What Causes Persistent Neural Activity?

Vishal Verma[1]

[1]The Institute of Mathematical Sciences, CIT Campus, Taramani, Chennai 600113, India

The persistent neural activity at a global scale, either stationary or oscillatory, can be explained by the use of the excitatory inhibitory neural network models. This state of the network is, as can be inferred, crucial for the information processing and the memorizing ability of the brain. Though the goal for persistence to exists is visible; but from where the network achieves its ability to show rich variety of the persistent dynamical states is not clear. The following study investigates the possible reasons for the persistence in neuronal networks and shows that the action of the inhibitory components, among other favorable factors in the network, plays a key role in stabilizing neural activity, once it starts. The results strongly support previous research conducted with simpler or more specialized neural network models, as well as neurophysiological experiments.

Excitation | Inhibition | Persistence | Bifurcation
Correspondence: ***vv0747970@gmail.com***

Introduction

What is the simplest network that can generate complex sustained dynamics, shedding light on the mechanism by which such dynamics are produced in the brain? Since a network consisting of excitatory and inhibitory (EI) neurons is considered a canonical model for understanding cortical network activity, I will attempt to answer the above question using this model while invoking a minimal number of parameters.

The Model. The use of computational models to study neurons began in 1952 with the conductance-based Hodgkin and Huxley model, which aimed to explain dynamics in the squid giant axon. One simplified version was presented by Dr. Richard FitzHugh in 1961 and independently by Jinichi Nagumo *et al.* in 1962[13,14,15]. According to the theory, the neuron's potential is a dynamical variable with its differential exhibiting cubic nonlinearity and modulated by another variable that varies at a timescale $1/\epsilon = 100$ times slower than itself. Dynamically, the system can undergo supercritical and subcritical Andronov-Hopf bifurcations with respect to the increasing stimulus, as shown in Figure 1. It possesses canard solutions. Remarkably, the nonlinear dynamics of the model not only explain neuron behavior but also elucidate dynamics of chemical oscillatory reactions, arrhythmia, and naturally occurring spatiotemporal patterns. Furthermore, successful simulations of logic gates have been achieved using the model's ability to create and switch between robust spatiotemporal patterns, underscoring its potential role in understanding the dynamics of the computational[1,6,18,19]. The mathematically synaptically connected network system is written as follows.

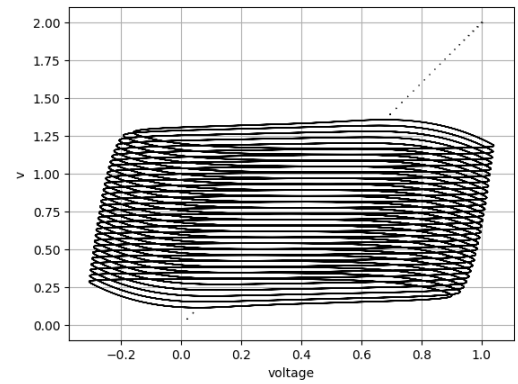

Fig. 1. u on X axis and v on Y axis in the above phase space refers to the neuron's excitation and the modulating variable that operates on a slower time scale respectively are shown. The neuron's stable dynamical state in its phase space moves upward as the current *I* increases from null to 2 mA, being driven first through the supercritical and then subcritical Hopf bifurcation.

$$\varepsilon \frac{du_i}{dt} = u_i(u_i + c)(1 - u_i) - v_i + I_i - \sum_j s_{ij} g_{ij}(u_i - E_j)$$

$$\frac{dv_i}{dt} = u_i - bv_i$$

$$\frac{ds_{ij}}{dt} = A(-s_{ij}) \ + \ B(1 - s_{ij}) \ \ 0.5\ 1 + \tanh(\frac{u_i - u_{\text{threshold}}}{u_{\text{sl}}})]$$

Parameters.

- u_i and u_j are the presynaptic and postsynaptic neural potentials, respectively.
- v_i and v_j are slow modulation variables for presynaptic and postsynaptic neurons, respectively.
- The parameters $c = -0.1$ and $b = 0.5$ describe the model kinetics, and $\epsilon = 0.01$, except in Figure 3 where it is 0.075, is the variable controlling the time scale differences between slow and fast variables. These values are chosen such that each uncoupled neuron is an excitable system.
- I_i is the external current or stimulus and varies throughout the study.
- s_{ji} denotes the synaptic gating variable.
- g_{ij} represents the entries of the synaptic weight matrix (or the adjacency matrix).
- E_{syn} represents the synaptic reversal potential, with $E_{syn} = 5$ for excitatory and $E_{syn} = -5$ for inhibitory neurons, respectively.
- Here, $A = 3$ and $B = 3$ are the rate constants, and $u_{th} = 0.3$ and $u_{sl} = 0.001$ are the parameters determining the shape of the synaptic term. The equation

DRAFT

for the gating variable s_{ij} depends only on the membrane potential of the presynaptic neuron V_j.

- $\frac{1+\tanh(x)}{2}$ is a step-up function.

Results

Dynamics of Coupled Neurons. A couple of nonlinear (relaxation) oscillators is different from a couple of linear oscillators because the superposition principle does not apply in the former system. Therefore, it is capable of producing rich dynamical states that the latter cannot produce. It can switch between these dynamical states (or bifurcate in a variety of ways) passing through intermittent states if the model parameters change. Here, these parameters can be I_i, E_i, I_j, E_j, g_{ij}, *et cetera*. References[9,10,17] provides ample information on this subject. Thus, without delving into the study of bifurcations, this section simply discusses whether two recurrently coupled nodes with synaptic connections can sustain activity through self-driving each other when transiently stimulated. It is well-known that the activity patterns of coupled neurons vary depending on (1) the type of synapses/neurons, i.e., excitatory or inhibitory, and (2) the coupling strengths. Through numerical simulations, I found that when one or both of the neurons (or equivalently synaptic connections) are inhibitory, the postinhibitory rebound occurs, i.e., in the case of an inhibitory presynaptic neuron, the postsynaptic neuron fires an action potential after being released from the suppressing effect of the inhibitory presynaptic neuron. This rebound effect is a factor that is found responsible for the persisting neural oscillation in the system of synaptically coupled FitzHugh-Nagumo neurons. Thus, if both the synapses (or equivalently neurons here) are excitatory, activity cannot be sustained. Futhermore, strong synaptic conductance can convert this rebound to a sustained activity pattern. In the case of EI or equivalently IE pairs, the strength of the synaptic conductance plays a key role in maintaining sustained oscillations. Previous analyses of two mutually coupled neurons, or networks operating in regular firing mode, have shown that the oscillatory properties, particularly the frequency of the global oscillation, depend strongly on the decay time of inhibitory postsynaptic currents (see, for example, van Vreeswijk et al., 1994; Hansel et al., 1995; Terman et al., 1998; Chow, 1998). Therefore, the results and reasoning of the present study are in agreement with the conclusions of these landmark studies. For example, refer to Figure 2. Changing either neuron to excitatory results in the loss of persistent oscillatory activity, which can be regained by increasing g to 0.9[check Supplementary Material and Code Availability]. Example: Figure 2 shows two systems self-oscillating in response to a 0.2 ms impulse.

Sparsely Connected EI Network. The realistic form of sparseness is the one in which a synapse is present with probability C/N at each pair of cells, independently from pair to pair, and therefore the number of arriving synaptic inputs varies from neuron to neuron. Also, since the Neuronal networks are random networks, their properties can be

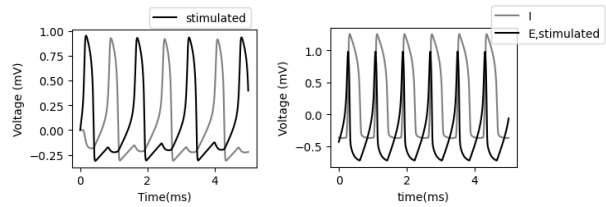

Fig. 2. Left. Both the neurons are Inhibitory and bidirectionally synaptically connected with g = 0.05 units. Right. Stimulated neuron was changed to Excitatory and g was changed to 0.9 units. Black neuron was stimulated for 0.2 ms. For both the cases, Sustained oscillations in response to transient stimulus can be observed.

studied with the help of Erdos Renyi random graphs. As the number of nodes in the net tends to achieve infinity, i.e., assuming the thermodynamic limit for the number of nodes in the graph, then the probability of having a specific type of edge, say, the one that represents self-connection; is vanishingly small or zero. Also because of the observed absence of self-connections in real neuronal networks, we do not model self-connections[16]. In this study, a supercritical Hopf bifurcation with respect to the decreasing Excitation Inhibition ratio has been found that separates the network activity regions with stationary and oscillatory global activity (Figure 3). This finding of oscillatory activity in a networks of mostly as well as purely inhibitory neurons agrees with previous modeling studies with either simpler or detailed conductance based neural models (e.g., van Vreeswijk et al., 1994; Wang and Buzsaki, 1996; Traub et al., 1996; White et al., 1998) and with evidence from both in vivo (McLeod & Laurent, 1996) and in vitro Whittington et al., 1995; Traub et al., 1996; Fisahn et al., 1998) experiments suggesting inhibition plays an important role in the generation of network oscillations[4].

Discussion

The results suggest that persistent neural activity stems from inhibitory synaptic actions, making it susceptible to the influence of transmission delays and the probabilistic distribution of synaptic time scales inherent in the brain. These factors can induce synchronization within the network, leading to regularities in neuronal firing patterns and subsequently impacting global activity to either its advantage or otherwise[12]. This hypothesis finds support in previous *in vitro* experiments (Whittington et al., 1995), as well as modeling studies (Whittington et al., 1995; Traub et al., 1996; White et al., 1998; Brunel, 2000)[4]. Recent work by Christopher M. Kim et al., building upon the approach of Nicolas Brunel using an EI population model, significantly addresses this aspect, thus obviating the need for repetition here[2]. Memory, defined as enduring alterations in system states in response to environmental cues, enables the retention of information about transient signals long after exposure[11]. Nicolas Brunel[5] in brain and more recently, Mitra et al.[12] in cellular signalling, have directly linked persistent activity to memory functions. In addition, this model interfaces intricately with the realm of analog computing[6], an arena cur-

DRAFT

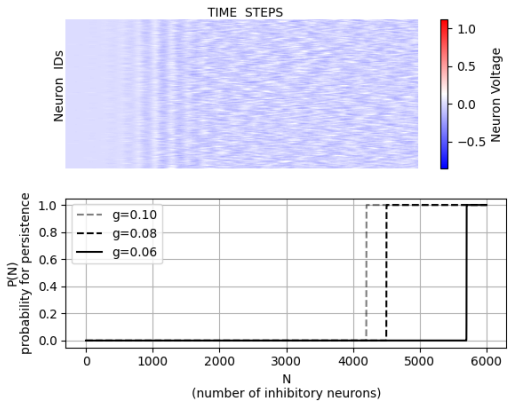

Fig. 3. The P(N) on Y axis is indicative of the probability of persistence with respect to the number of inhibitory neurons N in the EI network with 6000 nodes. Hopf Bifurcation occurs on increasing inhibition in the network. Effect of synaptic conductance *g* is indicated. Top figure shows the spatiotemporal pattern for neural persistent activity for 25 ms at N = 4800 and g = 0.10

rently undergoing a notable resurgence of industrial fascination[18]. Therefore, it shall also be interesting to incorporate the energy consumption constraint on the neural network model and observe its activity; a practice that may open gates to understand the emergence of the seizures (e.g., infantile myoclonic epileptic encephalopathies)[19] as well.

Supplementary Note 1: Methods

The model was numerically integrated using Runge Kutta 4 method using step size of 0.01 using Python. The parameters that were varied in The Model are as follows:

Figure	*epsilon*	*Stimulus*
1	0.010	0 to 2 mA
2	0.010	0.03 mA
3	0.075	0.07 mA

To produce Figure 3, (a) five randomly chosen nodes in the network were provided stimulus valued 0.07 mA for 1 ms. The persistent activity is shown in figure for 25 ms but it continues beyond (b) among network measures only percolation and the entailing First Order Phase Transition is discussed[16].

Supplementary Note 2: Code Availability

Code has been made available on internet and can be accessed on GitHub.

ACKNOWLEDGEMENTS
The author is grateful to Dr. Shakti Narayana Menon for many helpful discussions.

Bibliography

[1] Moritz Gerster et al. FitzHugh-Nagumo oscillators on complex networks mimic epileptic-seizure-related synchronization phenomena.(2020)

[2] Christopher M. Kim et al. Dynamics of multiple interacting excitatory and inhibitory populations with delays.(2018)

[3] A. Parveena Shamim et al. Lateral inhibition in relaxation oscillators provides a basis for computation.(2023)

[4] Nicolas Brunel. Dynamics of Sparsely Connected Networks of Excitatory and Inhibitory Spiking Neurons.(1999)

[5] Nicolas Brunel. Persistent activity and the single-cell frequency–current curve in a cortical network model.(2000)

[6] Robert Paz. Analog Computing Technique.

[7] Wang and Buzsaki. Gamma oscillation by synaptic inhibition in a hippocampal interneuronal network model.(1996)

[8] G. Bard Ermentrout and David H. Terman. Mathematical Foundations of Neuroscience. (2010)

[9] Eugene M. Izhikevich. Dynamical Systems in Neuroscience: The Geometry of Excitability and Bursting.(2010). MIT Press. ISBN:9780262514200, 0262514206

[10] Janaki et al. Lateral inhibition provides a unifying framework for spatiotemporal pattern formation in media comprising relaxation oscillators.(2019)

[11] Inniss, M. C. & Silver, P. A. Building synthetic memory. Curr. Biol. 23, R812–R816 (2013)

[12] Mitra, T., Menon, S.N. & Sinha, S. Emergent memory in cell signaling: Persistent adaptive dynamics in cascades can arise from the diversity of relaxation time-scales. Sci Rep 8, 13230 (2018)

[13] FitzHugh, Richard. "Impulses and Physiological States in Theoretical Models of Nerve Membrane". Biophysical Journal.(1961)

[14] Nagumo, J.; Arimoto, S.; Yoshizawa, S. (October 1962). "An Active Pulse Transmission Line Simulating Nerve Axon". Proceedings of the IRE.

[15] Hodgkin AL, Huxley AF (August 1952). "A quantitative description of membrane current and its application to conduction and excitation in nerve".

[16] Newman, Mark, Networks: An Introduction, 1st edn (Oxford, 2010; online edn, Oxford Academic, 1 Sept. 2010)

[17] P. Berge et al. Order within Chaos: Towards a Deterministic Approach to Turbulence. Publisher: Wiley VCH (29 April 1987)

[18] Research Projects in Analog AI at IBM.

[18] O. Dulac. Epileptic encephalopathy with suppression-bursts and nonketotic hyperglycinemia.(2013)

DRAFT