Mechanism for Microbial Population Collapse in a Fluctuating Resource Environment

Serdar Turkarslan[1]*(sturkarslan@systemsbiology.org), Arjun V Raman[1], Anne W Thompson[1], Mark A Gillespie[1], Kristina L Hillesland[4], Christina E Arens[1], Sergey Stolyar[1], Adrian López García de Lomana[1], David J Reiss[1], Frederick von Netzer[2], Drew Gorman-Lewis[5], Grant M Zane[3], Jeffrey A Ranish[1], Judy D Wall[3], David A Stahl[2], and **Nitin S Baliga[1],** Adam P Arkin[6], Paul D. Adams[6]

[1]Institute for Systems Biology, Seattle, WA, [2]Civil and Environmental Engineering, University of Washington, Seattle, WA, [3]Department of Biochemistry, University of Missouri, Columbia, MO, [4]Biological Sciences, University of Washington Bothell, Bothell, WA, [5]Earth and Space Sciences, University of Washington, Seattle, WA, [6]Lawrence Berkeley National Laboratory, Berkeley, CA.

Project URL: enigma.lbl.gov**,** http://networks.systemsbiology.net/syntrophy

Project Goals:

Microbial generalists are metabolically versatile and able to cope with periodically or randomly fluctuating natural environments by appropriately up- or down-regulating genes to optimize resource utilization. Not surprisingly, many experimental evolution studies have reported that mutations accumulate in regulatory genes during metabolic specialization of a generalist to a single resource environment. However, it is generally assumed and not demonstrated whether or how regulatory mutations foster adaptive evolution to new environments. The goal of this project is to provide insight into the complex intertwined relationship between regulatory architecture of a generalist and the spatiotemporal structure of environmental changes. We aim to bring together technologies and concepts in a systems biology framework to provide comprehensive characterization of microbial resilience from genome-wide and population scale to detailed molecular and single cell level.

Abstract:

Managing tradeoffs through gene regulation is believed to confer resilience to a microbial community in a fluctuating resource environment. To investigate this hypothesis we imposed a fluctuating environment that required the sulfate-reducer *Desulfovibrio vulgaris* to undergo repeated ecologically-relevant shifts between retaining metabolic independence (active capacity for sulfate respiration) and becoming metabolically specialized to a mutualistic association with the hydrogen consuming *Methanococcus maripaludis*. Strikingly, the microbial community became progressively less proficient at restoring the environmentally-relevant physiological state

after each perturbation and most cultures collapsed within 3-7 shifts. Counter-intuitively, the collapse phenomenon was prevented by a single regulatory mutation. We have characterized the mechanism for collapse by conducting RNA-seq analysis, proteomics, microcalorimetry, and single cell transcriptome analysis. We demonstrate that the collapse was caused by conditional gene regulation, which drove precipitous decline in intracellular abundance of essential transcripts and proteins, imposing greater energetic burden of regulation to restore function in a fluctuating environment.

Publications:

Turkarslan S., Raman AV., Thompson AW., Gillespie MA., Hillesland KL., Arens CE., Stolyar S., López García de Lomana A., Reiss DJ., von Netzer F., Gorman-Lewis D., Zane GM., Ranish JA., Wall JD., Stahl DA., and Baliga NS. (2016) Mechanism for Microbial Population Collapse in a Fluctuating Resource Environment. *Mol Sys Biol* (in revision)

"This material by ENIGMA- Ecosystems and Networks Integrated with Genes and Molecular Assemblies (http://enigma.lbl.gov), a Scientific Focus Area Program at Lawrence Berkeley National Laboratory is based upon work supported by the U.S. Department of Energy, Office of Science, Office of Biological & Environmental Research under contract number DE-AC02-05CH11231"