Lecture 5.2: (09:55-10:20)

Nonparametric mediation analysis: beyond the mean

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Mediation analyses estimate the effect of an exposure on an outcome mediated by a mediator. However, most methods focus only on the mean effect of the outcome. In our study, the biological effect of a cancer mutation may have affected the variation of a downstream outcome, such as gene expression, without even changing the mean outcome. To this end, we characterize the effect on the cumulative distribution function (cdf) of an outcome under the identifiability assumptions not stronger than the conventional ones. Consequently, one can easily summarize the effect of an outcome on any specific moment, with the effect on the mean outcome as a special case. We propose a nonparametric estimator based on kernel estimators for the cdf of the mediator given the exposure and that of the outcome given the exposure and mediator. We study the asymptotic results of the proposed nonparametric estimator. Extensive simulation studies were conducted to evaluate the performance of finite samples. We applied our methods to two studies: one investigates how IDH1 (isocitrate dehydrogenase 1) mutations in glioma patients affect EGFR (epidermal growth factor receptor) expression by altering its DNA methylation, and another investigates the influence of childhood socioeconomic adversity on adult adiposity via DNA methylation of the FASN (fatty acid synthase) gene.