

Automated Synthesis of Boolean Networks for Biological System Modeling



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Logical models of biological networks allow for abstracting details of biological network and capturing multiple layers of signaling. However, the current manual approach for logic rule design and minimization is time-consuming and error-prone. Hence, automated tools must be developed before large-scale networks can be efficiently modeled and analyzed.

In this work, we developed an automated approach to design and minimize biological circuit models, relying on available tools such as *Espresso* Boolean logic minimization. We start with the model interaction map (Fig. 1) and influence tables (Fig. 2 (table)) of activators/inhibitors, obtained through an extensive literature survey and consultation with experts. This is followed by defining the number of critical thresholds of model variables from existing knowledge or experimental time series data. We built upon *Espresso's* functionality by providing capabilities for handling multi-state logic (states 0,1,2 and 0i, Fig. 2 (table)) with variable delays (states 0d, Odd, 1d, 1dd, 2d, 2dd are implemented in the circuit shown in Figure 2). These additional features help us to identify timing relationships between different pathways. In cases where links between elements are not known, defining influence table components with several alternative values allows us to locate and predict the outcomes of gaps in our knowledge.

Our current result is a multi-staged tool capable of translating influence tables into minimized logic rules (Fig. 2 (bottom)), including delay effects to facilitate efficient biological network studies. We have applied our methodology to develop a discrete model for the circuitry (Fig. 1) that implements effects of malaria in mosquito cells. Preliminary results using developed rules for different initial conditions are shown in plots in Fig. 2 (right). Future work will include an intelligent automated system that indicates key inhibitors/activators, which are critical to the cell behavior, and suggests future experiments.

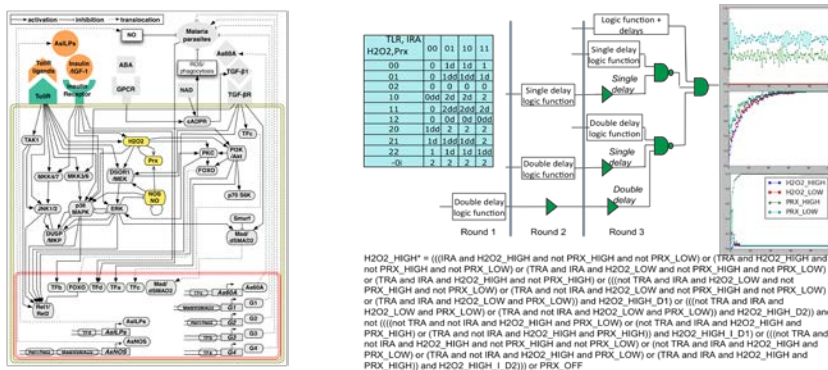


Fig. 1: Interaction network example. Fig 2: Delay logic circuit, logic rule and result examples.