iFunMed: Integrative Functional Mediation analysis of GWAS and eQTL with data-driven prior information

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Large consortia projects are cataloging DNA elements of RNA transcription, DNA accessibility, chromatin states, and DNA methylation across wide variety of tissues and cell types at an unprecedented rate and producing large collections of functional annotation information. Although there has been many advances in incorporating prior information into prioritization of trait-associated variants in genome wide association studies (GWAS), functional annotation data rarely played more than an indirect role in assessing evidence for association in these approaches. Furthermore, functional annotation information has not been utilized at all in the joint analysis of GWAS and molecular (i.e., expression) quantitative loci data, commonly known as genetical genomics data. This is a significant barrier in understanding the regulatory roles of variants in expression and disease progression.

We develop a novel Empirical Bayes method to utilize data-driven prior information in mediation analysis of GWAS and eQTL. We present different classes of available prior information, discuss implementation challenges, and present preliminary results on genetical genomic data from the Framingham Heart Study.

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