CSoI Project Team Report – Investigation of Metabolic Phenomena Using Information Theory

A. Problem Statement

As outlined in the seed grant proposal, the main problem that this group concerns itself with is determining the specific nature of metabolic regulation in single cellular organisms with the help of information theoretic tools. Building from previous work developed in the Ramkrishna research group on cybernetic models of metabolism, this project team's work attempts to determine how effectively the concept of dynamic metabolic regulation applies to real, natural cells. To do this, two thrusts are being taken to determine the validity of cybernetic concepts. One is assessing the predictive ability of cybernetic models in terms of how well model predictions match up with data. The other direction seeks to show how cybernetic models properly balance the concepts of model simplicity and accuracy of data fitting. Models that are simple and fit data well are the ideal in this case. With success in demonstrating that cybernetic models are predictive with low amounts of input data, benefits can be reaped by biologist who want useful these tools to study intricate metabolic systems.

B. Progress and Insights

Through the collaboration taking place in this project, a suitable method to compare systems biological models has been determined. This model comparison technique will be the subject of an upcoming conference presentation and paper in the coming fall; it has already been discussed in a publication in Current Opinion in Chemical Engineering which has already completed its review process.

C. Posters / Presentations / Papers

a) Posters:
DeVilbiss, F. and Ramkrishna, D. *Investigating Metabolic Phenomena Using Information Theory.* Poster Presented at Chemical Engineering Graduate Research Symposium, West Lafayette, IN, 2013.

b) Presentations
DeVilbiss, F., Song, H.-S., & Ramkrishna, D. *Developing An Information Theoretic Framework for Model Selection in Systems Biology,* 2013 AIChEAnnual Meeting, San Francisco, CA.

c) Papers
Song, H.-S, DeVilbiss, F. & Ramkrishna, D. *Modeling Metabolic Systems. The Need for Dynamics.* Publication Pending in Current Opinion in Chemical Engineering. Fall 2013
   - Paper features an introduction to model comparison techniques discussion

DeVilbiss, F., Raginsky, M., Song, H-S., & Ramkrishna, D. *A Comprehensive Information Theoretic Framework for Model Selection in Systems Biology*. (upcoming publication)

D. Team Member Interactions

Over the course of the past year, over 15 meetings occurred with various combinations of group members to discuss the progress of this project. Insights gained from these interactions have led to the aforementioned model comparison technique. The meetings have been useful towards analyzing proposed directions of investigation as a multidisciplinary team. Such meetings have saved time in the project's implementation and have also exposed the investigation to new ideas that would not have come about without having a group with diverse backgrounds.

E. Future Meetings and Conference Presentations

There is one planned conference presentation listed above in section C. This will discuss the information theoretic techniques to be used for analyzing a model's ability to compress data.

Future meetings among this project group are planned. It may, however, be useful to change the nature of the discussion. In the problem statement above, there are two directions. One is weighing the utility of various models using information theoretic tools. This has been a successful effort thus far. However, the other direction, analyzing the ability of cybernetic metabolic models to predict a range of bioinformatics data has yet to be completed. The validity of cybernetic models can truly be tested through comparing them to metabonomic, fluxomic and transcriptomic data. Professor Shankar Subramaniam's group at UCSD, also part of the center, is in the process of generating much relevant data related to lipid metabolism in mammalian cells. Extending the cybernetic framework to describe such models would be a very useful way to analyze the framework's ability to describe a range of data sets. We are already in discussion with his group related to the matter, but it would be appropriate to include him and some of his students in this project. As his group is out at UCSD, funding for travel would be needed to get the most out of this collaboration.

F. Desire to Extend Project

There is a strong desire to extend this project as a multidisciplinary team has been very useful in the completion of this project. As stated above, we would like to include Professor Subramaniam in this project. Such metabolic descriptions of mammalian metabolism could have impact in patient treatment and medicine.

G. Additional Comments

Comments related to improving the team have been stated above in section E. To reiterate, including Professor Subramaniam's group in this work would be useful towards achieving our goal of using the models to describe a range of different biological data.