

Evolvability of proteins in a signaling cascade: the importance of network topology

Shankar Mukherji<sup>1</sup>, Qiong Yang<sup>2</sup>, Alexander van Oudenaarden<sup>2</sup>

<sup>1</sup>Harvard-MIT Division of Health Sciences and Technology, Harvard University and  
Massachusetts Institute of Technology

<sup>2</sup>Department of Physics, Massachusetts Institute of Technology

The question of what determines the evolvability of a protein has recently attracted the attention of systems biologists. We examined this question from a functional standpoint. Using the budding yeast high osmolarity glycerol (HOG) pathway as a model system, we replaced each *Saccharomyces cerevisiae* pathway component with its ortholog from the evolutionarily diverged yeasts *Candida glabrata* and *Candida albicans*. Using a quantitative fluorescence microscopy based assay, we measured the ability of these ortholog-substitutions to recapitulate the signaling dynamics of the wildtype *S. cerevisiae* HOG pathway. The results are consistent with mathematical work and pathway simulations that point to the importance of network architecture in determining the evolvability of pathway components.