

National Academies Keck *Futures Initiative* Conference

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

Analysis of Network Architecture

Molecular Epistemics - A Novel Approach to Causal Modeling and Its Application to the Analysis of Type II Diabetes

Keith O. Elliston, PhD
President & CEO
Genstruct, Incorporated

Abstract:

The mental process of reasoning can deal with tens or even hundreds of distinct molecules present within a cell, but is fully incapable of dealing with tens of thousands or even hundreds of thousands of molecules and the relationships between them. To reason over this information to interpret the thousands of individual state changes determined through systems biology is clearly impossible. To accomplish this requires a computable approach to biological inference and reasoning. We have created a large-scale computable model to reason about the molecular actions and effects of insulin on muscle gene expression, The Diabetes Knowledge Assembly™ Model. The model enables computer-aided reasoning using over 170,000 relationships that we have assembled from the DM2 literature. We have been able to validate the model and our computer-aided reasoning approach by correctly predicting many of the gene expression changes previously observed in the two skeletal muscle studies, presuming those expression changes arose from known molecular processes downstream of impaired insulin sensitivity. These results demonstrate that our novel knowledge-based modeling and computer-aided causal reasoning approach is predictive and can be used not only to define the molecular causes of the disease but also potentially to identify new molecular targets for intervention.