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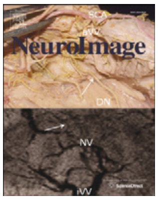

Technical Note

Anatomical connectivity and the resting state activity of large cortical networks

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ABSTRACT

This paper uses mathematical modelling and simulations to explore the dynamics that emerge in large scale cortical networks, with a particular focus on the topological properties of the structural connectivity and its relationship to functional connectivity. We exploit realistic anatomical connectivity matrices (from diffusion spectrum imaging) and investigate their capacity to generate various types of resting state activity. In particular, we study emergent patterns of activity for realistic connectivity configurations together with approximations formulated in terms of neural mass or field models. We find that homogenous connectivity matrices, of the sort of assumed in certain neural field models give rise to damped spatially periodic modes, while more localised modes reflect heterogeneous coupling topologies. When simulating resting state fluctuations under realistic connectivity, we find no evidence for a spectrum of spatially periodic patterns, even when grouping together cortical nodes into communities, using graph theory. We conclude that neural field models with translationally invariant connectivity may be best applied at the mesoscopic scale and that more general models of cortical networks that embed local neural fields, may provide appropriate models of macroscopic cortical dynamics over the whole brain.

Introduction

This paper is about modelling the dynamics in large scale brain networks with both realistic and analytic connectivity matrices. It focuses on the large scale structure of cortical dynamics and considers the effect of heterogeneities in connectivity in terms of the relationship between structural and functional connectivity (Honey et al., 2007; Zhou et al., 2006). The study of anatomical connectivity in the human brain – in parallel with the spatiotemporal activity of resting state networks – has attracted significant attention during recent years, e.g. (Arieli et al., 1996; Biswal et al., 1995; Damoiseaux et al., 2006; Smith et al., 2009; Vincent et al., 2007). Despite the inherent structure of this activity being well-known (engaging the posterior cingulate, precuneus, lateral parietal and elements of the prefrontal cortex), an understanding of how anatomical connectivity produces brain dynamics at various temporal and spatial scales is only partial. This is, in part, due to the lack of detailed biophysical data as well as computational power, both of which have only recently become available. In the past ten years, a wealth of data from tracing studies has revealed the complexity of anatomical connections in the macaque brain, while an aim over the next few years is to provide a full description of the connectivity of the human brain — the "connectome" (Biswal et al., 2010; Sporns et al., 2005).

Here, we use anatomical connectivity matrices and focus on the implications that their form might have for the dynamical repertoire of resting state activity and how this activity could be modelled. We assume that anatomical connectivity will predict certain aspects of functional connectivity (defined as the correlations among activity in different parts of the brain), and the dynamics of resting state activity; in other words, we assume that the dynamics of the resting state reflects some inherent aspect of anatomical connectivity. Our agenda was to establish the sorts of dynamics that could be seen under particular forms of anatomical connectivity and to relate them formally from basic principles.

Before detailed connectome data were available, simplifying assumptions about the connectivity needed to be made to study the network dynamics on the full brain scale. These assumptions included the translational invariance of the connectivity commonly referred to as homogeneous (e.g. Jirsa and Kelso, 2000). In particular for the temporal domain these assumptions proved to be powerful (Jirsa and Haken, 1996, 1997; Robinson et al., 1997), but naturally suffered when applied to the spatiotemporal domain. The symmetry present in the connectivity expressed itself as a constraint imposed upon the emergent brain dynamics. This led researchers to the proposal to use tractographic data as a connectivity skeleton of network models for the exploration of neural dynamics on the full brain scale (Jirsa et al., 2002). Here we were interested in exploring these connectivity constraints systematically. To address this, we use simulations to verify theoretically motivated characterisations of resting state dynamics and then use these characterisations to see whether

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homogeneity assumptions were justified when using realistic (DSI) connectivity matrices.

Our theoretical analyses focus on fixed-point attractor networks, where self-sustained oscillations are precluded (Jirsa and Ding, 2004) and, by definition, the network dynamics depend only upon the anatomical or structural connectivity matrix. This matrix allows us to express the dependence of spatiotemporal dynamics, arising from the collective activity over the network nodes, in terms of a few sufficient modes, which correspond to the dominant patterns of cortical activity observed at rest. To allow for some mathematical treatment, we simplify the mean field formulation of Brunel and Wang populations to a stable fixed-point attractor absorbing both effects of excitatory and inhibitory activity. Attractor networks have been demonstrated to show non-oscillatory instabilities for excitatory coupling with random connection topology and constant identical time delay for all couplings (Feng et al., 2006; Jirsa and Ding, 2004). There are currently no results available extending this work to multiple time delays. For our purposes, we focus on the (sub)set of non-oscillatory solutions arising at instabilities. This assumption does not exclude complex dynamics within a population as demonstrated by Brunel and Wang (2001) who considered mean fields of populations of spiking neurons based on the integrate-and-fire neuronal model. It is the mean field of the population activity that demonstrates the attractor state, which is the level of description chosen here. This result generalizes to more complex situations under certain conditions on the dispersion of neural activity and noise (Assisi et al., 2005; Jirsa, 2007; Stefanescu and Jirsa, 2008). In short, our focus is on fixed-point solutions of mean field formulations of Brunel and Wang neuronal populations. Noise induced in a population of spiking neurons will change the spiking dynamics, but the mean field will have a particular constant value as long as all other characteristics stay the same and this noise is small. Jirsa and Ding showed that inhibition is crucial in order to generate a delay-induced oscillatory instability for the network. However, this result holds only for random connectivity and when delay is the same across the whole network.

Our paper follows a series of studies focusing on the relationship between the structural properties of the brain and the nature of dynamics on brain networks. In particular, we take up the themes motivated by a graph theoretical approach to complex systems (Newman, 2003; Watts and Strogatz, 1998). This approach started with the paper of Watts and Strogatz — who studied the anatomical connectivity of *Caenorhabditis elegans*. Graph theory has been used to delineate significant traits of neuroanatomical networks (He and Evans, 2010; Stam and Reijneveld, 2007), such as their small-world architecture and derive measures that can be associated with dysfunction (Ponten et al., 2007; Schindler et al., 2008). Furthermore, graph theory has been used to identify plausible brain systems in a mind-wandering state, often called a default mode network, e.g. (Buckner et al., 2008; Raichle et al., 2001). Recent research has also focused on describing pathological brain states by associated graph theoretical measures, reflecting clinico-pathological processes (Bassett and Bullmore, 2009; Guye et al., 2010) and has used neural fields to analyse large scale cortical networks (Gray and Robinson, 2007, 2009; Gray et al., 2009; Henderson and Robinson, 2011; Robinson et al., 2008, 2009) and neural masses to model local sources (Jansen and Rit, 1995; Lopes da Silva et al., 1974; Van Rotterdam et al., 1982) or construct neurocognitive networks (Dhamala et al., 2007). We here focus on notions such as community structure, to motivate similar approximations of translational invariance (Amari, 1977; Breakspear et al., 2006; Coombes, 2010; Deco et al., 2008; Robinson et al., 2003; Wilson and Cowan, 1972) and consider the role of inhomogeneities in producing endogenous brain dynamics. As pointed out by a reviewer, there is a huge literature on the analysis and interpretation of fields in the physics literature — ranging from optics and electromagnetics to acoustics and quantum fields. Also, it is well known that localised modes will be produced by inhomogeneities (e.g., impurities in condensed matter), and that translation-invariant systems will have plane eigenmodes (this goes back to Nother in the early 1900s, see e.g. Bloch, 1929). Our focus is on heterogeneities of the sort assumed in neural field theory and whether they have a similar effect as “matrix impurities”. For instance, in condensed matter physics, impurities act only locally which is different from the combination of long-range interactions and local homogeneous kernels we consider here.

This paper comprises three sections: in the first, we discuss the anatomical data that form the basis of our investigation and introduce some notions from graph theory that we will use to characterise inhomogeneities in realistic and analytic connectivity matrices. In the second, we formulate cortical dynamics in terms of an integro-differential equation, thereby providing an analytical characterisation of resting state activity; that is dominated by eigenmodes of the connectivity matrix. We also consider a homogeneity approximation to the connectivity matrix; namely, we replace a sparse connectivity matrix by translationally invariant coupling (modelling lateral interactions on the cortical sheet), and provide a mathematical explanation for the emergence of damped spatially periodic patterns. In the third section, we turn to numerical investigations and study the emergent dynamics from various connectivity configurations and exemplar matrices. We demonstrate the relationship between graph theory measures of clustering and principal eigenmodes. In addition to our focus on symmetric (undirected) connectivity matrices, we also discuss the importance of asymmetries and coherent fluctuations, such as those observed in resting state fMRI by exploiting connectivity configurations including short range excitatory and inhibitory effects. Finally, we used the theoretical predictions to assess the adequacy of translationally invariant connectivity matrices to explain the principal patterns of activity associated with realistic anatomical connections.

Large scale brain networks

The analysis of large connectivity datasets, using graph theory, considers brain networks as weighted graphs, whose nodes represent cortical sources of measurable activity and whose edges correspond to anatomical connections. Each of these edges can be associated with a number corresponding to the weight that characterises the strength of the relevant connection; for example, as obtained through tracing studies. These weights then form a matrix, which describes anatomical connectivity.

Diffusion spectrum imaging matrix

We use an anatomical connectivity matrix denoted by κ obtained via diffusion spectrum imaging (DSI) and white matter tractography (Hagmann et al., 2008). This matrix consists of $N = 66$ nodes representing both hemispheres of the human brain (see Fig. 1).

The matrix entries κ_{ij} are the corresponding connection weights that range from 0 to 1 (in an arbitrary scale) and are based on tract density. The upper left and lower right quadrants represent intrahemispheric connections. Elements of a band structure in this matrix reflect prominent fibre-tracts connecting homologous regions in the two hemispheres. Since the DSI technique yields non-directional connections $\kappa_{ij} = \kappa_{ji}$. With each entry $\kappa_{ij} \in \kappa$ we can associate two regions x_i and x_j corresponding to source and target regions respectively. We will denote the space spanned by all such regions by W, namely $W = \{\cup x_l\}_{l=1}^{N}$. The matrix κ can be represented as a function in a two-dimensional space $\kappa(x,y)$, where the variables x and y parameterise the location of target and source regions respectively, assuming, for simplicity, one-dimensional cortical manifolds.

Optimal community structure, modularity and clustering coefficient

Here, we briefly review certain notions from graph theory, used in this paper, that have proven very useful for a quantifying brain network topology. For the evaluation of graph theoretic quantities we used the