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Pathway Models from RNAi Data

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In RNA interference (RNAi) small double-stranded RNA molecules are designed to specifically target cellular mRNAs for degradation. The method allows to knock-down expression of candidate genes. Effects of RNAi interventions are measured by microarrays. I work on methods to combine information from effects of gene silencing into pathway models. My talk will focus on two topics specific to RNAi data:

Probabilistic soft interventions We model data from silencing experiments in a Bayesian framework and discuss differences knock-outs. In Markowetz et al. (2005) we introduce a general concept of probabilistic interventions in Bayesian networks. This generalizes deterministic interventions, which fix nodes to certain states. We propose pushing variables in the direction of target states without fixing them. We formalize this idea in a Bayesian framework based on Conditional Gaussian networks.

Reconstructing signaling pathways The effect of silencing one candidate gene on other candidate genes may not be observable on microarrays when signaling happens on protein level. In this situation, genes have to be treated as hidden or latent variables. I will demonstrate a method of learning network structure on hidden variables from interventional data.

References:

[1] F. Markowetz. A bibliography on learning causal networks of gene interactions, 2005. URL http: //www.molgen.mpg.de/ markowet/docs/network-bib.pdf.