

Principles of Synthetic & Systems Biology
Agricultural & Biological Engineering
West Lafayette, IN 47907

To: Dr. Kevin Solomon

From: Designer BAAKteria (Katie Atherton, Archana Kikla, Barbara McAnulty, Adrian Ortiz-Velez)

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Subject: TinkerCell Software Review

TinkerCell is a CAD software tool for synthetic biology that incorporates visual design and code. From the built-in library, the user can choose parts and connections to build biological systems with user-specified quantitative parameters to customize rates, concentrations, etc. Parts include small-scale items like a ribosome binding site or an enzyme as well as large-scale parts like a cell or even a microscope. A built-in library of commonly-used biological inputs includes activation, repression, allosteric inhibition, and even a (de-)phosphorylation cycle. Expected outputs are clean graphs produced from a timed running of the constructed model.

TinkerCell is a graphical user interface that hosts C-based programming languages such as Python. Plug-ins and module files are stored in the repository, tinkercellextra.sf.net. TinkerCell API uses C data structures that don't return in Python or Octave, but are still available to the user through functions named "toTC" and "fromTC" to convert them to the preferred language. TinkerCell supposedly can connect with RegulonDB, an external database. Unfortunately, the software is not successfully connecting to parts databases which would aid in modeling realistic behavior of parts, systems, devices, and chassis. As such, the user must manually input the parameters and know how parts fit together in order to make up for this failure.

One example of a common biological system being represented in TinkerCell is the repressilator. Drawn in TinkerCell, Figure 1 shows X repressing Y, which represses Z, which completes the cycle to repress X. Each gene circuit is made of a promoter, repressor binding site, ribosome binding site, coding region for a monomer, and finally a terminator. The rates associated with each building block are customizable as shown in Appendix 1 Figure 2. Double clicking on the repression lines brings up Appendix 1 Figure 3, which details the mechanism by which repression occurs--via a monomer binding to a repression binding site. Some TinkerCell features, such as the "empty" circles with slashes are shown in Appendix 1 Figure 3 at the left and right to indicate nothing else exists in that space to interact with this repression system.

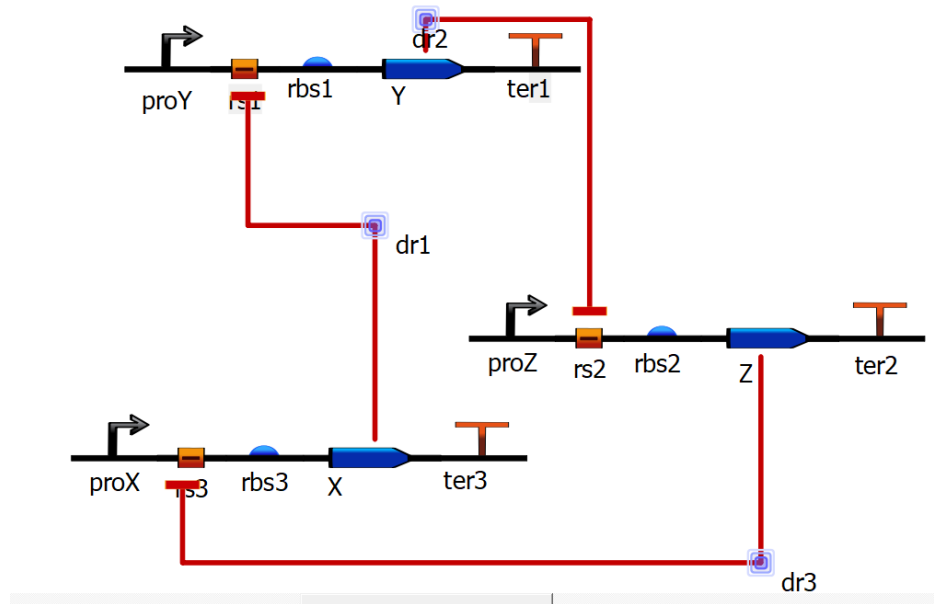


Figure 1: Repressilator in TinkerCell

TinkerCell's limitations include no longer being developed and being unable to open on a Mac machine. Even when plug-ins like Python, Octave, and Ruby are downloaded, the software often fails to initialize and interact with them. The parts library is comprised of general elements, which require manual input of parameters in order to create an accurate part in the system. When running the software, there is no indication of when the program begins or ends. In general, its graphical user interface can be improved to make it easier to use and understand.

Given TinkerCell's current state, recommended use for this is during the preliminary steps of design. This tool would be most useful in situations where the user knows and understands the different components their parameters of their system. Once an idea for a gene circuit is drawn or a series of logic gates are hypothesized, this would be an appropriate tool to translate the initial idea into general biological parts, devices, systems, and chassis. Since this hierarchical design is a core part of this tool, visualization with this tool is quite good. On the other hand, development has stopped and tools associated with TinkerCell do not load appropriately anymore so the ability to do the calculation have not been kept up with. Because of lagging development of the TinkerCell, the model can be inaccurate, but general trends align with expected trends. TinkerCell is also useful for any of the pre-loaded biological models like feed forward loops and a (de-)phosphorylation cycle. All in all, TinkerCell is best used under preliminary design to visualize gene circuits and obtain an initial behavior characteristics.

Appendix 1: Supplemental Figures



Figure 2: TinkerCell Quantitative Parameters

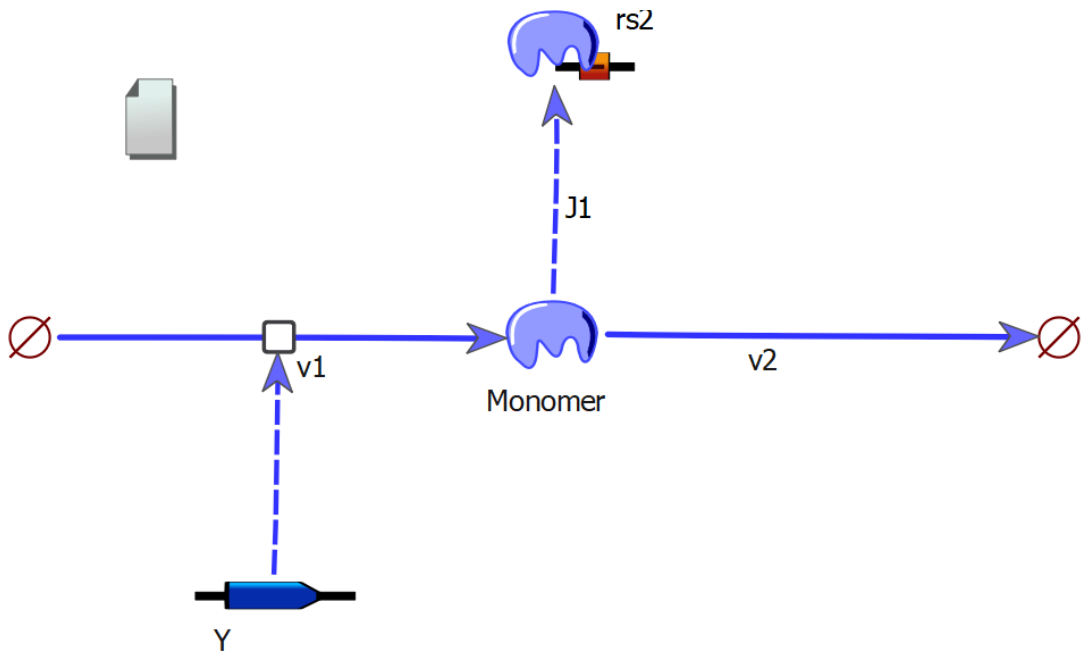


Figure 3: Repression Mechanism

Appendix 2: References

- Chandran, D., Bergmann, F.T., Sauro, H.M., (2009). TinkerCell: modular CAD tool for synthetic biology. *Journal of Biological Engineering* 3(19). doi: 10.1186/1754-1611-3-19
- TinkerCell Repository. Tinkercellextra.sf.net. Accessed 26 Sept 2018.
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<https://docs.google.com/document/d/1cYKSnAE3r0x6HBNJzsR1UUgCNc7n2kYGoFUYUgtT5C8/edit#heading=h.efcb844718ac>. Accessed 26 Sept 2018.