What Causes Persistent Neural Activity? Part I

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 exist is visible; from where the network achieves its ability to show a 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 starting and stabilizing neural activity. The results strongly support previous research conducted with simpler or more specialized neural network models, as well as neurophysiological experiments. This work shall be completed in two parts; first, computational methods shall help to take an experimental approach to the question of persistence in the brain in Part I, and second, theoretical methods shall advance our understanding of the persistent neural activity in Part II.

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 Network 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 concerning 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

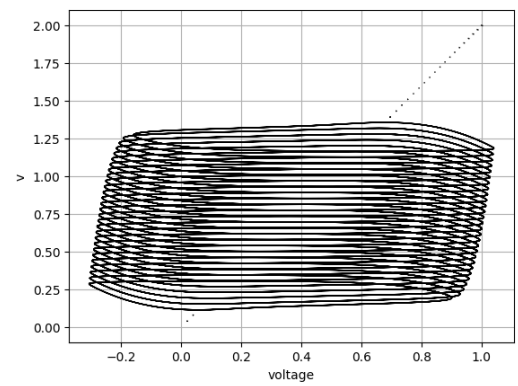


Fig. 1. In the depicted phase space, the horizontal axis denotes the excitation (u) of the neuron, while the vertical axis represents the slow modulating variable (v). The stable dynamical state of the neuron within this phase space ascends with the incremental rise of current (I) from null to 2 mA, traversing initially through the supercritical and subsequently the subcritical Hopf bifurcation regimes. Noteworthy is the absence of persistent response to transient stimuli.

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.

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

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

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

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.

DRAFT

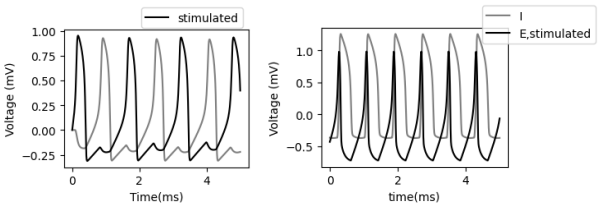


Fig. 2. Left. Both the neurons are Inhibitory and bidirectionally synaptically connected with g = 0.05 units. Right. Stimulated neuron was changed to Excitatory and g was changed to 0.9 units. Black neuron was stimulated for 0.2 ms. For both cases, Sustained oscillations in response to a transient stimulus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

- 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 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.

Firing Rate Model. Wilson Cowan Model equations describe the neural firing rates F_E and F_I of the interconnected excitatory and Inhibitory populations with weighted recurrent and lateral synapses that model the point stochastic process going on in the, say, spiking neural networks using coupled ordinary differential equations with the form as following [23]:

$$\tau_i \frac{dF_i}{dt} = -F_i \ + \ (1 - F_i) \ h(S_i)$$

where $h(S_i) = \frac{1}{1+\frac{1}{s^3}}$ is the Firing Rate Response function.

The specific functional form of $h(S)$ varies in the literature. S_E and S_I are the synaptic currents entering excitatory and inhibitory populations and *h* is the monotonically increasing firing rate response function ranging between zero and one. Synaptic current into node i coming from node j is related to synaptic weights and biases of the connection as $S_i = W_{ij}F_i \ + \ b_i$ and can be positive or negative.

Results

Dynamics of Coupled Neurons. A couple of nonlinear (relaxation) oscillators are 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] provide 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 post-inhibitory 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. Furthermore, 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, their properties can be 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 concerning 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 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

DRAFT

et al., 1998) experiments suggesting inhibition plays an important role in the generation of network oscillations [4]. To produce Figure 3, (a) five randomly chosen nodes in the network were provided stimulus valued at 0.07 mA for 1 ms. The persistent activity is shown in the figure for 25 ms but it continues beyond (b) among network theory measures, only the study of the percolation process on a random graph (called directed percolation) alongside its entailing First Order Phase Transition is conducted [16,20]; as we vary *N*, i.e., number of inhibitors. The observed activity can be explained using a model with comparatively fewer variables and equations than used here as below:

Firing Rate Model. The spatiotemporal pattern shown in Figure 3 is subtle. Network activity undergoes three phases: No firing, Synchronized Firing, and asynchronous Firing all by itself through self-organized criticality. The goal of using the Firing Rate Model is to test the above hypothesis that the synaptic strengths alone are driving the network towards persistence in the way observed in Figure three, i.e., (a) why activity remains suppressed initially (b) why synchrony (c) why transition to asynchronous firing from synchronized firing. Moreover, the firing rate model helps to connect the above result to the EEG patterns observed clinically say during anesthesia, seizures, sleep *et cetera* [20,21,22]. The results obtained are shown in Figure 4.

Three effects can be observed in the spatiotemporal pattern in the figure 3. One, No activity for the first 80 ms. Second, initiation of the activity in the form of synchronized neural firing or equivalently oscillating firing rate of the global activity and continuing of it for nearly 100 ms. Third, transitioning of this oscillating firing rate to a stationary one or equivalently asynchronous neural firing which is stable/saturated. I hypothesize that the observed phase transitions twice are caused by synapses only instead of any other network measure like structure, finite size effect, complexity, *et cetera.* While testing for this hypothesis in the investigation, theory must hold for neural activity caused by the neurons in the brain. This all can be achieved using the Wilson Cowan model.

Figure 4a shows the circuit of the neural populations I considered to recreate the observations. The third EI population inhibits the first population through either exciting its locally coupled inhibitory population or directly inhibiting it using I_3. This mimics long-range connections of the brain. However, the inhibitory population can't make long-range connections, so, the former case is biophysical. The inhibitory population is locally coupled to the self-feeding excitatory population. Excitatory populations connect and these connections mimic long-range range connections in the brain. This configuration of three WC EI nodes can produce a wide variety of dynamical patterns that are observed in the EEGs.

As can be seen below the circuits, the oscillating inhibitory firing population can be seen when Wc is low. Wc represents the synaptic weight of the long-range connection going from the E_3 to I_3. This represents that the synaptic current in SNN in Figure 3a is rising slowly after being stimulated and therefore the network moves from no activity to oscillating global activity. However, as the current was cut off, as in Figure 4b, the circuit could not sustain activity. Then, as Figure 4c indicates, the doubling of the synaptic weight W_c causes the sustained firing of the neurons to begin, as the duration of the "applied current" crosses a certain threshold (here 400 ms). This is equivalent to saying that, in Figure 3a, sustained firing with a global stationary firing rate began when the synaptic input going into each neuron was par some threshold value. This threshold value was "decided" By the network itself through a phenomenon called self-organized criticality or SOC.

Network of Pyramidal Neurons To preempt the possibility of the propagation of the claim through my work that the neural network models constituted by the excitatory nodes and synapses can not have persistence as their dynamical state, I present my results on this subject using a detailed neural network model constituted by separate Soma and Dendrite compartments, synaptic gates, two different synapses *AMPA* and *NMDA*. It is the Pinsky Rinzel Model [24]. Figure 5 Right shows the result of a homogeneous network of 1000 Pinsky Rinzel Neurons, out of whom 40 random neurons were stimulated for 1 ms. The resulting persistence is shown for 50 ms. This persistence has been seen to go on for at least 500 ms in the code. The result of the interaction among soma, dendrite, and many currents that build up in the network to finally cross the first threshold gives neural persistence. The global oscillatory frequency has been seen to increase, as the g_{AMPA} strength is manually increased from 0.005 to 0.01 to 0.015 to 0.02 keeping $NMDA$ synapse non-functional. This result is completely in favor of the work conducted by the Pinsky and Rinzel themselves; though in their work the persistence as a possible dynamical was not studied [24]. In conclusion, though the network system constituted all or most of the excitatory can not show persistence but equipped with synaptic gates modulating currents as in the Pinsky Rinzel model, the system expands its dynamical phase space to a large number of dimensions and hence finds the possibility for persistence.

Nonlinear Dynamics. Figure 3 (top) shows a semiflow defining the spatiotemporal evolution of the Fitzhugh Nagumo network on its state space, say X, a set consisting of discrete time steps J and a map or function Φ such that; it maps either a subset of or entire $J \times X \to X$ satisfying the semiflow property:

$$\Phi(t+r,x) \;=\; \Phi(t,\Phi(r,x)) \;\; r,t \in J, \;\; x \in X$$

We ask whether the dynamical system persists as a whole or at least in parts. This question can be formulated by

DRAFT

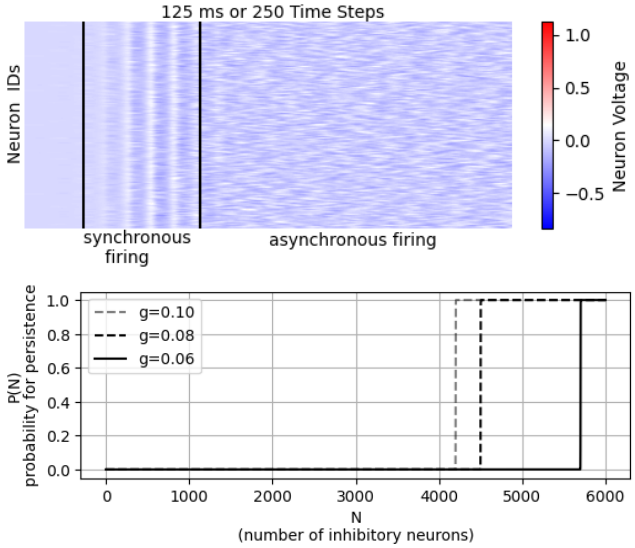


Fig. 3. The P(N) on the Y axis is indicative of the probability of persistence concerning the number of inhibitory neurons N in the EI network with 6000 nodes. Hopf Bifurcation occurs on increasing inhibition in the network. Effect of synaptic conductance *g* is indicated. The top figure shows the spatiotemporal pattern for a neural persistent activity for 25 ms at N = 4800 and g = 0.10 The effect of initially being held by the inhibitory synapses on neural network activity and then being released from it can be seen as persistent neural network activity in *mV*.

using a *persistence function* (here, collective neuron voltage or global potential as shown in the colorbars) such that it maps state space to the $\mathbb{R}^+$. So has been done in Figure 3 (lower part). Now, we have observed two types of persistent behaviors which we now characterize as uniformly weakly persistent and uniformly persistent behavior. The semiflow is called uniformly persistent if $\exists$ some $\epsilon > 0$ such that

$$\liminf_{t\to\infty} \ \rho(\Phi(t,x)) \geq \epsilon \ \text{ wherever } \ x \in X, \rho(x) > 0$$

Such behavior can be seen in the state labeled *asynchronous firing*. Then, if the above equation is true if *lim-inf* is replaced with *lim-sup*, the condition is satisfied by the network dynamical state labeled *synchronous firing*. This is a uniformly weakly persistent dynamical state. As can again be seen in the figure itself, a weakly uniformly persistent dynamical state is a stepping stone to the uniformly persistent dynamical state of the network. We asked two questions: 1. How does the network get uniform weak persistence 2. How the network transitioned from uniform weak to uniform persistence. We answered both through a computational approach[25]. We can see through Figure 3 that there are some global attractors. If so, what is its stability categorized as using the theory of Aleksandr Lyapunov? Is its existence a necessary condition for the system to transition from uniform weak to uniform persistence? Under what conditions, shall uniform weak persistence shall begin? All these are answered by the Nonlinear dynamical methods and Integral Transforms and can help us generalize our view on the conditions that must be imposed on a neural network system to ensure its robust persisting behavior. This shall constitute Part 2 of this work and shall be conducted.

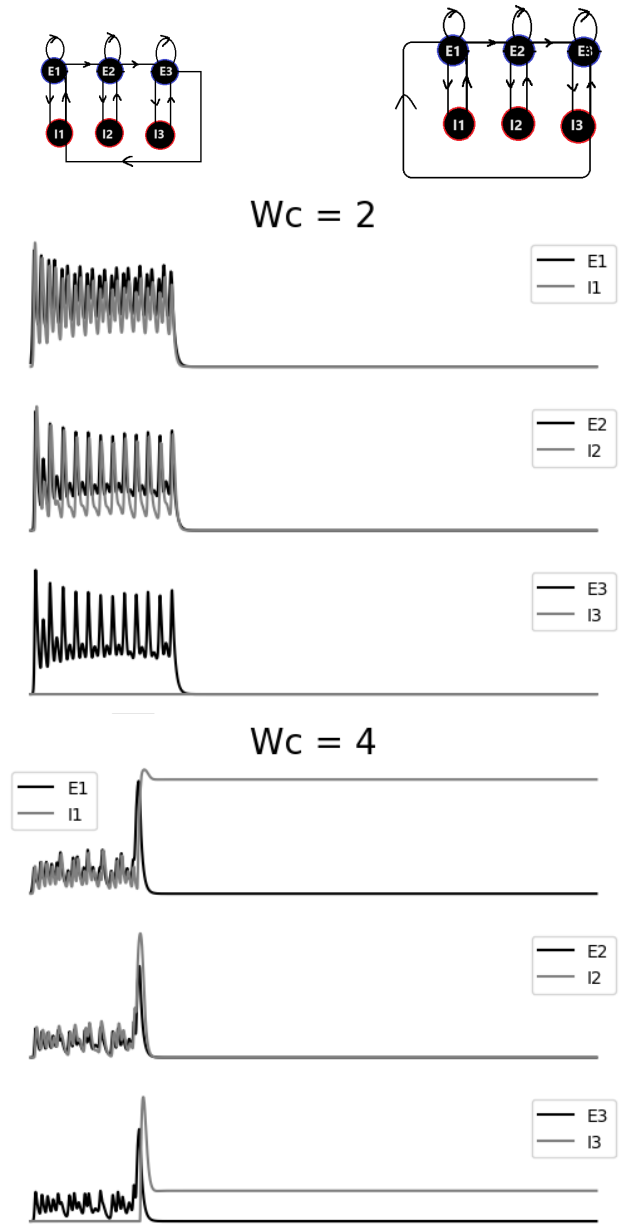


Fig. 4. Firing Rate Model. Stimulus was provided to E_1 for 0.5 seconds. The x-axis shows 2 seconds. The y-axis is the Firing Rate. Initially, the buildup of the synaptic current going into the nodes was insufficient to cause persistent firing in the Fitzhugh Nagumo neurons in Figure 3a. But as the current built up, synchronous firing started. This hypothesis is proved using the WC model (middle figure); As the inhibitory current into the node E_1 was 2, synchronous firing started. This circuit was incapable of sustaining its activity. However, as the W_c is increased, keeping every other parameter the same, the inhibitory node achieved a saturated firing rate when the current was supplied for 400 ms or more, but no less. This represents the third phase in the SNN, whereas the synaptic current built up enough in the network, that a saturated firing rate was achieved.

Supplementary Note 1: Conclusion

We discussed the percolation effect on a sparse and random network of FitzHugh Nagumo excitatory neurons by converting its excitatory neurons to inhibitory neurons and observed an adiabatic phase transition from dead to persistent network activity. This happened due to the post-inhibitory rebound effect of the inhibitory synapses. Other types of percolation effects are also possible. This constitutes ***synaptic*** cause for persistence. We also saw the ion channels in a neuron that may lead to persistence. This constitutes ***intrinsic*** cause for persistence. Then, the role that can be played by the Nonlinear Dynamics to find out the necessary mathematical constraints on the neural network system is highlighted.

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 shall be equivalent to tuning synaptic weights in the neural population (e.g., Wilson Cowan) model. 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 the brain and more recently, Mitra *et al.* [12] in cellular signaling, have directly linked persistent activity to memory functions. In addition, this model interfaces intricately with the realm of analog computing [6], an arena currently 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 understanding the emergence of the seizures (e.g., infantile myoclonic epileptic encephalopathies) [19] as well.

Supplementary Note 2: Methods

Both the models were numerically integrated using the Runge Kutta 4 method using step sizes of 0.01 and 0.001 respectively in *Python*. The parameters that were varied in The Fitzhugh Nagumo 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

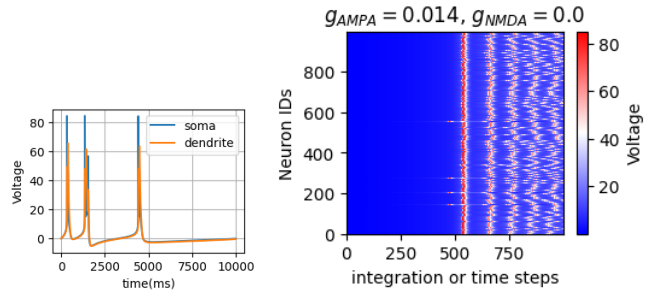


Fig. 5. Left. Single Pinsky Rinzel Neuron. Vs is somatic voltage (mV) and Vd is dendritic voltage (mV). 0.5 mA current was provided consistently. Right. A network of 1000 such neurons was stimulated for 50 ms. The current of 0.5mA was provided to 40 random neurons for 1 ms. Oscillating collective neural voltage (in mV) was observed.

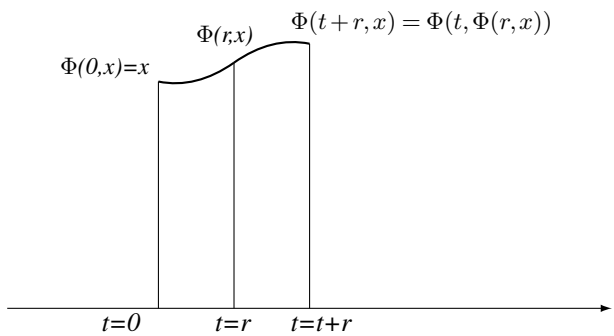
Network structure is sparse and random with each neuron having the probability of having some link being 0.006, as a way to constitute a small world network [16].
The parameters that were varied in The Wilson Cowan Model are as follows:

Population	*Parameters*	*Values*
Crossed	W_a, W_b, W_c	0 to 2 mA
1	W_1, W_2, W_3, W_4	6.5,6.5,6.5,0
2	W_1, W_2, W_3, W_4	6.5,6.5,6.5,0
3	W_1, W_2, W_3, W_4	4,2,1.2,0
1	Stimulus	0.32 for 0.5 s to E_1
all	τ_{E1},τ_{E2},τ_{E3}	0.010,0.010,0.010 s
all	τ_{I1},τ_{I2},τ_{I3}	0.007,0.007,0.007 s

W_a, W_b, W_c are the synaptic weights of the connections that connect E_1 to E_2, E_2 to E_3 and E_3 to I_1 (or equivalently I_3 to E_1) respectively. W_1, W_2, W_3, W_4 are the synaptic weights of the connections that carry current from E_1 to itself, I_1 to E_1, E_1 to I_1 and I_1 to I_1 for anyone WC node. Some connections are zero because of their absence in the brain. Biases are zero, except for the synaptic connection that connects E_1 to E_1, which is 0.32 for the first half second and otherwise zero. The inhibitory population is faster than the Excitatory population, as, for example, Interneurons are faster than the Pyramidal Neurons.
For Figure 5, the equations and parameters used were taken from Reference 24 and implied exactly. The network structure is sparse and random with each neuron having the probability of having some link being 0.006, as a way to constitute a small world network [16].

DRAFT

Supplementary Note 3: Semiflow Property



"Semigroup property" or "Chapman-Kolmogorov equation." This property is often associated with stochastic processes, particularly Markov processes, and it essentially states that the evolution of the system over disjoint intervals of time is consistent whether considered sequentially or all at once. In simpler terms, if one has a system evolving over time according to some dynamics or transition probabilities, and he wants to consider its evolution over two consecutive time intervals, say r and t, he can either: 1. Evolve the system for time r, observe the resulting state, then evolve that state for time t, or 2. Evolve the system for the combined time $t+r$ directly from the initial state. Mathematically, this property is expressed as follows also:

$$\boxed{\mathrm{P}(\mathrm{X}_{t+r} = y | X_r = x) = \int P(X_{t+r} = y | X_t = z) P(X_t = z | X_r = x)\, dz}$$

where X_t denotes the state of the system at time t, and $P(\cdot)$ denotes the probability of the event in parentheses occurring.

This property is foundational in the study of stochastic processes and is crucial in understanding their behavior over time. It ensures that the process maintains a certain consistency in its evolution, which is a desirable property in many applications, including modeling physical systems, financial markets, biological processes, and more.

Supplementary Note 4: Code Availability

Code has been made available on the internet and can be accessed on GitHub (link available here).

ACKNOWLEDGEMENTS

The author is grateful to Dr. Shakti Narayana Menon at The Institute of Mathematical Sciences, Chennai, India 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.

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

[20] Cowan, J.D., Neuman, J. & van Drongelen, W. Wilson–Cowan Equations for Neocortical Dynamics. J. Math. Neurosc. 6, 1 (2016)

[21] Meijer, H.G.E., Eissa, T.L., Kiewiet, B. *et al.* Modeling Focal Epileptic Activity in the Wilson–Cowan Model with Depolarization Block. J. Math. Neurosc. 5, 7 (2015).

[22] Liu, S., Ching, S. Homeostatic dynamics, hysteresis and synchronization in a low-dimensional model of burst suppression. J. Math. Biol. 74, 1011–1035 (2017).

DRAFT

[23] Wilson, H.R.; Cowan, J.D. (1972). "Excitatory and inhibitory interactions in localized populations of model neurons". Biophys. J. 12 (1): 1–24.

[24] Paul F. Pinsky and John Rinzel. Intrinsic and Network Rythmogenesis in a Reduced Traub Model for CA3 Neurons. 1994

[25] Steven Strogatz. Nonlinear Dynamics and Chaos. CRC Press. (1994)

[26] Pikovsky, Rosenblum and Kurths. Synchronization A Universal Concept in Nonlinear Sciences. Cambridge University Press, 2001. Online ISBN 9780511755743

DRAFT

Supplementary Note 5: Pinsky Rinzel Model

$$C_m \frac{dV_s}{dt} = -g_L(V_s - V_L) - \left(g_{Na} \left(\frac{-0.32(V_s - 13.1)}{\left(\exp\left(\frac{-(V_s-13.1)}{4.0}\right) - 1.0\right)} \right)^2 h(V_s - V_{Na}) \right.$$
$$\left. - g_{K_{DR}} n(V_s - V_K) + \frac{g_c}{p}(V_d - V_s) + \frac{I_s}{p} \right)$$

$$C_m \frac{dV_d}{dt} = -g_L(V_d - V_L) - g_{Ca} s^2 (V_d - V_{Ca}) - g_{K_{AHP}} q (V_d - V_K)$$
$$- g_{K_C} c \min\left(\frac{Ca}{250}, 0, 1\right)(V_d - V_K) + \frac{g_c}{1-p}(V_s - V_d) + \frac{I_d}{1-p}$$

$$\frac{dCa}{dt} = -0.13 \cdot \left(g_{Ca} \cdot s^2 \cdot (V_d - V_{Ca})\right) - 0.075 \cdot Ca$$

$$\frac{dh}{dt} = 0.128 \cdot \exp\left(\frac{17.0 - V_s}{18.0}\right) \cdot (1-h) - \frac{4.0}{\exp\left(\frac{-V_s+40.0}{5.0}\right) + 1.0} \cdot h$$

$$\frac{dn}{dt} = -0.016 \cdot \frac{V_s - 35.1}{\exp\left(\frac{-(V_s-35.1)}{5}\right) - 1.0} \cdot (1-n) - 0.25 \cdot \exp(-0.025 \cdot V_s + 0.5) \cdot n$$

$$\frac{ds}{dt} = \frac{1.6}{1.0 + \exp(-0.072 \cdot (V_d - 65.0))} \cdot (1-s) - \frac{0.02 \cdot (V_d - 51.1)}{\left(\exp\left(\frac{V_d-51.1}{5.0}\right) - 1.0\right)} \cdot s$$

$$\frac{dc}{dt} = \left(0.5 \cdot (1 - \tanh(V_d - 50.0)) \cdot \left(\frac{1}{18.975}\right) \cdot \left(\exp\left(\frac{V_d - 10.0}{11.0} - \frac{V_d - 6.5}{27.0}\right)\right)\right.$$
$$+0.5 \cdot (1 + \tanh(V_d - 50.0)) \cdot 2.0 \cdot \exp\left(\frac{6.5 - V_d}{27.0}\right)\Bigg) \cdot (1-c)$$
$$- \left(0.5 \cdot (1 - \tanh(V_d - 50)) \cdot 2.0 \cdot \exp\left(\frac{6.5 - V_d}{27.0}\right)\right.$$
$$\left. - \left(\frac{1}{18.975}\right) \cdot \left(\exp\left(\frac{V_d - 10.0}{11.0} - \frac{V_d - 6.5}{27.0}\right)\right) + 0.5 \cdot (1 + \tanh(V_d + 10)) \cdot 0\right) \cdot c$$

$$\frac{dq}{dt} = f(0.00002 \cdot Ca) \cdot (1-q) - 0.001 \cdot q$$

where $f(x)$ is a function that limits its input between 0 and 0.01. You can choose an appropriate function depending on the behavior you want to model. Some common choices include:

$$f(x) = \begin{cases} 0 & \text{if } x < 0 \\ x & \text{if } 0 \le x \le 0.01 \\ 0.01 & \text{if } x > 0.01 \end{cases}$$

or

$$f(x) = \frac{1}{1 + e^{-k(x - x_0)}}$$

where k controls the steepness of the function and x_0 is the point at which the function transitions from near 0 to near 1.

The values of the parameters used in Figure 5 are as follows.

p	gc	Is	Id	gL	gNa	gK_{DR}	gK_C	gCa	gK_{AHP}	$gKCa$	Cm	V_L	V_{Na}	V_K	V_{Ca}	V_{syn}
0.5	2.1	0.5	0.0	0.1	30.0	15.0	15.0	10.0	0.8	15.0	3.0	0	120	−15.0	140	30

DRAFT

In mathematics, the Heaviside step function is often denoted as $H(x)$ or $u(x)$. It is defined as:

$$H(x) = \begin{cases} 0 & \text{if } x < 0 \\ 1 & \text{if } x \geq 0 \end{cases}$$

The synaptic connections equations are as follows:

$$\frac{dS}{dt} = -\frac{S}{150} + \text{Heaviside}(V_s, 10) \cdot G$$

$$\frac{dW}{dt} = -\frac{W}{2} + \text{Heaviside}(V_s, 20) \cdot G$$

The parameters for the network model were the same as before.

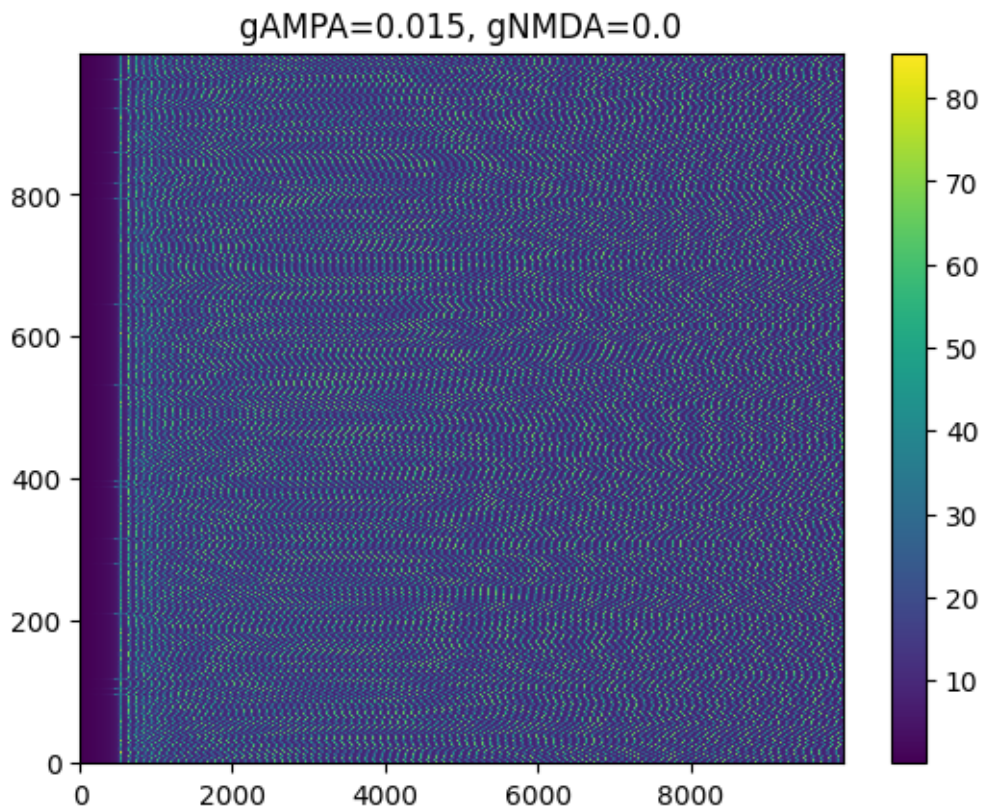


Fig. 6. Pinsky Rinzel Network Model. The x-axis is neuron ID. The y-axis is Time Steps such that each integration step counts 0.05. It makes up 500 ms. The colorbar gives Neuron Voltage. Current supplied to 40 neurons for 1ms. The semiflow Pattern is shown.

Reference:

[1] Paul F. Pinsky and John Rinzel. Intrinsic and Network Rythmogenesis in a Reduced Traub Model for CA3 Neurons. 1994