

FUNCTIONAL JOINT MODELS FOR IMAGING GENETIC DATA

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Abstract: We propose a functional joint modeling (FJM) framework for correlating imaging responses with genetic markers and clinical variables. Our FJM consists of a nonlinear multivariate functional principal component analysis (NMFPCA) and a functional multiple-index varying coefficient model (FMVCM). The NMFPCA, with unknown link functions, is used to extract meaningful functional principal component (FPC) scores of genetic markers, while the FMVCM identifies the varying association of the extracted FPC scores and clinical variables with imaging data. We propose an efficient estimation procedure to estimate unknown functions in our FJM and a regularization approach to simultaneously select relevant features from infinite-dimensional functional data and learn the model structure. The asymptotic convergence rate of estimators and model selection consistency are investigated. The proposed method is evaluated through simulation studies and applied to an imaging genetic data set extracted from the Alzheimer's Disease Neuroimaging Initiative (ADNI) study.

Key words and phrases: Functional joint model, functional principal component, imaging genetics, neuroimaging data analysis, varying coefficient.

1. Introduction

This study aims to integrate multimodal data to clarify the biological pathways that connect genetic factors to brain and, ultimately, to clinical outcomes (e.g., cognition, disease stage, and progression status) (Elliott et al., 2018; Zhu, Li and Zhao, 2023). By exploring these connections, we hope to gain valuable insights into brain development, healthy aging, and disease progression. One such pathway is reflected in Jack's hypothetical models for Alzheimer's disease (AD) (Jack Jr et al., 2013). This information could offer a comprehensive view of how behavioral outcomes relate to the genetic pathways of AD, as mediated by brain structure and function. Additionally, it could deepen our understanding of the interplay between genetic and environmental risk factors, and how modifying environmental influences might benefit individuals with genetic predispositions. Ultimately, this approach aims to inform more effective interventions and treatments (Veitch et al., 2022).

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