What is TinkerCell?

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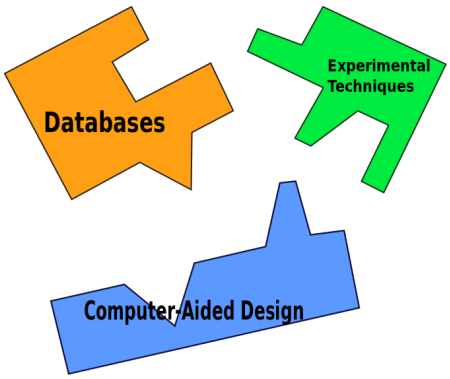
Computer-aided design in Synthetic Biology

TinkerCell is a Computer-Aided Design (CAD) tool for synthetic biology. Since synthetic biology is a rapidly evolving field, here are the issues which were taken into consideration when designing TinkerCell:

- modeling techniques in biology are still at a developmental stage
- experimental techniques are constantly evolving, especially automation and directed evolution methods
- databases of biological components are still maturing

In summary, TinkerCell is designed with the anticipation that the future of synthetic biology will be an intricate interplay between a variety of experimental techniques, databases that store results from experiments, and mathematical models explaining different aspects of the experiments.



The use-case of the *ideal* CAD program would be like this:

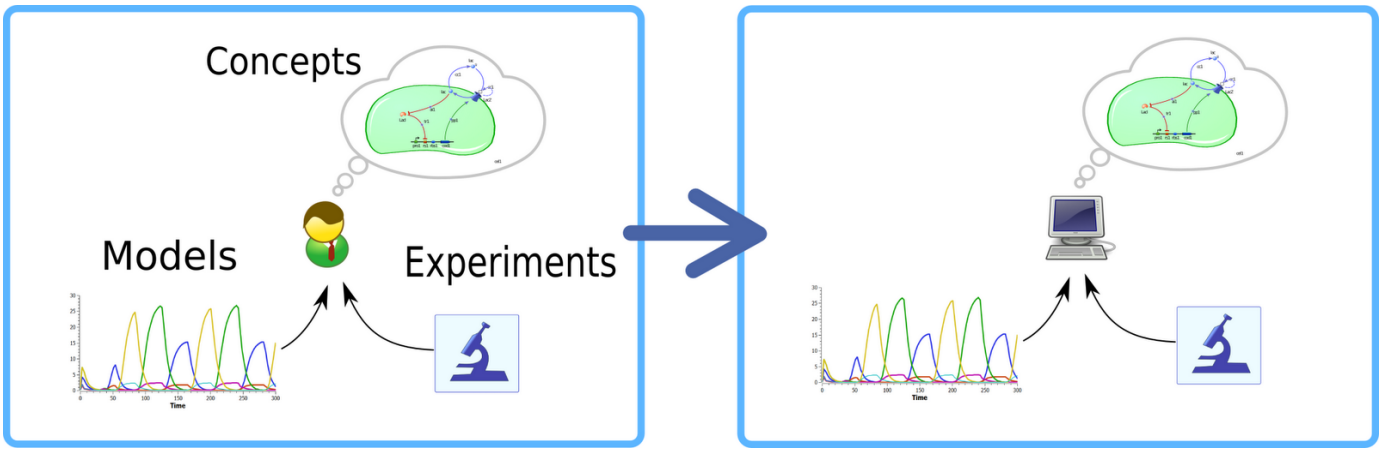
step 1: user *draws* a biological system
step 2: user performs some *analysis*
step 3: go back to step 1 if analysis is not satisfactory

The *analysis* step can potentially include:

- mathematical analysis of non-linear systems
- stochastic simulations, structural analysis, and other methods from systems biology
- prediction of evolutionary trajectories for directed evolution
- analysis and optimization of the DNA sequence
- database look-up to find suitable components
- generate different versions of the same design
- load experimental data from database(s) and relate them to the diagram
- ...more...

It is too much to have all of these functions in TinkerCell from the start. So TinkerCell uses a flexible plug-in framework, which will allow others to contribute new functions to TinkerCell. The plug-ins can be written in C, C++, Python, or Octave. Other languages, e.g. Java, might also get added to this list.

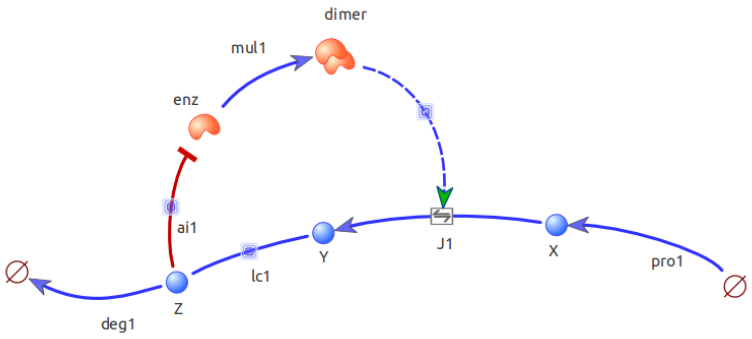
The basic idea behind TinkerCell is to represent a diagram that is detailed enough so that it can be mapped to models or experimental results. A human researcher is able to connect models and experiments because they are able to link them using a conceptual understanding of the system. TinkerCell enables that capability in software.



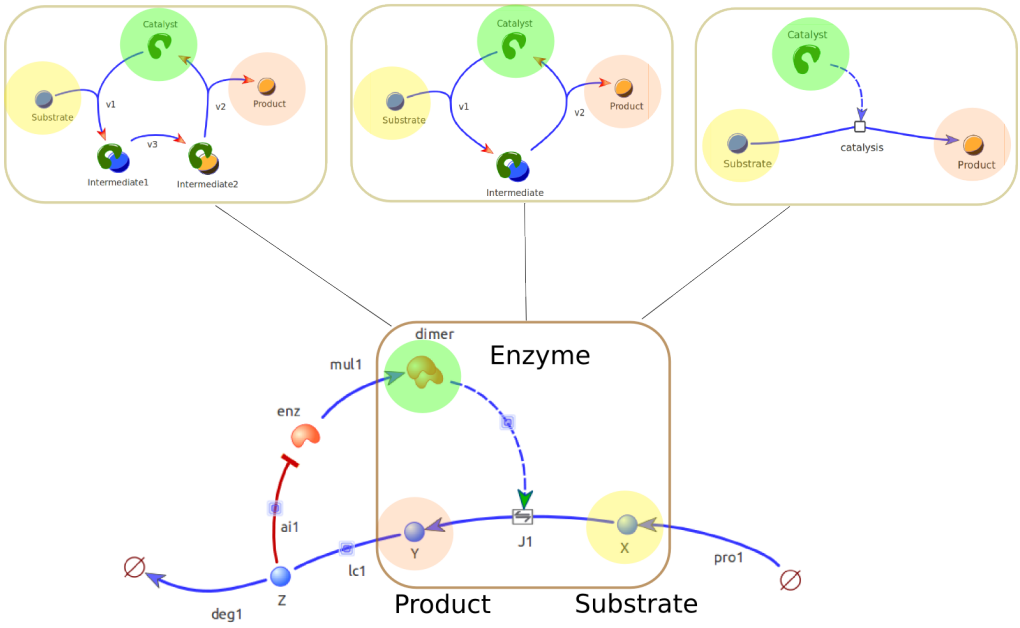
Abstract yet detailed diagrams

It is not entirely correct to provide a single mathematical model for a biological system because one mathematical model is just one hypothesis. There can be multiple hypotheses for the same system. TinkerCell distinguishes a “model” from a “diagram”.

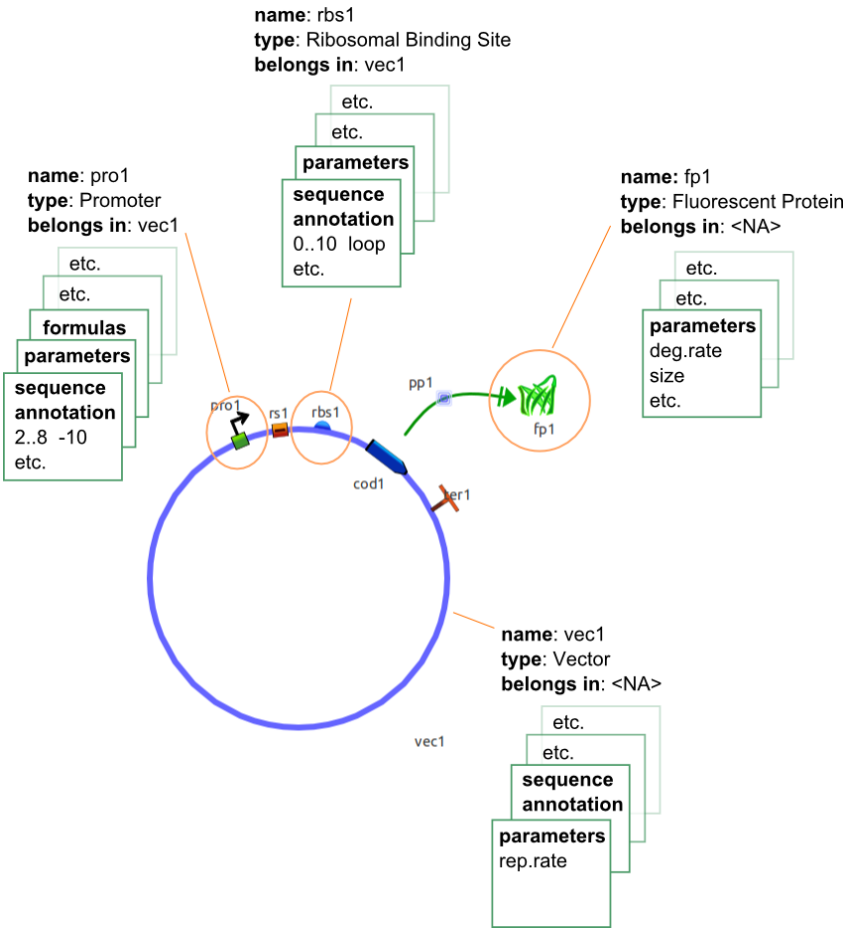
While TinkerCell diagrams are very abstract, they also contain all the details needed for different types of analysis. A diagram is not a model itself, but it has enough information for generating one or more models. For example, here is an abstract diagram.



TinkerCell is modular, meaning that each process in the above diagram can consist of subprocesses. In the example diagram above, the enzyme catalysis process has processes within it. The inner-processes can be changed without changing the outer diagram. The illustration below shows how the subprocesses are mapped to the main diagram by identifying the “types” of each component.



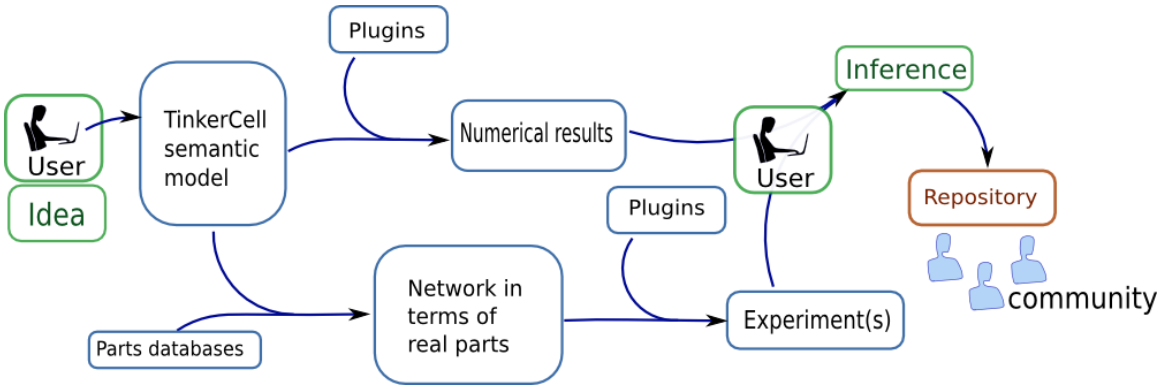
Within each component in the diagram, TinkerCell stores numerous data tables. Examples of data tables include parameters, text attributes such as sequence annotations, and equations. Each component also has a “family” which indicates the type of component it is.



Using the type of each component and their data tables, TinkerCell plug-ins perform different types of analysis. For example, a database-lookup plugin can identify whether a component is a promoter or coding sequence.

Long term goals

The long term goal of TinkerCell is to become one of the key applications involved in efficient engineering of biological (cellular) systems. The way this will work is by connecting TinkerCell to lab automation tools. In this situation, users would draw a system in TinkerCell. Some TinkerCell plugin would send the information to a remote robot. When the results from the experiments return, another TinkerCell plugin would automatically recommend the models to use based on the experimental evidence. In order to enable this pipeline, it is important to represent the initial model is a generic yet detailed format; existing software tools cannot do this, which is why one of the many reasons why pipe is not possible at present.



Current analysis capabilities

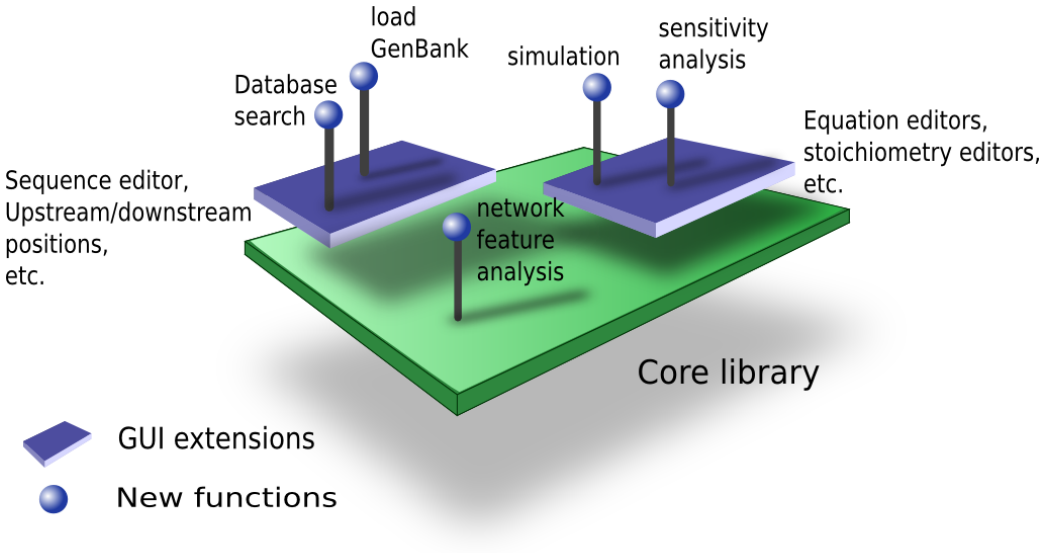
- deterministic simulation (using COPASI)
- stochastic simulation (using COPASI)
- steady state computation (using COPASI)
- jacobian computation (using COPASI)
- eigenvalue computation (using COPASI)
- exact stochastic simulation (using COPASI)
- tau-leap based stochastic simulation (using COPASI)
- hybrid simulation (using COPASI)
- stoichiometry matrix structural analysis (using libStructural)
- analysis of model assumptions, such as equilibrium assumptions
- parameter scan (Monte Carlo and steady state analysis)

TinkerCell is for the community

The purpose of TinkerCell's plugin interface is to welcome contributions from the community. Additionally, the TinkerCell source code is open-source (BSD) and the application itself is free of charge. All this is intended to make TinkerCell open to the community.

TinkerCell has a plugin interface that allows anyone to write code in C++, C, Python, Octave, or Ruby programming languages. The new code will appear as a button to all other TinkerCell users, making it convenient for anyone to distribute new methods. Plugins written in C++ can add new GUI features (e.g. equations editors, sequence editors) and provide new C, Python,

and Octave functions. Plugins written in C, Python, and Octave can use those GUI features to provide new functions (e.g. simulation, database search).



TinkerCell models are composed of “modules”, or sub-models. These sub-models can also be constructed and shared between users.