Computer tools are needed in systems biology to analyse qualitatively the dynamics of interaction networks, to discover the organisation of the cell’s molecular components. In this context, the objective is to develop a general tool which, based on a unique specification, allows to explore the properties of the model’s parameters and behaviours, and also to propose new experiments, by a mix of inference and simulation.

This work is based on the multi-valued asynchronous networks proposed by R. Thomas and E. Snoussi. This formalism, which can be seen as a discrete abstraction of a special class of piecewise affine differential equations, allows a qualitative analysis of the dynamic behaviour of such systems. This formalism has been recently extended by H. de Jong to take into account trajectories “sliding” along discretisation thresholds.

The goal of this research is to investigate how a formal description of such a biological switching network can be exploited through an implementation in Constraint Logic Programming (CLP) in order to obtain the variety of functionalities desired.

This tool will be applied to the construction of several biological networks from observed properties.

The state of knowledge, and also to partly known parameters and behaviours, is to develop a general tool which, based on a unique specification, allows to explore the properties of the model’s parameters and behaviours, and also to propose new experiments, by a mix of inference and simulation.

Efficiency: by using the structure of the discrete equations to enhance the tool (current work).

Extension of models: in order to be more accurate regarding biology and so to obtain a correct abstraction.

Interface: in order to provide a usable tool for a biologist (not trivial in the context).

Discrete equations giving the concentration’s tendency for each species:

\[
X = K_1 \cdot s^+(x,s_x) \cdot s^-(y,s_y) + K_2 \cdot s^-(x,s_x) \cdot s^+(y,s_y) + K_3 \cdot s^+(x,s_x) \cdot s^-(y,s_y)
\]

Example: for the state \([x,y] = [0,1]\) the tendency is the state \([X,Y] = [K_2,0]\)

Better abstraction with the extension: a path from \([1,1]\) to \([1,0]\) exists.

Example of mixed query:

K1=1, Path=[\([1,1]\), S1,S2,\([1,0]\)], predicate(Path,[K1,K2,K3],Model), enumerate(Path).

with 2 solutions:

Path=[\([1,1]\), \([sx,1]\), \([sx,sy]\), \([1,0]\)], K2=1;
Path=[\([1,1]\), \([1, sy]\), \([1,0]\), \([1,0]\)], K3=0.

State of knowledge: Model known

Parameters partially known

Behaviours partially known

Modeling, Inference and Simulation of Biological Networks using Constraint Logic Programming

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