Non-linear methods to characterize brain dynamics

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During the last 20 years (since [1]), extensive research on the brain's functional connectivity (FC) has been performed, caused by the understanding that brain activation research (based on comparing the BOLD signal's amplitude between conditions) should not be the only way of explaining how the brain works. But most of the research has been performed on the idea that connectivity has a static behavior, where a single value (for each pair of regions) can be obtained from the whole functional magnetic resonance scan (fMRI), usually Pearson, Partial or other variations of correlation [2]. All this research has been able to characterize many processes and behaviors in healthy subjects and patients, but does not consider one of the most relevant aspects of the brain, its dynamics. As an example, the connectivity between the thalamus and other brain areas in pain regulation has been widely reported, increasing their interaction when pain perception is not adaptive anymore (pain regulation), so when focusing on acute pain episodes induced by short events, this method usually fails.

To address this limitation and go further on what FC can provide to the brain's understanding, here we propose a variety of non-linear methods. These methods have been developed by our research group and used recently to address questions about several neurodegenerative disorders. Although these methods were defined in the early part of the decade [3], they were not studied in the detail they might deserve, motivating our work in a past project funded by the Spanish government (ref. PSI2017-82397-R), where we conducted extensive research on their functioning and capabilities with various publications on the subject (for instance [4]).

First, we will explain the so-called Point Process Analysis, This method is based on considering as relevant only the points in the BOLD signal that exceed a certain threshold of amplitude (usually a standard deviation of the normalized signal), thus constructing a discrete signal composed of $\{-1, 0, 1\}$. After this discretization, these can be analyzed as co-activation matrices at time T or as an accumulated matrix of these co-activations. It can be observed that, far from suffering a loss of relevant information, the method estimates perfectly the results obtained by conventional FC techniques while greatly reducing the computational burden and providing the opportunity to address short event questions. The second method proposed is called non-linear dynamic Functional Connectivity (nldFC). This method can be understood as an extension of the point process, as it incorporates samples that precede and follow the peaks (and/or valleys) of the BOLD signal, allowing new metrics such as directionality or delay, which are hard to compute using other FC methods.

In summary, we will review the state of the art in FC methods, focusing on new advances in non-linear ones to characterize brain dynamics, including their caveats and future implementations.

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References

[1] V. M. Eguíluz *et al.*, *Phys. Rev. Lett.* **94**, (2005). DOI: 10.1103/PhysRevLett.94.018102.

[2] I. Cifre *et al.*, *Psychosom. Med.* **74**, 1 (2012). DOI: 10.1097/PSY.0b013e3182408f04.

[3] E. Tagliazucchi *et al.*, *Front in Phys.* **15**, (2012). DOI: 10.3389/fphys.2012.00015.

[4] I. Cifre *et al.*, *Front in Neu.* **1194**, (2021). DOI: 10.3389/fnins.2021.700171.