**Origins and Properties of the Human Brain at Rest: a Comparative NIRS and fMRI Study**

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**Introduction:** Recent studies from near-infrared spectroscopy (NIRS) and functional magnetic resonance imaging (fMRI) have agreed that, at rest, spontaneous brain activity (SBA) across different brain regions is connected through some sort of network structure, presenting several complex features. In fact, graph theory has been a successful methodology to characterize the human brain at rest. In this work, we present our most recent advances on combining NIRS and fMRI to investigate low-frequency SBA over the whole head with graph theory.

**Materials and Methods:** We simultaneously performed NIRS (continuous-wave NIRScout, NIRx Medical Systems) and fMRI (3T Philips) in 28 healthy subjects during resting-state. For each subject, 300-s baseline runs were performed from 2 to 6 times. The NIRS geometry was designed to cover the whole head, employing 16 sources (760 and 850 nm each) and 32 detectors. The fMRI protocol included acquisition of structural and functional (TR 2s) images (TR 2s) sequences. For pre-processing, we employed standard procedures from NIRS1 and fMRI2 to extract hemoglobin concentration changes and BOLD time courses, respectively. We employed our graph analysis methods3 to estimate global network parameters and network topological organization. In parallel, we simulated the Ising Modelin two dimensions with periodic boundary conditions at the critical, super-critical and sub-critical temperatures, with the aim to understand the origins of the interactions that yield the network parameters measured by fMRI and NIRS.

**Results and Discussion:** Our results suggest that during the resting state brain networks present a high density of local connections with few long-range links. Brain regions that are symmetrically located or that share the same functionality are highly connected. We also observed that although networks built from graphs are variable over short periods of time, global network properties remain stable. This stability suggests that the human brain at rest is capable to organize itself in such a way that preserves its global topological properties. We identified that the distribution of hubs from oxy-hemoglobin-, deoxy-hemoglobin-, total-hemoglobin- and BOLD-time courses are very similar. The network hubs were located mostly in the frontal and parietal lobes, with slight predominance in the left hemisphere. Regarding differences in the NIRS contrasts, networks derived from BOLD and deoxy-hemoglobin exhibit a similar behavior as function of the correlation coefficient, while they differ from oxy- and total-hemoglobin networks. Last, we could successfully simulate the main network features from deoxy-hemoglobin and BOLD networks by analyzing spontaneous fluctuations of the Ising model. Near the phase transition of the system, the model strikes several properties of the brain networks during the resting state.

**Conclusion:** Overall, our methodology opens new directions to the investigation of the human brain connectivity at rest as a complex system. We developed an efficient approach to generate networks based on the most robust connections that is capable to elucidate fundamental questions regarding brain network topology, such as the presence of hubs and brain asymmetry. In addition, our results suggest that deoxy-hemoglobin and BOLD networks have similar properties but oxy- and total hemoglobin may provide different information that can be valuable to comprehend the human brain. Last, by simulating and analyzing spontaneous fluctuations of the Ising Model at several temperatures, we provided evidences to support the conjecture that, at rest, the human brain behaves like a dynamical system near the critical point. This work enhances the importance of multimodal experiments to better understand brain function and organization.

**References:** [1] Mesquita et al., Biomed. Opt. express 1(1): 324-336, 2010; [2] Power et al., NeuroImage 84: 320-341, 2013; [3] Novi et al., Biomed. Opt. Express 7(7): 2524:2537, 2016.