Modeling the Hsp70-mediated Protein Folding in *E.coli*

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Abstract:

The 70 kDa heat shock protein (Hsp70) chaperone system is the major molecular chaperone system that assists protein-folding processes in *Escherichia coli*. During the heat shock response, the Hsp70 chaperone system protects the cell by increasing its production and preventing protein aggregation. Traditional biochemical studies demonstrated a great power in revealing the complex mechanism of the system. However, understanding the regulation of the pathway of the Hsp70 system experimentally is difficult due to various limitations of current biochemical and biophysical technologies, primarily because denatured, aggregating protein species are not amenable to biophysical experiments. Detailed computer simulation based on real biochemical data with a comprehensive comparison with experimental results is a promising approach to better appreciate the functionality of the system.

In this work, we developed the first kinetic model of Hsp70-mediated protein folding and analyzed the kinetic characteristics of this system during folding of an unfolded protein using computer simulations. Rate constants used for the model were derived from recent literature or were determined by Dr. Matthias P. Mayer (ZMBH, University of Heidelberg). Many of the simulation results were validated by experiments. By simulating the model at different temperatures with lab measured rate constants, we evaluated how temperature may affect the system during the heat shock response. Our model suggests that the Hsp70 system is robust in assisting protein folding and for the final release of folded substrates GrpE is the most efficient regulator of this system. Discrepency of our model and experimental results are discussed.

References:

B. Hu and M. Tomita. *The Hsp70 chaperone system maintains high concentrations of active proteins and suppresses ATP consumption during heat shock.* Systems and Synthetic Biology , in press.

B. Hu, M.P. Mayer and M. Tomita. *Modeling Hsp70-mediated protein folding*. Biophys J , 91(2):496-507, 2006.