Voxel-wise Intermodal Coupling Analysis of Two or More Modalities using Local Covariance Decomposition

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02 December, 2021

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# 1 CRediT author statement

Fengling Hu: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Writing - Original Draft, Writing - Review & Editing, Visualization

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# 2 Abstract

When individual subjects undergo imaging with multiple modalities, biological data is present not only within each modality, but also between modalities - that is, in how modalities covary at the voxel level. Previous studies have shown that the covariance structures between modalities, or intermodal coupling (IMCo), can be estimated between two modalities, and that two-modality IMCo reveals otherwise undiscovered patterns in neurodevelopment as well as other processes. However, previous IMCo methods are based on the slopes of local weighted linear regression lines, which are inherently asymmetric and limited to the two-modality setting. Here, we present a PCA-based generalization of IMCo which uses local covariance decompositions to define a symmetric, voxel-wise coupling coefficient valid for two or more modalities. We then demonstrate this method is spatially heterogeneous and varies with respect to age and sex over the course of neurodevelopment. As availability of multi-modal data increases, PCA-based IMCo offers a natural approach for summarizing relationships between multiple aspects of brain structure and function. An R package is provided.

# 3 Introduction

Hello test!

# 4 Methods

## 4.1 Participants

We included 803 participants (340 males) ages 8-23 (mean = 15.6; sd = 3.3) from the Philadelphia Neurodevelopmental Cohort (PNC). Of the 1445 PNC participants who underwent neuroimaging, we initially excluded those meeting any of the following criteria: history of psychoactive medication (n = 165), history of inpatient psychiatric hospitalization (n = 51), or history of medical disorders that could impact brain function (n = 166). From the remaining 1113 participants, we included those who underwent the combination of T1-weighted MRI, arterial spin labeling MRI (ASL), and resting state fMRI (rfMRI) scanning, each of acceptable image quality as determined based on automated and manual screening. This resulted in the final set of 803 participants used for this study. The Institutional Review Boards of the University of Pennsylvania and the Children’s Hospital of Pennsylvania approved all study procedures. All study participants gave informed consent; for participants under the age of 18, parents or guardians provided consent and participants provided assent. Additional details of the PNC study have been previously described.

## 4.2 Image acquisition

## 4.3 Estimation of intermodal coupling

## 4.4 Statistical analysis

# 5 Results

# 6 Discussion

# 7 Supplementary Materials