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Timing Analysis of Genetic Logic Circuits using D-VASim

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Abstract – A genetic logic circuit is a gene regulator network implemented by re-engineering the DNA of a cell, in order to control gene expression or metabolic pathways, through a logic combination of external signals, such as chemicals or proteins. As for electronic logic circuits, timing and propagation delay analysis may play a very significant role in the designing of genetic logic circuits. In this demonstration, we present the capability of D-VASim (Dynamic Virtual Analyzer and Simulator) to perform the timing and propagation delay analysis of genetic logic circuits. Using D-VASim, the timing and propagation delay analysis of single as well as cascaded genetic logic circuits can be performed. D-VASim allows user to change the circuit parameters during runtime simulation to observe its effects on circuit's timing behavior. The results obtained from D-VASim can be used not only to characterize the timing behavior of genetic logic circuits but also to analyze the timing constraints of cascaded genetic logic circuits.

Brief Introduction – D-VASim, which stands for dynamic virtual analyser and simulator, is an interactive virtual laboratory environment for the simulation and analysis of genetic logic circuits [1]. It takes a genetic logic circuit model, developed in Systems Biology Mark-up Language (SBML) [2] and lets the users analyse the model's components in a friendly manner. For each logic circuit model, D-VASim generates a separate virtual laboratory environment to perform deterministic and stochastic simulation. This virtual environment serves as a standalone virtual instrument or virtual apparatus for the specific logic circuit model, which allow users to interact with the model, observe its behavior, and make the direct changes in the concentration of input species, all during runtime. Besides providing users an ability to interact with the model during runtime, D-VASim is also capable of verifying the logic function of a genetic logic circuit. Moreover, D-VASim can be used to analyse the timing and propagation delays of genetic logic circuits.

The genetic logic gates proposed in [3] are used for the experimentation in D-VASim. Figure 1 shows the simulation results of a genetic NAND gate which produces the output green-fluorescent protein (GFP) only when both of the inputs, lactose inducer (LacI) and tetracycline repressor (TetR), are present in the significant amount in the cell. This significant amount is the threshold concentration, which triggers the concentration of output specie. This is similar to the digital components in electronic circuits, which have a certain threshold value of input voltages to trigger the output. However, in genetic logic circuits, each circuit may have different input threshold concentration for triggering the concentration of output specie, and thus needs to be identified. D-VASim is equipped with an algorithm to estimate the threshold value and a propagation delay of genetic logic circuits. Figure 1 shows the simulation results of genetic NAND gate proposed in [3]. Figure 1(c) shows the results of threshold value and an input-output propagation delay of a given genetic circuit (NAND gate) estimated by D-VASim algorithm, which approximately matches the results obtained by the stochastic simulation shown in Figure 1(d). Figure 1(d) shows the virtual instrument generated by D-VASim to perform the stochastic simulations of genetic NAND gate. This figure indicates that when LacI and TetR are present in the significant amount i.e. above their threshold concentration level (12.5 units in this case), the concentration of GFP is gradually decreased (takes ≈230 time units) to pass-by the threshold concentration level, thus exhibiting the behavior of NAND gate.

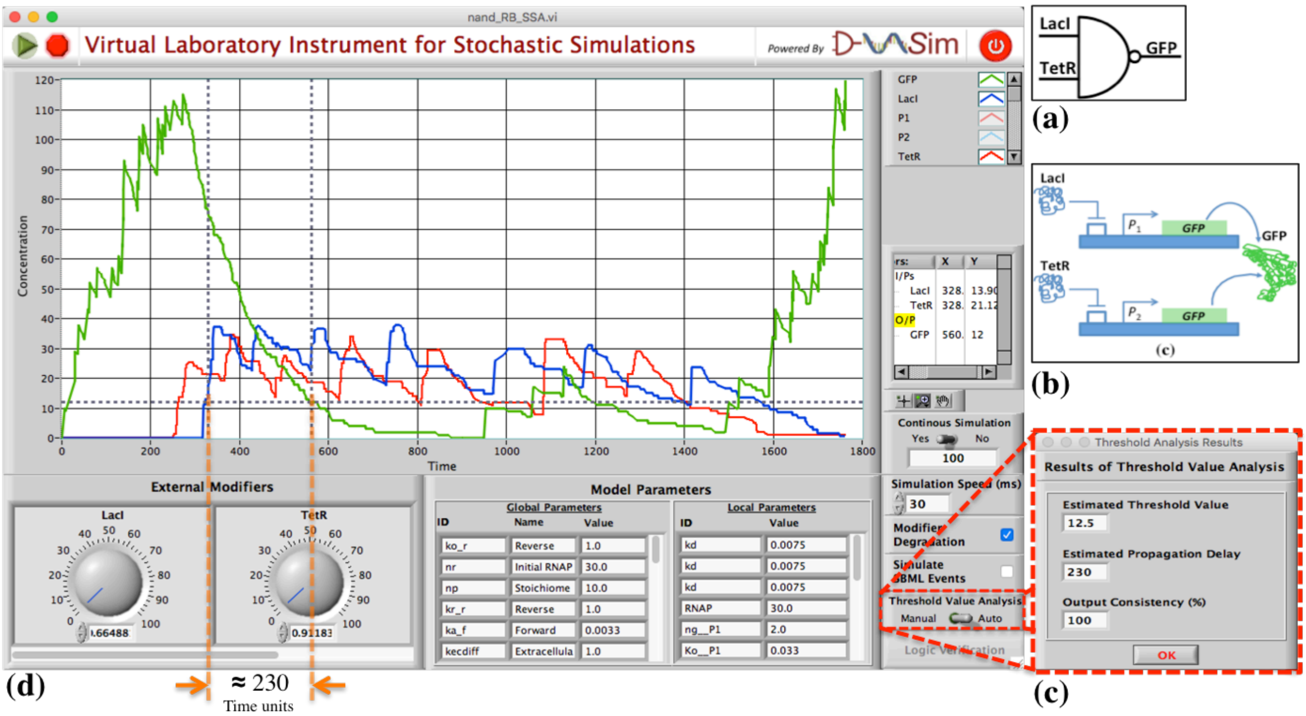

Figure 1. Simulation results of genetic NAND gate using D-VASim. (a) Schematic symbol of genetic NAND gate. (b) Genetic implementation. (c) Threshold value and timing analysis results. (d) The virtual instrument generated by D-VASim for the stochastic simulations of genetic NAND gate.

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