Title: *High-dimensional Multivariate Mediation with Application to Neuroimaging Data*

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Abstract

Mediation analysis is an important tool in the behavioral sciences for investigating the role of intermediate variables that lie in the path between a treatment and an outcome variable. The influence of the intermediate variable on the outcome is often explored using a linear structural equation model (LSEM) with model coefficients interpreted as possible effects. While there has been significant research on the topic, little work has been done when the intermediate variable (mediator) is a high-dimensional vector. In this work we introduce a novel method for identifying potential mediators in this setting called the principal directions of mediation (PDMs). PDMs linearly combine potential mediators into a smaller number of orthogonal components, with components ranked by the proportion of the mediation effects each accounts for. We demonstrate the method using a functional magnetic resonance imaging (fMRI) study of thermal pain where we are interested in determining which brain locations mediate the relationship between the application of a thermal stimulus and self-reported pain.