Title: Experimental Systems-Biology Approaches for Clostridia-Based Bioenergy Production: The Metabolite Stress-Response System in Solventogenic Clostridia

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http://research.bioinformatics.udel.edu/clostridia-stress-response

Project Goals: The objectives of this project are to engage enabling experimental systems-biology approaches to support the development of integrated, predictive models of the metabolic and regulatory networks underlying the metabolite stress response in solventogenic clostridia. Clostridia are Gram$^+$, obligate anaerobic, endospore-forming bacteria of major importance to fermentative biofuel production. Here, we focus on understanding and modeling the stress-response of *Clostridium acetobutylicum* to two important toxic metabolites: butanol and butyrate. Systems-level understanding is expected to lead to better strategies for industrial-strain development, as well as bioprocessing strategies taking advantage of the stress response to achieve superior bioprocessing outcomes.

Solventogenic and other clostridia are of major importance for developing technologies for biofuel production (3). A major and unique advantage is their ability to utilize a large variety of substrats (hexoses, pentoses, oligosaccharides, xylan, and starches). Among the two sequenced solventogenic clostridia, *C. acetobutylicum* is the only one that contains a full cellulosome (2) and may thus directly utilize cellulosic material for production of fuels and chemicals.

The toxic-metabolite stress response is a problem of major and general importance not only in clostridial biotechnologies but in all microbial systems of interest to bioenergy production (1). Achieving the goals of this project will solve a long-standing problem of both fundamental and practical importance. The significant broader impact is that the approaches and tools developed here can be applied to other cellular systems, aiming to achieve the ultimate goal of comprehensive multidimensional understanding of cells via Genome Scale Model (GSM) multidimensional platforms and models. The outcomes of this project aim to become an enabling paradigm for modeling complex programs of organisms and biological systems of importance to DOE's mission on energy and the environment.

To achieve these goals, we apply genomic tools for collecting extensive transcriptomic (based on both deep sequencing and microarray analyses) and targeted fluxomic and proteomic data, and couple omics data integration with building stress models and modeling platforms that can be linked, as an added modeling dimension, to a 2nd generation GSM of this organism. Successful completion of this project aims to the following deliverables: (i) experimental omics data of the metabolite stress response in *C. acetobutylicum* for deposition to public repositories and that can be mined for systems-level predictive modelling; (ii) an in-depth systems-level molecular understanding at multiple genome-scale levels of the metabolite stress response; (iii) two models and modeling frameworks for the metabolite stress responses linking them to the constructed 2nd generation GSM; and, (iv) computational and bioinformatic tools and frameworks that can be applied to modeling other cellular programs.

References

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