Effects of time-delays on neural dynamics on functional brain networks

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The purpose of the project is to study neural dynamics on empirically derived networks by means of numerical simulations. Here, these networks arise from functional magnetic resonance imaging (fMRI) data yielding functional networks. Thus, the project combines experimental and modelling approaches.

Complex, but highly structured, dynamic phenomena have been reported in resting brain activity, i.e., under no stimulations and in the absence of any overt-directed behavior, revealing resting-state functional networks [BIS95, DAM06, BRE10b]. However, the question, how these well-organized patterns of activity emerge from intrinsic brain dynamics, remains essentially unexplored. Resting state functional connectivity is commonly assumed to be shaped by the underlying anatomical connectivity. Furthermore, it has been suggested that its strength, persistence and spatial properties are constrained by the large-scale anatomical structure of the cortex [VIN07, KAI07, HON09].

However, strong functional connectivity is often observed between remote cortical regions suggesting that indirect connections, interregional distance and collective effects governed by network properties of the cortex play significant role in generation of the functional connectivity in the resting state. Here, we aim to address these questions by studying topology of an empirically derived resting state network from fMRI data and modelling the dynamics on these network. This will contribute to long-term research efforts addressing the comparison of results based functional and structural networks and will provide deeper insight to the underlying processes involved in the observed functional connectivity.

The resting-state functional networks are comprised of N cortical regions as adapted from a studies of functional segmentation of the human cortex [TZO02, KIV09]. From each region the mean time series of blood-oxygen-level-dependent (BOLD) activity are extracted. Then the $N \times N$ correlation matrix $\{f_{ij}\}$, $i, j = 1, \ldots, N$, is constructed by calculating the Pearson correlation coefficient on all possible pairwise combinations of the time series. Any correlation in the correlation matrix greater than a given threshold is kept as a link between corresponding regions in the adjacency matrix.

The distances d_{ij} between the nodes are taken into account as the distances between the centers of the regions from which BOLD time series are extracted [KAI06]. In contrast to the simplifying assumption of the Euclidean distance between regions, we will be able to use the actual trajectory length of the fiber tract, which could be significantly longer for highly curved tracts. The obtained lengths help to account for the finite speed v of the signal propagation along the axons, and the interactions in the network are modeled with corresponding time delays $\Delta t_{ij} = d_{ij}/v$ [GHO08, GHO08a, DEC09].

In a general notation, the network model can be written as follows [VUK13]:

$$\dot{\mathbf{x}}_i = \mathbf{g}\left(\mathbf{x}_i\right) - c\sum_{j=1}^{N} f_{ij}\mathbf{h}\left[\mathbf{x}_i(t - \Delta t_{ij})\right] + \mathbf{n}_i, \qquad i = 1, \ldots, N$$

where $\mathbf{x}_i \in \mathbb{R}^n$ denotes the dynamical variables of the node i, c is the coupling strength, $\mathbf{h}$ specifies the local coupling, and $\mathbf{n}_i$ describes n independent additive white Gaussian noise terms. The coupling configuration of the network is specified by the adjacency matrix $\{f_{ij}\}$, $i,j = 1,\ldots,N$, which will be extracted from empirical data. In practice, the local dynamics $\mathbf{g}(\mathbf{x}_i)$ will be described by a two-dimensional nonlinear system as summarized in the following.

The large-scale neural models will be used as a tool for the the local dynamics to explore a non-trivial question of correlated behavior of distant cortical regions, i.e., functional connections, in resting-state brain dynamics. The model of choice will be the FitzHugh-Nagumo model [FIT61, NAG62, GHO08, GHO08a], but other models could also be discussed in passing: the saddle-node infinite period bifurcation (SNIPER/SNIC) [HU93a], stochastic models for the firing rate [CAB12], Wilson-Cowan model [DEC09], or other dynamical models [IZH07]. The FitzHugh-Nagumo model describing the local dynamics of the nodes is given by in the notation of [GHO08, GHO08a]:

$$\dot{u} = g(u,v) = \tau\left(v + \gamma u - \frac{u^3}{3}\right) \tag{1a}$$

$$\dot{v} = h(u,v) = -\frac{1}{\tau}\left(u - \alpha + bv - I\right), \tag{1b}$$

where I is magnitude of an external stimulus, which is assumed to be 0 in our model of the resting state dynamics. The other system parameters are chosen as $\alpha = 0.85$, $\beta = 0.2$, $\gamma = 1.0$ and $\tau = 1.25$ to render solutions with damped oscillatory behavior of a node dynamics, i.e., at the onset of instability, in the absence of the connectivity in the network. The resulting time-series of the neural activity can be used to infer the BOLD signal observed in the fMRI data via the Baloon-Windkessel hemodynamic model [FRI00].

Using the described configuration, we investigate how correlated behavior of distant regions emerges from different topologies of empirically derived functional resting-state networks. We discuss physiologically realistic values of the coupling delays as well as different coupling strengths and correlation thresholds, for which the simulated networks have graph-theoretical measures [KAI04a, KAI07a, RUB10, NEW10] very similar to those of experimentally derived networks.

The following steps will be taken:

1. Literature study on nonlinear dynamics in neuroscience, network dynamics, functional and structural networks of the human brain...

2. Numerical simulation of neural models on the network topology derived from fMRI data (functional networks); in particular, scan of ranges for time-delays/propagation velocities.

3. Time-series analysis, calculation of functional connectivity from simulations, and comparison of results obtained for structural and functional networks

This lab rotation will be focused on the simulation of neural dynamics on realistic network topologies and extends recent research in the junior research group of Dr. Hövel [VUK13]. The work is embedded in the *Bernstein Center of Computational Neuroscience Berlin* and it also is part of international and national collaborations on nonlinear dynamics and neuroscience, in particular with the working group of Marcus Kaiser (*Newcastle University*).

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