single to burst spike S_{14} . According to superposition theory whenever we measure the output of system, most likely it will give us the state which has a higher probability (c_i). Therefore when we want to measure S_{14} it will give us either S_0 which is single spike or S_1 which is burst pattern according to c_0 and c_1 .

If after measurement we single spike the next step would be adjusting c_1 to get S_1 for the next phase. Note that after getting S_0 we can simply put c_0 to zero, so the next step would definitely gives us S_1 , but since in actual recordings

of STN neurons sometimes we have two more phases of single spikes (S_0), we can not put the probability of seeing S_0 for the second time to zero. The solution would be setting c_0 smaller enough in comparison to c_1 in order to have a high chance of seeing S_1 after S_0 as stated in Figure 4.

In STN neurons, we can see this single to burst switching pattern but what is scientist concern nowadays is that the STN neurons of patient with Parkinson's disease would create abnormal pattern in rebound burst area (Figure 4). In Parkinson's disease this area would have a longer duration along with lower voltage. Biological reasons for this rebound behavior can be considered in some sequential steps which starts with depolarization of membrane potential due to calcium channel opening in STN cells. Then the depolarization to burst phase would happen because of low calcium current. After this step we have a high frequency spiking pattern in which each of these spikes would increase calcium velocity, resulting activation of potassium in the STN membrane. Due to potassium current the membrane potential would be repolarized and when it reaches to a minimum threshold (which is lower for Parkinson's disease), again the rebound burst phase would appear as is showed in Figure 5.

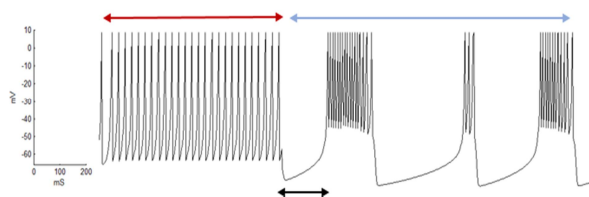


Figure 4. Single to burst switching pattern generated by our model using the superposed system explained in figure 2. Here red arrow indicates the single spike pattern and blue arrow shows the burst firing pattern. Black arrow in this figure clarifies a phenomena called rebound burst which is interestingly lower value (in term of membrane potential) for people with Parkinson's disease or dopamine deficiency.

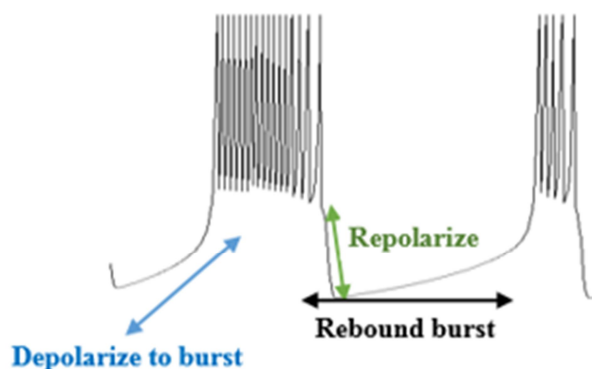


Figure 5. Rebound burst steps.

5. Conclusion

Mathematical models that can cover most of known brain spiking patterns, are difficult to extract. Most of these models use ordinary differential equations, which are not able to generate all patterns of spikes, especially when we want to investigate the abnormal patterns happening due to various types of disorders. Coming up with an adjustable model that can combine spiking pattern together and generate different abnormal pattern would be a great opportunity for scientists to investigate brain abnormalities. Considering the fact that in a quantum superposed system any combination of states can be a new state itself, we can propose a model of brain neurons that can generate normal primary spikes (states) and using quantum superposition, further spikes coming from combination of primary spikes would be obtainable.

Studying the chemical reaction in a neuron leading to an abnormal pattern can be well established by this proposed system. Suppose in an abnormal spikes three types of primary spikes such as tonic spike, frequency adaptation and bistable spike are involved. Knowing the chemical reaction in the cell membrane for each of these patterns and of course their sequence of occurrence can help us to see which ion has low or high velocity in a desired cell, that causes an abnormal pattern and therefore we can come up with some medicine to compensate it. This can be an interesting field for future works to somehow understand the ionic reaction in brain disorders through spikes generated by a quantum superposed system and furthermore cure these disorders with related medicine or activating cell membrane by some electrical stimulus designed on small circuits. These circuits in future can be an intelligent way to solve abnormality in brain spiking patterns due to wide variety of disorders.

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