Model-free inference of neuronal connectivity via embedding dimensionality

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A two-photon calcium imaging system is used to capture the in vivo activities of hundreds of neurons in different regions of the awaken mouse visual cortex under different visual stimuli. We infer neural connectivity in these regions from the time series (signals) of neural activity, extracted from the images. Our inference method is based on a novel connectivity measure first proposed in a recent work by S. Emrani and H. Krim [1]. This measure, called embedding dimensionality metric (EDM), provides a causality metric between two neuron signals by interpreting pairs of observations at different instants as individual points in a two-dimensional space and estimating a fractal dimension of the resulting point cloud. The EDM leads itself suitably to establishing nonlinear relations among neurons, which are often elusive to traditional correlational analysis. We compute the ED between each pair of neurons and use it as a weight on the corresponding edge in the connectivity graph. We observe intriguing patterns in the resulting functional network such as information hubs and topological invariant features, corresponding to different visual stimuli. Our method is validated in various aspects, including robustness against trial-to-trial variability and noise, similarity with some other model-free methods and also dissimilarity to null model networks.

More details: We collect N neuron signals $\{\{x_i(t)\}\}_{i=1}^{N}$ from 20 trials of an experiment, where a mouse watches a sequence of shifting grating movies, followed by two different natural movies. Corresponding activities of 590 neurons in the primary visual cortex (V1) and 301 neurons in the anterolateral area (AL) are recorded. Given a pair of neuron signals $\{x_1(t)\}$ and $\{x_2(t)\}$, the point cloud $\{(x_1(t), x_2(t))\}_t$ is embedded in the phase space $\mathbb{R}^2$. The EDM is defined as the reciprocal (inverse) of the fractal dimension of the point cloud, which for the sake of computational efficiency and robustness against noise, uses the correlation dimension [1,2]. The idea behind the application of the EDM for estimating connectivity networks is that dependent neuron signals lead to a structured point cloud with lower fractal dimension. An extreme case is when two neurons have a one-to-one correspondence, either linearly or nonlinearly, in which case the corresponding point cloud lies on a one-dimensional curve in the two dimensional space. Conversely, independent neuron activities correspond to a point cloud spanning homogenously, thus having the same dimensionality as the embedding space.

To assess the robustness against trial-to-trial variability, we infer the connectivity networks for different trials of different stimuli. We show that the resulting adjacency matrices for different trials have relatively high correlation for the same stimulus, in contrast to low correlation between different stimuli. The networks distinguish quite well between drifting grating and natural movies, and to our surprise, they still differentiate two rather similar natural movies to some degree. Consistent high-degree (hub) neurons are identified for the same stimulus in different trials. When treating networks as filtrated simplicial complexes [3], we are able to study the topological invariant features using sequences of Betti numbers (dimension of the homology group of the simplicial complex) in both zero and one dimension. The derived Betti curves show consistency among natural movies and clear distinction with drifting grating movie.

For further validation, we build null networks for comparison. A set of edge-shuffled networks are generated, and their degree distributions are observed. Degree distribution of networks from real data is following the power-law more significantly than the null networks. Moreover, we compare our connectivity inference method with the statistical correlation and mutual information (MI) approaches [4]. By inspecting the set of top 50 neurons with the highest weighted degree in networks obtained by different approaches, we discover 15 common neurons between EDM and MI, two common neurons between EDM and correlation, and only one common neuron between MI and correlation. This calls for a more careful study of the properties of the common neurons. Finally, we analyze the robustness of the embedding measure against noise, by examining the results of adding different levels of white Gaussian noise to the signal, and we identified a relatively broad noise range where the results remain consistent.

References

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