Modeling Signal Transduction Using Process Algebra

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Recent years have shown a rapid accumulation of molecular information about inter-cellular and signal transduction communication systems, which play a pivotal role in evolution, development and disease [1]. However, this information is diverse, disparate and fraught with detail, rendering analysis difficult. We propose a novel formal unifying view of signal transduction as a pure communication system. We establish this correspondence, and employ the π-calculus [2, 3], a process algebra originally designed for describing networks of inter-connected concurrent computational processes, to model signal transduction systems.

The model is mathematically well defined and biologically visible. It represents both the dynamic behavior of the system over time, and the structural molecular implementation that underlies this behavior. We demonstrate the power of the π-calculus to represent complex molecular networks by constructing a model for the receptor tyrosine kinase (RTK)-MAP kinase cascade pathway. The low-level molecular details (e.g. residues, domains) fit clearly and visibly within the representation and serve as the basis for the entire scope of global network behavior (e.g. feedback, cross talk).

This uniform, integrated, scalable theoretical framework based on the π-calculus, can be employed to study signal transduction at molecular, evolutionary and cybernetic levels: 1. Simulation and formal mathematical verification allow to predict the effect of changes in low-level components (molecules and below) on global outcome. This can serve for functional as well as evolutionary studies. 2. Formal methods for the comparison of processes represented in process algebras (e.g. bisimulation) serve as a basis for a novel measure of homology of pathways, the *homology of process* [1]. Since our π- calculus representation includes both the structure and the dynamics of signaling pathways, we are able to define a distance measure that incorporates both differences in molecular components and in their interactions. 3. The final network representation can be reified to an object, in itself amenable to cybernetic studies on general properties of different communication systems, molecular and others.

References

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