Executing multicellular differentiation: quantitative predictive modelling of *C. elegans* vulval development

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We present a mechanistic model that accurately reproduces observed cell fate patterns in the developing *C. elegans* vulva. The model was implemented using Petri nets, and contains 600 nodes and 1000 connections spread over the six vulval precursor cells, describing known mechanistic interactions: transcription, protein interaction and activation, degradation, trafficking, and multi-cellular signaling. Two published hypothetical interactions are shown to be crucial to reproducing all known fate patterns. The first involved a very subtle change: downregulation of a protein should occur via endocytosis instead of gene inhibition. The other hypothesis involves a micro-RNA interaction, which appears to play a tuning-type of role.

The design of executable computer algorithms and formal models in biological research gained lately a favorable momentum (e.g. Nature, vol. 462, pp. 408-410). Our modeling exercise is a clear example of the potential of executable biology to provide models that can support continued progress in biological research.

Anton Feenstra obtained an MSc in molecular sciences from the University of Wageningen, in 1996. For his PhD research in biophysical chemistry, he moved to Groningen. He graduated in 2001 with a thesis titled “Long term dynamics of proteins and peptides”. After post-doc positions in both molecular toxicology and in bioinformatics at the Vrije Universiteit Amsterdam, he became assistant professor in bioinformatics at the same university in 2007, working with Jaap Heringa.

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