MAR06-2005-001114

Abstract for an Invited Paper
for the MAR06 Meeting of
the American Physical Society

Unraveling Biological Design Principles Using Engineering Methods: The Heat Shock Response as a Case Study

HANA EL-SAMAD, Biochemistry and Biophysics, QB3, UC San Francisco

The bacterial heat shock response refers to the mechanism by which bacteria react to a sudden increase in the ambient temperature. The consequences of such an unmediated temperature increase at the cellular level is the unfolding, misfolding, or aggregation of cell proteins, which threatens the life of the cell. To combat such effects, cells have evolved an intricate set of feedback and feedforward mechanisms. In this talk, we present a mathematical model that describes the core functionality of these mechanisms. We illustrate how such a model provides valuable insight, explaining dynamic phenomena exhibited by wild type and mutant heat shock responses, corroborating experimental data and guiding novel biological experiments. Furthermore, we demonstrate, through the careful control analysis of the model, several design principles that appear to have shaped the feedback structure of the heat shock system. Specifically, we itemize the roles of the various feedback strategies and demonstrate their necessity in achieving performance objectives such as efficiency, robustness, stability, good transient response, and noise rejection in the presence of limited cellular energies and materials. Examined from this perspective, the heat shock model can be decomposed, both conceptually and mathematically, into functional modules. These modules possess the characteristics of more familiar modular structures: sensors, actuators and controllers present in a typical technological control system. We finally point to various theoretical research challenges inspired by the heat shock response system, and discuss the crucial relevance of these challenges in the modeling and analysis of many classes of systems that are likely to arise in the study of gene regulatory networks.