

Constructing Mathematical Models of Biological Signal Transduction Pathways

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Living organisms detect and respond to a variety of environmental cues (e.g., light, attractants, hormones, etc.) through receptor-mediated signal transduction pathways. The majority of pharmaceutical agents act by modulating the behavior of these biological networks. Many of the signaling systems possess remarkable performance characteristics including exquisite sensitivity, broad dynamic range, and robustness. Using techniques from control and dynamical systems theory, we have studied three well-characterized signaling pathways: (1) bacterial chemotaxis (two-component) , (2) mammalian visual phototransduction (G-protein), and (3) yeast pheromone response (G-protein). We have found that the dynamics of these complex networks are carefully regulated through feedback control in order to achieve the desired performance. In addition, constructing a mathematical model allows one to make predictions about the input/output relationship when the system is subjected to both external (ligand) and internal (mutations) perturbations.