Executable biology -- Computer science sheds light on animal development

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By applying the techniques of computer engineering to a mechanistic diagram describing the development of the Nematode C. elegans, a group of researchers in Switzerland has been able to tease out what laboratory experiments have not – how and when the crucial cross-talk between cellular signaling pathways takes place in order to determine the fates of individual cells. The novel in silico model is described in a paper appearing May 18, 2007 in the open-access journal *PLoS Computational Biology*.

During C. elegans development, uncommitted precursor cells differentiate into two distinct cell types in response to a series of complex biochemical signaling events. Cancer cells respond to the same cellular signals, so understanding the dynamic orchestration in the cellular environment has important implications in our understanding of cancer metastasis as well as normal development.

Traditional biological models give a fairly static picture of cellular processes, and this limits understanding of the details involved. Biologists and computer scientists from the EPFL (Ecole Polytechnique Federale de Lausanne) and the University of Zurich have taken a new approach, using formal methods of computer science to translate this picture into a dynamic representation that can capture time-dependent processes. Results from the model can then be compared to data from the lab, revealing gaps in our understanding of the processes taking place. Researchers can use the model to test hypotheses that would fill in the missing pieces in silico before performing actual lab experiments.

By running their model with a wide variety of gene mutation scenarios and comparing results with available laboratory data, they found that the fate of C. elegans vulval precursor cells depends upon the time-sequence of two cellular signaling pathways, as well as a negative feedback loop that had not been described before.

These kinds of models hold great promise for future exploration of a variety of biological systems, explains lead EPFL researcher and biologist Dr. Jasmin Fisher. "Once a robust model has been built of a particular system, it can be used to get a global, dynamic picture of how the system responds to a variation – such as a drug or a genetic mutation. Preliminary studies could be quickly done using the model, saving valuable laboratory time and resources for only the most promising research avenues. We call this Executable Biology."

Source: Public Library of Science