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Connectivity and phase coherence in neural network models of interconnected Z^4-bi-stable units.*

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Abstract— **A phenomenological neural network model with bi-stable oscillatory units is used to model up- and down-states. These states have been observed in vivo in biological neuronal systems and feature oscillatory, limit cycle type of behavior in the up-states. A network is formed by a set of interconnected units. Two different types of network layouts are considered in this work: networks with hierarchical connections and hubs and networks with random connections. The phase coherence between the different units is analyzed and compared to the connectivity distance between nodes. In addition the connectivity degree of a node is associated to the average phase coherence with all other units. The results show that we may be able to identify the set of hubs in a network based on the phase coherence estimates between the different nodes. If the network is very dense or randomly connected, the underlying network structure, however, can not be derived uniquely from the phase coherence.**

I. Introduction

Computational modeling is a powerful tool for understanding pathological conditions of the central nervous system such as epilepsy. In our previous models we have shown that both realistic models [1] and phenomenological, metaphoric [2] models can explain and even predict certain features of the dynamics of real biological systems. In this article we continue the analysis of analytical, effective models of neuronal tissue concentrating on the network properties and collective behavior of distributed networks. One property of such behavior is the phase coherence, or phase locking, of the system. In recent years a lot of attention has been devoted to the apparent or measurable network topology [3-5]; nonetheless a clear correspondence to the underlying unit connectivity is purely hypothetical. In the present study we show that a more systematic approach is possible, that eventually can provide the translation between the connectivity topology and the large scale collective behavior of a distributed system within the model assumptions. Such correspondence can be a valuable asset in both directions: (1) By measuring functional characteristics of the system such as phase coherence, we can infer properties of the architecture of the structural connectivity, in this way eventually the origin of a pathological functional state may be estimated; (2) in the context of neural engineering, we may be able to program a given connectivity topology in order to reach a certain functional state.

The model of the individual units used in this work displays bi-stable behavior. Their functional state can either be in an up- or down-state; an oscillatory component, with a limit cycle type of dynamics, is active in the up-state only. A similar behavior is observed during in vivo animal experiments [6, 7], where fast oscillations are present during positive baseline shifts of the ongoing activity. These different states that each individual unit can occupy determine the dynamics of coherence within the network. A set of units within the network can only synchronize when fast oscillations are present in these units.

II. Methods

A. Model

In this work we use an analytical model of a bi-stable oscillator, which may serve as a metaphoric model of a lumped neural network. The behavior of the model is described by:

$$\frac{d}{dt}Z = -Z(|Z|^2 - u) + i\omega(|Z|)Z \qquad (1)$$

$$\frac{d}{dt}u = -u(u^2 - 1), \qquad (2)$$

where ω is the angular speed of the rotator and u defines the up- and down-state of the system.

Due to random fluctuations the system can either be in an up-state ($u = 1$) or in a down-state ($u = -1$). The rotator is only present in the up-state and in the down-state the unit behaves as a harmonic oscillator with a steady state attractor. The up-state can represent paroxysmal type of behavior with large oscillations (epileptic seizures) and the down-state can represent inter-ictal behavior with output resembling filtered noise.

Different units can be coupled together through a connectivity matrix to form a network. The connectivity is added to the Z component of the model:

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$$\frac{d}{dt}Z_m = -Z_m(|Z_m|^2 - u) + i\omega(|Z_m|)Z_m + \sum_{k,k\neq m}^{N} C_{mk}Z_k \quad , \quad (3)$$

where C_{mk} is the connection strength between the k–th and m–th unit and N the total number of units. The topology of these connections can determine the collective behavior of the system and in particular the phase coherence between units.

The phase coherence between two complex signals $Z_m(t)$ and $Z_n(t)$ of two units is computed using:

$$X_{mn} = \frac{\sum_{t=0}^{T} Z_m(t)conj(Z_n(t))}{\sum_{t=0}^{T} |Z_m(t)Z_n(t)|}. \quad (4)$$

B. Hubs

By defining connections between units we create networks of various topological signatures. As an example, the network used in this work consists of ten units and all connections are symmetrical: $C_{mk} = C_{km}$. Furthermore, here we only consider binary connections. The strength of the connection can be either zero, no connection, or one. In order to analyze the behavior of the network we start with a simple graph structure consisting of just two highly connected nodes (hubs) while each of the other nodes is connected to only one of these hubs. The graph of this network is shown in the upper panel of Figure 2.

C. Random network

It would be of high value if we were able to reconstruct the network connectivity based on the determined synchronization of the different units. Therefore we create a random network where the weights of the connections are, as above, either zero, no connection, or one, connected. From this connection matrix C, the minimal path length, between two different nodes can be computed. Also the degree (total amount of connections) of each node can be extracted from the connectivity matrix.

D. Nonlinear association index

To quantify the relation of the phase locking and the minimal path length between two nodes over the entire network the nonlinear association index, known as h^2, is used [8]. This index measures the best signal to noise ratio of any nonlinear map between two signals and it has values between h^2=1, which indicates the existence of an exact functional mapping between signals, and h^2=0, which shows no such functional mapping.

E. Simulations

All simulations are performed for 50000 simulation seconds. Gaussian noise is added with a mean of zero and a variance of one, a multiplication factor of 0.4 is used. In order to avoid spurious synchrony due to parameter fine tuning, the angular speed, ω, is different in each unit of the network and is randomly selected during the initialization from a normal distribution with a mean of five and a standard deviation of 0.5. The connectivity parameters depend on the experiment. Simulink ® (Mathworks Inc, Natick, MA) was used for the simulations and MatLab® (Mathworks Inc, Natick, MA) for analysis of the results.

III. Results

In Figure 1 the signal of one unit is shown. It is clearly visible that it has up- and down-states. The oscillatory behavior starts increasing during the transition from down- to up-state and it is maximal when the up-state is reached.

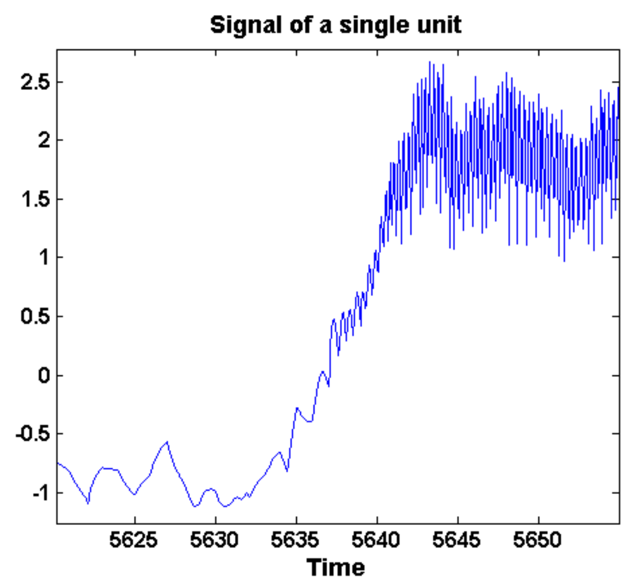

Figure 1. The signal of a single unit of the model. The down-state, until t=5635, shows no oscillations, while the up-state, starting at about t=5640, shows clear oscillatory behaviour.

A. Hubs

The upper panel of Figure 2 shows a network, with connections as described by (3), consisting of two hubs, nodes 1 and 8. The other nodes are only connected to one of these hubs and the hubs are connected to each other. The lower panel shows the phase locking between the nodes. The hubs show a high phase locking with directly connected nodes. Nodes that are not directly connected, but connected with the same hub show less phase locking, although still significant. Even nodes connected to one hub show significant phase locking with the other hub. The non hub nodes do not show phase locking with nodes directly connected to the other hub.

Figure 3 shows the distance, or minimal path length, matrix (upper panel) and the relation of the phase locking with the distance between nodes (lower panel). The box plot shows that the phase locking of pairs of nodes with the same distance is well clustered. The nonlinear association index between phase locking and distance is h^2=0.97.

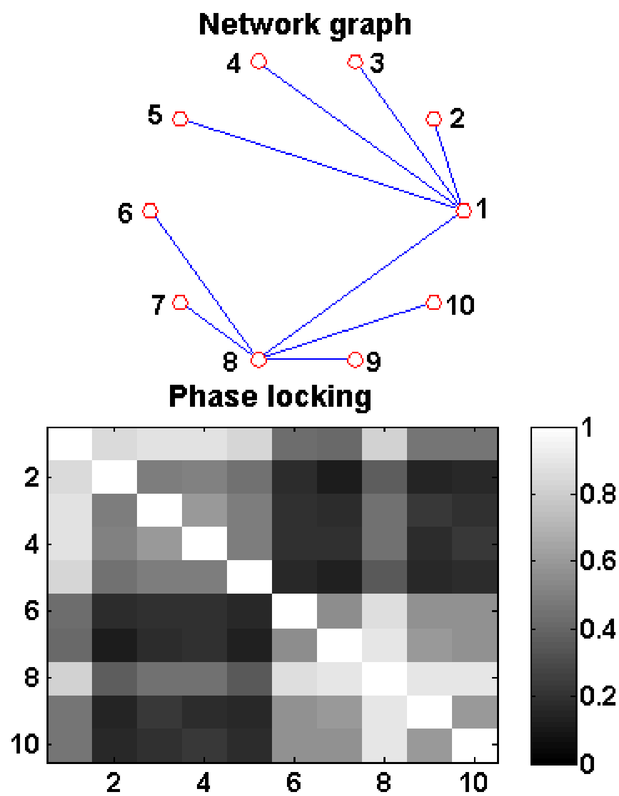

Figure 2. Top: Graph of the network of units. Node 1 and 8 are the hubs. Bottom: Phase locking of the different units. Zero (black) means no synchronisation and one (white) denotes fully synchronised units.

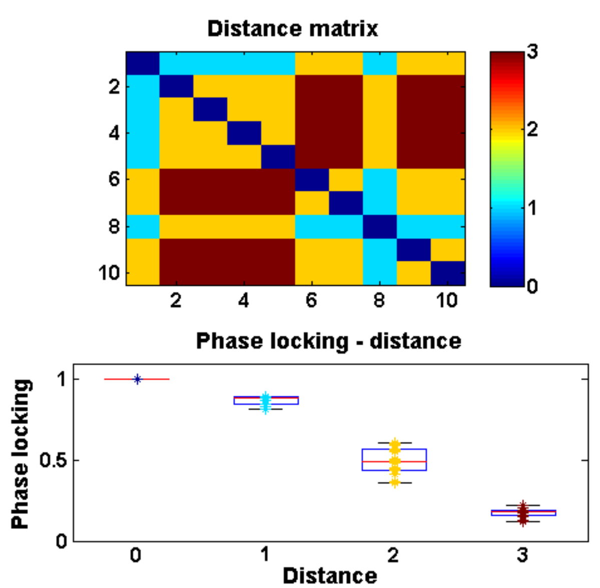

Figure 3. Top: Distance matrix of the graph as shown in Figure 2 upper panel. Bottom: Box plot of the phase locking as shown in Figure 2, lower panel, grouped by distance. The coloured dots correspond to the colours in the upper panel.

B. *Random network*

The upper panel of Figure 4 shows a randomly connected network. In contrast to the previous network, where the network is very sparsely connected we now obtain a very densely connected network. This is also reflected in the phase locking diagram in the lower panel of Figure 4. In general the nodes are highly synchronized with other nodes, although at some positions we can observe significant less phase locking, especially the phase coherence of node 7 with node 2 and node 10 is very low. In the distance matrix, shown in the upper panel of Figure 5 , it is shown that the distance between those nodes has the value three, which is the maximum distance found in this network.

In the center panel of Figure 5 the relation between the inter-node distances and the phase locking becomes more diffused in comparison with the sparse network. Clusters overlap and are not separable anymore. The h^2 index between phase locking and distance is h^2=0.81, which is slightly lower than for the previous network. In the lower panel of Figure 5 the relation between the degree of a node and the average phase locking with all other nodes is shown. It shows that the average phase locking increases with the number of connections, but not linearly.

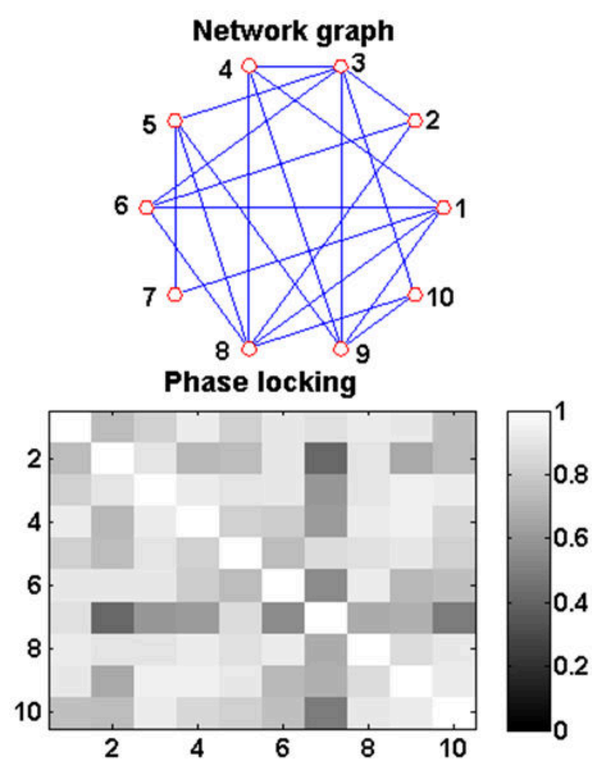

Figure 4. Top: Graph of the network of units. Bottom: Phase locking of the different units. Zero (black) means no synchronisation and one (white denotes fully synchronised units.

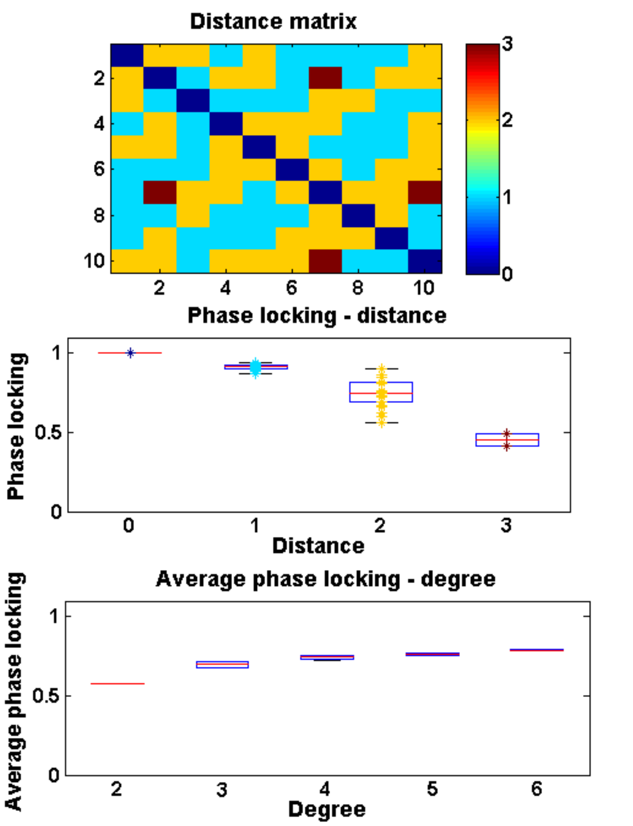

Figure 5. Top: Distance matrix of the graph as shown in Figure 4 upper panel. Center: Box plot of the phase locking a shown in Figure 4, lower panel, grouped by distance. The coloured dots correspond to the colours of the distance matrix in the upper panel. Bottom: Boxplot of the average phase locking of a node with all other nodes grouped by degree of the node.

IV. Conclusions and Discussion

We show that in a network of model units eliciting bi-stable behavior calculating the phase coherence between different units can provide information on the connectivity topology of the network. The phase locking is only present in the up-state of the model units when they are in a state of limit cycle, since the down-state has no oscillatory component. Therefore the transitions between up- and down-states in the model are part of the phase locking mechanism.

The experiments with clearly defined hubs in the network show a distinct difference in phase locking in relation to the distance from one node to another node. The larger the distance between nodes, the less phase locking occurs. In the random network analysis this effect is much less pronounced, which is also shown in the lower value of h^2. One of the reasons for this is that the minimal path between two nodes is not necessarily the only path. Especially in highly connected networks there are more routes from one node to the other. All these distinct different routes contribute to the phase locking of two nodes. This causes more diffusion of the phase coherence and the clusters start to overlap. When viewing only the phase coherence of the signals, it is not possible to trace back to the underlying network topology. However, if some nodes in the network have a significant higher degree, what we may call super hubs, this might still be visible in the phase locking of the signals. Also very sparsely connected nodes, with a large distance to other nodes are to be recognizable by looking at the phase coherence.

In this study we have only investigated the contribution of the $Z-Z$-connections of the model. These are not the only type of connections contributing to the total network behavior. We can, for example, think of some collective couplings, where the total amount of synchronization can force the units to go back to the down-state. Also internal couplings within one unit can be realized. One type of self connection can be self termination of an up-state. This type of connection can produce effects reminding those of hyper polarization activated inward currents in a neural network [9].

References

1. Suffczynski, P., S. Kalitzin, and F.H. Lopes Da Silva, *Dynamics of non-convulsive epileptic phenomena modeled by a bistable neuronal network.* Neuroscience, 2004. **126**(2): p. 467-484.
2. Kalitzin, S., et al., *Computational model prospective on the observation of proictal states in epileptic neuronal systems.* Epilepsy Behav, 2011. **22 Suppl 1**: p. S102-9.
3. Rubinov, M., et al., *Small-world properties of nonlinear brain activity in schizophrenia.* Hum Brain Mapp, 2009. **30**(2): p. 403-16.
4. Wilke, C., G. Worrell, and B. He, *Graph analysis of epileptogenic networks in human partial epilepsy.* Epilepsia, 2011. **52**(1): p. 84-93.
5. Martini, M., et al., *Inferring directional interactions from transient signals with symbolic transfer entropy.* Phys Rev E Stat Nonlin Soft Matter Phys, 2011. **83**(1-1): p. 011919.
6. Bragin, A., et al., *High-frequency oscillations after status epilepticus: epileptogenesis and seizure genesis.* Epilepsia, 2004. **45**(9): p. 1017-23.
7. Bragin, A., C.L. Wilson, and J. Engel, Jr., *Voltage depth profiles of high-frequency oscillations after kainic acid-induced status epilepticus.* Epilepsia, 2007. **48 Suppl 5**: p. 35-40.
8. Kalitzin, S.N., et al., *Quantification of unidirectional nonlinear associations between multidimensional signals.* IEEE Trans Biomed Eng, 2007. **54**(3): p. 454-61.
9. Koppert, M.M., et al., *Plasticity-modulated seizure dynamics for seizure termination in realistic neuronal models.* J Neural Eng, 2011. **8**(4): p. 046027.