Introduction

Synthetic genetic circuits created by synthetic biologists have yielded exciting applications. However, these circuits are often difficult to engineer, requiring months to research, design, build, and test each individual genetic device involved in the circuit. The UCSD Software iGEM team will address this challenge by creating a web-tool that leverages existing genetic devices to lower the barrier of entry into the field of synthetic biology. This web tool consists of three parts: a database of genetic parts, a network-based search algorithm, and a web application for visualizing the data.

Database Schema
The database is structured such that it leverages Petri-Net Modeling to represent the interactions between chemical species in genetic circuits. Additionally, we used atomization to refine relationships between genetic circuits and related concepts. Finally, we also used chemical specificity to capture the mechanism through which genetic expression is governed. The attached figure is a representation of our database schema.

Network Analysis

We quantified the increase in genetic circuits by comparing the input-degree and output-degree distribution of the input circuitry (circuits contained in individual publications) to the integrated database circuitry. We then performed a topological motif search using CytoKavosh to further demonstrate the expected increase in potential genetic motifs.

Results

Our search algorithms return a sub-network of paths from the input species sets to the output species sets through the SBiDer Network. Because each path is calculated individually, each path through the sub-network can be highlighted.

SBiDer has two search algorithms based on multiple breadth first searches (BFS). Each algorithm creates paths from a list of input species (AND and OR logic accepted). The first algorithm, Linear Successional Activation Search (LSAS), generates a sub-network of operon paths where in each operon path, the output species of a preceding operon produces all of the required input species for the succeeding operon. For instances where multiple operons are needed produce all input species for the next operon, we use Non-Linear Successional Activation Search (NLSAS). NLSAS has a unique traceback algorithm from the output species on a sub-network created by LSAS to capture this non-linearity.

SBiDer: Synthetic Biocircuit Developer

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Functionality

Users can submit a circuit topology in terms of the desired input species and output species of the circuit with logical operators such as AND and OR (eg. lara AND arac = gfp). Users are provided a network visualization of the circuit topology as well as a table of useful information about individual plasmids and species.

Future Directions

- Integrating with NDEx. NDEx allows for more community development of our network.
- As a result of OWL (Web Ontology Language) integration, SBiDer can represent the biological reality of synthetic biology in a much more complex, sophisticated, and realistic manner.
- Factor graphs have been considered to help improve our modeling accuracy in dynamic systems.

References


SBiDer was developed off of CyNetShare, a simple web application to share CytoscapeJS generated network visualizations as interactive web-based views. SBiDer was developed using modern web technology technology such as AngularJS and Bootstrap CSS.

On the server end of the tool, we leveraged popular tools and languages for scientific computing such as Python, Java, and SQL.

SBiDer utilizes and extends the web-application architecture used by the Owl Datasheet generator project from iGEM 2013.

Software

The network structure is encoded using the SBML Level 3 format with its extension for qualitative networks. Images of devices are provided by SBOL (Systems Biology Ontology Language) development of our network.

Algorithms

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Network

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Web Application

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Database

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