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Prediction of unknown connections in cortical networks

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Introduction

The cerebral cortex is probably the most prominent example of natural information processing networks. It is therefore of major importance how this network is organised. At the lowest level the cortical network is composed by physically (i.e. via chemical and electrical synapses) connected nerve cells. At a higher organizational level, the cortex consists of a set of structurally and functionally specialised regions or areas with highly variable shape and size [5]. Since the use of sensitive and powerful tract tracing techniques is not feasible in humans, the neuronal connections between the areas have been being studied intensely in non-human primates, especially in the macaque, which serves as a model of the human cortex [5]. Kötter and Stephan [3] pointed out the importance of the consideration of "missing data" – connections that have never been checked experimentally, therefore possibly erroneously being treated as missing. An accurate network model should take into account that a disconnected pair of vertices can represent either a pair of areas that are known to be disconnected, or a pair of areas whose connectivity has not been checked yet.
Because it is reasonable to assume that a considerable part of the large-scale cortical network is still unknown, it is an important problem to predict the location of additional connections that have not been charted yet. The two studies published up to now present data on such predictions of yet unknown connections in the cortex [1, 2]. However, they also report a relatively large number of violations, where known existent connections were predicted as non-existent and known non-existent connections to be existent in the reconstructed graphs. This suggests that using other approaches could result in better reconstruction of the cortical network. The aim of the present study was therefore to find a reconstruction algorithm that predicts unknown edges in an arbitrary network under some very general assumptions that do not rely on domain-specific a priori knowledge.

Results

We introduced a simple stochastic graph model based on vertex types and connection probabilities depending on them [4]. Loosely speaking, the model assumes that vertices belong to one of k distinct vertex types, and the probability of a connection between two vertices depend solely on the types of the two vertices involved, governed by a parametrizable probability matrix. This model is called the preference model from now on. We will discuss two methods for fitting the parameters of the preference model to an arbitrary network being studied. One of the methods is a simple greedy algorithm, while the other one is a stochastic method based on the

Metropolis-Hastings algorithm. The two methods complement each other in the sense that the initial burn-in phase of the stochastic method can be substituted by the greedy method in order to achieve faster convergence. The general algorithm was applied to the large-scale visual cortical network, which was reconstructed more accurately than with other models [1, 2] (true positives 93.1%, true negatives 84.8%), while assuming less about the connectional patterns of the network. For the first time, the effect of extension of the visual cortex on graph reconstruction was also examined after complementing it with the subnetwork of the sensorimotor cortex (true positives 92.7%, true negatives 83.1%).

Discussion

One of our major findings is that knowledge of definitely nonexistent connections may significantly improve the understanding of large-scale cortical organisation and the prediction quality of previously uncharted edges, especially in the case of the whole visuo-tactile cortex, where most of the heteromodal connections (going between the visual and the sensorimotor cortex) are completely unknown. It is therefore highly prompted by our results that neurobiologists notice the absence of connections in addition to the existence in their experiments. Nevertheless, our method achieved the highest success rate so far in the visual cortex (compared to [1] and [2]) while mostly agreeing with previous studies in the major connectional patterns of the predicted connections.

We note that although the data on which we operate is cortex specific, the model can be fitted to any kind of graphs, so our prediction methodology can presumably be applied to other networks as well. Being a stochastic method, it is also useful for constructing null models for specific networks and checking whether a given property of the network being studied deviates significantly from the same property of the network ensemble generated by the null model.

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