


# National Academies Keck *Futures Initiative* Conference

## Mathematical Models in Signaling Systems - June 16-18, 2004

### ***Experimental Approaches to Understanding Networks***

#### *Towards a Molecular Spectrometer of the Cell*

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#### ***Abstract:***

Cellular biochemical machineries, what we call pathways, consist of dynamically assembling and disassembling macromolecular complexes. While our models for the organization of biochemical machines are derived largely from *in vitro* experiments, do they reflect their organization in intact, living cells? We have developed a general experimental strategy that addresses this question by allowing for quantitative probing of molecular interactions in intact, living cells. The experimental strategy is based on Protein fragment Complementation Assays (PCA), a method whereby protein interactions are coupled to refolding of enzymes from cognate fragments where reconstitution of enzyme activity acts as the detector of a protein interaction. A biochemical machine or pathway is defined “spectroscopically” by grouping interacting proteins into those that are perturbed in the same way by common factors (hormones, metabolites, enzyme inhibitors, etc). I will describe how we go from descriptive to quantitative representations of biochemical networks at an individual to whole genome level and how our approach will lead ultimately to better descriptions of the biochemical machineries that underlie living processes.