Towards Integration of "Cello", the Computer-Aided Design Platform for Genetic Circuits, into KBase.

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http://kbase.us/ , **https://narrative.kbase.us/#appcatalog/module//cello** , **http://cidarlab.org/cello/**

Project Goals: Cello is a suite of tools for biological circuit design and functional prediction created by the Voigt and Densmore Labs. Our objective is to allow biologists to easily design and analyze custom genetic circuits using this framework while also leveraging the interlinked resources within the DOE Systems Biology Knowledgebase to support advanced information and modeling capabilities for gene and organismal function. KBase will also ultimately enable sharing of the design, build, test and learn processes that are transferable and generalizable across applications. We seek to increase the efficacy of biological design procedures to reduce the number of experimental implementation iterations necessary for product optimization.

Advances in DNA reading and writing technologies are driving the adoption of new paradigms for engineering of biology. One of the current challenges is to be able to decide which genetic parts must be rewired to achieve higher production of desired bioproducts. To do this, there must be standards for rapid design and testing of custom gene regulatory systems. Therefore, this project aims to develop a smart platform in which engineers can synthesize and test their circuits *in silico* within one virtual location and test the circuits in an environment that allows leverage of diverse information and models of diverse biological function in variable environments through multiple programs. In addition, engineers will avoid having to deal with the laborious process of managing the configuration of the program on their personal computers. Toward this goal, we used the KBase Software Development Kit to add the Cello biocircuit design software into the system and established the framework for design and analysis of synthetic genetic circuits.

Cello is a computer-aided-design program created by CIDAR labs (Boston University), the Synthetic Biology Center at MIT, and the Biosystems and Biomaterials Division at the NIST. The program applies the concept of Circuit-Design Automation from computer circuit design to genetic parts in living organisms. It uses the modularity of transcription factors such as repressors and promoters to control the gene regulatory system. One of the inputs to the program is a set of instructions which lists relationships between certain promoters and their related outputs (e.g. the presence of compound A implies Gene B is being expressed, the presence of compound B means Gene C is not being expressed); the other inputs are the

promoters and outputs themselves. This information is used to generate the instructions for a plasmid which would realize these relationships and predict its operation in the target organism.

Now that Cello is packaged in KBase, users can design genetic circuits that are predicted to express target pathways under different environmental conditions, and produce and visualize a plasmid design to implement this circuit. While still under development and being optimized for integration with the rest of KBase capabilities, this brings a powerful design tool into a powerful environment for everyone to use and build upon.

Ultimately, this research will enable predictable and dynamic control of multiple economically important traits such as growth on plant-derived feedstocks, tolerance to toxic byproducts and other stresses, and production of multiple and complex target molecules. By deploying these new biological engineering platforms for non-model microorganisms with potential industrial relevance, this project will advance the DOE's mission to develop sustainable biofuel production from renewable sources.

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