A Markov Chain Model of the MAPK Signaling Cascade

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ABSTRACT

The mitogen-activated protein kinase (MAPK) cascade is an essential component of a wide variety of eukaryotic cell signaling pathways including ones involved in growth, differentiation, and apoptosis. This highly conserved series of three enzymes has been extensively studied, and a wide range of steady state as well as dynamic data has been published [1][2]. Here, we present a statistical model for the MAP Kinase cascade using Markov chain theory. Unlike previously developed biochemical reaction models [2], the Markov model has very few parameters and its dynamic properties are a consequence of the topology of the Markov chain as opposed to some particular set of parameter values. The model predictions include ultrasensitivity and adaptation and correlate with experimental findings. We also investigate the effect of scaffolding [3] on MAPK activity and incorporate it into the model leading to a new set of predictions and suggested experiments. This Markov chain representation of cascades is

finally extended to other signaling cascades including the bacterical chemotaxis signaling pathway.

REFER ENCES

- Huang, C.F., and Ferrell, J.E. Ultrasensitivity in the Mitogen-Activated Protein Kinase Cascade. Proc. Natl. Acad. Sci. USA, Vol. 93, 10078-10083, September 1996.
- [2] Asthagiri, A.R., and Lauffenbuger, D.A. A Computational Study of Feedback Effects on Signal Dynamics in a Mitogen-Activated Protein Kinase (MAPK) Pathway Model. Biotechnol. Prog. 2001, 17, 227-239.
- [3] Levchenko, A., Bruck, J., and Sternberg, P.W. Scaffold Proteins may Biphasically Affect the Levels of Mitogenactivated Protein Kinase Signaling and Reduce its Threshold Properties. Proc. Natl. Acad. Sci. USA, Vol. 97, 5818-1823, May 2000.