

Dynamic Modelling of Signal Transduction Pathways

“Simulating what cannot be simulated”

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Abstract

Many neuro- and cancer-related diseases can be considered a failure of communication at molecular level. The area of **cell signaling** [1] investigates the transmission of information from receptors at the cell surface to gene activation in the nucleus. Signals are relayed by means of biochemical reactions occurring in space and time and organized in **pathways**.

There are principally two conceptual frameworks in which to model and/or simulate biochemical reaction networks: a) stochastic simulation of the *chemical master equation* (CME), derived from the Chapman-Kolmogorov equation [2] and b) *generalized mass action* (GMA) models, employing nonlinear differential equations [3,4]. I am going to compare the two frameworks with respect to their mathematical roots and application to signal transduction pathways. This will include a critical review of some conclusions made in recent publications.

Although we are now beginning to have technologies that enable us to generate **signal-response time series** at the molecular level, I am going to describe the problems arising in modeling **intracellular dynamics** [5,6] using such data. On the other hand, despite the lack of reliable, accurate and sufficiently rich data sets, we find that even simple simulations and the modeling process itself can provide the bio/medical researcher with useful information, guiding the **design of experiments**, helping to identify which variables to measure and why.

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