Transitions in a Metastable Neuronal Network

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Abstract

Recent experimentation has found that while newborn rats follow an exponential distribution for wake bout distributions, older rats follow a power law distribution. Understanding possible explanations for this phenomenon requires understanding how transitions occur in metastable systems. Here we review some useful mathematical results and terminology in relation to networks and explore how several different network structures affect the dynamics of this sleep-wake system. We also employ several methods to identify possible transition mechanisms to help uncover biological and mathematical reasons for the change in bout distributions. Studying each mechanism, we relate the most prevalent transition mechanism for a system with a given network architecture to the type of bout distribution observed and correlate power law behavior to a gradual degradation mechanism and exponential behavior to a mechanism involving the firing of well-connected nodes.

1 Introduction

Biological processes can be governed by or modeled with network dynamics. One such example is the transition between sleep and wake states governed by two mutually inhibitory and self-excitatory neuronal networks. This is hypothesized to be a possible network structure or sub-structure in the brains of many species [1, 2, 3]. Experiments have shown that the wake bout distribution observed in infant rats is exponentially distributed, while older rats produced a power law distribution [4]. This implies a change in the neuronal network structure present in the part of the brain that regulates this sleep-wake system. Knowing what behavior to expect from different network architectures becomes vital in predicting the causes and implications of this change in network structure.

The actual sleep-wake rhythms are also important by themselves. The amount of time spent in sleep and wake states is directly related to the amount of REM sleep obtained, which is hypothesized to be a crucial component of many biological processes, such as long term memory consolidation [16]. A power law distribution for older rats implies a higher probability to be asleep for a shorter period of time. Extending this to humans makes sense, as humans tend to need, or at least get, less sleep as they grow older, compared to when they are infants. The question is whether the brain needs less sleep to function at the same level which causes a change in brain structure, or if some natural, or unnatural, change in the structure of the brain causes the bouts to be shorter. We aim to test the plausibility of the latter question by considering the same dynamical rules for a neuronal network under different architectures.

Although much is known about the brain, there are also many unknowns in terms of specific structures responsible for the physiology that is observed in experiment. Because of this, it is difficult to produce an accurate model of specific processes. Instead of modeling a known system with pre-determined parameters, assumptions are made and are put to use in various models. These models are then tested with different mechanisms and parameters until the desired behavior is consistently reproduced. One such model is a stochastically driven, competitive, firing rate model. However, simply having this basis for a competitive network is not enough, as there are many ways to create a network that satisfies this condition. It has been found that parts of the brain display complex network connections; that is that they contain an inhomogeneous mixture of features characteristic of different types of networks. The key distinguishing feature among these types of networks is how ordered or how random they are. Erdos and Renyi developed the tools to create random graphs [12] and by extension, networks, which are binomially degree distributed. If some kind of order is desired, scale free and small-world networks have predictable degree distributions in the form of a power law, and have been used to accurately model many real-world systems.[10]

The network model we used to describe this sleep-wake system was found to be metastable [13], staying in one state for a long time and then suddenly changing states. The distribution of the amount of time spent in each state has been shown to exhibit characteristics of both exponential and power law distributions, dependent on the structure of the network. An important factor in understanding these distributions is the transition mechanism between states. Knowing how the system goes from one state to the other allows us to predict when transitions will occur given a set of precursors, determine how often these precursors appear, and validate conceptually the power law that has been observed in experiment and simulation.

In this paper, we simulate the dynamics of a stochastic, competitive neuronal network that has been shown to produce exponential and power law bout distributions for certain choices of parameters. We study how network structure affects the dynamics, transitions between states, and the amount of time spent in each state. Transition mechanisms are identified, formally defined, and then statistically associated with the network architecture.

The rest of the paper is organized as such. Section 2 introduces the structure and dynamics of the neuronal network model used. In Section 3, transition mechanisms for varying network structures are discussed. Next, Section 4 describes the effect of changing the intermediate state boundaries on bout length. Section 5 details an attempt at a perturbation approach to find transition mechanisms and Section 6 concludes with a summary of the important findings.

2 Description of Network

2.1 Network Terminology and Definitions

Cluster: A group of neurons responsible for one type of behavior, eg sleep or wake.
Directed: Networks can be directed or undirected. A directed network is one in which a connection existing from node i to node j guarantees one way communication from i to j, but not necessarily from j to i.
Degree: The degree of a node i, typically denoted by n, is the number of nodes connected to node i, in an undirected network. In a directed network, there exists an in degree and out degree. The in degree of node i refers to the number of nodes, j, that communicate with node i, but node i does not necessarily communicate with any of the j nodes, though this is possible. Similarly, the out degree is the number of nodes, j, that i communicates with, but does not necessarily receive communication from.
Degree Distribution: The probability, $P(n)$, that a randomly selected node has degree n.

2.2 Network Architectures

2.2.1 Erdos-Renyi

An Erdos-Renyi network is a random network in which there is an equal probability for any node to be connected to any other node, independent from the rest of the network. It is created by considering each possible connection between two nodes i and j, generating a uniform random number between 0 and 1, and creating the connection if said number is less than p, the desired mean degree, divided by the total number of nodes in the system, N. The produced degree distribution is binomial. The degree distribution of any particular node is given by

$$P(n) = \binom{N-1}{n} \left(\frac{p}{N}\right)^n \left(1 - \frac{p}{N}\right)^{N-1-n}$$

where n is the degree of the node.

2.2.2 Scale Free

Scale Free networks follow a power law degree distribution and are created by defining a higher probability for a neuron to be connected to a neuron with more connections. The network begins with m initial nodes and n initial connections. Nodes are then added to the system one at a time until a desired amount, N, is reached. Every time a node is added, it is connected to m other nodes with probabilities proportional to the sum of each existing nodes in and out degree. Once the connecting nodes are chosen, the new node is given out connections and the existing neurons are given an in connection. This creates well-connected hubs that accurately model many real life systems [10]. The distribution is given by

$$P(n) \propto n^{-c}$$

where c generally satisfies the inequality $2 < c < 3$ [11].

2.3 Description of Network Dynamics

The system [13, 14, 15] is a directed, stochastic neural network progressing in time as a **continuous time** Markov Chain utilizing the Gillepsie Algorithm to ensure a statistically correct trajectory. Events are probabilistically generated by firing rates and depend only on the current state of the system. This competitive network composed of two clusters, one sleep and one wake, contain neurons that can be excited, inhibited, or in a base state. These clusters are mutually inhibitory and self-excitatory, such that when one neuron fires, it excites neighboring neurons in the same cluster and inhibits neighboring neurons in the opposite cluster (Figure 1) in the following way. When neuron i fires, we look at the state of all neurons with an incoming connection from neuron i. If in the same cluster, the receiving neuron is excited to the next state, i.e. inhibited to base, or base to excited. There is no effect on other excited nodes. If in the opposite cluster, the receiving neuron is inhibited to the next state down, i.e. excited to base or base to inhibited. There is no effect on already inhibited neurons. A neuron that is in an inhibited or excited state may also relax, which returns the neuron to the base state. At any time step, one neuron can fire or relax based on the rate of each event. Let f_j and r_j denote the firing rate and relaxation rate, respectively, for a neuron in state j, where j can be excited (e), basal (b), or inhibited (i). Rates were as follows for all simulations: $f_e = 0.016$, $f_b = 0.03$, $f_i = 0.001$, $r_e = 0.005$, and $r_i = 0.001$. Neural connections were made in one of two ways; Erdos-Renyi (Directed) and Scale-Free (Directed). Both inter-cluster and intra-cluster connections were made in the same way. For the Scale-Free Network, preferential attachment was performed across networks in the same way it was performed in a single network, but with $\frac{N}{2}$ added to the index of node j.

Two quantities are measured during the course of the simulation, $W_E(t)$ and $S_E(t)$, the fraction of excited nodes in the wake and sleep cluster, respectively. These quantities are plotted against simulation time and used to determine when transitions occur. A sample plot is shown in Figure 2 for scale free network couplings. The value of p is the mean excitatory degree of nodes, q the mean inhibitory degree of nodes, and N the number of neurons in the system.

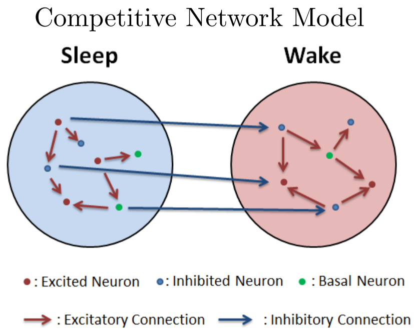


Figure 1
A simple example network showing the wiring for the two mutually inhibitory and self excitatory networks.

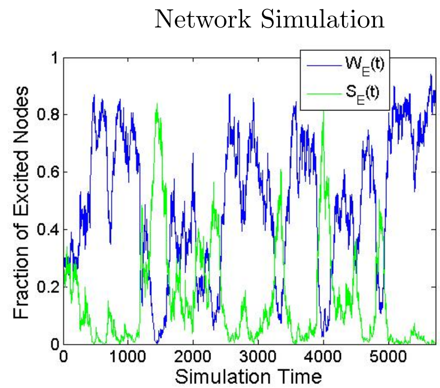


Figure 2
Example simulation using scale free connections. $N = 1000$, $p = 3.4$, $q = 4.08$.

3 Transition Mechanisms

The first network type that was studied was an Erdos-Renyi connected network, with $N = 100$ and various values for the mean excitatory and inhibitory degrees, ranging from 1 to about 7. It was observed that for every transition the fraction of excited nodes in the active cluster would decrease until the fraction of excited nodes went down to approximately 0.3, at which point neurons in the suppressed cluster would fire several times and overtake the active cluster. Several quantities related to inhibition were calculated and tested to see if they could accurately predict transitions. The number of neurons in the active cluster that got inhibited and that got excited over ten time steps were calculated, the difference between the two was taken, and it was compared to ten times the number of inhibitory connections. This quantity was successful in finding transitions, but not predicting them. By the time the measured quantity became greater than the criteria it was compared to, the active cluster was already inhibited down to less than 0.3 fraction of excited nodes, so that criteria might as well be used as a predictor, which is unacceptable. Several more quantities were tested including ratios of the previous two quantities and the number of excited and inhibited neurons from the inhibited cluster. Nearly the same results were obtained for all quantities. These quantities predicted better with some network connections over others, with the best predicting a transition when the fraction of excited nodes was reduced to 0.45 and in the worst case, not predicting transitions at all.

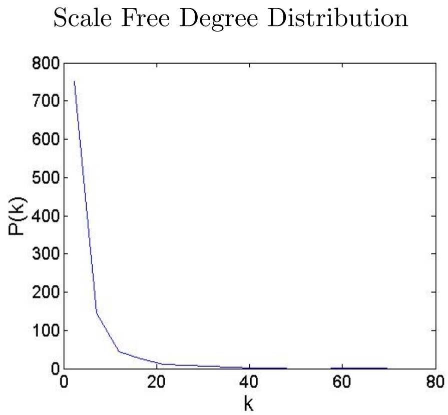
A scale free network was constructed next using a preferential attachment algorithm and the degree distribution was verified to be power law distributed by using a log-log plot (Figure 3). Using a line of best fit approximation on the continuous part of the distribution we find a slope of approximately -2.23. We can write the function in log-log coordinates as

$$ln(P(k)) = -2.23 * ln(k) + 9.95$$

where -2.23 is the power law exponent and $e^{9.95} = 20952$ is the proportionality constant in the power law expression for $P(k)$. Using this we get a degree distribution of

$$P(k) = 20952 * k^{-2.23}$$

This falls within the usual range of exponents for a scale free distribution, satisfying $2 < m < 3$.



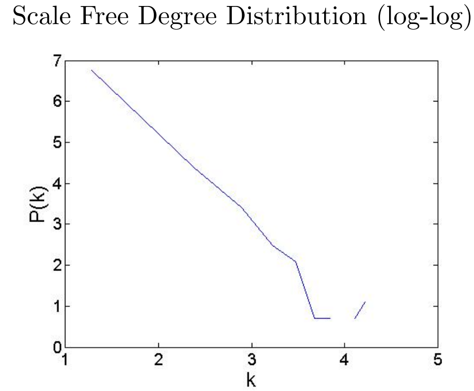


Figure 3
The measured degree distribution for our scale free network algorithm. Note the straight line on the log-log plot, verifying the power law distribution. Logs taken are the natural logarithm.

Mass simulations were run using two different degree distributions for both the Erdos-Renyi and scale free networks. A log-log plot of the bout distributions was constructed for each network, which lead to observing small power law distributed regions followed by an exponential tail for Erdos-Renyi network, and much larger power law regions again followed by an exponential tail for the scale free network. Studying the network with the largest power law distributed region, $N = 100$, $p = 3.4$, and $q = 4.08$, it seems that there are two possible ways for a transition to occur. A well-connected excitatory node can fire in the suppressed cluster and excite enough nodes to cause a cascade effect which will excite the cluster even more while simultaneously inhibiting the opposite cluster. Define this to be an excitatory Single Fire transition. The other possibility is similar to what was noticed for Erdos-Renyi, where a well-connected inhibitory node in the suppressed cluster fires which inhibits the active cluster and more easily allows for the possibility that the suppressed cluster can fire and overtake the active cluster and become excited. Define this to be an inhibitory Single Fire transition. In addition to this, there is a secondary inhibitory transition that is not present for excitatory transitions, where the active cluster is slowly withered down, as opposed to all at once inhibition, until the suppressed cluster can overtake it to become excited. Define this to be a Gradual Degradation Transition.

Determining which mechanism any particular transition followed requires a discussion of how the states are defined. First a base line average of W_E and S_E is computed over many simulations for a fixed parameter set, N, p, and q. Boundaries are placed at some point below and some point above this average value, and these boundaries define the points at which a cluster is considered suppressed(mostly inhibited) and active(mostly excited), respectively. We discuss how to choose these boundaries and how different choices affect the results in Section 4. A general transition occurs when the active cluster dips below the lower boundary and the suppressed cluster rises above the upper boundary. Now we can define a Single Fire Transition to be a transition in which a cluster goes either directly from the active region to the suppressed region or directly from the suppressed region to the active region, without entering the intermediate region between the two boundaries. Let any transition that doesn't satisfy this condition be a Gradual Degradation transition.

The excitation first and inhibition first transition mechanisms that were identified can be related to the ideas of escape and release in a mutually inhibitory neuronal network, discovered by Wang and Rinzel [17]. In escape, the inhibited neuron can overcome the inhibiting signal of the active neuron, under certain conductance conditions, and become active itself. This is similar to the excitation first mechanism, in which a well-connected excitatory node in the suppressed cluster fires, which allows more nodes to become excited and fire, until a transition occurs, or the cluster is suppressed again. In release, the active neuron sends a signal to the suppressed neuron, causing it to send a rebound signal that inhibits the active neuron. This does not have an exact analogue in our network, as it is mutually inhibitory as well as self excitatory, in addition to our model being a firing rate model, and not directly dependent on voltage and currents. The inhibition first mechanism is initiated by a well connected inhibitory neuron in the suppressed cluster, but we can not know if some activity in the active cluster causes it. Which of these two occurs more often is dependent on which degree is higher, excitatory or inhibitory. The same goes for the gradual degradation transitions, whichever degree is higher corresponds to which of either inhibition or excitation occurs first, on average.

Distinguishing between inhibition first and excitation first transitions and recording bout lengths, it was observed that the excitatory transitions follow a bout that is nearly completely exponentially distributed; there is a very small power law distributed region followed by an exponential tail. However, the inhibitory transitions follow a bout that has the largest power law distributed region seen in any other measured bout distribution, again followed by an exponential tail (Figure 4). These inhibitory transitions are approximately 8 times more frequent than excitatory as well.

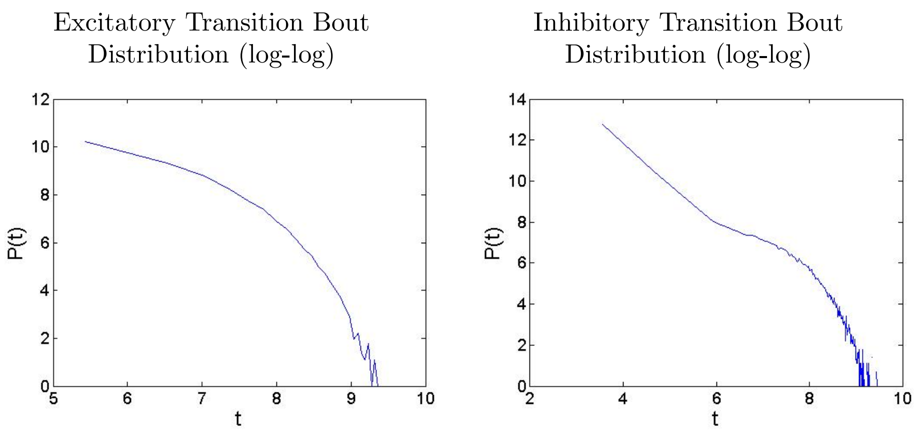


Figure 4
Comparison of the bout distributions from excitatory and inhibitory transitions. Note that the excitatory transitions are possibly power law distributed over no more than 1.25 units on the log scale while the inhibitory transitions span nearly 3 units. For these simulations, $N = 100$, $p = 3.4$, $q = 4.08$. The logs taken are the natural logarithm.

Using these same connections and conditions, the system was run again, except this time distinguishing between inhibitory transitions caused by the Single Fire Mechanism and the Gradual Degradation Mechanism. One would expect to see a nearly completely exponential distribution when waiting for a specific node to fire, and a power law distribution otherwise. This is exactly what was observed of the bout distributions, as shown in Figure 5.

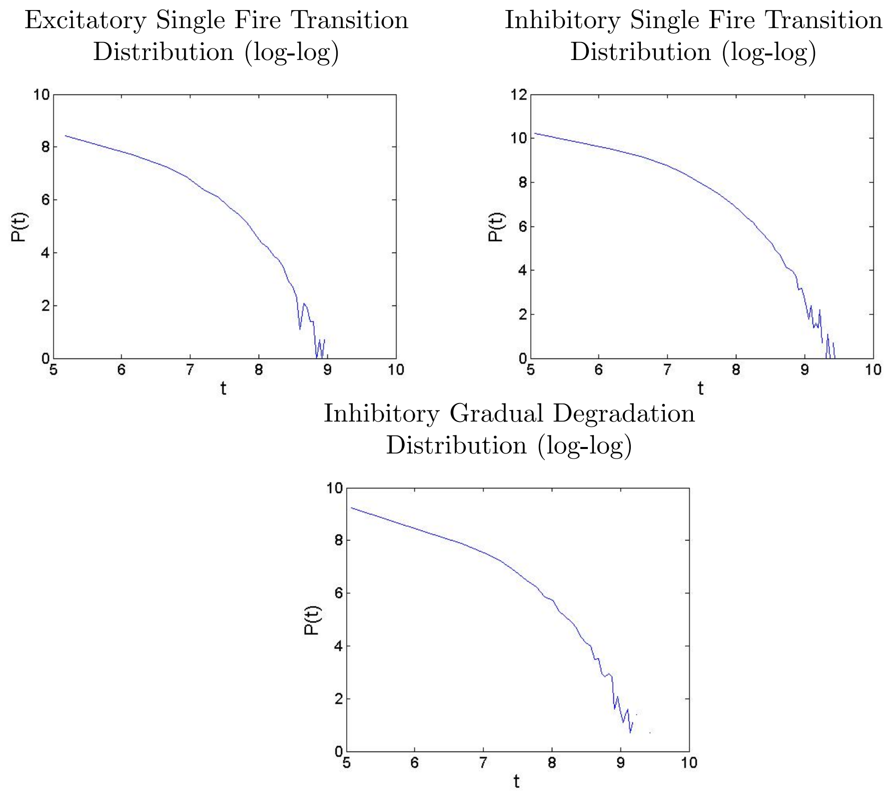
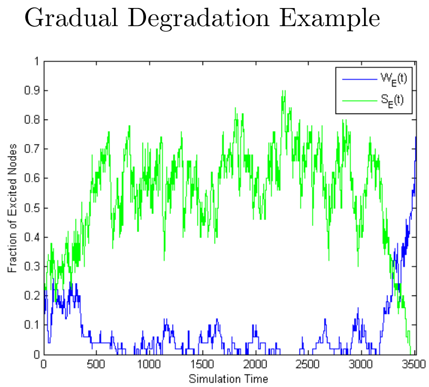


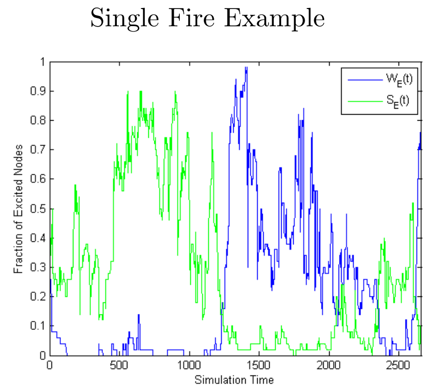
Figure 5
Bout distributions measured after distinguishing between all types of transition mechanisms. Note the gradual transition mechanism is the only one that has any behavior that can be thought of as power law distributed. Logs taken are the natural logarithm.

To quantitatively verify the identified transition mechanisms, phase plane diagrams were constructed by plotting $W_E(t)$ against $S_E(t)$ for 50 to 75 time steps before and after transitions of each type. Some example diagrams are shown in Figure 6, with the trajectory following the path in the blue to red direction. Single-Fire Transitions that are characterized by a sudden spike in the fraction of excited nodes are apparent in the phase plane diagrams as an initial large spike followed by a transition to the other state. Gradual Degradation Transitions on the other hand follow a somewhat erratic path, but with a general flow in one direction over time. These plots show that there are at least two distinct methods in which a transition can occur, and they correspond to the two mechanisms found qualitatively.

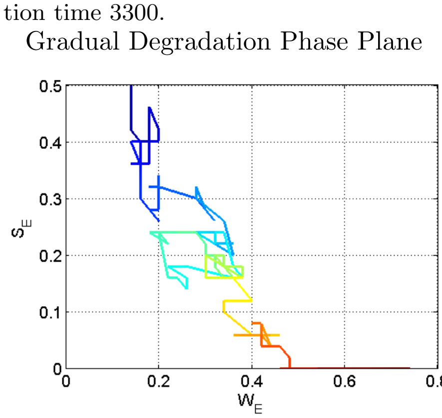
In a simpler 2 neuron inhibitory model from Patel and Joshi [18], the notions of inhibition first and excitation first transitions are also prevalent. Transitions in their system also seem to behave more like the Single Fire mechanism than the Gradual Degradation mechanism that we have identified, due to the nature of the system. Inhibition is received from signals from the opposing neuron while excitation is maintained through noise. As soon as a spike in the noise or inhibition is seen, the system is almost guaranteed to transition, which sounds like the Single Fire mechanism in our system. They also find that bout distributions are all exponentially distributed. This is a good verification for the Single Fire bout distributions measured here. It seems that adding an additional layer to the network that is responsible for excitation, rather than leaving it up to noise, changes the dynamics enough to allow for the Gradual Degradation mechanism, and possibly the power law behavior observed in experiment and simulation.



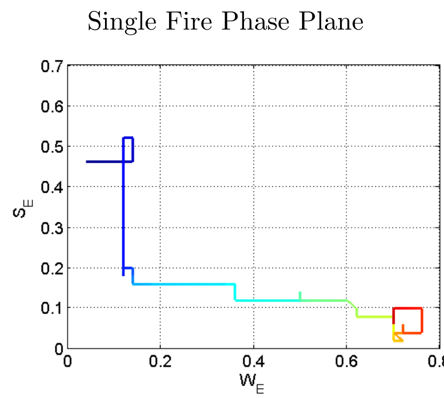
a) An example system with a Gradual Degradation Transition around simulation time 3300.



b) An example system with a Single Fire Transition around simulation time 1250.



c) Phase plane diagram for the system in a) near the transition at simulation time 3300. The trajectory goes from blue to red. The path followed is erratic but generally trends slowly in a single direction towards the new state.



d) Phase plane diagram for the system in b) near the transition at simulation time 1250. The trajectory goes from blue to red. The path consists of an initial spike followed by an almost immediate transition to the new state.

Figure 6
Example system realizations that contain a Gradual Degradation Transition (a) and a Single Fire Transition (b) and the corresponding phase plane diagrams near the transitions.

4 Change of Intermediate State Boundaries

In choosing boundaries for the intermediate state, a question of what values to select for them arises. A good choice of boundary values would result in a small disturbance or no disturbance in the measured bout distributions for a small change in the boundary values, since the boundaries exist only to provide a more accurate way of finding and defining transitions. Given this criterion, it would be expected that the Single Fire Mechanism's distribution would not change at all but the Gradual Degradation Mechanism's distribution would slightly increase or decrease, depending on if the intermediate boundary was pushed further or closer to the sleep or wake states.

The bout distributions shown in Figures 4 and 5 were obtained using the average value of W_E and S_E to define a base line, at 0.35, and placing the boundaries at 0.25 and 0.55. The boundaries were chosen asymmetrically in order to have as big a sleep region as possible for the lower boundary, since the average value of 0.35 is significantly less than 0.5, while still accurately choosing an upper boundary to mark where transitions start and finish. The bout distributions were measured again using 0.35 as a base line and 0.35 ± 0.1 as boundaries. The plots are shown in Figure 7.

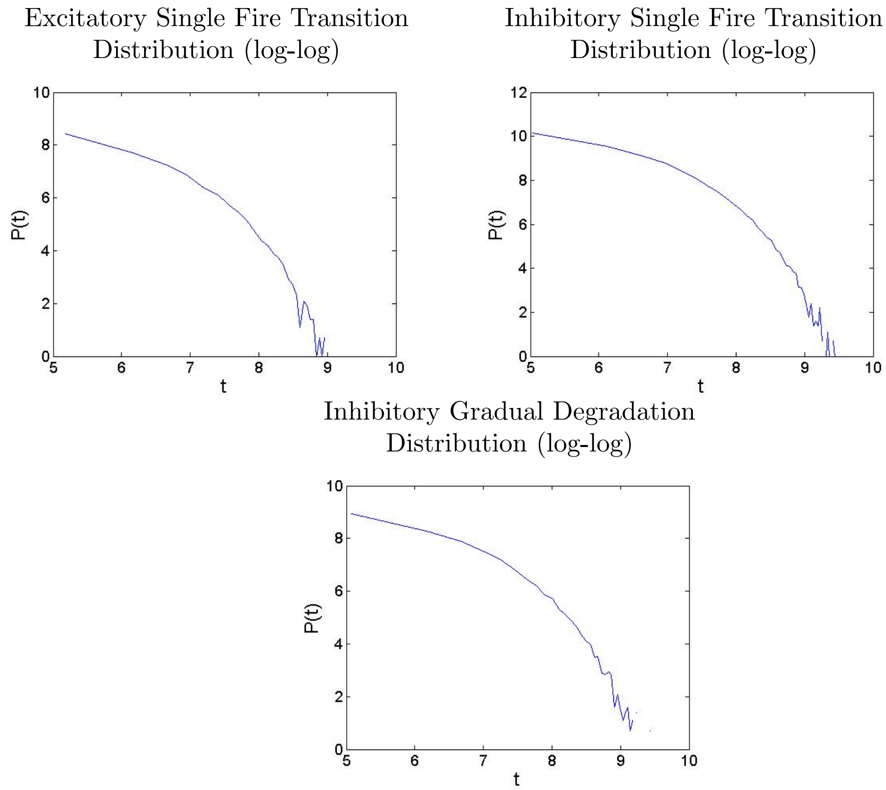


Figure 7
The same bout distributions measured in Figure 5 using symmetric boundaries for the intermediate state. Note the plots are nearly identical with a slight bias toward shorter bouts for the Gradual Degradation Mechanism. Logs taken are the natural logarithm.

As expected, the plots for the Single Fire Mechanism are unaffected by the change in boundary, since the large spikes push W_E and S_E well past the boundary in essentially all instances. On the other hand, the Gradual Degradation bout distribution displays a subtle shift toward shorter bout lengths and a more pronounced power law distributed region. To see how big of a difference there is between the two distributions, the power law distribution was recovered from the log-log plot for the symmetric and asymmetric case, using the same method to determine the degree distribution of the scale free network. For the symmetric boundaries the power law region can be described as

$$P(t) = e^{15.03} * t^{-1.04}$$

and for the asymmetric boundaries

$$P(t) = e^{14.75} * t^{-0.98}$$

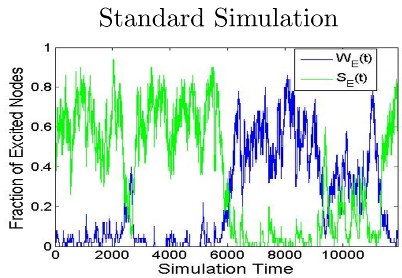
This shows that there is indeed a small change in the Gradual Degradation bout distribution for the symmetric boundaries and there is a more pronounced power law, as expected. Since the intermediate state is 0.1 units smaller and only transitions caused by a large amount of small inhibitions are considered, it makes sense that transitions would be on the order of 5-10 time steps shorter, accounting for the difference in these two distributions.

5 Perturbation Approach

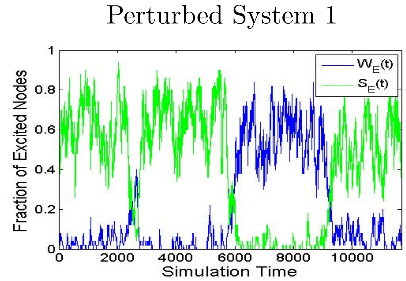
The first attempt at uncovering a transition mechanism was to do a perturbation analysis similar to the one outlined in Ansmann [6] on the Erdos-Renyi connected neural network.

The setup we made use of is summarized as follows. In a system of N coupled differential equations for excitable units, the average state value was measured. An extreme event was defined as a spike in this average that went above a specified value. A perturbation analysis was performed in which perturbations were made in increasing magnitude at a specified time before a spike and also at a specified magnitude at increasing times before a spike. The probability that the spike could no longer be observed was estimated by generating many realizations of the perturbed system with perturbations of equal magnitude but different direction, and taking the ratio of cases the extreme event was not observed to the total number of trials. This probability was found to generally be linear and increasing with decreasing time before a spike and increasing magnitude of perturbation. Generating mechanisms were therefore hypothesized to come into play a short time before extreme events. This provided a way to narrow the search to a specific region and search for patterns consistent among the extreme events.

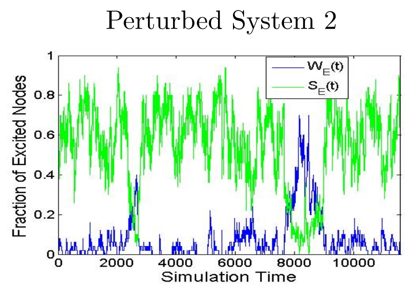
To extend this approach to our network, the system was run undisturbed and the time of transitions was first noted manually by a guess and check method where the fraction of excited nodes in the excited cluster went below 0.5 and the inhibited cluster above 0.5. At varying times before the marked transition a single node or group of nodes was disturbed by changing their state from either excited to inhibited or vice versa or by changing the node that fired during that time step. The purpose was to see the effect this would have on the transition; either destroying it, delaying it, or not really affecting it. Numerous trials on different realizations of the network showed that small to medium sized perturbations (changing any less than about half of the nodes) did not have a short term enough effect to disturb the transition, but caused wildly different behavior much later on, implying the system was chaotic. Making perturbations that affected greater than half of the nodes or changing the state of a well-connected node responsible for the transition would generally delay the transition, but the delay would increase when perturbations were made a longer time before the transition, implying it was due to the chaotic nature of the system and not some underlying mechanism. (Figure 8) This is likely due to the stochastic nature of our system compared to the deterministic differential equation model used in Ansmann.



a) An example system run undisturbed with $N = 100$, $p = 6$, and $q = 9$. W_E and S_E are the fraction of excited nodes in the wake cluster and sleep cluster, respectively. Note the transition from sleep to wake at simulation time 6000.



b) The same system as a) but with the neuron responsible for the transition inhibited two time steps prior to the transition. The transition still occurs but the bout length has been decreased.



c) The same system as a) but with the neuron responsible for the transition inhibited fifty time steps prior to the transition. In this trial the transition has been destroyed and the system exhibits radically different end behavior.

Figure 8

6 Conclusion

The dynamics of our neural network under various architectures and node connections have been described. The original goal was to identify possible transition mechanisms, see how they depend on the network type used, and use this to determine the origin of the observed power law behavior. A Single-Fire Mechanism was identified, where a single well-connected node firing can cause a transition from a cascade effect. Also identified was a Gradual Degradation Mechanism in which the active cluster is slowly withered from firing in the suppressed cluster until it can be overtaken in a gradual transition. These mechanisms were verified and a visualization of each was shown by plotting a phase plane diagram around different transitions.

From the data, it is safe to conclude that something present in the Gradual Degradation Transition Mechanism causes this power law phenomenon. Comparing to the Single Fire Transitions, we can see that waiting for a specific neuron to fire will cause the bout distribution to be exponential, as one would expect, so it is the Gradual Degradation Mechanism that is responsible for the power law regions. Exponential distributions can be thought of as representing independent attempts at overcoming a potential barrier [7], which makes sense in the context of waiting for a neuron with enough connections to fire. Power law distributions on the other hand, are more complex. Power laws emerging for certain quantities in a thermodynamic system have been associated with phase transitions[8]. This result makes sense in the context of our system as well, however it remains to figure out what exactly about this mechanism causes the power law behavior and how to predict when transitions will occur.

7 Acknowledgments

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