Comparative Analysis of Metabolic Robustness: *E. coli* and *Synechocystis*

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***Short Abstract* — The metabolic network comprises of a network of reactions that catalyze the transformation of substrates essential for cellular growth into biomass and energy, and a set of enzymes that catalyze the reactions. We use computational constraint based techniques to ask how the evolutionary niche that organisms occupy affect the metabolic network. In this work we present a comparison of a photosynthetic cyanobacterium, *Synechocystis* with *E. coli* and show how metabolic network topology, in particular the enzyme-reaction association, plays a significant role in determining the robustness of microorganisms.**

***Keywords* — Metabolism, metabolic network, flux balance analysis**

I. INTRODUCTION

THE metabolic network comprises of a network of reactions that catalyze the transformation of substrates essential for cellular growth into biomass and energy. This network has been well studied for its topological properties such as the degree distribution and scale-free properties. However metabolic reactions are catalyzed by enzymes, and the relation between the enzymes and the reactions they constrain form an additional layer of complexity that has not yet been well characterized.

In this study we carry out a computational analysis of the structure of enzyme-reaction associations and ask how they impact metabolic robustness by a comparative analysis of two organisms, E. coli and Synechocystis.

II. METHODS AND RESULTS

Our computational analysis is based on constraint-based modeling techniques[1] that have been shown to predict effects of single gene deletions with good accuracy [2,3]. The metabolic network is drawn from a recent genome scale model, iJN678, of *Synechocystis sp.* PCC6803[4] and iAF1260, of *E. Coli* MG1655[2].

A. Synechocystis is more susceptible to gene deletions

In agreement with earlier results [4] we found that Synechocystis is more susceptible to gene deletions, with about 65% of functional enzyme complexes in the metabolic network resulting in lethality on deletion, compared to about 21% for E. coli. The differences were most stark especially in autotrophic energy metabolism.

B. Gene Reaction Association distribution resembles a power-law

We found that for both E. coli and Synechocystis, the distribution of the number of reactions constrained by enzymes resembles a power law. We tested this relationship in two other microorganisms and found a similar power law behavior. While the decadal span of the data is too small for more sophisticated statistical analysis, what is intriguing is the similarity across all organisms studied.

C. Essentiality of multifunctional enzymes in Synechocystis suggests fitness benefits

Despite the similarity in the structure of the gene-reaction association distribution, multifunctional enzymes are more essential in Synechocystis. Simulations suggest that the multifunctional nature of these enzymes should have fitness benefits.

D. Comparative mapping of gene deletions highlight differences in enzyme-reaction association as well as network structure

We mapped lethal gene deletions from one organism to the other and studied all non-lethal deletions in the other organism. We found that E. coli escapes from many deletions that are lethal in Synechocystis due to metabolic network topology, in particular differences in specific gene-reaction associations.

III. CONCLUSION

The structure or topology of the metabolic network can have a significant effect on metabolic robustness, especially when the gene-reaction associations are taken into account.

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