Dear Professor Eickhoff,

It is our pleasure to submit our manuscript titled “Voxel-wise Intermodal Coupling Analysis of Two or More Modalities using Local Covariance Decomposition" for possible publication as an original research paper in *Human Brain Mapping*.

In this study, we present a novel method for estimating intermodal coupling (IMCo), which can be thought of as how two or more modalities relate to one another, at the single-voxel level. Over the past decade, as the availability of multi-modal datasets has increased, there has been great interest in studying the relationships between these modalities. Such efforts, carried out at the resolution of whole brains and regions of interest, have allowed for increased understanding of structure-function relationships, metabolism-function interactions, and much more. Recently, a method for studying voxel-level IMCo has shown single voxel resolution may hold the key to furthering our understanding of complex intermodal relationships. While that method has been a significant advancement in our ability to study IMCo, it is limited by a few shortcomings; namely, the method cannot estimate IMCo between more than two modalities and provides IMCo estimates that differ based on an arbitrary specification. Here, we provide an improved single-voxel resolution method that can be used to study IMCo between any number of modalities and resolves the issue of inconsistent IMCo estimates in the two-modality setting. We use our method to uncover how coupling of cerebral blood flow, resting state fluctuations, and local connectivity changes in neurodevelopment.

We believe this method will be of great interest to the readers of *Human Brain Mapping*. The method presented allows for improved high-resolution study of IMCo, a field that is rapidly growing. For descriptive analyses, it provides a manageable, consistent, and easily interpretable IMCo estimate, even in settings where the covariance structure is complex. For predictive analyses or in efforts to identify biomarkers, it can allow for more efficient use of the data collected. As a journal committed to advancing understanding of the brain and translating that understanding to clinical practice, *Human Brain Mapping* is the perfect journal for work that enables the study of complex intermodal relationships.

We confirm this manuscript has not been published elsewhere and is not under consideration by another journal. It has been uploaded as a preprint to bioRxiv. All authors have approved the manuscript. The authors report no conflicts of interest.

Thank you for your time and consideration.

Sincerely,

Fengling Hu