Modeling Cell Fate Specification in the Sea Urchin Embryo

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***Short Abstract* — The sea urchin is a model organism for experiments on early embryonic development. A detailed picture of the gene regulatory network (GRN) governing cell fate specification in the endomesoderm is being pieced together from several types of experiments. [1] We construct an autonomous Boolean model of the GRN, including signaling between neighboring cells in the growing embryo, and ask whether it can account for observed patterns of gene expression, with particular emphasis on the transfating pathway followed by nonskeletal mesoderm cells after microsurgical removal of skeletogenic cells.**

***Keywords* —Transcriptional regulatory networks; Boolean networks; Embryonic development.**

THE sea urchin embryo provides the a unique platform for studying the dynamics of a gene regulatory network. Experiments over the past several decades have identified more than 70 key transcription factors and signaling molecules that regulate each other, and the interactions between various subsets of these factors have been invoked to explain a wide array of processes involved in cell differentiation. [1,2] Experimental techniques are now available for measuring expression of a given gene in a particular cell, tagging cells according to lineage, and performing microsurgery to coax the embryo into generating tissues through pathways not found in normal development.

The GRN underlying cell fate specification in the early embryo is complex enough to make it hard to tell whether the whole picture constructed to date is internally capable of explaining the 3D patterns of gene expression observed in wild-type and perturbed embryos. To reveal the full implications of the current picture of the GRN, a mathematical model capable of producing the such patterns is needed. Autonomous Boolean models represent a good compromise between the full detail required for capturing all relevant biomolecular processes and the simplicity of synchronous Boolean models that are known to produce dynamical artifacts not inherent to physical systems. [3] Boolean reasoning, in which genes are said to be either ON or OFF and finer distinctions are ignored, is commonly employed by biologists describing the logic of experimental results on the sea urchin embryo. Autonomous updating rules allow modeling of different delay times associated with activation or repression through different network links and with different decay times of molecular species, and avoid spurious effects associated with other update schemes.

We have constructed a framework for modeling endomesoderm specification in the sea urchin embryo. Cell positions are specified on the surface of a sphere, where the spatiotemporal pattern of cells and cell divisions is taken from experimental images from the 16-cell stage up to the beginning of ingression of the primary mesenchymal cells. The cells are assumed to be running identical copies of the GRN, which includes links for signaling between adjacent cells. When a cell divides, the two resulting cells inherit the state of gene expression of the mother. The differences in gene expression between cells result from differences in maternal signals to the micromeres and macromeres at the 16-cell stage and the subsequent dynamics of the intracellular GRNs and the signals passed between cells. We will report on progress made toward finding time-delay parameters and Boolean logic assignments that yield known patterns of expression and on experiments probing the expression of Pmar1, a crucial early gene in the skeletogenic lineage, during transfating in micromereless embryos.

The dynamics of generic autonomous Boolean networks is itself a topic of current research. To properly capture the behavior of underlying physical systems, appropriate filtering of pulses of short duration is crucial and certain memory effects may also be important. These points are illustrated by the analysis of two types of analytically tractable networks: simple rings of copiers and inverters, and a single XOR gate with two self-inputs. [4]

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