## Causal inference for gene-gene and gene-environment interactions

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## Abstract

Causal inference methods for inference about gene-gene and gene-environment interaction will be discussed. Statistical interactions will be compared and contrasted with causal interactions including sufficient cause interactions and "compositional epistasis" in the genetics literature. Compositional epistasis refers to the setting in which the effect of a particular genetic variant is masked by a variant at another locus. Contrary to prior claims in the genetics literature, it is shown that compositional epistasis can be detected from statistical data. Testing and estimation methods for causal interactions are discussed. The methods are illustrated with a number of examples drawn from the existing literature on gene-gene and gene-environment interaction. Questions of mediation and interaction between genetic and environmental factors are discussed and illustrated by considering the extent to which effects of polymorphisms at chromosome 15q25 on lung cancer are mediated by nicotine addiction.