

# *BioBLESS* User Guide

*BioBLESS* Developers

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## 1 What is BioBLESS? What can it do?

*BioBLESS* (Biological Boolean Logic Evaluation & Systematization based on Simulation) is an integrated development environment that can automatically design and stochastically simulate the gene network that can conduct a specific logic computing task.

Hoping to generate a more direct and rational circuit design, we develop *BioBLESS* that can automatically compute the structure of a digital gene circuit. Instead of looking for a general solution to the computational design challenge, we focus on digital circuits. Given a truth table where the inputs and outputs of Boolean gates take only 0/1 values, we convert it into Boolean Formula and get possible circuit schemes.

To get reliable circuits, we select well-behaved circuits with the introduction of fitness scores which sufficiently consider the practical realizability. Performance simulation and robustness analysis constituting the core of our evaluation module will shed light on how our devised circuits behave and examine the correspondence with truth tables. Moreover, our software keeps the compatibility and various methods or algorithms and reserves the space for users to redesign.

## 2 Major Modules in BioBLESS

In the following description, we use background color to specify the meaning of a word:

- Green color as background means a feature name: *Feature*
- Blue color as background means a module name: *Module*
- Purple color as background means the action name you should take: *Action*
- Orange color as background means the button you should find: *Button*

A very common statement will be “In *some module*, to achieve *some feature* you can *double click some button* to do something”. In the following modules guide, you should always *click* the corresponding *icon* on the left of the canvas.

## 2.1 The Logic Module

The main function of **Logic** module is the construction of logic circuit in abstract logic gate scheme. One can easily set up a logic circuit by using simple clicks and drags. Another main function of this part is to transform the logical truth table into simplified logic gates construction using the famous **ESPRESSO** algorithm.

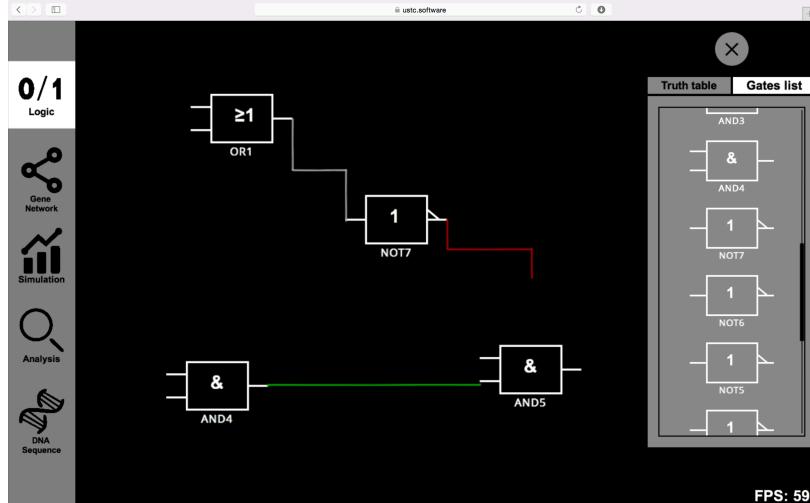


Figure 1: Gate Manipulation View

The first important feature of **Logic** is that you can **manipulate logic gates** by some mouse clicks and drags.

- To **add a logic gate**, *click +* on the right of the canvas, *click* the **Gates list**, and then *drag* the **gate** to any position of the canvas.
- To **delete a logic gate**, *move the mouse* to the gate, then *click* the **-** above the gate. When you delete a logic gate, every existing wire binding to this gate will also be deleted.

The second important feature of the **Logic** module is that one can easily construct the system up with wires.

- To **add a wire** between current logic gates ports, *click* the **port** you want to begin with, then *click* the **port** you want to end with.
- To **delete a wire**, *move the mouse* to the gate, then *click* the **-** above the wire.

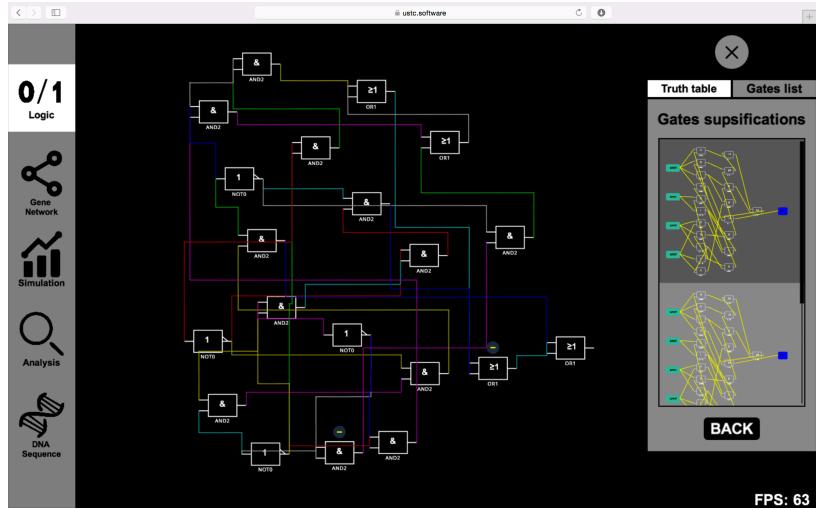


Figure 2: ESPRESSO view

You can also **input the truth table** and let *BioBLESS* to automatically calculate the logical circuit using **ESPRESSO** and archived gene circuit score function.

- To **use design automation**, click + at the right of the canvas, press the corresponding **input number** on the right of the canvas, input the truth table by press the "turn-on" button on the right, then press **create**. A algorithm using **ESPRESSO** and builtin score function will generate an optimized logic circuit.
- This automatically generated logic circuit can be treated as your self-made circuit, which means arbitrary modification is also allowed in this scheme. Say, you can delete a logic gate as you like. But once modified, the correctness of the truth-table is not guaranteed.

You also can zoom in and out to make a more detailed and overall view of the current circuit configuration.

- To **zoom in**, scroll up the mouse wheel at **any position on the canvas**.
- To **zoom out**, scroll down the mouse wheel at **any position on the canvas**.

## 2.2 The Gene Network Module

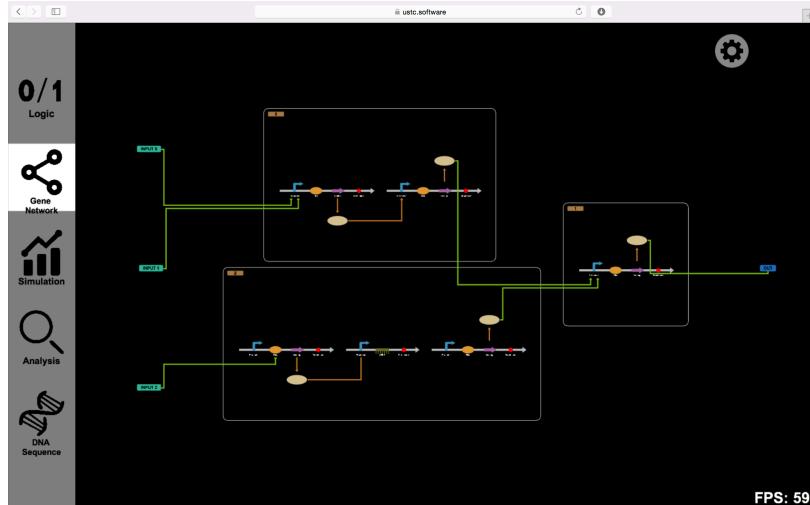


Figure 3: Gene Network View

The main function of **Gene Network** module is to represent the concrete biological entity of each logic gates. Each gate's gene content is drawn in a rounded rectangle. Another main function is that one can easily modify gene circuit parameters in this scheme using parameter modifier.

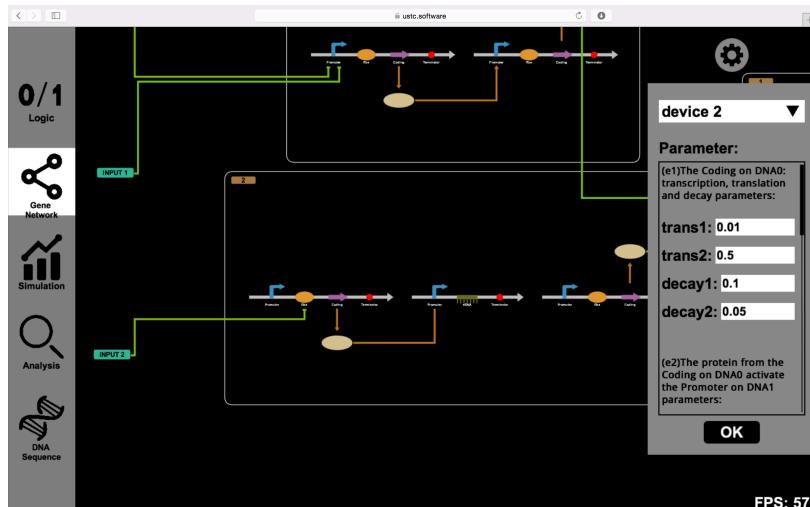


Figure 4: Parameter Manipulation View

You can modify every parameters used in the simulation, including transla-

tional and transcriptional parameters, regulational parameters and so on. And the kernel of *BioBLESS* will take these parameters as the input data of the simulation. Every parameter has a default value. If a parameter remains unmodified, the default value will be taken.

- To show the parameters list, click the gear button on the right of the canvas, click to open the drop-down menu, click the gate you want. Then the parameters list will be displayed.
- To alter the simulation parameters, open the parameters list using the above sequence, select the parameter you want to alter, type in a new value.

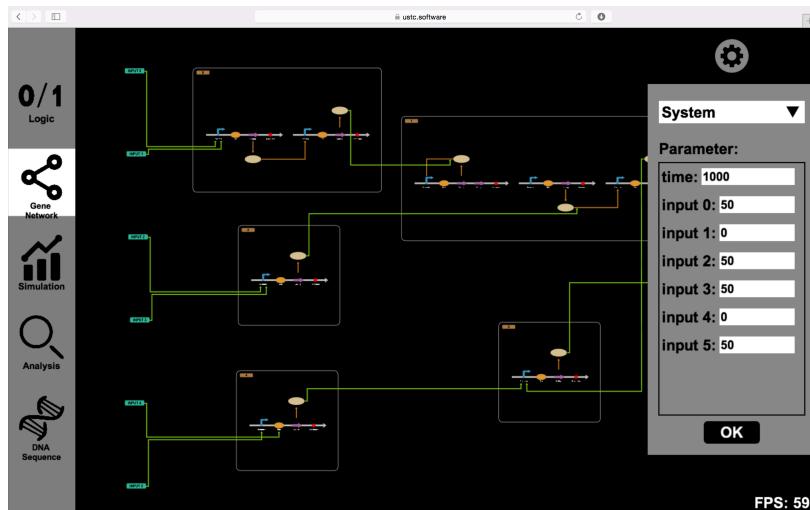


Figure 5: System Parameter View

Apart from the parameters describing the chemicals interaction, other parameters such as the total simulation time and the input chemicals concentration are needed to carry out the simulation. These parameters are also inputted in this scheme.

- To set the simulation time, click the gear button on the right of the canvas, click to open the drop-down menu, click the item *system*, type in the simulation time.
- To set the input chemicals concentration, click the gear button on the right of the canvas, click to open the drop-down menu, click the item *system*, type in the corresponding input concentration.

Up to now, you can use *BioBLESS Simulation* module to simulate the system defined above in a abstract chemical interaction style, in which the chemical species are considered as abstract substance. But you can also give

every part of the DNA sequence a concrete meaning by selecting one real part in iGEM BioBrick database. This will benefit the **DNA Sequence** module to be able to output the DNA sequence of our design.

- To fill the blank part using BioBrick database, click the *part* you want to fill, type in the BioBrick information to search in the BioBrick database. Then click the *BioBrick* to implement the fill.
- To change the filled part, click the *part* you want to change, type in the BioBrick information to search in the BioBrick database. Then click the *BioBrick* to implement the change.

You also can zoom in and out to make a more detailed and overall view of the current gene network configuration.

- To zoom in, scroll up the mouse wheel at any position on the canvas.
- To zoom out, scroll down the mouse wheel at any position on the canvas.

### 2.3 The **Simulation** Module

The **Simulation** module accepts the parameters in **Gene Network** module and passes them to the simulation kernel of **BioBLESS**. Using the Gillespie Algorithm, the **BioBLESS** kernel simulate the system stochastically.

- To trigger the simulation, click the *simulate* button on the left of the canvas.

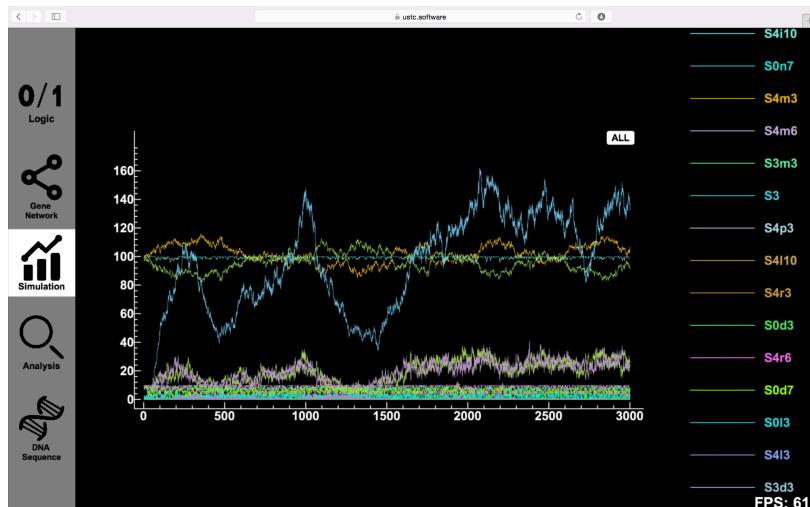


Figure 6: Simulation View

The simulation results will be sent form **BioBLESS** kernel to your computer immediately. By default, the time evolution of all species is displayed on the canvas. The following functions are useful when observing the simulation result.

- To show a specific molecule, click the corresponding *legend* on the right of the simulation result.
- To zoom in, scroll up the mouse wheel at *any position on the canvas*.
- To zoom out, scroll down the mouse wheel at *any position on the canvas*.

## 2.4 The *Analysis* module

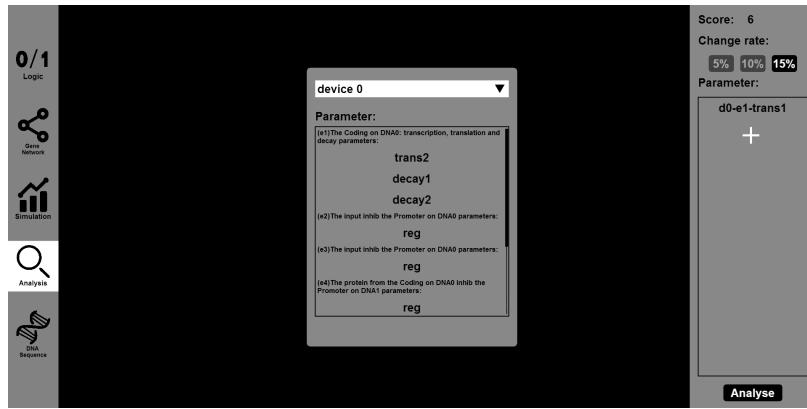


Figure 7: System Analysis View

The *Analysis* module provides users with a way to analyse the stability of the system constructed in previous section. In this module, you choose a set of parameters to be tested and then decide the fluctuation range in percentage. The *Analysis* module reads your setup and alters the parameters value. Each value is taken as the information for an independent simulation (which means that *BioBLES* tests the stability with respect to every parameter independently). Then the *Analysis* module outputs the result.

- The *score* of the system using a archived score function is printed on the right of the canvas. The score is small if the system is relatively more stable.
- To add a parameter to be tested, click the *+* on the right of the canvas, and then click the *parameter name* to open the drop-down menu.
- To trigger the analysis, click *OK* button on the right of the canvas.

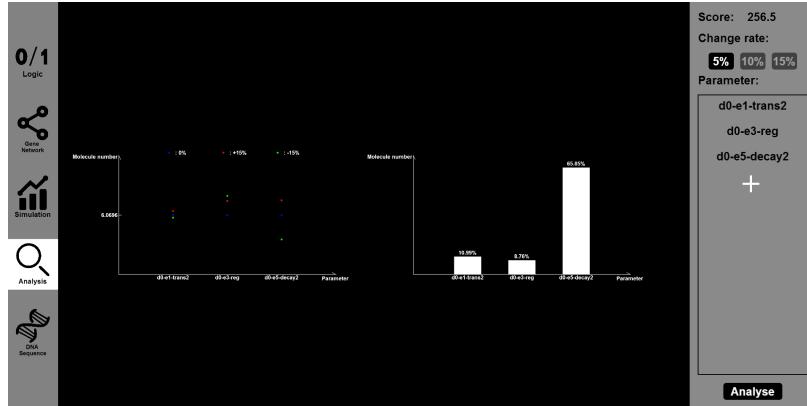


Figure 8: Analysis Result View

The result of the [Analysis](#) will be displayed in 2 graphics. The left one shows the last-30%-time-averaged output value relative to the original output and the right one shows the last-30%-time-averaged output value change occurring in the parameter fluctuation relative to the original value.

## 2.5 The [DNA Sequence](#) Module



Figure 9: DNA Sequence View

The [DNA Sequence](#) module generates the DNA sequence of the system designed. If the simulation result satisfies the user's intended logic feature, this module can serve as the reference of the first step for wet-lab synthesizing.

- To copy the sequence, mark the part you want to search, release the mouse button.

### 3 About Developers

If any problem arises, please contact us in the following ways.

- GitHub: <https://github.com/igemsoftware/USTC-Software2015>
- E-Mail: [igemustc2015@gmail.com](mailto:igemustc2015@gmail.com)
- Facebook: @USTCSoftware
- Address: *East Campus, USTC, No.96 Jinzhai Rd., Baohe Distr., Hefei, Anhui, P.R.C.*