An algorithm to describe cellular brain connectivity

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The brain is a complex system composed by neurons connected in a way that is largely unknown. Discovering the general rules that can underlie brain connectivity, at the single neuron level, can provide fundamental insights into how information is integrated and propagated within and between brain regions. However, this problem is next to impossible to be adequately studied experimentally and, in spite of the intense efforts in the field, a mathematical description has so far escaped any satisfying solution. In this poster, we present a general algorithm based on graph-theoretical considerations that is able, starting from experimental data obtained from a few small subsets of neurons, to quantitatively explain and predict the single-cell connectivity properties of neuronal networks of any size. We started from two well known classes of random graphs, called exponential (introduced in [1]) and power law (described in [2]). In the exponential model, the probability that exist an edge starting from node i and arriving at node j is exactly p, a constant, for any distinct i and j nodes. For this type of graphs, which we will call ER (from Erdős and Rényi, who first introduced them [1]), the distribution of the incoming connections (indegree) in a network of N nodes is

$$P(D^I_{ER} = k) = p^k(1-p)^{N-1-k}\binom{N-1}{k},$$

and the distribution of outgoing connections (outdegree) is

$$P(D^O_{ER} = k) = p^k(1-p)^{N-1-k}\binom{N-1}{k}.$$

The model is called exponential because the tail of the functions, describing the indegree and outdegree, decays faster than any power law. Indeed, the tail behavior is a very important property of the distributions, because it gives a direct estimation of the network hubs, which are correlated to the way in which information flows in the brain. However, networks rarely exhibit this type of tail in their distributions [3]. More often, tails following a power law are observed. In this networks the underlying assumption is the existence of a preferential connection between nodes; they are called BA models (from Barabási and & Albert, which first described them [4]). Here we used a particular implementation, the Price's model [2]. In this case the indegree and outdegree distributions of a graph of N nodes are defined as

$$P(D^I_{PR} = k) = \frac{B(k+a, 2+\frac{a}{c})}{B(a, 1+\frac{a}{c})} \approx k^{-(2+\frac{a}{c})},$$

and

$$P(D^O_{PR} = k) = \left(\frac{m_0}{N}\delta_0(k) + \frac{N-m_0}{N}\gamma_k\right),$$

where B is the Beta function, $\delta_0(k)$ the discrete Dirac's delta distribution, γ_k is a parameter distribution, a and m_0 are free parameters and $c = \mathbb{E}(\gamma_k)$ a function described in [2]. The major problem is that, in contrast with what has been found in brain networks, pure power law models have too many nodes with low connectivity, instead of the expected linear increase of the degree distributions around zero. This is an important property, and for these models it is in striking contrast with the experimental observation that all neurons are highly connected. On the other extreme, exponential models have an exponential tail, instead of the power law expected for brain networks. For these reasons, in this poster we suggest a method to mix these models, by creating a network starting from two disjoint networks, A and B, which are generated from the same power law model with the same parameters. We create a graph F as the disjoint union $F = A \cup B$. We have thus a copy in F of A and viceversa. We then add edges from A to B (and viceversa) with simple rules inspired by the exponential model. We demonstrate how to obtain indegree and outdegree distributions withe the characteristics to exhibit a linear increase close to 0 and, at the same time, maintain the same power law tail of the original graphs A and B.

We tested our model with the available experimental data and with a large-scale accurate model of cortical circuitry [5]. In all cases we were able to obtain a quantitative agreement between model and data. The results suggest that, using our model, brain connectivity can be accurately described, and algorithmically predicted, using sparse data experimentally obtained from a few sets of small neuronal subnetworks.

References

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