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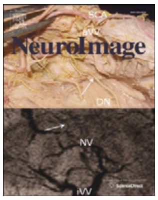

Mapping the dynamic repertoire of the resting brain

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ABSTRACT

The resting state dynamics of the brain shows robust features of spatiotemporal pattern formation but the actual nature of its time evolution remains unclear. Computational models propose specific state space organization which defines the dynamic repertoire of the resting brain. Nevertheless, methods devoted to the characterization of the organization of brain state space from empirical data still lack and thus preclude comparison of the hypothetical dynamical repertoire of the brain with the actual one.

We propose here an algorithm based on set oriented approach of dynamical system to extract a coarse-grained organization of brain state space on the basis of EEG signals. We use it for comparing the organization of the state space of large-scale simulation of brain dynamics with actual brain dynamics of resting activity in healthy subjects.

The dynamical skeleton obtained for both simulated brain dynamics and EEG data depicts similar structures. The skeleton comprised chains of macro-states that are compatible with current interpretations of brain functioning as series of metastable states. Moreover, macro-scale dynamics depicts correlation features that differentiate them from random dynamics.

We here propose a procedure for the extraction and characterization of brain dynamics at a macro-scale level. It allows for the comparison between models of brain dynamics and empirical measurements and leads to the definition of an effective coarse-grained dynamical skeleton of spatiotemporal brain dynamics.

1. Introduction

Brain activity is a spatiotemporal signal with deterministic and stochastic characteristics. As time evolves the brain dynamics traces out a trajectory in a high-dimensional state space. The objective of all analysis methods is to provide a characterization of this trajectory. The most frequently used approaches apply some sort of information compression with the objective that the achieved reduction in complexity is still sufficiently informative to allow for comparisons between data sets, let it be different experimental conditions, different subject groups or between model and empirical data. Such approaches include entropy, dimension estimates, various forms of complexity, Lyapunov exponents, and covariances just to name a few (see e.g. Stam (2005) and Subha et al. (2010), for reviews). For each of these measures multiple derivatives exist with various degrees of sophistication. All of these approaches have in common by construction that they lose their sense of dynamics, that is the actual notion of temporal evolution is lost. As a consequence quantitative descriptions of brain activity are impoverished and only capture limited aspects of the brain trajectory and none of its temporal nature.

We illustrate this thought along a hotly debated example in neuroscience, that is the resting state dynamics of the brain, which is typically accessed through functional magnetic resonance imaging (fMRI), electroencephalographic (EEG) and magnetoencephalographic (MEG) measurements. The fMRI measures the blood oxygenation dependent level (BOLD) signals of the hemodynamic response on high resolution spatial scales (mm) and slow temporal scales (sec). Here a limited number of 8–10 robust network patterns of BOLD activity have been observed in the primate brain during rest in the BOLD signals (Biswal et al., 1995; Damoiseau et al., 2006; Raichle et al., 2001). These patterns are characterized by spontaneous intermittent coherent fluctuations on an ultraslow scale of <0.1 Hz. Correlation patterns amongst the resting state networks with strong positive and negative correlations have been observed (Fox et al., 2005). Though this finding provides a constraint on the permissible spatiotemporal brain dynamics, the details remain still unclear. We still do not know if this temporal dynamics translates into an oscillatory coactivation of selected resting state networks, or a pattern competition, or even a hopping process

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from one resting state network to another. These important details will express themselves through features of the trajectories in the state space of the brain network, including their geometry and topology, as well as zones of increased convergence and divergence of the trajectory densities. The total loss of temporal dynamics has been nicely demonstrated by Wen et al. (2012) who applied common techniques of prevailing statistical approaches to surrogate fMRI data (subjected to covariant randomization of the temporal order) and obtained identical results regarding the resting state networks.

We find a similar situation in electroencephalographic data. First of all, the BOLD signal and its electrophysiological correlate show a clear but non-trivial relationship. To investigate this relationship between the BOLD signal and its underlying neural activity Logothetis et al. (2001) demonstrated in anesthetized monkeys that simultaneous fMRI and intracortical electrical recordings of local field potentials show positively correlated spontaneous fluctuations. Laufs et al. (2003) recorded simultaneous fMRI and EEG in awake human subjects at rest and found that the β-band power was positively correlated with the BOLD signals in the posterior cingulate, the precuneus, the temporo-parietal and dorsomedial prefrontal areas. These areas are known from one of the resting state network patterns referred to as the Default Mode Network (DMN), which is characterized by a reduced activation during task conditions and elevated activation in absence of any task. Mantini et al. (2007) also showed that different frequency bands correlate differently with the various resting state network patterns, whereas a recent study by Scheeringa et al. (2011) demonstrated that the BOLD signal in humans performing a cognitive task is related to synchronization across different frequency bands. In the latter, trial-by-trial BOLD fluctuations correlated positively with high γ power of the EEG and negatively with α and β. Hence, there is empirical evidence that the spatiotemporal dynamics of the BOLD signal is related to the spatiotemporal dynamics of electroencephalographic signals, but the actual nature of the spatiotemporal organization, in particular its time evolution is not clear.

The situation is similar for the theoretical studies in the resting state literature, certainly motivated by the objective to achieve correspondence with empirical data (see Deco et al. (2011), for a recent review). Essentially, in a series of theoretical studies (Deco et al., 2009; Ghosh et al., 2008; Honey et al., 2007) the authors demonstrate that the resting state pattern formation can be understood as emerging from the network interactions of a brain network with a full brain connectivity derived from either the CoCoMac database or using tractographic data (DTI/DSI). Convergent evidence based on these theoretical models was provided that multiple states exist during the resting state, which are explored in a stochastic process driven by noise. Such models agree on the importance of noise-driven exploration of the brain dynamical repertoire, but do not fully agree on the deterministic skeleton of this “dynamical repertoire”. The dynamic repertoire is the set of all the macrostates that may be occupied during the resting state dynamics and the “deterministic skeleton” is the set of transitions between these macrostates. Taken together they thus include the geometry and topology of the trajectories, as well as their convergence properties indicating stability. One can view the ensemble of dynamic repertoire and skeleton as a graph composed of macrostates on the nodes and the edges indicating the possible transitions. Such a visualization is effectively a discrete representation of the continuous time evolution of the brain network in its state space. Ghosh et al. (2008) named the noise driven exploration of such a brain dynamics graph “the exploration of the dynamic repertoire of the human brain” due to the similarity between the resting state patterns and network activations known from task-related conditions.

Initial interpretations of neuronal dynamics have mainly focused on attractor dynamics (Amit, 1989; Hopfield, 1982), leading to a clear hypothesis concerning the organization of the brain state space. Nevertheless, it soon appeared that transients and metastability play an important role due to e.g. high dimension or sparse connectivity (Friston, 1997; Tsuda, 2001). This leads to the proposal that such a complex coordinated system as the brain is best understood as a multistable and metastable system at many levels from multifunctional neural circuits to large-scale neural circuits (Kelso, 2012). Nevertheless, these proposals have been quantitatively compared with real data (fMRI, EEG or MEG) mainly on the basis of the comparison of time-series of spectral contents (Freyer et al., 2011) or the comparisons of covariance matrices (functional connectivity) (Deco and Jirsa, 2012) between experiment and model. For example, Deco and Jirsa (2012) recently correlated the functional connectivity matrices of the simulated brain network data with the experimental BOLD signals and obtained high correspondence. They also demonstrated the existence of five resting state patterns for an elevated value of coupling strength but also found that the best fit of functional connectivity is obtained at a lower level of coupling, i.e. when the resting state patterns do not exist as stable states in the state space, but are close to their creation (a so-called bifurcation). For this reason, Deco and Jirsa named them ghost attractors, which comprise the dynamic repertoire of the brain network. Here a subtle distinction plays an important role: These ghost attractors are assumed to exist due to their parametric proximity to the bifurcation. This situation is called criticality. The assumption behind this hypothesis is that below the bifurcation point (subcritical) and above (supercritical), the density of the trajectories in the state space changes smoothly. Though this assumption is reasonable, it still remains to be shown that the ghost attractors indeed exist in the subcritical regime. Once their existence, and thus the dynamic repertoire, is established, then this will be the first step towards the full characterization of the trajectories within the state space connecting the ghost attractors, and hence the full characterization of the spatiotemporal brain dynamics.

As we illustrated above, although the presence of a spatio-temporal organization in brain activity has clear empirical support, the understanding and interpretation of this organization remains an open problem. Moreover, the deterministic dynamical skeleton in the state space is not easily characterized at the level of scalar metrics (spectral analysis or even correlation) and render the comparison of model and empirical brain activity in its state space indispensable. From the view point of dynamical system theory the only unambiguous representation of a dynamic system is given by its flow in the state space. Said differently, two dynamical systems are different from each other if and only if the topology of their flow is different. If not, then they belong to the same class of systems. The flow prescribes the evolution of the state vector of the system as a function of its current state and is most commonly written as a set of differential equations. In terms of state space analysis, two approaches are typically taken in the literature. The first approach is based on nonlinear time series analysis derived from dynamical systems theory (see e.g. Kantz and Schreiber (2004)) and has mostly focused on the properties of continuous trajectories in the brain's state space. The second approach is based on the stochastic approach of dynamical systems (Lasota and Mackey, 1994). The main difference between these two *complementary* approaches lies in the fact that the first one supposes a differential structure of the trajectory, whereas the second one does not and thus allows one to link dynamical systems and stochastic processes. The stochastic approach of dynamical systems thus becomes a natural theoretical setting for the characterization of brain dynamics all the more that high dimensional dynamics can be hardly differentiated from stochastic processes (Lachaux et al., 1997). Nevertheless, there are subtleties that go beyond the scope of this article, but should be kept in mind when interpreting data. To some extent noise, which is invariably present in biological systems, can obscure the underlying difference but not always: A subcritical bifurcation is only smoothed into an apparent supercritical bifurcation by additive noise of a sufficient amplitude — otherwise the discontinuity of the former remains. In the presence of multiplicative noise, the statistics of the system will be also qualitatively different. Similarly, the symmetry of noise

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