NeuroImage 162 (2017) 32–44

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/neuroimage

Multi-Connection Pattern Analysis: Decoding the representational content of neural communication

Yuanning Li [a,b,c,*], Robert Mark Richardson [a,c], Avniel Singh Ghuman [a,b,c]

[a] Center for the Neural Basis of Cognition, Carnegie Mellon University and University of Pittsburgh, USA
[b] Program in Neural Computation, Carnegie Mellon University and University of Pittsburgh, USA
[c] Department of Neurological Surgery, University of Pittsburgh, USA

ARTICLE INFO

Keywords:
Functional connectivity
Multivariate statistical analysis
Decoding
Representation similarity analysis
Functional magnetic resonance imaging (fMRI)
Intracranial electroencephalography (iEEG)

ABSTRACT

The lack of multivariate methods for decoding the representational content of interregional neural communication has left it difficult to know what information is represented in distributed brain circuit interactions. Here we present Multi-Connection Pattern Analysis (MCPA), which works by learning mappings between the activity patterns of the populations as a factor of the information being processed. These maps are used to predict the activity from one neural population based on the activity from the other population. Successful MCPA-based decoding indicates the involvement of distributed computational processing and provides a framework for probing the representational structure of the interaction. Simulations demonstrate the efficacy of MCPA in realistic circumstances. In addition, we demonstrate that MCPA can be applied to different signal modalities to evaluate a variety of hypothesis associated with information coding in neural communications. We apply MCPA to fMRI and human intracranial electrophysiological data to provide a proof-of-concept of the utility of this method for decoding individual natural images and faces in functional connectivity data. We further use a MCPA-based representational similarity analysis to illustrate how MCPA may be used to test computational models of information transfer among regions of the visual processing stream. Thus, MCPA can be used to assess the information represented in the coupled activity of interacting neural circuits and probe the underlying principles of information transformation between regions.

1. Introduction

Since at least the seminal studies of Hubel and Wiesel (1959) the computational role that neurons and neural populations play in processing has defined, and has been defined by, how they are tuned to represent information. The classical approach to address this question has been to determine how the activity recorded from different neurons or neural populations varies in response to parametric changes in the information being processed. Single unit studies have revealed tuning curves for neurons from different areas in the visual system responsive to features ranging from the orientation of a line, shapes, and even high level properties such as properties of the face (Desimone et al., 1984; Hubel and Wiesel, 1959; Tsao et al., 2006). Multivariate methods, especially pattern classification methods from modern statistics and machine learning, such as multivariate pattern analysis (MVPA), have gained popularity in recent years and have been used to study neural population tuning and the information represented via population coding in neuroimaging and multiunit activity (Cox and Savoy, 2003; Ghuman et al., 2014; Haxby et al., 2001; Haynes and Rees, 2006; Hirshorn et al., 2016; Kamitani and Tong, 2005; Poldrack, 2011; Polyn et al., 2005). These methods allow one to go beyond examining involvement in a particular neural process by probing the nature of the representational space contained in the pattern of population activity (Edelman et al., 1998; Haxby et al., 2014; Kriegeskorte and Kievit, 2013).

Neural populations do not act in isolation, rather the brain is highly

* Corresponding author. S906 Scaife Hall, 3550 Terrace Street, Pittsburgh, PA, 15261, USA.
E-mail address: ynli@cmu.edu (Y. Li).

http://dx.doi.org/10.1016/j.neuroimage.2017.08.033
Received 6 June 2017; Received in revised form 20 July 2017; Accepted 10 August 2017
Available online 13 August 2017

interconnected and cognitive processes occur through the interaction of multiple populations. Indeed, many models of neural processing suggest that information is not represented solely in the activity of local neural populations, but rather at the level of recurrent interactions between regions (Grossberg, 1980; Kveraga et al., 2007; Lee and Mumford, 2003). However previous studies only focused on the information representation within a specific population (Freiwald et al., 2009; Ghuman et al., 2014; Haxby et al., 2001; Hirshorn et al., 2016; Nestor et al., 2011; Tsao et al., 2006), as no current multivariate methods allow one to directly assess what information is represented in the pattern of functional connections between distinct and interacting neural populations with practical amounts of data. Such a method would allow one to assess the content and organization of the information represented in the neural interaction. Thus, it remains unknown whether functional connections passively transfer information between encapsulated modules (Fodor, 1983) or whether these interactions play an adaptive computational role in processing. Note that our definition of non-adaptive information transfer is equivalent to a static linear projection where no computational "work" is done in the interaction between the regions and therefore no information is added (from an information theory perspective). Adaptive information transfer is one in which computational work related to the behavioral state or condition is performed and therefore state or condition specific information is added through the interaction between regions; this is equivalent to a non-linear function.

Univariate methods that go beyond assessing the degree of coupling between populations to assess changes in the relationship between the activity as a factor of condition also examine adaptive communication between regions. For example the psychophysiological interactions (PPI; (Friston et al., 1997)) and dynamic causal modeling methods (Friston et al., 2003) are sensitive to adaptive interregional communication. Multivariate methods, however, in comparison to univariate methods, allow for "more sensitive detection of cognitive states," "relating brain activity to behavior on a trial-by-trial basis," and "characterizing the structure of the neural code" (Norman et al., 2006). Thus, a multivariate pattern analysis method for functional connectivity analysis is critical for decoding the representational structure of interregional interactions.

In this paper, we introduce a multivariate analysis algorithm combining functional connectivity and pattern recognition analyses that we term Multi-Connection Pattern Analysis (MCPA). MCPA works by learning the discriminant information represented in the shared activity between distinct neural populations by combining multivariate correlational methods with pattern classification techniques from machine learning in a novel way. Much the way that MVPA goes beyond a *t*-test or ANOVA by building a multivariate model of local activity that is then used for single-trial prediction and classification, MCPA goes beyond PPI by building a multivariate connectivity model that is then used for single-trial prediction and classification. This single-trial prediction and classification makes MCPA distinct from previous connectivity approaches that only statistically test the absolute or relative functional connectivity between two populations (Cribben et al., 2012; Finn et al., 2015; Richiardi et al., 2011; Shirer et al., 2012; Wang et al., 2015) and allows for a detailed probe of the representational structure of the interaction.

The MCPA method consists of an integrated process of learning connectivity maps based on the pattern of coupled activity between two populations A and B conditioned on the stimulus information and using these maps to classify the information representation in shared activity between A and B in test data. The rationale for MCPA is that if the activity in one area can be predicted based on the activity in the other area and the mapping that allows for this prediction is sensitive to the information being processed, then this suggests that the areas are communicating with one another and the communication pattern is sensitive to the information being processed. Thus, MCPA simultaneously asks two questions: 1) Are the multivariate patterns of activity from two neural populations correlated? (i.e. is there functional connectivity?) and 2) Does the connectivity pattern change based on the information being processed? This is operationalized by learning a connectivity map that maximizes the multivariate correlation between the activities of the two populations in each condition. This map can be thought of like the regression weights that transform the activity pattern in area A to the activity pattern in area B (properly termed "canonical coefficients" because a canonical correlation analysis [CCA] is used to learn the map). These maps are then used to generate the predictions as part of the classification algorithm. Specifically, a prediction of the activity pattern in one region is generated for each condition based on the activity pattern in the other region projected through each mapping. Single trial classification is achieved by comparing these predicted activity patterns with the true activity pattern (see Fig. 1 for illustration). With MCPA single trial classification based on multivariate functional connectivity patterns is achieved allowing the nature of the representational space of the interaction to be probed.

We present a number of simulations to validate MCPA for a realistic range of signal-to-noise ratios (SNR) and to show that MCPA is insensitive to local information processing. We apply MCPA to examine the inter-regional representation for natural visual stimuli in visual cortex using functional magnetic resonance imaging (fMRI) data. Specifically, we show that the interactions between regions of the visual stream (V1, V2, V3, V4, and lateral occipital cortex [LO]) are sensitive to information about individual natural images. We combine MCPA with representational similarity analysis to demonstrate that MCPA can be used to evaluate computational models and make inferences regarding the underlying neural mechanism of information transferring. To demonstrate MCPA's applicability to electrophysiological signals and

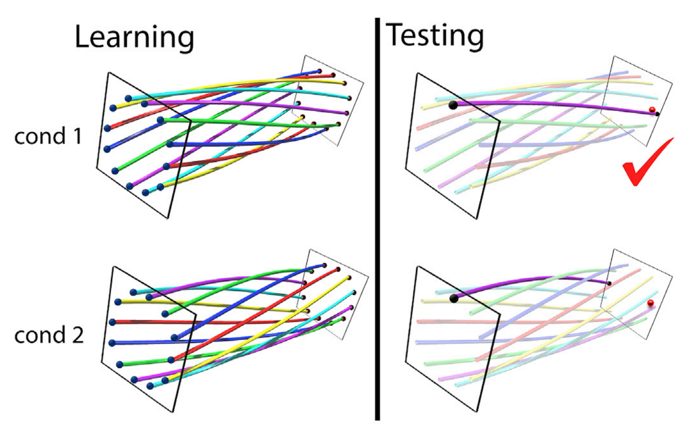

Fig. 1. Illustration of the connectivity map and classifier of MCPA. The MCPA framework is demonstrated as a two-phase process: learning and testing. **Top left:** an illustration of the learned functional information mapping between two populations under condition 1. The representational state spaces of the two populations are shown as two planes and each pair of blue and red dots correspond to an observed data point from the populations. The functional information mapping is demonstrated as the colored pipes that project points from one space onto another (in this case, a 90° clockwise rotation). **Bottom left:** an illustration of the learned functional information mapping between two populations under condition 2 (in this case, a 90° counter-clockwise rotation). **Top right:** an illustration of the predicted signal by mapping the observed neural activity from one population onto another using the mapping patterns learned from condition 1. The real signal in the second population is shown by the red dot. **Bottom right:** an illustration of the predicted signal by mapping the observed neural activity from one population onto another using the mapping patterns learned from condition 2.
In this case, MCPA would classify the activity as arising from condition 1 because of the better match between the predicted and real signal.