Hamilton Institute

Some Theoretical Aspects of Cell Signaling: Receptor-ligand Interactions and Signal Amplification Cascades

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Abstract

Understanding the connection between receptor activity and cell signaling is a major issue in the research and development of new drugs. The signal transduction process that eventually leads to the cell's response includes various regulatory and feedback mechanisms, as well as signal amplification. The analysis of each signaling module, in a control theoretic framework, may help understand the interactions among the different modules in signaling pathways.

In a first step, we develop a model of receptor/ligand interactions, by considering various possible receptor conformations and the respective receptor+ligand complexes. While some drugs block receptors (antagonists), others may even supress a receptor's constitutive activity (inverse agonists). These properties are characterized experimentally by "dose-response" curves: for each concentration of drug, the corresponding receptor+ligand activity is measured. Our model reproduces the dose-response curves and identifies the agonism class of a ligand through a minimal set of kinetic parameters.

In a second step, we focus on a model of protein kinase cascades, and consider a characterization of signal amplification, in terms of the input-to-output transfer function and gain of the system. The effect of the length of the cascade on signal amplification is analyzed, from the point of view of optimizing the balance between signal duration and amplitude.

Venue: Seminar Room, Hamilton Institute, Rye Hall, NUI Maynooth

Time: 1.00 - 2.00pm (followed by tea/coffee)

Travel directions are available at www.hamilton.ie

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