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Functional networks from inverse modeling of neural population activity

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Abstract

The availability of large-scale neural multi-electrode or optical recordings make now possible the modelling of the simultaneous activities of tens to thousand of neurons. One promising approach relies on the inference of detailed functional connectivity between the recorded cells, that is, of an effective coupling network reproducing the correlation structure of the spiking events. Here we report some recent applications of those approaches to retinal, hippocampal, and cortical data, illustrating in particular how functional coupling networks may be useful to decode complex brain representations, and how their changes may be tracked in behaving animals, with a possible connection to behavioral learning. Statistical, theoretical, and neurobiological issues raised by the inverse modeling of population activity are discussed.

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Introduction

Functional connectivity across neurons has long been investigated through pairwise correlations [1,2], independently of the activity of the other recorded neurons. The availability of large population neural recordings, with tens to thousands of cells [3–9], has recently fostered interest for inverse approaches to reconstruct functional connectivity [10,11], in particular from snapshots of the activity [12,13] (Box 1). These approaches are coherent in that they process all recorded cells together, and are able to disentangle direct correlations between cells from indirect effects mediated through other recorded neurons [11,14]. We report below some applications to various brain areas, in connection with the following issues:

1. Functional couplings a priori vary with the sampling conditions (Box 2), such as brain state or external stimuli (Box 2). How strong is this variation, and what features remain invariant across different states?
2. Are functional models accurate enough to identify (decode) brain states [15–17], even in the absence of any sensory correlate?
3. Can we measure experience-related changes in functional couplings [18,19], and do they reflect properties expected for physiological plasticity [20,21]?
4. Are functional networks helpful to identify cell assemblies, postulated by Hebb to be the central units of neural computation and memories [22,7,23,18,24]?

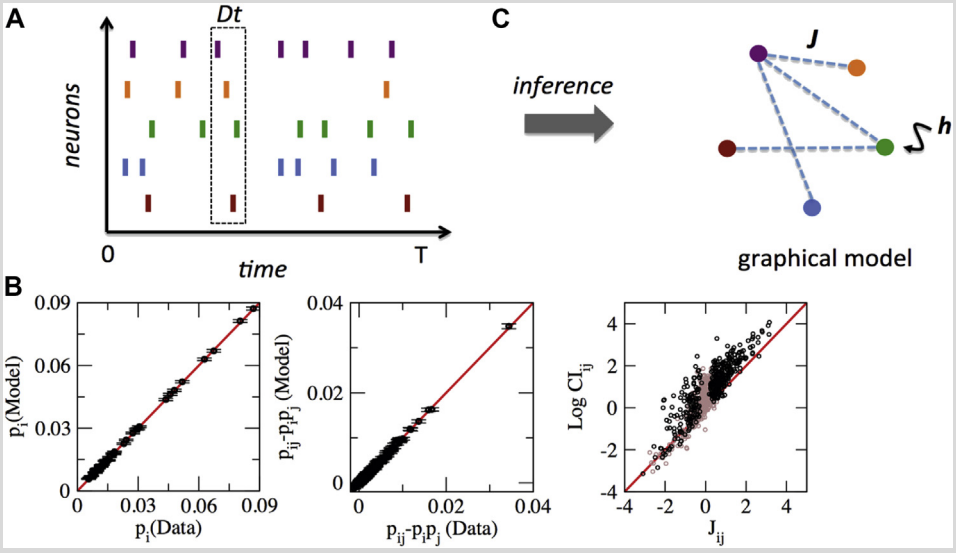
Functional networks show both invariant structure and specificity with respect to neural states

Functional connectivity reproduces the patterns of correlations in the neural activity across the recorded population. Those correlations reflect both the synaptic underlying interactions, as well as common inputs specific to the environmental, sensorial or cognitive state. To study the importance of both contributions we focus on three multi-electrode recording data sets (DS), in which the same cells were recorded with different external stimuli or conditions:

(DS1) salamander Retina ganglion cell (RGC) were recorded in the absence of light (dark) and with a randomly flickering checkerboard stimulus (flicker) [4]. Figure 1a shows the effective couplings between RGC, located at the centers of their receptive fields in the retinal plane [14]. In both dark and flickers stimuli a short-range network of large and positive couplings is found, similarly to [13], presumably due to gap junctions

Box 1. Functional connectivity models for neural data

Data consists of the times of all spikes emitted by a population of *N* neurons during a recording of duration *T* (***A***). We first discretize the data into time bins $t = 1,\ldots, T/Dt$ of width *Dt*, and define for each bin a variable $s_{i,t} = 1$ if neuron i has emitted one or more spikes, and *0* otherwise. Typical *Dt* values range from 10 to 100 ms depending on the recorded brain area.



Inference of functional model. A. *Multi-electrode or optical recordings are analyzed to obtain the raster plot of the neural activity (left). Activities are binned into time windows of duration Dt (dashed box) to define the configuration* $S_t = (s_{1t}, s_{2t},\ldots,s_{Nt})$. *The functional network* J_{ij} *describing the spiking dependencies among the neuron activities is then inferred, together with the local inputs* h_i *acting on the neurons.* ***B.*** *Single-cell firing probabilities* p_i *and pairwise correlations* $p_{ij} - p_ip_j$ *in data (x-axis) vs. predictions from inferred Ising model (y-axis).* ***C.*** *Scatterplot of inferred couplings* J_{ij} *vs. log. correlation indices* $CI_{ij} = p_{ij}/p_ip_j$ [42]. *Data in* ***B*** *and* ***C*** *are RGC recordings from* Ref. [12].

We look for a distribution model over the set of activity configurations in time bins, $S_t = (s_{1t},s_{2t},\ldots,s_{Nt})$. In the simplest model, neural cells are supposed to spike independently of each other. This model is generally poor, as it cannot reproduce correlations between spiking events [12]. In functional-connectivity models the probability that neuron *i* is active ($s_i = 1$) is conditioned to the activities s_j of the other neurons *j*:

$$P_{cond}\left(s_i = 1 | \{s_j, j \neq i\}\right) = \Phi\left(\sum_{j \neq i} J_{ij} s_j + h_i\right) \quad [1]$$

where $\Phi(x)$ is a sigmoidal increasing function of its argument *x*. The local input h_i controls the average activity of neuron *i* (the higher the input, the larger the activity), while the couplings J_{ij} encode the conditional dependence of the activities of neurons *i* and *j* (large positive, respectively, negative couplings correspond to pairs of neurons with correlated, respectively, anticorrelated activities). In practice the *N* inputs and *N(N – 1)/2* couplings are fitted to maximize the probability of the data configurations; this is a non-trivial computational problem, which can be tackled with various approximate inference techniques [56–59]. A natural choice is $\Phi(x) = \frac{e^x}{1+e^x}$, which corresponds to the well-studied Ising model of statistical physics, and to a simple expression of the probability of activity configurations,

$$P(s_1, s_2, \ldots s_N) \propto \exp\left(\sum_{j<i} J_{ij} s_i s_j + \sum_i h_i s_i\right), \quad [2]$$

up to some multiplicative normalization factor.

When only $N = 2$ cells are recorded the unique coupling, J_{12}, is related to the correlation index, C_{12}, equal to the ratio of the probability that neurons 1 and 2 both spike in a time bin, over the product of their individual spiking probabilities, through $J_{12} = \log C_{12}$. When more cells are recorded no general relationship exists between couplings and correlation indices [42], unless the activity is extremely sparse [41].

We stress that Eqs. [1] & [2] are approximate; modified Ising models, including non linear combinations of the neural activities in the argument of Φ, have been proposed [53].