Effect of grouped neural connectivity on network synchronization

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Abstract

There are many different components to the organization of neurons in the brain (e.g. regions, cortical layers) but some are better understood than others. In this work we explore the apparent organization of neurons into columnar structures and test whether connectivity of neurons grouped locally effect the network synchronization differently than neurons which are grouped randomly (independent of poisition). We find that for our systems of purely excitatory neurons at very low propogation speeds ($\sim 10^{-3}$m/s), there is a clear difference of the behavior of locally grouped versus randomly grouped systems. This difference is most apparent for high connectivity (~ 40 connections per neuron) and large bias towards connectivity within the neural group. This scenario is also explored with systems of excitatory and inhibitory neurons. The results are in some ways consistent with the excitatory case but do not seem to highlight the same dramatic differences between locally and randomly grouped systems. Future work is proposed which would alter the connectivity of the inhibitory neurons, explore larger systems, and examine the similarity of these networks to the 'small-world network' description of neural connectivity.

1 INTRODUCTION

We understand a great deal about the makeup of neurons and how they communicate. We also understand a good deal about how different regions of the brain interact with the rest of the body. What is still left to be learned about the brain is what lies inbetween. How does the neural organization and connectivity give rise to the amazing abilities and functions of the network as a whole? The more specific question we seek to answer is: does the apparent columnar or locally grouped architecture of neurons in the neocortex have any measurable influence on the performance (specifically the synchronization) of the network?

1.1 The Brain and its Components

The human brain consists of a very complex network of billions of neurons. It is capable of storing, processing, and transmitting large amounts of information beyond that already stored in the genetic material of the organism. Much work has been done in studying how the brain works on a macroscopic level, for example, identifying which regions of the brain are associated with certain functions (speech,

hearing, vision etc.). Still it is important when studying the larger system to fully understand its components.

The region I will focus on in this work is that of the neocortex. This region is densely populated by diverse types of neurons divided into six layers and is responsible for many high-order functions, including sensory perception and cognition [1, 2, 3]. Of these six layers, the outermost layers (I-III) are more highly interconnected and, for the most part, any connections into or out of these layers are to the lower layers. The innermost layers (IV-VI) not only connect with the outer layers but also have long range connections which propogate information to and from other regions of the brain as well as sources of sensory information (e.g. eyes, ears, whiskers in mice) [1]. Therefore, in the upper regions, especially layer III, we have more complex interconnected networks, but we can more confidently study local regions of these layers using smaller (less computationally expensive) simulations with external stimulations to represent their connection to layers IV-VI.

1.2 Columnar Structure in the Neocortex

The neocortex can also be subdivided into less discrete units within the planes of the layers. On the largest scale these are radially connected regions, often on the order of a few hundred microns wide, which can be assosciated with specific functions, but can be classified more sepcifically as cortical columns [4, 5, 3]. This columnar view of the organization of the brain is less well defined, and it is sometimes disputed whether they have any noticable effect on function, but these columns are well accepted as a real undeniable feature of cortical structure [6].

Before we get down to the neurons, the cellular units of the brain, we encounter one more possibly important unit of structure. In the neocortex of the brains of humans, primates, and other mammals, cortical neurons appear to be arranged into microcolumnar (minicolumnar) structures [7, 8, 9, 10, 11, 12]. These structures are only a few micrometers thick ($\sim$1 neuron wide), but can extend through multiple layers of the neocortex [4]. It is still, however, an open question wether these structures serve a purpose in terms of the performance of the brain. Whether related to function or not, there have been many studies correlating loss of microcolumnar structure with cognitive decline. It has been shown that changes in structure of these microcolumns is correlated with aging in monkeys and humans [13, 14, 15, 16, 17] as well as neurological disorders such as Alzheimer's, Lewy body dimentia, schizophrenia, and autism [18, 19, 20, 21, 22, 23]. These structures are expecially prominent in layer III and so we will focus our work here [14].

According to Mountcastle's description of this columnar structure, many microcolumns combine to form the larger cortical columns which are so widely accepted and observed [4]. In this work the systems do not have a microcolumnar structure, but the features do fall somewhere just under his characteristic size for cortical columns. The work then does not seek to specifically justify this particular view but to instead investigate the significance to columnar structure and connectivity as compared with random connectivity.

1.3 Synchronization of Neurons

The cognitive performance of a living brain can be tested in many ways but it can be more difficult to develop a metric for a computational simulation of a network of neurons. One useful and relatively simple measure is the synchronization of neurons in the network. Synchronization (and changes in the degree of synchronization) of pairs of cortical neurons has been linked with the performance of different attention related tasks in primates [24, 25, 26]. Although the synchronization of neurons

itself does not tell us anything specific about the activity of the brain itself, it does appear that the arrival of this synchronization or changes to the way neuronal outputs are correlated is closely related to function [27] Therefore, finding conditions which directly effect the synchronization of a network of neurons may be a useful method of determining important variables that determine the performance of the brain.

To approach this problem, we examine a neural network broken up into local clusters, inspired by a combination of the small-world network (discussed in future work) and columnar models of the brain. Using the ratio of inter-column to intra-column connectivity and the porportion of connections present as our variables we measure network synchronization as a tool of discovering the possible function and importance of local network structure in brain activity.

2 METHODS

The main progression of the simulations involved in the work consisted of: (1) splitting a random network of neurons into a grid pattern, (2) connecting the neurons according to a specified bias towards connections within grid blocks, and (3) running a simulation of the network by providing a series of stimulating action potentials to each neuron. This process is repeated on systems of neurons which are randomly assigned to groups as opposed to grouping by grid. The intent is to provide a clear comparison between the behavior of locally connected networks and those whose connections have no dependence on proximity.

Previous student Michael Royster, building on work of Max Henderson, PhD, developed a suite of programs which handled much of the placement, connectivity, and simulation control with little interaction from the user. This suite also incorporates neuronal placement software developed by advisor Luis Cruz Cruz, PhD. I have contributed some changes to the program and run simulations to reproduce features seen in previous work as well as to explore the effect of inhibitory neurons on these features. The following description of methods follows essentially the same progression as the work done by Michael Royster, aside from a few additions, and data and figures obtained from M. Roster's work are noted as such.

2.1 Neuronal Placement

A set of three dimensional neural positions are generated in a box of side length L_b in a microcolumnar organization using the 'slicegen' program[28]. Each neuron then follows a random walk with hard-sphere interaction to randomize the positions (see Fig 1a). We acheive a network of neurons with completely random positions, but by starting with the microcolumnar organization, we can use the same method and retain some microcolumnar structure in the future. Two types of system with different sizes were generated with $L_b = 256\mu m$, $384\mu m$, containing an average $N_E = 554.2$, 1942.7 excitatory neurons respectively. For the systems with inhibitory neurons included (only done for smaller L_b), an average of $N_I = 138.9$ inhibitory neurons were added to bring the density of inhibitory neurons to $\sim 20\%$. The work done by M. Roster included only excitatory neurons and only explored the smaller size system.

Neurons are labeled as belonging to a certain group according to two different methods. In the first method, an $n \times n$ grid is overlayed onto the xy coordinates of the neural ensemble (2x2 for smaller system and 3x3 for larger system). Each neuron is assigned to the group that contains its xy-coordinates, as shown in Fig 1b. In the second method, neurons are assigned to groups randomly such that each

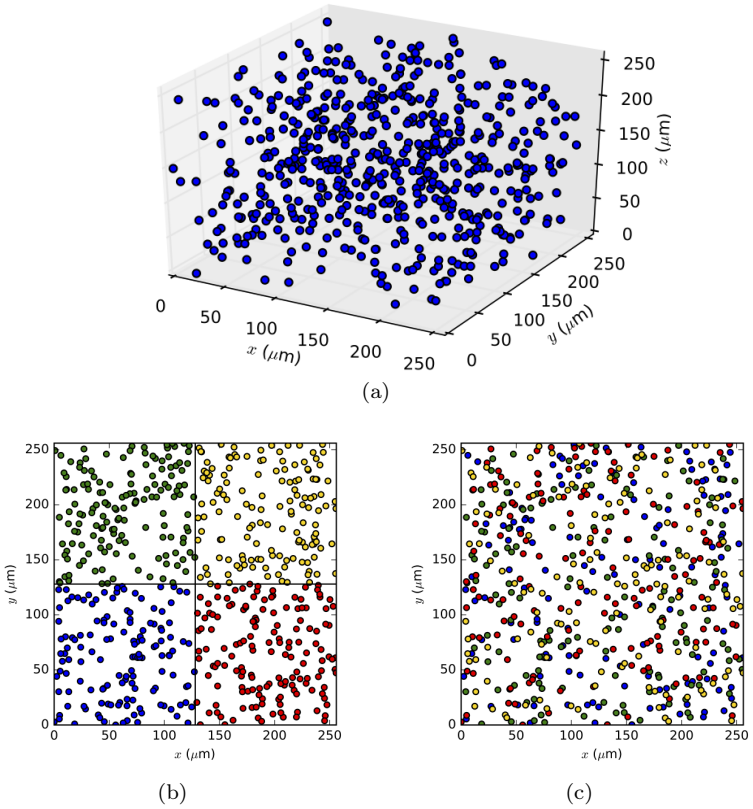


Figure 1: Creation and labelling of neuronal distribution. (a) A random distribution of ~ 554 neurons is created in a 256μm edged box. (b) Example of grid assignment process: 2x2 grid is placed in xy plane and neurons are assigned to groups based on xy position. (c) Example of mixed group assignments: neurons are randomly assigned to 4 different groups, corresponding to the grid assignment in (b).

group has the same number of neurons as in the first method, as shown in Fig 1c. We will refer to these grouping methods as segregated groups and mixed groups respectively.

2.2 Connections

The purpose of assigning the neurons to groups is essentially to give some sort of context for local versus non-local connections which also mirrors the columnar picture of the cortex. To implement this, neurons are connected with a bias to form intra-group connections. Every pair of neurons is assigned a certain probability of forming a connection, and pairs in the same group have a higher probability of forming a connection based upon the bias parameter. For a desired number of connections per neuron

m and bias parameter δ, this results in a symmetric probability matrix $\mathbf{P}$ such that

$$\mathbf{P}_{ij} = \begin{cases} 0 & i = j \\ p_{rand} + p_{intra} & B_i = B_j \\ p_{rand} & \text{otherwise} \end{cases} \tag{1}$$

where

$$p_{rand} = \frac{m\,(1-\delta)}{N-1} \qquad p_{intra} = \frac{m\delta}{M^{(G_i)}-1} \tag{2}$$

N is the number of neurons in the system, $M^{(G_i)}$ is the number of neurons in the ith neuron's group, and G_i is the label identifying the ith neuron's group. When $\delta = 0$, this recovers a uniform random distribution of connections and when $\delta = 1$, all connections are within each group (see Figures 2a and 2c respectively for examples of each case). The probabilities in (2) satisfy the constraint

$$m = (N-1)\,p_{rand} + \left(M^{(G_i)} - 1\right) p_{intra} \tag{3}$$

independent of changes to δ except in the case of saturation.

Saturation occurs when the number of intra-group connections desired $m^{(i)}_{group}$ is greater than the total number of possible connections within the group $M^{(B_i)} - 1$. Modifying (3) shows that the expected value of $m^{(i)}_{group}$ is

$$\langle m_{group} \rangle = m \left[\delta \left(1 - \frac{\langle M \rangle - 1}{N-1} \right) + \frac{\langle M \rangle - 1}{N-1} \right] \tag{4}$$

$$\langle M \rangle = \frac{N}{\text{number of groups}} \tag{5}$$

The maximum m that can be used without saturation for all values of δ is then

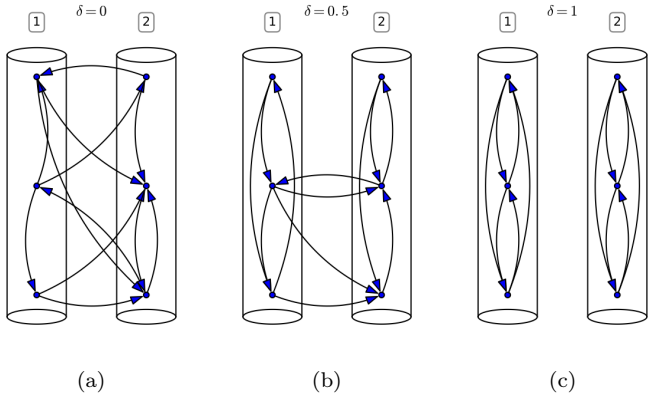
$$m = \langle M \rangle - 1 \tag{6}$$

This maximum m is also the reason why we use a larger system when breaking up the box into a 3x3 grid. We can reach value of m because our number of neurons per group remains the same. For now, inhibitory neurons are connected in the same way as excitatory neurons. The probability of connection does not depend at all on the type of neurons involved, only whether or not they belong to the same group.

2.3 Simulation

To simulate the firing of the neurons, the package NEURON was used. This allowed us to model the membrane potential using Hodgkin-Huxley mechanisms. To stimulate the system (and simulate incoming connections) each neuron receives a series of action potentials (APs) drawn from a Poisson distribution with average interval 35 ms. These series drive the system and are independent for each neuron. Each driving AP raises the target neuron's membrane conductance g by $1\mu S$ and generates a membrane current $I = gV$. The membrane conuductance decays exponentialy such that

$$\frac{dg}{dt} = -g/\tau$$



(a) (b) (c)

Figure 2: Connections between groups 1 and 2 as δ is changed ($m = 2$). (a) Completely random connections with $\delta = 0$. Predicted number of intra-group connections is 0.8, with measured values of 0.67 and 1.0 for blocks 1 and 2 respectively. (b) Bias towards intra-group connections with $\delta = 0.5$. Predicted number of intra-group connections is 1.4, with measured values of 1.3 for both groups. (c) Completely isolated inside the macrocolumn with $\delta = 1$. Predicted number of intra-group connections is 2, with measured values of 2 for both blocks. These figures generated by M. Royster

where $\tau = 1$ms.

Once the ith neuron's membrane potential rises above a threshold (10 mV in our experiments), an AP is transmitted to each connected neuron j. The effect of this AP depends on the type of connection. When an excitatory (E) neuron is sending the signal, the membrane conductance is raised, increasing likelihood of target neuron firing. Conversely, a signal from an inhibitory (I) neuron lowers the conductance of the target. The increases and decreases for each type of connection are listed:

$$\begin{aligned} \text{E} \to \text{E} \quad & + 0.45\mu S \\ \text{E} \to \text{I} \quad & + 0.20\mu S \\ \text{I} \to \text{E} \quad & - 0.05\mu S \\ \text{I} \to \text{I} \quad & - 0.10\mu S \end{aligned}$$

To simulate the time the signal takes to travel along the axon, transmit, and travel along dendrite, each AP arrives after a delay time

$$t_{ij} = \begin{cases} d_{ij}/v_1 & d_{ij} < 155\mu m \\ d_{ij}/v_2 & d_{ij} \geq 155\mu m \end{cases}$$

where $v_2 > v_1$. This approach of separating delay times for large and small distances, accounts for the increased transmission speed found on axons with myleinated sheaths. These speeds are not well documented for neurons in the neocortex so these parameters were varied from 6.38 to 150μm/ms for v_1 and 12.77 to 300μm/ms for v_2.

2.4 Statistics

We generated a total of 10 sample systems with only excitatory neruons to reproduce the work of M. Royster and 10 sample systems with inhibitory neurons included. Each grouping system was applied to create a segregated and mixed groups case for each of these systems. When generating connections, a range of $m = [1, 45]$ and $\delta = [0, 1)$ was used allowing us to scan the phase space. Values of m and δ were picked randomly. The propogation speeds v_1 and v_2 became variables to use in our search for features. A large range of propogation speeds were explored and those which demonstrated interesting features will be shown below.

3 RESULTS

3.1 Synchronization

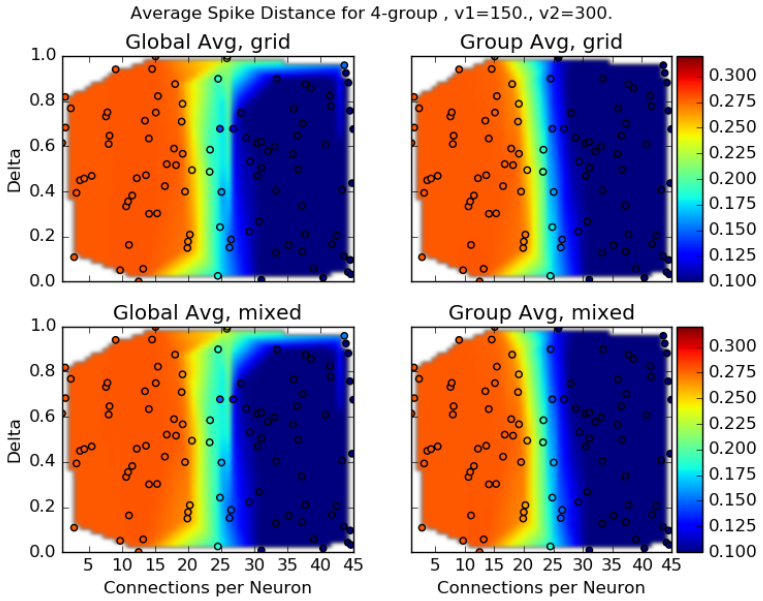
Using the changes in membrane potential of each neuron, we found the times each neuron generated an action potential. This sequence of spiking events is referred to as a neuron's spike train. We measured the synchronization between every pair of neurons in the system using the SPIKE-distance method created by Kreuz [29, 30]. This metric is bounded on the interval $[0, 1]$, where 0 indicates complete synchronization and 1 indicates complete asynchronization. Averaging the synchronization of every neuron yields the system's global synchronization. The average synchronization was calculated for each group and averaged together to define the group synchronization.

We first examine the systems without inhibitory neurons. Figure 3a shows a synchronization phase diagrams for 4-group (2x2 grid) systems at high speeds of propogation (150μm/ms, 300μm/ms). We see a sharp transition around $m = 25$ inditcating some sort of critical number of connections per neuron to enter the more synchronous regions on the right. There is also a small but definite difference between the global average and the group averages of synchronization. We see that there is a transition to asynchrony at $\delta = 0.9$ in the global average but not in the local average where there is little impact of δ. This can be rationalized by the fact that if each group has neurons that are synchronized with each other but not with the other groups, the group average will appear synchronous but the global average wiill not. This feature is much more apparent in the work of M. Royster which fills in the phase space more. This part of my work seaks to simply reproduce and confirm his results.

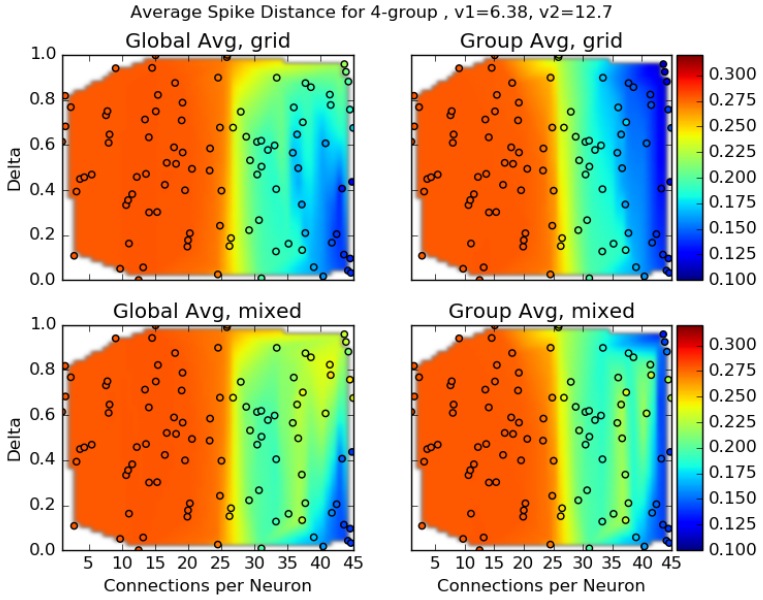
Figure 3b shows the same size system but with a much slower propogation speeds. Overall the system does not become as synchronous and our transition point seems to be slightly above $m = 25$. However, there arises a clear difference between the systems which have been connected based on segregated grouping (labelled 'grid') and those connected based on mixed grouping. In both the global and group averages there is an asynchronous region at high m and δ that appears only in the mixed grouping. This difference was discovered by M. Royster and was successfully recovered with these simulations.

We also examined larger systems to see whether there were any features which were artifacts of the size of the box. Figure 4 shows that the larger system exhibits some different behavior. Notably there is another asynchronous region at high m and low δ. Despite these new features there still appears to be the same discrepency between segregated grouping and mixed grouping: that is, at high m and high δ there is an asynchronous region that only appears in the mixed grouping system.

Once we add in inhibitory neurons, the whole system actually becomes less synchronous. This might be expected since the inhibitory neurons may have a similar effect to slowing down propogation speeds. When we look at Figure 5a, which shows the results of a simulation at high propogation



(a)



(b)

Figure 3: Average SPIKE-distance for 4-group (2x2 grid, $L_b = 256\mu$m) system of excitatory neurons. Each sub-figure shows global and group averages for segregated and mixed groups. a) Simulation at high propogation speeds ($v_1 = 150\mu$m/ms, $v_2 = 300\mu$m/ms). b) Simulation at low propogation speeds ($v_1 = 6.38\mu$m/ms, $v_2 = 12.77\mu$m/ms)

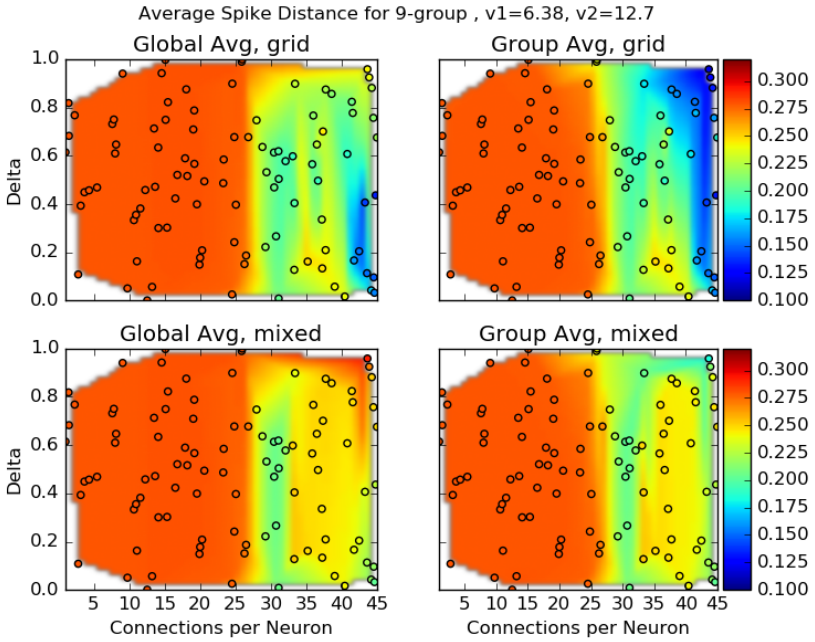
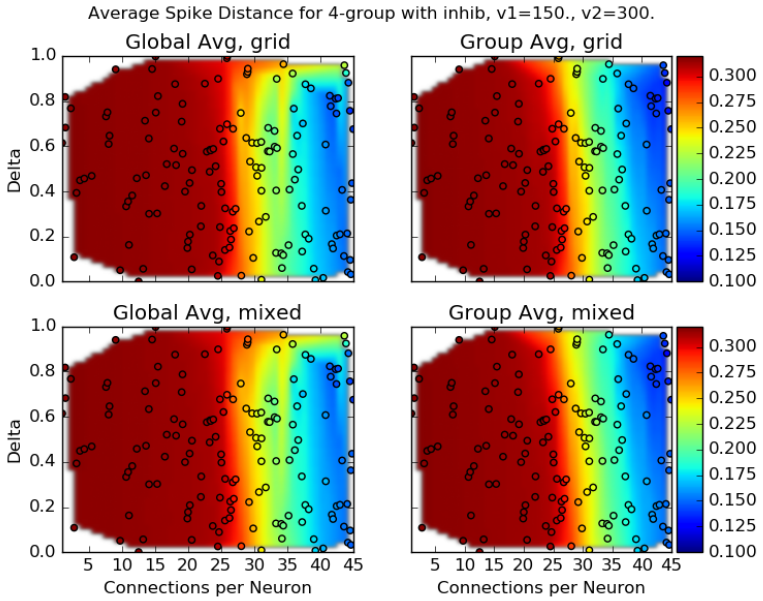
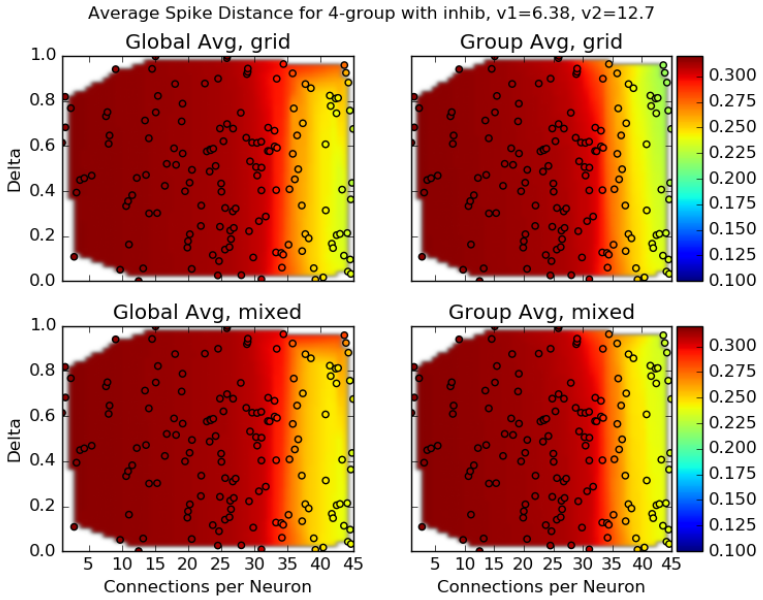


Figure 4: Average SPIKE-distance for 9-group (3x3 grid, $L_b = 384\mu$m) system of exitatory neurons at low propogation speed ($v_1 = 6.38\mu$m/ms, $v_2 = 12.77\mu$m/ms).



(a)



(b)

Figure 5: Average SPIKE-distance for 4-group system of excitatory and inhibitory ($\sim 20\%$) neurons. a) Simulation at high propogation speeds ($v_1 = 150\mu$m/ms, $v_2 = 300\mu$m/ms). b) Simulation at low propogation speeds ($v_1 = 6.38\mu$m/ms, $v_2 = 12.77\mu$m/ms)

speeds, we see a similar transition to that which we have seen in the purely excitatory systems. There are a few more features in the global averages which may be of interest. They do show some small asynchronous regions at higher m than we saw in the purely excitatory case. However, we do not see a large difference between the segregated and mixed grouping systems. If there is any difference (around $m = 35$, $\delta > 0.6$) it is minute. At slower speeds, Figure 5b, the system becomes much less synchronous but if we look closely at the region of very high m and δ, we can still see some differences between the grouping types.

4 DISCUSSION / FUTURE WORK

The results that recreated previous work show a clear difference between synchronization of systems with segregated (columnar) grouping and those with mixed grouping, but only at low speeds of propogation. These speeds however are not very biologically realistic. The presence of this feature at only slow speeds could be the result of a few things. The first reason could be the size of the system: a larger system could possibly recreate the feature at higher speeds because an increase in distance and decrease in speed both directly effect the delay time. The second reason could be the lack of inhibitory neurons. These inhibitory neurons could have a similar effect to slowing down the signal propogation by working against excitation. Without inhibitory neurons, the excitation of neurons in the brain would get out of control. Adding in neurons was one step in the right direction of making this simulation more biologically feasible, however it did not seem to recover the distinguishing feature at high speeds.

There are a few different steps forward from here. One is to change the connectivity of our inhibitory neurons. The columnar organization may only apply to projection (excitatory) neurons in which case bias towards connecting within a column (local group) would only apply to excitatory neurons. To test this, we would like to also run simulations for systems that connect inhibitory neurons randomly without bias. These connections would be either to the whole system or to radially close neighbors (with exponentially decaying probability). This would represent a system in which excitatory neurons are biased towards columnar connections but inhibitory are not, and actually act as a link between columns. Even though they are inhibitory they would transmit information about neuron firing between columns. This feature would be much more important at high δ values as systems with high δ have blocks which are nearly completely isolated from each other.

We would also like to explore the theoretical side of these networks. Clustering of neurons in the brain, along with relatively short average path length between neurons, leads to a possible mathematical description of the brain as a small-world network of neurons [31, 32, 33, 34, 35]. Our parmeter δ is essentially a measure of the clustering of our network. There is also evidence that this balance of clustering to long-range connection between neurons effects synchronization. For example, it has been shown that the balance of excitation and inhibition can disappear when a random model is replaced by a complex clustered model [36]. This description is a more theoretical one, but characterizing the degree to which our networks reflect this "small-world" network could give us insight into why certain regions of phase space exhibit certain behavior.

5 CONCLUSIONS

This work, along with the work of M. Royster, highlights a difference in the behavior of systems with locally and randomly connected blocks. By adding in inhibitory neurons we brought the simulation

closer to accurately representing a biological system of neurons in layer III of the neocortex. We also decreased the overall synchronization of the network (may or may not be relevant). We did not however find extremely interesting features differentiating randomly connected and locally connected blocks at high propogation speeds in these new networks. Further work may uncover these differences at higher propogation speeds with different systems and different inhibitory connectivity, but a large search through different combinations of parameters is in order. Theoretical analysis of the network is also in order as it may lead to a better understanding of the phase space we are scanning.

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References

[1] Somana Lodata and Paola Arlotta. Generating neuronal diversity in the mammalian cerebral cortex. *Annual Review of Cell and Developmental Biology*, 31:699–720, 2015.

[2] Jan H. Lui, David V. Hansen, and Arnold R. Kriegstein. Development and evolution of the human neocortex. *Cell*, 146(1):18–36, 2011.

[3] Brian G. Rash and Elizabeth A. Grove. Area and layer patterning in the developing cerebral cortex. *Current Opinion in Neurobiology*, 16(1):25–34, 2006.

[4] Vernon B. Mountcastle. The columnar organization of the neocortex. *Brain*, 120:701–722, 1997.

[5] Nuno Macarico da Costa and Kevin A. C. Martin. Whose cortical column would that be? *Fronteirs in Neuroanatomy*, 4(16), 2010.

[6] Jonathan C Horton and Daniel L Adams. The cortical column: a structure without a function. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 360(1456):837–862, 2005.

[7] DP Buxhoeveden, AE Switala, E Roy, M Litaker, and MF Casanova. Morphological differences between minicolumns in human and nonhuman primate cortex. *American Journal of Physical Anthropology*, 115(4):361–371, AUG 2001.

[8] DP Buxhoeveden and MF Casanova. The minicolumn hypothesis in neuroscience. *Brain*, 125:935–951, MAY 2002.

[9] DP Buxhoeveden and MF Casanova. The minicolumn and evolution of the brain. *Brain Behavior and Evolution*, 60(3):125–151, 2002.

[10] J Defelipe, S.H.C. Hendry, T Hashikawa, M Molinari, and E.G. Jones. A microcolumnar structure of monkey cerebral-cortex revealed by immunocytochemical studies of double bouquet cell axons. *Neuroscience*, 37(3):655–673, 1990.

[11] AE Vercelli, D Garbossa, R Curtetti, and GM Innocenti. Somatodendritic minicolumns of output neurons in the rat visual cortex. *European Journal of Neuroscience*, 20(2):495–502, JUL 2004.

[12] Noritaka Ichinohe. Small-scale module of the rat granular retrosplenial cortex: an example of the minicolumn-like structure of the cerebral cortex. *Frontiers in Neuroanatomy*, 5, JAN 10 2012.

[13] L Cruz, DL Roe, B Urbanc, H Cabral, HE Stanley, and DL Rosene. Age-related reduction in microcolumnar structure in area 46 of the rhesus monkey correlates with behavioral decline. *Proceedings of the National Academy of Sciences of the United States of America*, 101(45):15846–15851, NOV 9 2004.

[14] L. Cruz, D. L. Roe, B. Urbanc, A. Inglis, H. E. Stanley, and D. L. Rosene. Age-related reduction in microcolumnar structure correlates with cognitive decline in ventral but not dorsal area 46 of the rhesus monkey. *Neuroscience*, 158(4):1509–1520, FEB 18 2009.

[15] SA Chance, MF Casanova, AE Switala, TJ Crow, and MM Esiri. Minicolumn thinning in temporal lobe association cortex but not primary auditory cortex in normal human ageing. *Acta Neuropathologica*, 111(5):459–464, MAY 2006.

[16] Steven A. Chance, Linda Clover, Helena Cousijn, Leila Currah, Rosemary Pettingill, and Margaret M. Esiri. Microanatomical correlates of cognitive ability and decline: Normal ageing, mci, and alzheimer's disease. *Cerebral Cortex*, 21(8):1870–1878, AUG 2011.

[17] Susanne J. van Veluw, Eva K. Sawyer, Linda Clover, Helena Cousijn, Celeste De Jager, Margaret M. Esiri, and Steven A. Chance. Prefrontal cortex cytoarchitecture in normal aging and alzheimer's disease: a relationship with iq. *Brain Structure & Function*, 217(4):797–808, OCT 2012.

[18] SV Buldyrev, L Cruz, T Gomez-Isla, E Gomez-Tortosa, S Havlin, R Le, HE Stanley, B Urbanc, and BT Hyman. Description of microcolumnar ensembles in association cortex and their disruption in alzheimer and lewy body dementias. *Proceedings of the National Academy of Sciences of the United States of America*, 97(10):5039–5043, MAY 9 2000.

[19] F. M. Benes and E. D. Bird. An analysis of the arrangement of neurons in the cingulate cortex of schizophrenic-patients. *Archives of General Psychiatry*, 44(7):608–616, JUL 1987.

[20] M. F. Casanova. Schizophrenia as a neurological condition caused by a failure in the lateralisation of the brain: macro and microscopic observations. *Revista De Neurologia*, 49(3):136–142, AUG 1 2009.

[21] Enrica Di Rosa, Timothy John Crow, Mary Anne Walker, Georgia Black, and Steven Andrew Chance. Reduced neuron density, enlarged minicolumn spacing and altered ageing effects in fusiform cortex in schizophrenia. *Psychiatry Research*, 166(2-3):102–115, APR 30 2009.

[22] MF Casanova, I van Kooten, AE Switala, H van England, H Heinsen, HWM Steinbusch, PR Hof, J Trippe, J Stone, and C Schmitz. Minicolumnar width abnormalities in autism. *Biological Psychiatry*, 59(8, S):19S, APR 15 2006. 61st Annual Convention of the Society-of-Biological-Psychiatry, Toronto, Canada, MAY 18-20, 2006.

[23] M. F. Casanova, I. van Kooten, A. E. Switala, H. van Engeland, H. Heinsen, H. W. M. Steinbusch, P. R. Hof, and C. Schmitz. Abnormalities of cortical minicolumnar organization in the prefrontal lobes of autistic patients. *Clinical Neuroscience Research*, 6(3-4):127–133, OCT 2006. 85th Annual Conference of the Association-for-Reseach-in-Nervous-and-Mental-Disease, New York, NY, DEC 01-02, 2005.

[24] PN Steinmetz, A Roy, PJ Fitzgerald, SS Hsiao, KO Johnson, and E Niebur. Attention modulates synchronized neuronal firing in primate somatosensory cortex. *Nature*, 404(6774):187–190, MAR 9 2000.

[25] P Fries, JH Reynolds, AE Rorie, and R Desimone. Modulation of oscillatory neuronal synchronization by selective visual attention. *Science*, 291(5508):1560–1563, FEB 23 2001.

[26] A Riehle, S Grun, M Diesmann, and A Aertsen. Spike synchronization and rate modulation differentially involved in motor cortical function. *Science*, 278(5345):1950–1953, DEC 12 1997.

[27] E Salinas and TJ Sejnowski. Correlated neuronal activity and the flow of neural information. *Nature Reviews Neuroscience*, 2(8):539–550, AUG 2001.

[28] Luis Cruz, Brigita Urbanc, Andrew Inglis, Douglas L. Rosene, and H. E. Stanley. Generating a model of the three-dimensional spatial distribution of neurons using density maps. *Neuroimage*, 40(3):1105–1115, APR 15 2008.

[29] Thomas Kreuz, Daniel Chicharro, Martin Greschner, and Ralph G. Andrzejak. Time-resolved and time-scale adaptive measures of spike train synchrony. *Journal of Neuroscience Methods*, 195(1):92–106, JAN 30 2011.

[30] Thomas Kreuz, Daniel Chicharro, Conor Houghton, Ralph G. Andrzejak, and Florian Mormann. Monitoring spike train synchrony. *Journal of Neurophysiology*, 109(5):1457–1472, MAR 2013.

[31] Rodrigo Perin, Thomas K. Berger, and Henry Markram. A synaptic organizing principle for cortical neuronal groups. *Proceedings of the National Academy of Sciences of the United States of America*, 108(13):5419–5424, MAR 29 2011.

[32] CJ Stam. Functional connectivity patterns of human magnetoencephalographic recordings: a 'small-world' network? *Neuroscience Letters*, 355(1-2):25–28, JAN 23 2004.

[33] C. J. Stam and E. C. W. van Straaten. The organization of physiological brain networks. *Clinical Neurophysiology*, 123(6):1067–1087, JUN 2012.

[34] VM Eguiluz, DR Chialvo, GA Cecchi, M Baliki, and AV Apkarian. Scale-free brain functional networks. *Physical Review Letters*, 94(1), JAN 14 2005.

[35] Yong He, Zhang J. Chen, and Alan C. Evans. Small-world anatomical networks in the human brain revealed by cortical thickness from mri. *Cerebral Cortex*, 17(10):2407–2419, OCT 2007.

[36] Mark D. McDonnell and Lawrence M. Ward. Small modifications to network topology can induce stochastic bistable spiking dynamics in a balanced cortical model. *PLOS One*, 9(4), APR 17 2014.