Towards rationally redesigning bacterial signaling systems using information encoded in abundant sequence data[1] RYAN CHENG, FARUCK MORCOS, HERBERT LEVINE, JOSE ONUCHIC, Center for Theoretical Biological Physics, Rice University — An important challenge in biology is to distinguish the subset of residues that allow bacterial two-component signaling (TCS) proteins to preferentially interact with their correct TCS partner such that they can bind and transfer signal. Detailed knowledge of this information would allow one to search sequence-space for mutations that can systematically tune the signal transmission between TCS partners as well as re-encode a TCS protein to preferentially transfer signals to a non-partner. Motivated by the notion that this detailed information is found in sequence data, we explore the mutual sequence co-evolution between signaling partners to infer how mutations can positively or negatively alter their interaction. Using Direct Coupling Analysis (DCA) for determining evolutionarily conserved interprotein interactions, we apply a DCA-based metric to quantify mutational changes in the interaction between TCS proteins and demonstrate that it accurately correlates with experimental mutagenesis studies probing the mutational change in the *in vitro* phosphotransfer. Our methodology serves as a potential framework for the rational design of TCS systems as well as a framework for the system-level study of protein-protein interactions in sequence-rich systems.

Ryan Cheng
Center for Theoretical Biological Physics, Rice University

Date submitted: 12 Nov 2013   Electronic form version 1.4