



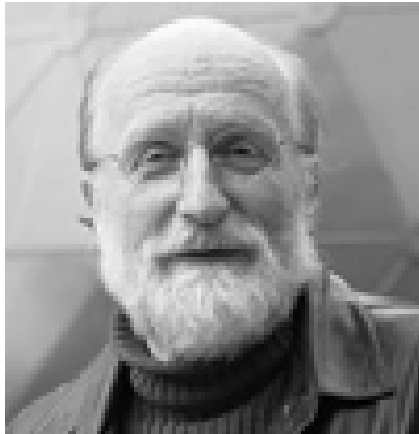
JOHNS HOPKINS

BIOMEDICAL ENGINEERING



Monday, March 23, 2009, 1:00 PM Rome Room, Clark 110

Light lunch will be provided at 12:15



Combinatorial drug perturbations of cancer cells

Chris Sander

Computational and Systems Biology
Memorial Sloan -Kettering Cancer Center

Hosted by Dr. Rachel Karchin

Abstract We have developed a novel method for deriving network models from molecular profiles of perturbed cellular systems. The network models aim to predict quantitative outcomes of combinatorial perturbations, such as drug pair treatments or multiple genetic alterations. Mathematically, we represent the system by a set of nodes, representing molecular concentrations or cellular processes, a perturbation vector and an interaction matrix. After perturbation, the system evolves in time according to differential equations with built-in nonlinearity, similar to Hopfield networks, capable of representing epistasis and saturation effects. For a particular set of experiments, we derive the interaction matrix by minimizing a composite error function, aiming at accuracy of prediction and simplicity of network structure. To evaluate the predictive potential of the method, we performed 21 drug pair treatment experiments in a human breast cancer cell line (MCF7) with observation of phospho-proteins and cell cycle markers. The best derived network model rediscovered known interactions and contained interesting predictions. Possible applications include the discovery of regulatory interactions, the design of targeted combination therapies and the engineering of molecular biological networks. Based on Nelander et al., *Molecular Systems Biology*, Sept. 2008

Upcoming Seminars
March 27: Lauren Black, University of Minnesota

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