Graph Models of Brain Connectivity Networks

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Final report presented for the degree of
Master 2 Sciences de la Cognition et Systemes Complexes

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June 2015

Abstract

We model brain connectivity networks by an exponential random graph (ERG) model formulated in terms of two important mechanisms with which the brain operates: segregation and integration. The model is first validated over a set of 5 networks that exhibit well-known properties ranging from lattice to random topology and pass through networks with small-world architecture. These network configurations have been shown exhibit by brain connectivity networks. We found a parameter space where the weights of the metrics in the ERG model lay and follow a trajectory according to the rewiring probabilities of the Watts and Strogatz model used to construct the networks. We also show how the parameters of the ERG models for brain connectivity networks in each frequency band of the EEG data lay in a small-world regime in the parameter space and are able to distinguish between eyes-open and eyes-closed resting state conditions.

Introduction

The representation of a system composed by agents and interactions among them by a complex network is an effective way to extract information on the nature and topology of such interactions. An example of such a system is the brain. Only recently the brain has been an object of study in the complex systems field. The microscopic scale of synaptic connections is too large to be analysed by classic complex network metrics and characterizations. Instead, other theoretical theories, such as random matrices theory, are used. But at a mesoscopic scale, one can represent the brain functioning with a brain connectivity network. The nodes of this network are anatomical regions of the brain and the links represents a statistical dependency of aggregate neuronal activity among two nodes.

As with other complex networks, one is interested in studying the intrinsic dynamics and forces that cause emergent behaviours and topologies. For example, in a social network one could be interested in understanding how new friendships are formed and a plausible hypothesis could be that friendships among people who have a friend in common are more likely to happen. In a functional connectivity network on is interested in study the statistical dependencies among remote neurophysiological events.

Even though already from the 19th century a good anatomical map related to specific tasks of the brain was known, today, still very little is known about functional connectivity of the brain. This discrepancy comes from the different nature of the tools used to explore the anatomical related brain functions and connectivity related brain functions. The instruments and techniques used to construct the anatomical map were more rudimentary. The anatomical brain map was mainly constructed form injured brains from which it was possible to conduct invasive explorations or, from very localized brain injures which affected only a specific motor or cognitive task[1]. On the other hand, the tools used to explore functional connectivity developed with the technological revolution. Now, the scientific community has access to sophisticated neuroimaging techniques which allows capturing quantitatively functional connectivity in a not invasive way.

Connectivity-based methods have had a prominent role in characterizing normal brain organization as well as alterations due to various brain disorders[2]. Nevertheless, it is necessary to go beyond descriptive and characterization analysis. Instead, we want to model and simulate the emergent behaviour that this system exhibits in order to to better understand the organizational mechanisms of the brain.

Results

We propose a model based on the family of exponential random graph (ERG) models [3]. The proposed model has the form

$$P(G) = \frac{exp(\theta_1 \langle K \rangle (G) + \theta_2 E_l(G) + \theta_3 E_g(G))}{Z} \tag{1}$$

Where $\langle K \rangle (G)$ measures the mean degree of a network G and is included in the model to control the density of the networks; $E_l(G), E_g(G)$ measures the local and global efficiency which are defined as

$$E_g(G) = \frac{1}{N(N-1)} \sum_{i,j=1}^{N} \frac{1}{d_{i,j}}$$
$$E_l(G) = \frac{1}{N} \sum_{i=1}^{N} E_g(G_i) \quad (2)$$

These particular metrics were chosen because they capture two important organizational mechanisms of the brain: functional segregation and functional integration[4, 5, 6]. Functional segregation refers to the distinct specialization of anatomical brain regions and; functional integration refers to the possible temporal dependences between the activity of anatomically separated regions of the brain[1].

This model is graph based and we estimated the model parameters using Monte Carlo estimation technique. We show results for: i) an ensemble of Small-world (SW) networks simulated with the Watts and Strogatz model; ii) application to brain connectivity networks constructed from EEG recordings.

The figure below shows the parameter space for the graph-based ERG models given by equation 1. It is interesting to see that there exists a trajectory on the space. Moreover, the trajectory is in correspondence with the topology transition of the SW ensemble. In the Watts-Strogatz model the transition is given by the rewiring probability p and produces networks with topologies that change form lattice topology to random and passes through small-world architectures.

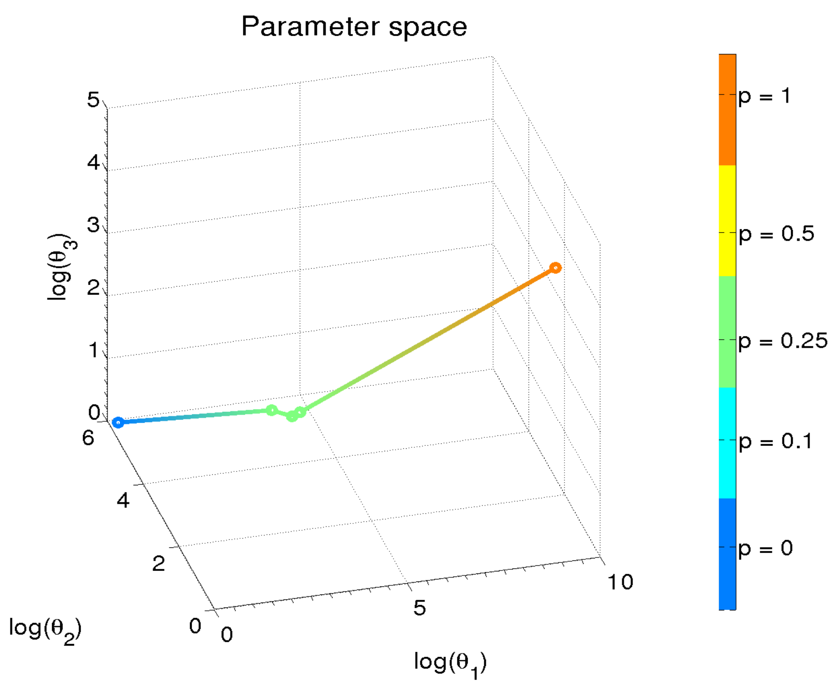

Figure 1: Parameter space of model $P(G) = \frac{exp(\theta_1 \langle K \rangle(G) + \theta_2 E_l(G) + \theta_3 E_g(G))}{Z}$ for the simulated SW networks. $\langle k \rangle$ corresponds to the mean degree metric, E_l to the local efficiency metric and E_g to the global efficiency metric.

We also examine how these models are able to simulate networks with similar topologies to the input networks. This was done by visual inspection and by comparing the values of local metrics. The metrics in model 1, i.e mean degree $\langle k \rangle$, local efficiency E_l and global efficiency E_g, are measured over the SW input networks and over 100 simulated networks using the models with estimated parameters. By comparing these values and the network visualization, we observed that the proposed model 1, estimates better networks with higher rewiring probabilities.

Next, we applied the proposed model 1 to brain connectivity EEG recordings data. The data used to construct brain connectivity networks were acquired by means of an electroencephalogram (EEG). EEG records electrical activity through electrodes placed on the scalp of subjects. The number of sensors used is 56 electrodes. The data was recorded for 100 subjects in two baseline conditions: one minute resting state with eyes open and one minute with eyes closed.

Given that the brain represented in a functional connectivity networks exhibits small-world architecture[7] we were expecting that the parameters of the subject-based ERG models given by equation 1 will fall in the trajectory and close to the point of network with rewiring probabilities larger than zero but smaller than one.

The figure below shows the same parameter space of figure 1 now including the estimated parameters of the ERG models with subject functional connectivity networks (constructed from EEG recordings) as input networks.

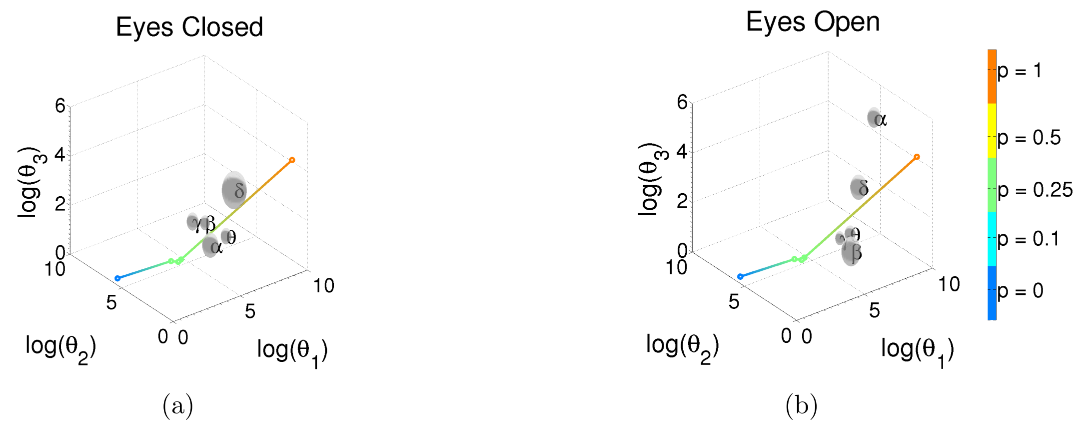

Figure 2: Subfigure a shows the parameter space for the model $P(G) = \frac{exp(\theta_1 \langle K \rangle (G) + \theta_2 E_l(G) + \theta_3 E_g(G))}{Z}$ over EEG data of subject undertaken base line rest-state eyes closed. Subfigure b shows the parameter space for the model over EEG data of subject undertaken base line rest-state eyes open.

It is interesting to observe that the the estimated parameters for the alpha frequency band is in correspondence with a well know effect of opening and closing the eyes during a rest state condition. In terms of functional connectivity when a subject open his or her eyes a decrease on the α peak frequency is observed[8]. The model is able to capture the difference as show by the upward shift in the eye open condition as compared to the eyes closed condition of the α sphere in figure 2.

Another important point is that the brain connectivity parameter estimates lay closer to the estimates of parameters associated to SW networks that are constructed with a higher rewiring probability. Since the ERG model in equation 1 performs better for input networks with a higher rewiring probability, and the brain connectivity networks have a topology closer to them, the fact that the parameters are in the same region validates the use of this model for EEG data.

Discussion

We showed that when formulating an ERG model for certain network it is important to use metrics which capture intrinsic topological properties. In the case of brain connectivity networks, we wanted to capture two important organizational mechanisms: functional segregation and functional integration. Then we proposed an ERG model that included the local efficiency and global efficiency metrics.

The proposed model is able to capture important feature of network ensembles generated with the Watts Strogatz model. It is able to reproduce the transition in topologies giving by changing the rewiring probability from zero to one.

When applied to brain connectivity EEG recordings data, the estimated model parameters give networks that exhibit a small-world topology. The model also captures an important effect of brain connectivity in the α frequency band when comparing eyes-open and eyes-closed resting state conditions.

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Graph Models of Brain Connectivity Networks

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ABSTRACT

We model brain connectivity networks by an exponential random graph (ERG) model formulated in terms of two important mechanisms with which the brain operates: segregation and integration. The model is first validated over a set of 5 networks that exhibit well-known properties ranging from lattice to random topology and pass through networks with small-world architecture. These network configurations have been shown exhibit by brain connectivity networks. We found a parameter space where the weights of the metrics in the ERG model lay and follow a trajectory according to the rewiring probabilities of the Watts and Strogatz model used to construct the networks. We also show how the parameters of the ERG models for brain connectivity networks in each frequency band of the EEG data lay in a small-world regime in the parameter space and are able to distinguish between eyes-open and eyes-closed resting state conditions.

Introduction

For many years, there has been a great interest on understanding brain functioning, but only until recently, research in this area has increased significantly. Such increase is mainly due to important improvements of neuroimaging techniques. New technological developments allowed the scientific community to quantify brain connectivity across different spatial and temporal space resolutions in a non-invasive and exhaustive manner.[1,2] On the other hand, the use of graph theory and complex network analysis in studying brain functioning has enriched our understanding of the topology of functional interactions. This approach has served to characterize the emergence of coherent behaviour and cognition,[3] or the capability to functionally reorganize after a brain lesion (i.e. brain plasticity)[4] by studying brain connectivity networks.

As any other complex network, brain connectivity networks characterized completely by defining its agents (nodes) and the interactions among them (links). In the case of brain connectivity networks the nodes are established in large part by the neuroimaging techniques used to record brain connectivity data, and the links are defined by a functional connectivity (FC) measure of the temporal dependence between nodes. For example, when using an electroencephalogram (EEG), which is a sensor-base modality, to record electrical brain activity then the brain nodes are commonly define as the electrodes.[5,6] If instead a voxel-base modality is used, such as fMRI, then today the most commonly way to define brain nodes is to use a fixed anatomical atlas.[7–9]

To define the links the researcher has to choose a FC measure, which is a function that measures the magnitude of the statistical interaction between nodes. Many measures have been proposed and the use of one or another depends mainly in the hypothesis the researcher has about brain connectivity patters under certain condition. The use of a particular FC measure will result in a directed or undirected weighted network and affect the results interpretation.

It is important to notice that even though a brain connectivity network is defined by its nodes and links, the links are a statistical representation of the true interaction. Therefore there exists an underlying methodological pipeline to follow in order to obtain a final unweighted filtered network which better represents functional connectivity and which is the object of study and analysis of brain functioning. Sensitive steps include choosing an appropriate FC measure and filtering the graph. The later refers to retain only statistical significant dependencies among nodes and to remove other links that are more likely to come from different sources of noise. All the steps for graph analysis of functional brain networks are well documented in the literature[10] including methodological issues and possible solutions.

The analysis of these complex brain networks by means of the use of different network metrics has certainly enrich our understanding of brain connectivity patterns.[11–14] However these results are limited to descriptive analysis and many issues remain unaddressed.[15] Instead a new method to model the organizational mechanisms in the neural activity to explain how the brain is functional organized is needed. We propose a statistical network analysis based on the family of exponential random graph (ERG) models.[16]

Statistical exponential family models where first proposed by Wasserman and Pattison in 1996[17] as an extension of Markov random graphs models proposed by Frank and Strauss in 1986.[18] These models have been widely used over social complex networks[19–22] and many of the theory has been developed by researchers working in this area or related.[23–27] The essence of ERGM theory is the formation of networks structure through the accumulation of small local substructures and, ultimately, through the information of individual links into the patterns of those substructures.[28] In other words, the aim is to create model networks with properties similar to those seen in real world network.

The model has an exponential form in function of a linear combination of network metrics (see equation 6). Well known examples of such network metrics are for instance the mean degree $\langle k \rangle$. The mean degree of network is the sum of all the links each node has divided by the total number of nodes in the network. The coefficients of the linear combination of the network metrics are parameters to be estimated. The estimation of the model parameters presents difficulties in several aspects (see section) and the simplification assumptions that holds for social networks[29] do not necessary have an interpretation on brain connectivity networks and therefore do not hold. It is then necessary to first explore the behaviour and capabilities of ERG models over brain functional connectivity data. We propose to do so first over a set of networks with well-studied topologies (lattice, small-world architecture and random) and next over brain connectivity networks constructed form EEG recordings over a population of 100 subjects undertaking eyes-open and eyes-closed resting state conditions

Results

We propose an ERG model form to model brain connectivity networks given by equation 8 (see section for details on the form derivation). We first investigate the capability and limitations of the model over a set of 5 networks with topologies that range from a lattice to random and pass through small-world architecture. These networks are constructed using the Watts and Strogatz model (see section), and we will refer to this set of networks as SW networks. Then, we estimate the parameters of model 8 with brain connectivity networks as input. The bran connectivity networks are constructed from EEG brain activity recordings.

Simulations: SW networks

The main aim of this first part was to determine if an ERG model could capture classical topology network structures. Also to find a space where the estimated parameters fall in a coherent way.

Let G be a random network with N nodes, analytically, one can show that the ERG model with the form

$$P(G) = \frac{exp(\theta E(G))}{Z} \tag{1}$$

Where $\langle E \rangle$ is the expected number of edges in the network is equivalent to the Bernoulli model.[30]

When estimating the model computationally, once can verify that it is able to reproduce networks with similar topologies. This can be done visually and by the goodness of fit of global properties of simulated networks. Figure 2a shows the input random network and Figure 2b shows a sample simulated network by model 1. The three sub-plots in Figure 1c shows the goodness of fit over a set of three graph statistics:[31]

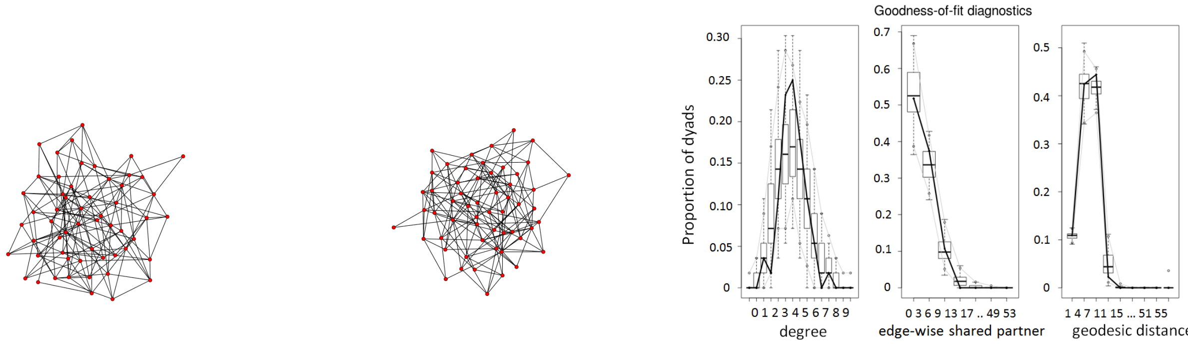
- The **degree** distribution: The statistics D_k equal to the number of nodes with degree k (with k links) for $k = 1, 2, ...$ divided by N
- The **edge-wise shared partner** distribution: The statistics EP_k equal to the number of edges in G between two nodes that share exactly k neighbours in common
- The **geodesic distance** distribution): The proportion of pairs of nodes whose shortest connecting path is of length k, for $k = 1, 2, ...$ and setting $k = \infty$ for pairs of nodes which are not connected

The solid line in Figure 1 is the values for each of the graph statistics define above for G the input random network, and the box plots show the distribution of those same graph statistics over 100 simulated network using model 1.

Now let G be a lattice with N nodes. A lattice is characterized by the number of neighbours each node has, then we expect that the model

$$P(G) = \frac{exp(\theta D(G))}{Z} \tag{2}$$

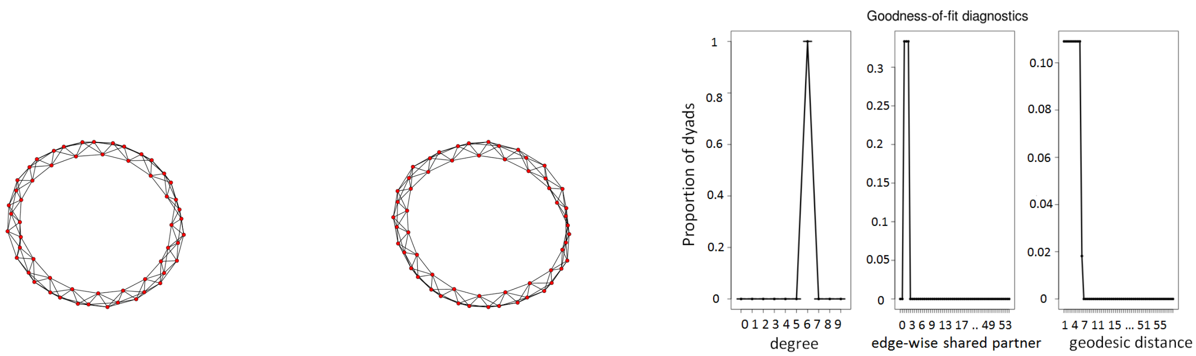
Where $D(G)$ is the degrees of network G, i.e. $D(G) = [D_1, D_2, ...]$ the degree distribution as describe before captures well the topology and its able to simulate similar networks.



(a) **(b)** **(c)**

Figure 1. a shows the input random network, b shows a simulated network using model 1 and the G as input network, and c shows the goodness of fit of the model over global topological properties.

Figure 2a is the input lattice network and Figure 2b is a sample simulated network by model 2. The three sub-plots in Figure 2c shows the goodness of fit over the set of graph statistics: degree, edge-wise shared partners and minimum geodesic distance



(a) **(b)** **(c)**

Figure 2. a shows the input lattice network, b shows a simulated network using model 1 and G as input network and c shows the goodness of fit of the model over global topological properties.

This shows that one can formulate ERG models to model networks with well-studied opposite topologies by choosing suitable graph metrics. Suitable metrics are the ones that adequate capture important features of the network topology. However, since our ultimate goal is to model brain connectivity networks, we propose the model given by equation 8 which incorporates the local efficiency E_l and global efficiency E_g measures. These are adequate metrics to capture brain connectivity topology which has been shown to exhibit small-world architecture.[32]See section to see the details of the model formulation.

We first investigate how this model behaves over the set of 5 SW networks constructed with the Watts and Strogatz model with rewiring probabilities $p = [0, 0.1, 0.25, 0.5, 1]$. Figure 3 shows the space of the estimated parameters of models with the form of equation 6 and with each of the SW networks input. The colour line shows the trajectory in $\mathbb{R}^3$ that the estimated parameters follow when increasing the rewiring probability from 0 to 1 in the Watts and Strogatz model.

The estimated parameters of the ERG model separate networks with lower and higher probabilities and cluster together networks that exhibit small world architecture. This shows that the model 8 is able, through the parameters, to resemble the transition the Watts-Strogatz model undergoes.

We are now interested in examine how well the model behaves when simulating new networks. We can compare visually the input SW networks (first row Figure 4) versus representative simulated networks using model 8 and each of the SW networks as input networks (second row Figure 4)

We then assessed property 4 for the models 8 for each SW network. We compute the values for the graph metrics $(\langle k \rangle, E_l, E_g)$ over the input SW networks, which are represented in Figure 5 by a green cross, and compare them with distribution of the

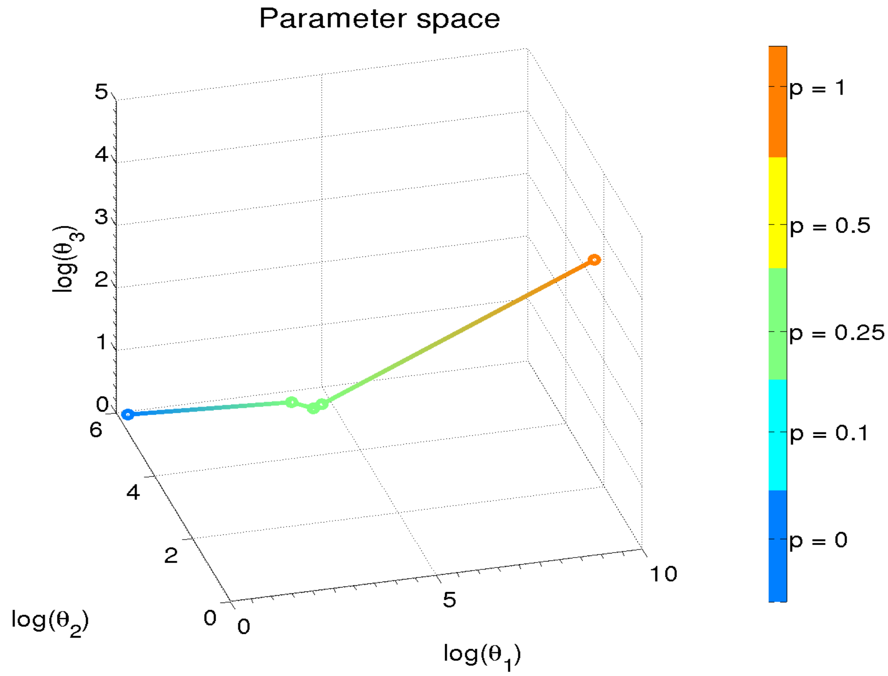


Figure 3. Parameter space of model $P(G) = \frac{exp(\theta_1 \langle K \rangle (G) + \theta_2 E_l(G) + \theta_3 E_g(G))}{Z}$ for the simulated SW networks. $\langle k \rangle$ corresponds to the mean degree metric, E_l to the local efficiency metric and E_g to the global efficiency metric.

values of the same metrics over 100 simulated networks by each model. These distributions are represented in Figure 5 by the box plots.

Both figures 4 and 5 show that model 8 does not perform very well at capturing and simulating input network topologies for small rewiring probabilities (≤ 0.1) but it does a better job for higher rewiring probabilities (≥ 0.25).

Before moving to brain connectivity networks application we explored the size and density effect on model in equation model 8. We estimate model 8 for a series of SW ensemble networks described below. Let $\bar{N} = [50, 100]$ be the network size vector and $\bar{\rho} = [0.04, 0.12, 0.5]$ the network density vector. Then we construct 6 ensembles of 5 networks each with the Watts and Strogatz model and for networks with size and density of all possible vector entries combination of $\bar{N}$ and $\bar{\rho}$.

Figure 6 shows for each rewiring probability $p = [0, 0.1, 0.25, 0.5, 1]$ the value of the estimated parameters changing across networks with different densities. The dark line represents estimated parameters for network of size equal to 50 nodes, and light blue equal to 100 nodes.

The dark and light blue lines are very close for almost all the sub-plots shown above. This suggests that there is no size effect on the sensitivity of the parameter estimation. However, there is a density effect on the sensitivity of parameter estimation which does not depend on a specific metric graph but instead seems more dependent on the rewiring probability, ultimately in the network topology.

Application: Brain connectivity networks

After validating the model over the SW networks we then used the EGG data (see section) to model and simulate brain connectivity networks of 100 subjects undertaken two base conditions: rest-state eyes closed and eyes open. We plot over the same parameter space given in Figure 3 the weights of the estimated parameters for the subject-based models with form given by equation 8 per frequency band. The sphere represents the cloud point of parameters per frequency band. The centre is given by the cloud point centroid of the estimated parameters and the radius by the cloud point mean standard deviation i.

For both base lines conditions, rest state eyes closed and eyes open, the cloud point of subject-based model's estimated parameters fall in the region of the trajectory where is expected to see network with small world architecture. A notorious difference among both conditions is the cloud estimated parameters in the α frequency band which is known to be related to attention cognitive tasks.[33]

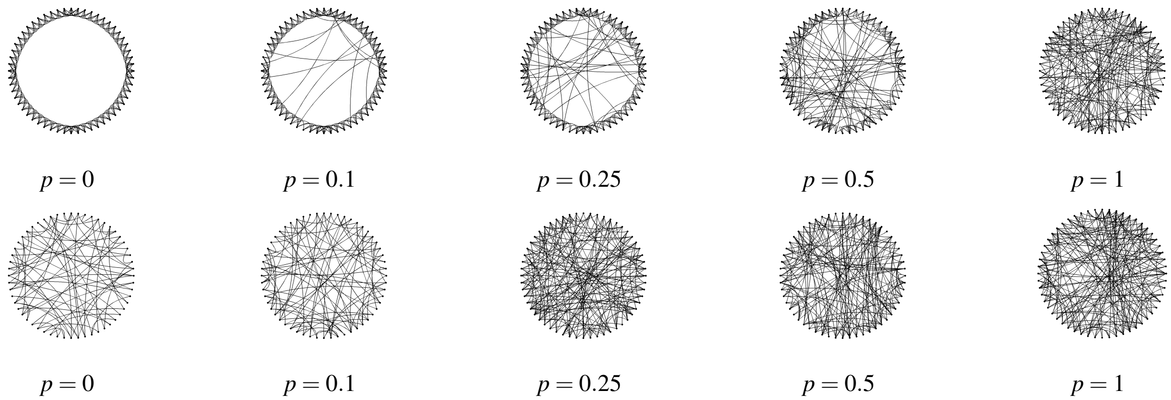


Figure 4. First row shows the input SW networks with rewiring probabilities $p = [0, 0.1, 0.25, 0.5, 1]$. Second row are the representative simulated networks when using the model 8 and each of the networks above as input.

Discussion

We found that networks exhibiting a lattice topology can be model using an ERGM with the degree distribution metrics. When including other metrics to the ERG model, specifically the local efficiency E_l and global efficiency E_g, the model does not satisfy condition 4 very well and is not good in simulating new networks with a similar topology. This was assessed visually and by comparing the values of the metrics in the model of the input network, i.e. lattice network, with the ones simulated by the models that converged.

For the random network we already knew analytically that the model 1 is equivalent to the Bernoulli model and therefore it models very well this type o network topologies. When including E_l and E_g to the ERG model it is still good at satisfying condition 4 and simulating networks which have a random topology.

For networks with small world architecture, these are SW networks with rewiring probabilities somewhere in between zero and one, the proposed model 8 satisfies condition 4 better and simulates new networks closer to the topology of the input network for larger values of the rewiring probability.

We propose ERG model 8 which includes metrics E_l and E_g that capture two very important organizational mechanisms of the brain: functional segregation and functional integration. We were interested in understanding how this model behaves for classical well-studied networks such as the SW networks and in this way validate the application to modelling brain connectivity networks. We found that the estimated model parameters follow a trajectory which resembles the transition of topologies of the SW networks.

We then estimate the parameters of model 8 for brain connectivity networks constructed from EEG data of 100 patients undertaken two baseline activities, eyes-open and eyes-closed resting state conditions. We observed that the estimated parameter fall into the parameter space previously defined by the SW networks ERG model. Moreover, the estimated parameters for each of the frequency band brain connectivity networks are in correspondence with a well know effect of opening and closing the eyes during rest state condition. In terms of functional connectivity when a subject open his or hers eyes a decrease on the α peak frequency is observed.[34] The model is able to capture the difference as show by the upward shift in the eye open condition as compare to the eyes closed condition of the α sphere in figure 7.

Methods

First, we explain the general theory of ERG models. Then we proposed an ERG model for brain connectivity networks. The model is first analyse over networks with well-studied topologies and then it is applied to brain connectivity EEG recordings data.

ERG General Model formulation

Let $G \in \mathscr{G}$ be a graph in a set of possible network realizations, $\{x_i\}_i = \{x_1, x_2, \ldots, x_r\}$ be graph metrics and $\{x_i^*\}_i = \{x_1^*, x_2^*, \ldots, x_r^*\}$ values of the graph metrics measured over G. The aim is to choose a probability distribution $P(G)$ over $\mathscr{G}$ such that conditions

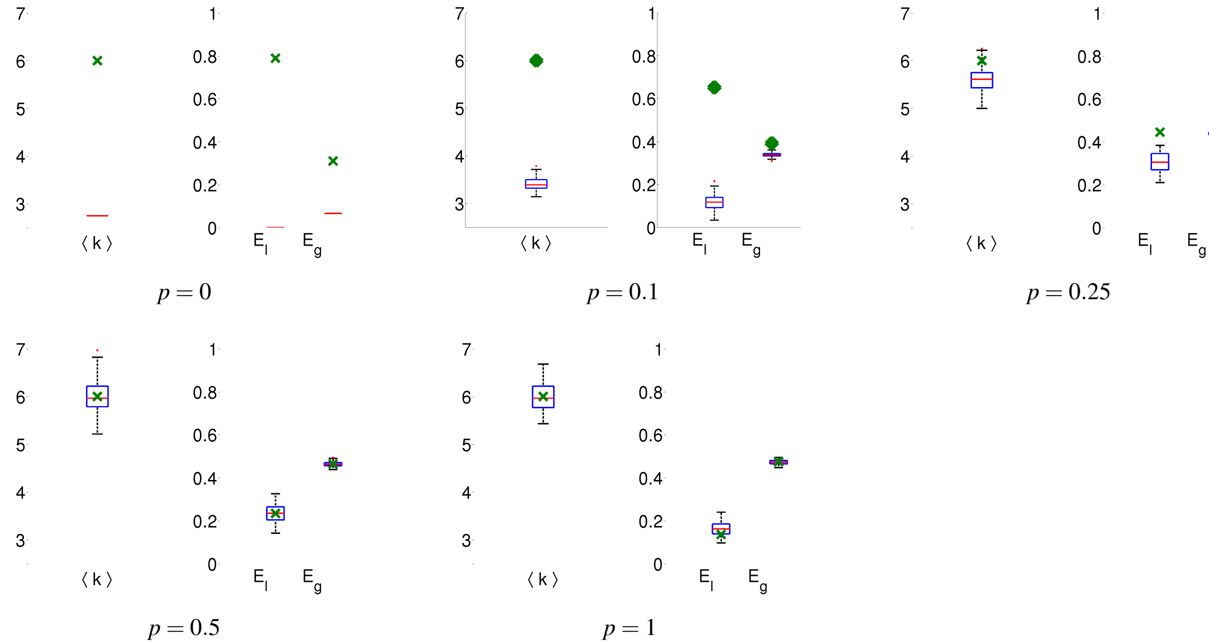


Figure 5. The green cross represents the value of the metric measured over the input SW networks. The box plot are the distribution of the values of the metrics measured over 100 simulated networks by model 8. The metrics are: mean degree ($\langle k \rangle$), local efficiency (E_l), global efficiency (E_g).

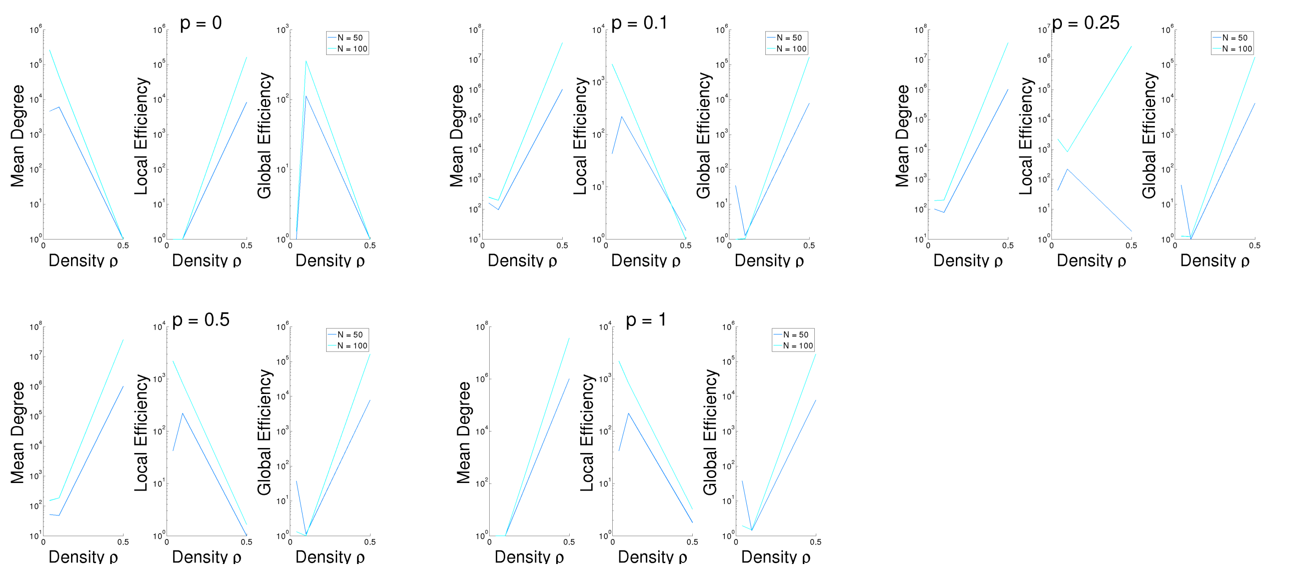


Figure 6. Size and density sensitivity analysis of parameter estimation. From left to right the rewiring probabilities increase, in the x-axis of each sub-plot is the density varying according to $\bar{\rho}$, and on the y-axis the values in logarithmic scale of the estimated parameter for the network metrics mean degree $8(\langle k \rangle)$, local efficiency (E_l) and global efficiency (E_g) which are included in model 8

3 and 4 are satisfied.

$$\sum_{G \in \mathscr{G}} P(G) = 1 \tag{3}$$

$$\langle x_i \rangle = \sum_{G \in \mathscr{G}} x_i(G) P(G) = x_i^* \tag{4}$$

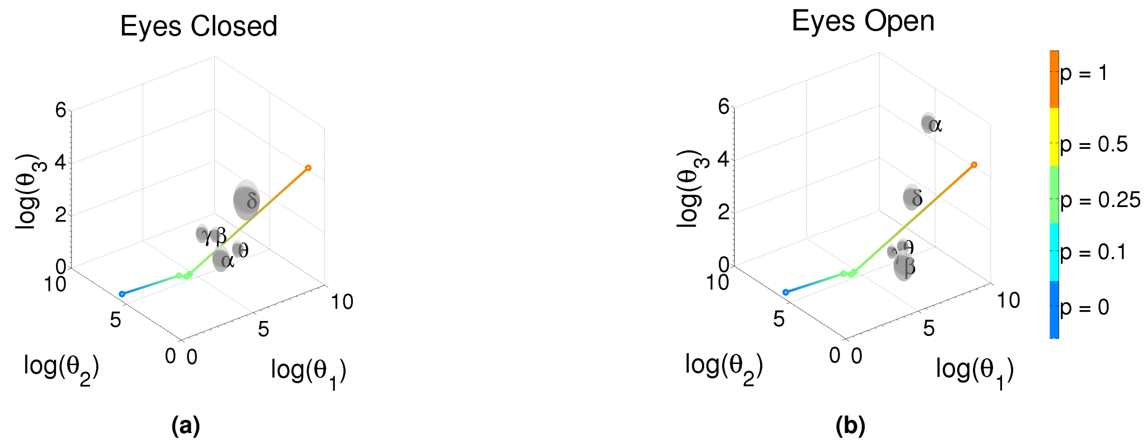


Figure 7. Subfigure a shows the parameter space for the model $P(G) = \frac{exp(\theta_1 \langle K \rangle(G) + \theta_2 E_l(G) + \theta_3 E_g(G))}{Z}$ over EEG data of 100 subjects undertaken base line rest-state eyes closed condition. Subfigure b shows the parameter space for the model over EEG data of 100 subjects undertaken base line rest-state eyes open condition. Each sphere correspond to a frequency band: $\delta(1-3)$Hz, $\theta(1-3)$Hz , $\alpha(1-3)$Hz , $\beta(1-3)$Hz, $\gamma(1-3)$Hz.

Due to maximum entropy principle of information theory,[35] which amounts to the second law of thermodynamics in statistical physics,[36] the *best choice* of probability distribution $P(G)$ is the one that maximizes the Shannon/Gibbs entropy (equation 5) subject to the constraints 3, 4. Where the *best choice* is the one that makes the minimum assumptions about the distribution.[37]

$$S = -\sum_{G \in \mathcal{G}} P(G) ln P(G) \tag{5}$$

The maximization problem of equation 5 subject to the constraints 3 and 4 takes the form

$$\frac{\partial}{\partial P(G)} \left[S - \alpha \left(1 - \sum_{G \in \mathcal{G}} P(G) \right) - \sum_{i=1}^{r} \theta_i \left(x_i^* - \sum_{G \in \mathcal{G}} x_i(G) P(G) \right) \right] = 0$$

$$\Rightarrow -ln(P(G)) - 1 + \alpha + \sum_{i=1}^{r} \theta_i x_i(G) = 0$$

$$\Rightarrow P(G) = exp \left[\alpha - 1 + \sum_{i=1}^{r} \theta_i x_i(G) \right]$$

$$\Rightarrow P(G) = \frac{e^{H(G)}}{Z} \tag{6}$$

where $H(G) = \sum_{i=1}^{r} \theta_i x_i(G)$ is the graph structural Hamiltonian and $Z = \sum_{G \in \mathcal{G}} e^{H(G)}$ is the partition function.

In general it is hard to estimate the parameters θ_i and only a few examples of models are analytical solvable.[30] For example, if one takes $i = 1$, and $x_1 = E$ where $\langle E \rangle$ is the number of expected links in a graph $G \in \mathcal{G}$. Then the model reduces to the well-known Erdös-Renyi model[38,39] and it can be show that there is a direct relationship between the ensemble parameter θ in the ERGM model and the connection probability in the classical Erdös-Renyi model.[30]

When more (complicated) metrics are included in an ERG model the main difficulty in estimating the parameters θ_i comes from the partition function Z in equation 6. Given that the space $\mathcal{G}$ of possible realizations of networks G is very large, calculating the term Z is infeasible and consequently so it is estimating the parameters analytically by maximum likelihood principle. Other techniques such as maximum pseudo-likelihood have been used in the literature but the main drawback is the difficulty of its interpretation.[40] A preferred technique and the most commonly used is Monte Carlo estimation.[41] Such technique consists in simulate a distribution of random graphs from a starting set of parameter values, and then refine the distribution according to condition 4 until parameter stabilization.

Another complication that may arise on an ERG model estimation is that it fails to fit observed real networks, this happens when the probability distribution exhibits one of the following[42]

- Near degenerate property: This is when a model implies that only a few simulated graphs had other than very low probability
- Binomial shape distribution.

In the case of social networks, which tend to have low density but higher levels of triangulation, this problems arise when including metrics such as the count of triangles or of two-stars which are the local properties that will better capture the expected emergent phenomena of social behaviour. New specifications for this metrics have been developed in an effort to avoid degeneracy issues.[43] Such new specifications are based in important mechanisms observed in social networks that do not necessarily are observed in brain connectivity networks. For example, the hypothesis of triangulation stating that two nodes that have a friend in common (are linked to a common node) are more likely to be friends (share a link too) does not apply. Thus, an important step is to recognize what are the intrinsic mechanisms of neural activity and determine the metrics to be included in the ERG model that will best capture them quantitatively. On the next subsection we address the ERG model brain connectivity formulation.

ERG Brain Connectivity Model formulation

Two important organizational mechanisms of the brain are functional segregation and functional integration.[44–46] Functional segregation refers to the localizationism of anatomical brain regions and; functional integrations refers to the connectionism or anatomically separated regions of the brain.[47]

In graph theory this two properties can be capture by the local efficiency and global efficiency measures define as follows[48]

$$\begin{aligned} E_g(G) &= \frac{1}{N(N-1)} \sum_{i,j=1}^{N} \frac{1}{d_{i,j}} \\ E_l(G) &= \frac{1}{N} \sum_{i=1}^{N} E_g(G_i) \end{aligned} \tag{7}$$

The ERG model for brain connectivity we propose takes then the following form

$$P(G) = \frac{exp(\theta_1 \langle K \rangle (G) + \theta_2 E_l(G) + \theta_3 E_g(G))}{Z} \tag{8}$$

Where $\langle K \rangle (G)$ measures the mean degree of network G and is included in the model to control the density of the networks; $E_l(G), E_g(G)$ measures the local and global efficiency (equations in 7)

Computational implementation

To estimate the models computationally we used the software R-version 3.1.3 and the package `statnet`,[49] which has incorporated the `ergm` package[31] that allows to estimate the parameters of an ERG model by the Monte Carlo technique and it has already incorporated a large list of metrics to be included in the model. The advantages of using this existing package instead of coding the algorithm is the robust Markov Chain Estimation algorithm that it has implemented.

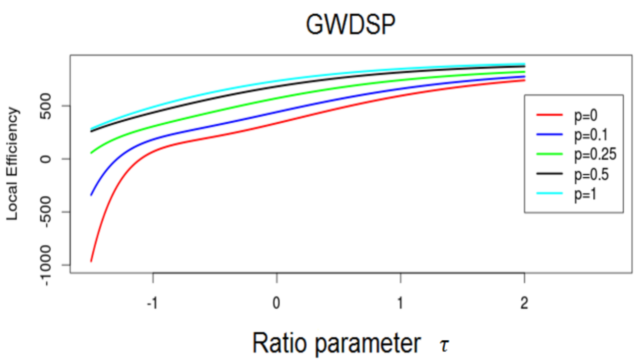
One thing to notice is that the metrics for E_l and E_g are not included exactly as in equations 7 because the way the estimation algorithm is implemented in the `ergm` package takes into account the change statistics and not the metrics itself.[50] The change statistics is the change of a metric value when changing one dyad of the graph G from being connected to disconnected. This value is hard to compute for either E_l or E_g because it highly depends in which dyad is being considered to be removed. For instance the value of the change statistic for E_g is very high when the considered dyad disconnects a network when removed, and very low when the dyad does not form part of any shortest path between nodes in G.

Instead what we used is two metrics *GWDSP* and *GWNSP* that are part of the `ergm` package and equivalent to E_l, E_g respectively.[?, 51]

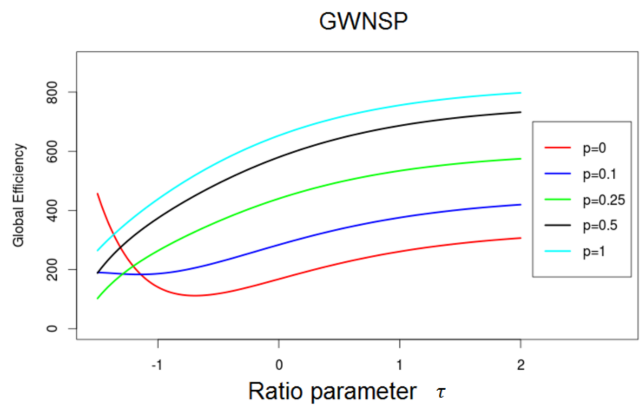
Watts-Strogatz Networks

We used the Watts and Strogatz model to generate 5 networks $G_{i}{}_{i=1}^{5}$ with topologies ranging from a lattice to random and passing through small-world architecture. To do this we created a lattice with $N = 56$ nodes and $k = 6$ neighbours per node. The number of the nodes was chosen like this because that is the number of electrodes used in the EEG data collection, more details on the data can be found below under the Brain Networks subsection. To obtain connected networks, we required that $N >> k >> ln(N)$[52] where k is the number of neighbours of a node, i.e. number of links a specific node has. When $N = 56$, $ln(N) \approx 4.02$. We took $k = 6$. Then a network is generated by setting the rewiring probability to one of the components of the vector $v_p = [0, 0.1, 0.25, 0.5, 1]$. The Watts-Strogatz applied to the vector v_p interpolates networks from lattice topology $p = 0$ to random $p = 1$ and in the middle it produces networks with the so called small-world property.

We then estimated the parameters of the ERG model given by equation 8 for each of the networks created as described above. The ratio parameter τ for each of the metrics *GWDSP* and *GWNSP* where chosen according to the results of Figure 8.



(a)



(b)

Figure 8. Sub-plot a shows how the value of the metric GWDSP (which is the equivalent to local efficiency) changes when the ratio parameter τ varies. Sub-figure b shows the same but for the metric GWNSP which is the equivalent to global efficiency.

We want the metrics GWDSP and GWNSP to differentiate different network topologies, therefore we want to choose values of τ for with the lines in figure 8 are well separated. Then, based in Figure 8a we take $\tau_{GWDSP} = 0.1$ and form Figure 8b we take $\tau_{GWNSP} = 1$. These values remain constant for all the models described in this paper for the sake of comparison.

Brain Networks

Data description

The data used to construct brain connectivity networks was acquired by use of an electroencephalogram (EEG). EEG records electrical activity through electrodes placed on the scalp of subjects. The number of sensors used is 56 electrodes. The data was recorded for 100 subjects undertaken two baseline conditions: rest state one minute with eyes open and one minute with eyes closed.

Network construction

The electrical recordings are represented by a set of time series which are then treated to extract the temporal dependencies among the sensor sites, i.e. apply the FC measure.

There are many FC measures that can be used[53] and. In our case we used the spectral coherence[54] given by equation 9. The spectral coherence FC measure quantifies the level of synchrony between two stationary signals at a specific frequency band. The result is for each dyad of electrodes and per frequency band an adjacency matrix A_i of size 56×56 where in each entry $(a_{jk})_i$ is the value of the spectral coherence between node j and k.

$$SC(x,y,f) = \frac{| S_{xy}(f) |^2}{S_{xx}(f)S_{yy}(f)} \tag{9}$$

We then average the FC measure over the 5 most characteristic frequency bands: $\delta(1-3\text{Hz})$, $\theta(4-7\text{Hz})$, $\alpha(8-14\text{Hz})$, $\beta(15-29\text{Hz})$, $\gamma(30-40\text{Hz})$. We are left with five adjacency symmetric matrices, each of which correspond to a frequency band and represent an undirected weighted network, where nodes are the regions of the brains which are associated to the electrodes and the links are weighted by the magnitude of the FC measure, the spectral coherence.

Then, to obtain the most relevant links, meaning the ones which represent the most significant FC measures and remove noise due to the spatial proximity of the nodes or to other sources of electrical activity, the adjacency matrices must be filtered.[10] Again, many techniques exists[11,55,56] and the choice of remove it is an open debate which strongly depends on the FC measure used to defined the links. In our case, we set a threshold $t \in \mathbb{R}$ such that when removing all the links which have a weight lower than t the density of the network was $\rho = 6/55$, in analogy with the implemented WS model for which the ring lattice had 6 neighbour nodes and therefore a mean degree equal to 6. Finally the networks are binarized, this is the remaining weighted links, i.e. entries in the adjacency matrix different from zero, are set to one.

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