An Algebraic Approach to Modeling Biological Communication Systems: The π-Calculus as a Formalism of Signal Transduction

Aviv Regev[1] and Eva Jablonka[2]
[1]Department of Cell Research and Immunology, The George S. Wise Faculty of Life Sciences, and [2]The Cohn Institute for the History and philosophy of Science and ideas, Tel Aviv University, Tel Aviv, Israel
e-mail: aviv5@netvision.net.il, jablonka@post.tau.ac.il

Recent years have shown a rapid accumulation of molecular information on inter-cellular and signal transduction communication systems, which play a pivotal role in evolution, development and disease(Gilbert, Opitz, and Raff, 1996). 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 (Milner, Parrow, and Walker, 1992; Milner, 1993), 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 behaviour of the system over time, and the structural molecular implementation underlying this behaviour. The power of the π-calculus to represent complex molecular networks is demonstrated by constructing a model for the receptor tyrosine kinase (RTK)-MAP kinase cancade 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 behaviour (e.g. feedback, cross-talk).

We employ this uniform, integrated, scalable theoretical framework based on the π-calculus, 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*. Since the the π-calculus formalism incorporates the structure as well as the dynamics of signalling processes both differences in molecular components and in their interactions are measured to determine the distance. 3. The final network representation can be reified to an an object, in itself amenable to cybernetic studies on general properties of different communication systems, molecular and others.

References

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