Dynamical analysis of the stress-induced heat-shock protein network in post-traumatic stress disorder (PTSD)

K. Sriram$^{1,2}$ and Francis J. Doyle III $^{1,2}$

1. Institute of Collaborative Biotechnologies, University of California, Santa Barbara, CA 93111-5100 USA
2. Department of Chemical Engineering, University of California, Santa Barbara CA 93111-5080 USA.

Tel: (805) 893-8133 E-mail: doyle@engineering.ucsb.edu

Summary: Dynamical analysis of heat shock protein network is carried out to determine its role in post-traumatic stress disorder under acute stress.

Physiological and psychological stresses, such as depression and post-traumatic stress disorder (PTSD), cause drastic changes at a molecular level in the brain. To counteract this stress, the heat–shock protein (HSP) network plays a vital role in restoring the homeostasis of the system. To study the stress-induced dynamics of heat-shock network, we constructed three modules of the HSP90 network–trimerization reactions, phosphorylation–dephosphorylation reactions, and the conversion of HSP90 from an open to a closed conformation (Fig. 1a), and analyzed the corresponding nonlinear differential equation model based on the laws of mass action kinetics with stress as a bifurcation parameter.

Codimension–1 bifurcation analysis with stress as a bifurcation parameter revealed the occurrence of “mushroom”, a type of complex dynamics, in which S–shaped and Z–shaped hysteretic bistable forms were present together (Fig. 1b). We mapped the molecular events in the HSP90 network responsible for generating the mushroom dynamics under stress, and interpreted the occurrences of S–shaped and Z–shaped hysteresis to a normal function, and the function within the stress–related disorders such as depression and PTSD, respectively. Finally, we studied the effect of parameter variations on the mushroom dynamics to get insight about the role of parameters in effecting complex dynamics such as isolas.