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Title: Heterogeneous mean field approximation for neural networks topology reconstruction

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The study of complex systems, that is, systems consisting of many degrees of freedom, is a branch of statistical mechanics that is developing rapidly. For a physicist who faces these systems the challenge is trying to describe them in mathematical terms, providing basic models with which to explain the experimental results. An important tool in this direction is certainly provided by network theory, a branch of mathematics that has found great application in the recent decades. Through the use of graphs, more commonly called networks, it is in fact possible to describe a great variety of systems characterized by the presence of binary interactions that can be independent of the relative spatial distance between the constituents that take part in them.

One of the most widely investigated network systems is certainly the brain. Like any network dynamics, neural dynamics depend strongly on the network topological structure on which they take place. However, considering the neurons have a small size and they are largely present inside the brain, obtaining a complete mapping of the connections is an extremely difficult task which is fulfilled only in the case of small and poorly evolved animals. Recent studies, which also includes my master's thesis work, have shown how to use mathematical models of neural networks to formulate and solve inverse problems that allow to extract information on the network structure starting from the global processes' evolution that are observed experimentally. These techniques allow to obtain an estimate of the connectivity distribution and other important properties of the system. They are based on a principle that is common to all dynamical systems on networks: the constituent elements of these systems (represented by network nodes) are indeed characterized both by their internal properties and by their connectivity (number of incoming or outgoing connections) that basically quantifies the number of interactions in which they are involved. The connectivity of the nodes is often the determining property for the emergence of the observed global dynamics. This allows us to formulate a description of the system in a particular approximation called Heterogeneous Mean Field (HMF). Such approximation can be considered as a middle course between a detailed description of the interactions and the mean field approximation. In the mean field theory, the binary interactions (in which a given component of the system is involved) are usually replaced by an interaction with a global field that depends on the average properties of the whole system. Instead, in the heterogeneous mean field approximation, the interaction with the global mean field is multiplied by the connectivity of the elementary component considered. In the above-mentioned works, the HMF approximation is used to define a self-consistency relationship, whose imposition enable to obtain an estimate of the connectivity distribution associated with the network. This imposition is equivalent to asking that the network have a connectivity distribution that justifies the emergence of the observed global dynamics.

During my master's degree thesis work, these techniques have been developed in order to be used in a more general class of neural networks, considering also the effects of the inhibitory. Then, working with the research group of biophysics at the European Laboratory for Non-Linear Spectroscopy (LENS), the reconstruction method has been successfully applied to some experimental data associated with neural activity in mice's brain and in a zebrafish larva, respectively. In particular, the zebrafish larva brain analysis returned interesting results, showing a distribution of connectivity which scales as a power law distribution, a distribution that seems to characterize many other real systems investigated and which, for this reason, has attracted the attention of many scholars.

During my PhD I will carry on the collaboration with the LENS researchers, in order to promote an integrated approach to data analysis. Indeed, the combination between the methods developed during my thesis and the experimental observations can prove successful in order to obtain low-cost information on biological neural networks' topology and structure.

The possible applications are manifold: for example, it is possible to use this kind of techniques to make useful comparisons between the functioning of brains in different clinical states (e.g.,

healthy state and epileptic state) or to provide evidence of the different properties of the same brain when subjected to different tasks. These latter properties, that are often only described qualitatively, can be quantified by using the above-stated techniques.

A further future development may consist in the formulation of a more sophisticated model. In fact, the experimental observations are usually based on the calcium fluorescence. The calcium concentration is considered to be a good proxy of the neurons membrane potential. However, this way of proceeding, although it is widely used, does not take into account the underlying dynamics. Indeed, the calcium concentration is connected to the membrane potential value through some not trivial processes. By properly describing these processes, it would be possible to obtain more correct information on the variation of the membrane potential from the observed data. We could introduce a new model that describe the calcium dynamics and this can be done with different approaches. The calcium dynamics model can be used to improve the reconstruction scheme formulated during my master's degree thesis, in order to extract topological information about the network taking into account also the underlying mechanisms.

Another possible development could come from the combination of reconstruction techniques (with or without the description of calcium dynamics) with other known methods of brain activity analysis as the study of the correlation matrix (one of the most widely used analyzes). Indeed, the information obtained through the reconstruction methods can provide constraints which need to be satisfied when analysing the correlations. Therefore, a methodology to extract not only global properties, such as connectivity distributions, but also detailed information on individual connections may be formulated, aiming to obtain a mapping of the brain connections.