A System-Theoretic Modeling Framework for Cellular Processes

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With the availability of technologies that allow us to obtain stimulus-response time series data for modeling and system identification, there is going to be an increasing need for conceptual frameworks in which to formulate and test hypotheses about intra- and inter-cellular dynamics, in general and not just dependent on a particular cell line, cell type, organism or technology. While the semantics can be quite different, biologists and systems scientists use in many cases a similar language (notion of feedback, regulation, etc.). A more abstract system-theoretic framework for signals, systems and control could provide the biologist with an interface between the domains. Apart from recent examples to identify functional elements and describing them in engineering terms, there have been various more abstract developments to describe dynamics at the cell level in the past. This includes Rosen's (M,R)-systems. This paper presents an abstract and general compact mathematical framework of intracellular dynamics, regulation and regime switching inspired by (M,R)-theory and based on hybrid automata. The theory of hybrid systems allows us to complement continuous dynamics, which form the basis for many pathway models, with other regulatory or response levels that include changes to the elementary structure of dynamics. The hybrid automaton may accept several executions and thus can represent the uncertainty of the cellular dynamics. Properties such as reachable set computations, liveness, and stability can be analyzed for these nondeterministic hybrid automata. The proposed mathematical model of cellular processes could form a basis for further discussions and extensions such as the inclusion of the diverse signaling used in cellular communication. Various alternative mathematical tools could be investigated including temporal logic, stochastic automata, etc. Despite of the uncertainty one faces in modeling intra-cellular dynamics, the encouraging experience is that even dramatically simplified models can provide useful practical guidance for the design of experiments, helping the experimentalist to decide what to measure and draw conclusions about experimental results.