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Statistical causal networks using multi-omics and the concept of granularity

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An emerging focus of biomedical research is the relationship, particularly the causal relationship, among components of a –multiomic system, such as genomics, transcriptomics, metabolomics and risk factors. We refer to these different levels of organization as different granularities. Powerful and advanced analysis strategies are required to identify the underlying causal network among variables within a level of biological hierarchy/granularity.

The most pragmatic and widely used tool for identification and visualization of causal relationships in large-scale data are Directed Acyclic Graphs (DAGs), which are compatible with Structural Equation Modeling. These causal networks are ideally suited for the analysis of multi-omics and heterogeneous data types, such as DNA sequence, metabolomics and risk factor data collected in a sample of deeply phenotyped individuals. However, if we do not include relevant basic knowledge about the causal relationship between granularities, we cannot generate robust DAGs within a level of granularity. Considering basic biological knowledge, such as genome variation is a causal factor of phenotypes, we use genome information embedded in principal components to robustly identify underlying network among phenotypes, and we call the resulting causal relationships a GDAG.

In particular, we extracted information from 1,034,945 genetic variants scattered across the genome to infer the statistical causal network among 122 reliable serum human metabolomics measurements. We then analyzed the network to reveal patterns. Application of the method to serum metabolomics data and subsequent comparison to existing metabolic pathway databases reveal that the results generally coincide with known metabolic relationships.

Given the metabolomics network, we entered risk factors in the model which are in yet a different granularity and identify the metabolites with direct and indirect effect on risk factor levels. Finally, finding genes harboring loss of function mutations with influence on metabolites, we could identify pathways from genome to risk factors via metabolites.

Biography

Azam Yazdani has completed her PhD from Cambridge University in England and Friedrich Schiller University of Jena in Germany in Statistical Causal Inference. She has been continuing her research in causal inference by integrating multi-omics and the concept of granularity at The University of Texas Health Science Center Houston. Dr. Yazdani is one of the investigators knowledgeable on how to handle and analyze multiple omics in a causal setting. Her research has been recognized as “exceptionally creative, skillful research in causal inference” at the Atlantic Causal Conference in May 2015 held in Pennsylvania State University.

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