The Use of Forced Oscillations to Study Biochemical Interactions.

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Investigating the response of protein interaction networks to external stimuli *in vivo* typically involves observing the step, or steady state response of individual cells, cell populations, or tissues in response to the stimulus of interest. Here recent work investigating the use of time varying stimuli to probe the dynamics of biochemical systems and protein interactions is discussed. This technique is analogous to frequency domain analysis techniques employed by engineers to characterize electrical and mechanical systems. By measuring the amplitude of the response of a pathway to a time varying signal as a function of the frequency of the input signal one can extract information about the dynamics of the pathway. A fast responding pathway for example will tend to pass higher frequency signals without attenuation than a slow responding pathway. By measuring the input frequency at which this attenuation occurs one can extract information about the rate at which the pathway is activated. In addition, time varying signals can potentially uncover interactions within multiple input/multiple output networks. By measuring the response of such a network as a function of the phase difference between two input signals, one can gather information about component interactions at common nodes within the network. In this situation, if both signals are simultaneously high at the common node, then one would expect a higher output signal than if both signals were low, whereas if the pathways being probed do not share common nodes, then one would not expect a correlation between the phase of the input signals, and the pathway outputs. As a first step towards validating this measurement technique we are investigating, experimentally and theoretically, how *E. coli* grows in response to sinusoidal temperature oscillations, and *S. cerevisae* responds to oscillating pheromone concentrations.