

Method for Simulating the Kinetics of Cell Growth and Division at the Molecular Level

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ABSTRACT

A long-term objective of computational systems biology is to simulate the kinetics of cell growth and division at the molecular level. Given the astronomical complexity of living systems as well as the lack of appropriate rate constants, copy-numbers and mechanistic details of the individual processes occurring therein, this objective is presently unattainable. Nevertheless, the rate at which such knowledge is being amassed is ever increasing, suggesting that this objective might be attainable eventually. The goal of this project is to develop methods that could be used if and when that day arrives. Our approach employs *Mechanical Cells*. These hypothetical living systems have properties symbolically reminiscent of real prokaryotic cells, but they are far simpler. In a sense, their use allows the complexity of living systems to become a variable that can be adjusted as available information and modeling capabilities change. Mechanical cells are composed of an explicit set of chemical reactions and components. The cell considered here (called MC4) has a membrane, cytoplasm and genome, all located within an environment that provides nutrients for growth and division. It

undergoes cell cycle processes, including genomic replication, partitioning, and midcell septal-constriction. It has a metabolism, in which environmental nutrients are converted into amino acid, nucleotide, and phospholipid molecules, and proteins that are synthesized by feedback-regulated genetic mechanisms.

Ordinary differential equations were generated from the chemical reactions that define these cells, and these were used to generate simulations that were fitted numerically to hypothetical microarray "data". This "data" was constructed from the known choreography of *Escherichia coli*'s cell-cycle, and adjusted to abide by the conservation relationships inherent in the MC4 mechanism. A method for determining the rate-constants that result in best-fit simulations to the "data" was developed. Spatial attributes for cell cycle components were constructed and used to prepare a 3D animation of the cell's dynamics, as dictated from output simulations. The poster will describe the properties of MC4, the methods employed for simulating it, and the resulting animation.