

Standard Enabled Model Generator for Genetic Circuit Design

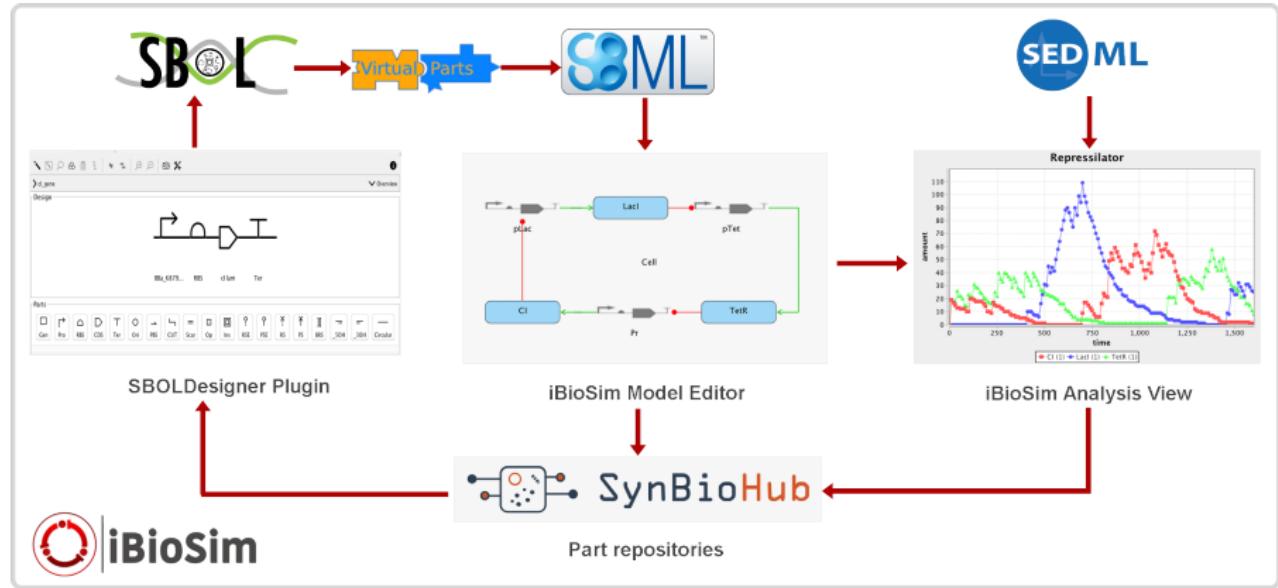
Göksel Mısırlı ² Tramy Nguyen ¹ James McLaughlin ²
Chris Myers ¹ Anil Wipat ²

University of Utah ¹

Newcastle University ²

9th International Workshop on Bio-Design Automation
August 9th, 2017

Recap



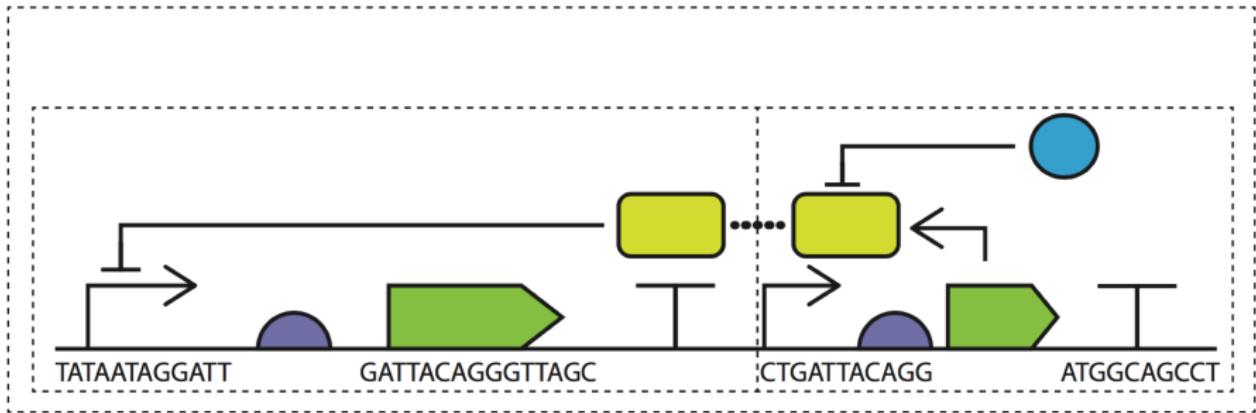
Motivation

- Large amount of information is being produced about biological parts that can be used to build complex designs.
- Computational modeling *in silico* are created manually to predict the behavior of designs implemented *in vivo* or *in vitro*.
- Models in these designs have functional relationships and design constraints between parts that can be used for simulation.
- Computational models can be created by extracting knowledge about the DNA components and their interacting entities.

Data Standards

- Important to facilitate design automation.
- Pass information between different computational tools.
- *Synthetic Biology Open Language* (SBOL): an **open standard** for representing *in silico* **biological designs**.
- *Systems Biology Markup Language* (SBML): an **open standard** to describe the behavioral models of **biological systems**.

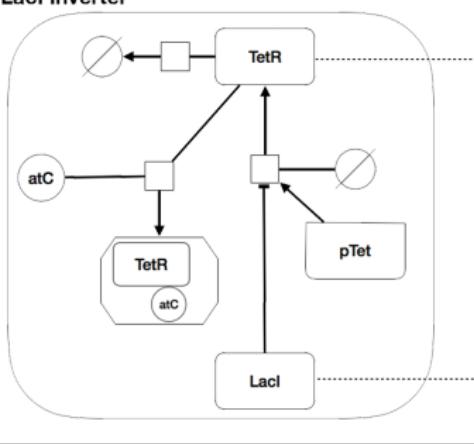
Synthetic Biology Open Language (SBOL)



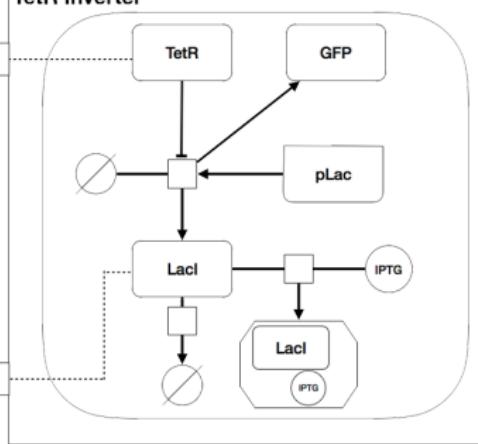
Systems Biology Markup Language (SBML)

Genetic Toggle Switch

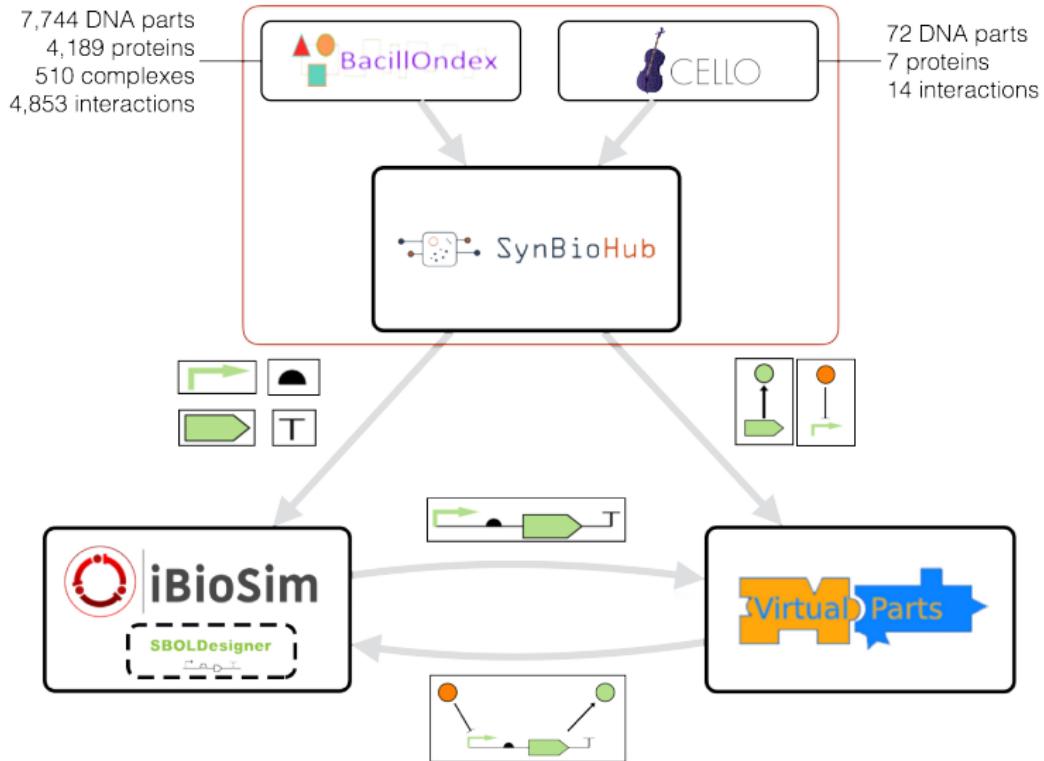
LacI Inverter



TetR Inverter

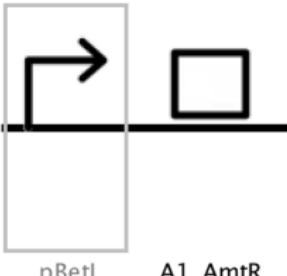


Data Integration



Genetic Circuit Construction

Design



Inverter1

Select a part from registry

Registry: Living Computing Project (<https://synbiohub.p...iology.org>)

Part type: DNA

Collection: Cello_Parts_collection

Part role: Pro (Promoter)

Role refinement: None

Import with subcomponents

Filter parts

Matching parts (7)

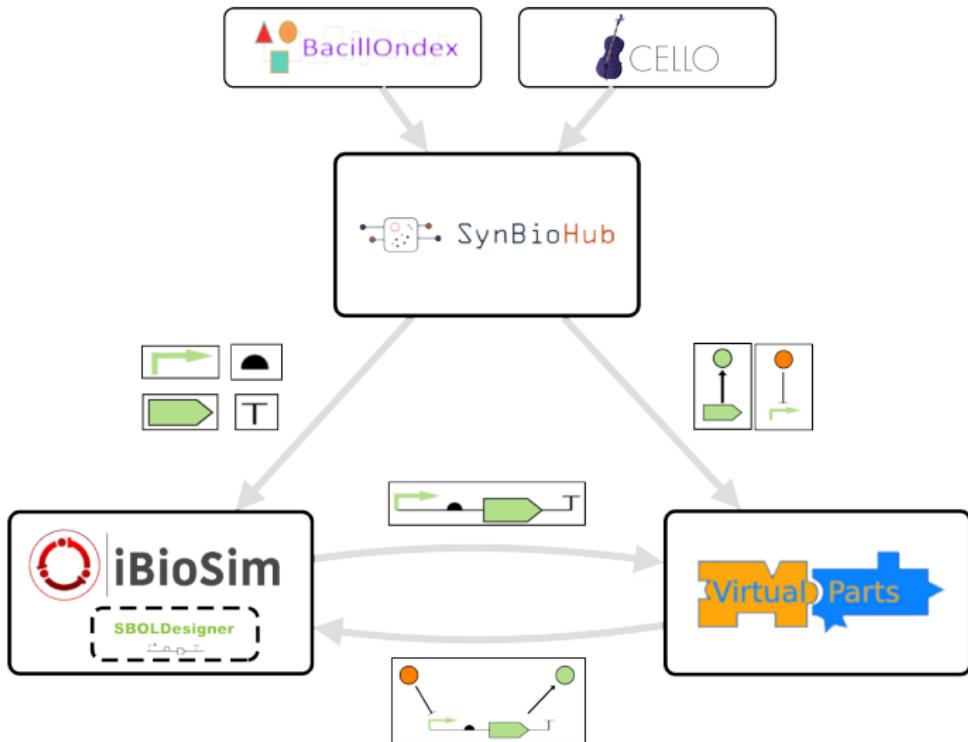
Type	Display Id	Name	Version	Description
Part	pBetI	pBetI	1	
Part	pAmrR	pAmrR	1	
Part	pAmrB	pAmrB	1	
Part	pHyBR	pHyBR	1	
Part	pSrpR	pSrpR	1	
Part	pBM3R1	pBM3R1	1	

Options Cancel OK

Parts

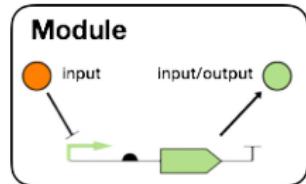
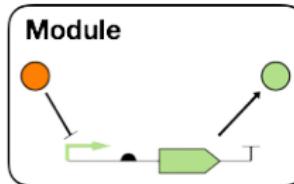
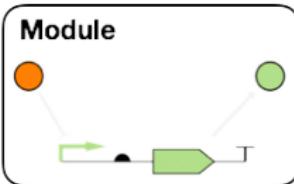
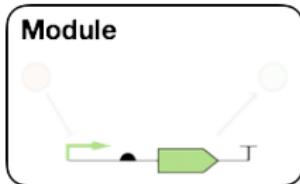
Gen Pro RBS CDS Ter Ori PBS CUT Scar Op Ins RSE PSE RS PS BRS _SOH _3OH Circular

Virtual Parts API



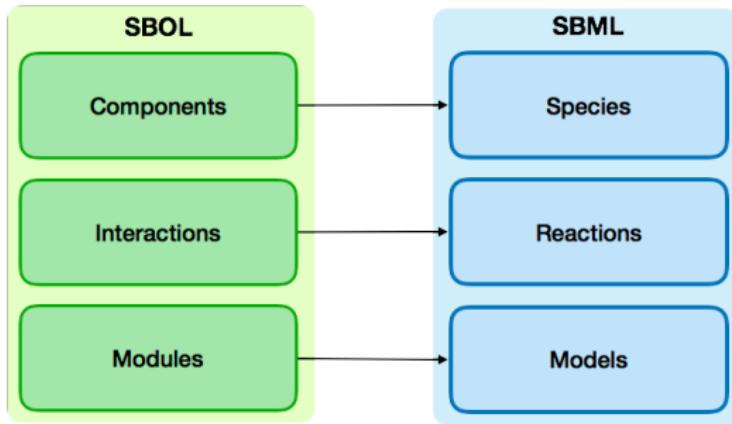
Enriching SBOL Designs Process

- Create a Module for each transcriptional unit in the design.
- Add to the Module biological molecules that interact with the DNA components.
- Adds Interactions between the components.
- Add directionality to the components.
 - Mark as input components for biological molecules that are not produced by the transcriptional unit.
 - Mark as input/output components for biological molecules that are produced by the transcriptional unit.

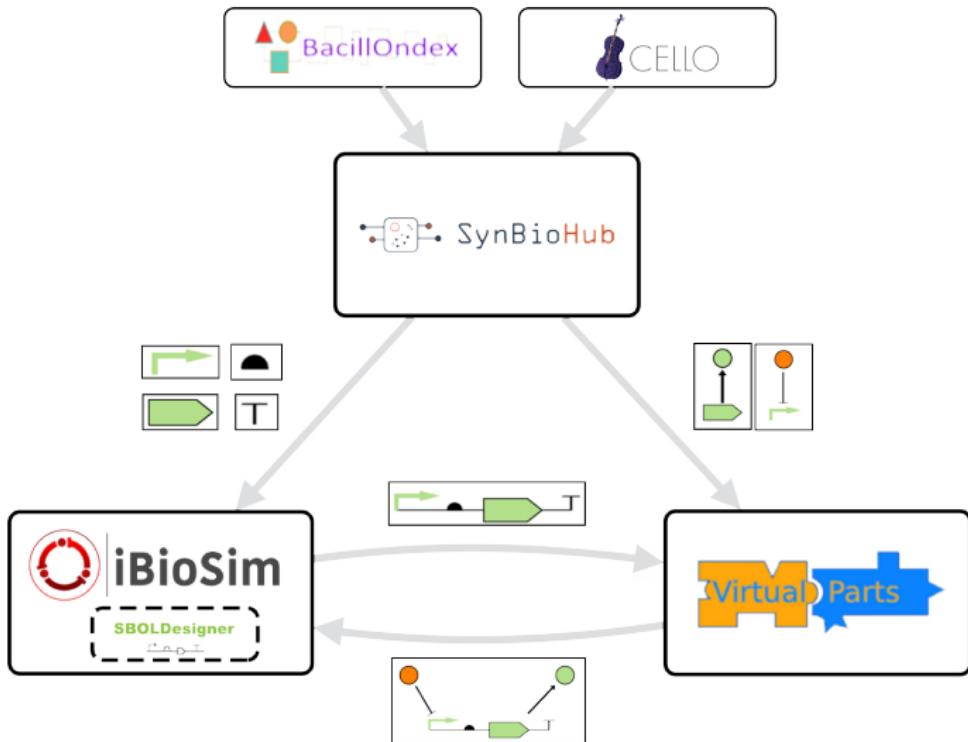


Deriving Dynamic Models

- SBOL to SBML conversion is applied to verify the behavior of a design.
- Ontology terms are used to translate components between standards.



Model Generation Workflow



Demo

Conclusion

- Abstract detail of complexity when dealing with computation models.
- Ease process of designing circuits using DNA parts while benefiting computational modeling.
- Facilitates automation.
- Explore large design space of biological systems.
- Data standards such as SBOL and SBML is critical for connecting tools within this workflow.
- Future work is to retrieve parameter values as annotation from the output model of the VPR API.

Acknowledgements



Göksel Mısırlı



James McLaughlin



Chris Myers



Anil Wipat



The Engineering and Physical Sciences Research Council grant EP/J02175X/1.



The National Science Foundation under Grant No. CCF-1218095 and DBI-1356041.