

Synthetic Biology Open Language Applications

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SBOL Chair: Chris Myers (University of Utah)

SBOL Workshop

July 8, 2019

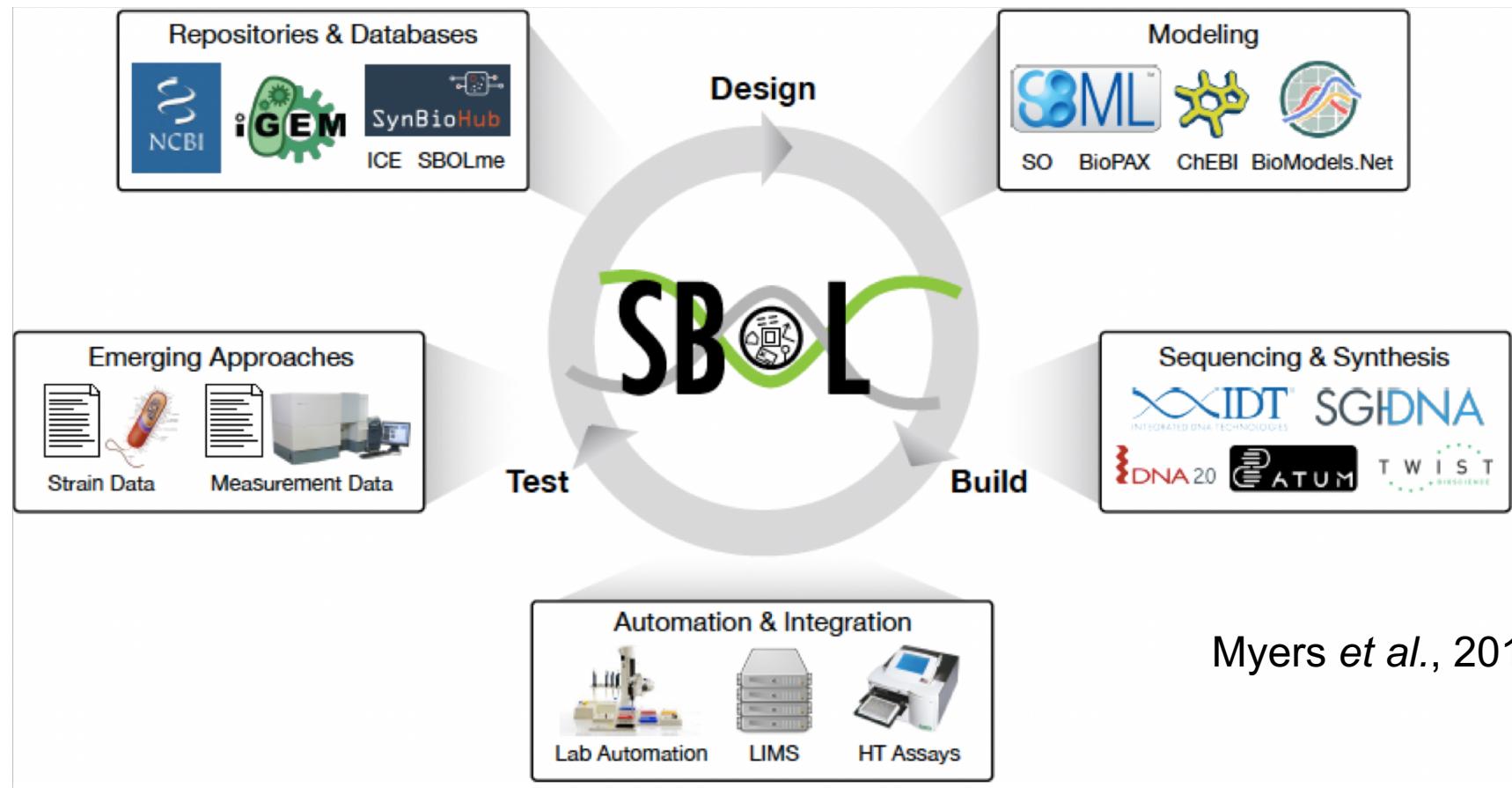


IWBDA 2019

July 8-10, 2019 · Cambridge, England

Slides were provided by Jacob Beal, Chris Myers and Anil Wipat
These slides were adapted and new slides were added by Göksel Mısırlı

Collaborating across different stages of (automation-assisted) synbio workflows



- Unambiguous **exchange** of information
- **Reuse** of information and existing tools
- **Extendible** data model to incorporate application specific data
- **Integrating** with existing technologies to **store, query** and **visualise** data

ACS Synthetic Biology has officially adopted SBOL as publication standard

- **SBOL Visual** is the recommended graphical notation for depicting genetic constructs
- **SBOL 2.0 Data Model** is the preferred format for nucleic acid sequences

ACS
Synthetic Biology

Viewpoint
pubs.acs.org/synthbio

Improving Synthetic Biology Communication: Recommended Practices for Visual Depiction and Digital Submission of Genetic Designs

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ABSTRACT: Research is communicated more effectively and reproducibly when articles depict genetic designs consistently and fully disclose the complete sequences of all reported constructs. ACS Synthetic Biology is now providing authors with updated guidance and piloting a new tool and publication workflow that facilitate compliance with these recommended practices and standards for visual representation and data exchange.



- Manuscript submission, review, and production process is linked to **SBOL-enabled repositories**
- Joint Bioenergy Institute (JBEI) has set up the initial repository

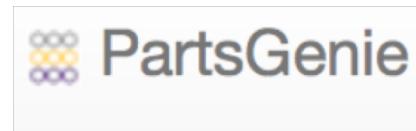
Applications



iBioSim



CELLO



Shortbol



Gene Designer

poolDesigner



DeviceEditor

SBOLDesigner



Applications - continued

APPLICATION	KNOWLEDGE MANAGEMENT	SEQUENCE DESIGN	CIRCUIT DESIGN	MODELING	VISUALIZATION	SBOL VISUAL	IM-PORT SBOL1	IM-PORT SBOL2	EX-PORT SBOL1	EXPORT SBOL2
Pigeon Visualizer					★	★				
DNAPlotlib					★	★	★	★	★	★
SBOLDesigner	★	★			★	★	★	★	★	★
ICE	★	★			★	★		★		★
j5		★		★		★	★	★		★
DeviceEditor	★	★	★		★	★	★		★	
Finch	★	★	★		★	★				★
Pool Designer		★					★	★	★	
Virtual Parts Repository	★		★	★		★	★	★	★	★
MoSeC		★	★						★	

Data Repositories: ICE



Search SEARCH Administrator

Create Entry ADD TO REMOVE MOVE TO EDIT DELETE EXPORT TRANSFER ACCEPT

Featured	64	Type	Name	Description	Status	Approve	Date
Personal	0	PLASMID	LCP_000117	pGOP35_pSB1C3-g13Op-minCMV-GFP-RBGpA The 2016 BostonU iGEM team designed a set of mutually orthogonal...	Complete		Dec 2, 2016
Shared	0	PLASMID	LCP_000116	pGOP30_pSB1C3-g8Op-minCMV-GFP-RBGpA The 2016 BostonU iGEM team designed a set of mutually orthogonal...	Complete		Dec 2, 2016
Drafts	0	PLASMID	LCP_000115	pGOP25_pSB1C3-g3Op-minCMV-GFP-RBGpA The 2016 BostonU iGEM team designed a set of mutually orthogonal...	Complete		Dec 2, 2016
Pending Approval	1	PLASMID	LCP_000079	pGOP110_pSB1C3-g13Op_mismatch_1bp_loc10-minCM... The 2016 BostonU iGEM team designed a set of mutually orthogonal...	Complete		Nov 28, 2016
	64	PLASMID	LCP_000078	pGOP90_pSB1C3-g13Op_3multi_24bp-minCMV-GFP-RB... The 2016 BostonU iGEM team designed a set of mutually orthogonal...	Complete		Nov 28, 2016
	0	PLASMID	LCP_000077	pGOP85_pSB1C3_g13Op-2-multi-24bp_minCMV_GFP_R... The 2016 BostonU iGEM team designed a set of mutually orthogonal...	Complete		Nov 28, 2016
	0	PLASMID	LCP_000076	pGOP23_pSB1C3_g1Op_min-CMV_GFP_RBG-A The 2016 BostonU iGEM team designed a set of mutually orthogonal...	Complete		Nov 28, 2016
	0	PLASMID	LCP_000074	pGEX108_pSB1C3_hU6_g6_SP-Cas9-gRNA-scaffold-RB... This part produces a guide RNA that pairs with an operator. This basi...	Complete		Nov 18, 2016
	0	PLASMID	LCP_000073	pGEX103_pSB1C3_hU6_g1_SP-Cas9-gRNA-scaffold-RB... This part produces a guide RNA that pairs with an operator. This basi...	Complete		Nov 18, 2016
	0	STRAIN	LCP_000072	Assembly #1 Recombinase_Level 1 Level 1 for assembly #1.	Complete		Nov 15, 2016
	0	STRAIN	LCP_000071	gfp_pich41276_gi MoClo level 0 part.	Complete		Nov 15, 2016
	0	STRAIN	LCP_000070	tp901p-ag-bxbip-gt-tp901p-tc-eg Level 0 part.	Complete		Nov 15, 2016
	0	STRAIN	LCP_000069	bfp-pich41258-de MoClo level 0 part.	Complete		Nov 15, 2016
	0	STRAIN	LCP_000068	bxbib-gt_cd MoClo level 0 part.	Complete		Nov 15, 2016



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Data Repositories: SynBioHub

The screenshot shows the SynBioHub homepage. At the top, there's a navigation bar with a logo, "SynBioHub", "Submit", "Login or Register", and a "Home" link. Below the header, the main title "SynBioHub" is displayed next to a central icon of a cell with DNA and protein components. A descriptive text block explains that SynBioHub is a design repository for biological constructs, enabling users to upload DNA and protein designs and search for existing parts. Three main functional sections are shown: 1) "Search for useful parts and designs" with a search bar and "Browse Design Collections" button. 2) "Upload your design for safekeeping" with a large upload icon and "Submit a Design" button. 3) "Share designs for publication or collaboration" with a share icon and "Manage Submissions" button.

- Supports storing and retrieving native SBOL and other related data
- Unified syntax and semantics via SBOL
- Data can be federated across multiple instances
 - A web of synbio registries
- Promotes data integration

McLaughlin *et al.*, ACS Synthetic Biology (2018)

Data Repositories: SBOLme

The screenshot shows the SBOLme repository interface. At the top left is the King Abdullah University of Science and Technology logo and the Computational Bioscience Research Center name. At the top right is the SBOLme logo and tagline. A navigation bar below has tabs for Query (selected), Catalog, Information, and About. The main content area contains a search form with dropdowns for 'Search for' (set to 'Compound') and 'Filter By' (set to 'Compound name or ID'). A value input field contains 'Pyruvate, C00022, ME_C00022'. To the right, a tooltip explains that the query can search by compound name or ID, mentioning KEGG and SBOLme IDs. Below the form are buttons for 'Search' and a dropdown for page size ('25'). A success message from 'Kuwahara et al., ACS Synthetic Biology (2017)' is displayed. At the bottom, a table shows the first result: SBOLme ID ME_R00006, KEGG ID R00006, and Name 2-acetolactate pyruvate-lyase (carboxylating).

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SBOLme
repository of **SBOL** parts for metabolic engineering

Query Catalog Information About

SBOLme is a repository of **SBOL 2.0-compliant** metabolic parts for metabolic engineering. Here, you can search for these biological parts from the SBOLme repository with convenient criteria for composing biosynthesis systems.

Search for

Compound

Filter By

Compound name or ID

Value

Pyruvate, C00022, ME_C00022

With this query, you can search for a compound by its name or its IDs. The acceptable IDs are the KEGG compound IDs and the SBOLme compound IDs.

Search 25

Page 1 of 1 results

SBOLme ID	KEGG ID	Name
ME_R00006	R00006	2-acetolactate pyruvate-lyase (carboxylating)

Kuwahara *et al.*, ACS Synthetic Biology (2017)

28,437 chemical compounds, 6,883 enzyme classes, 9,909 metabolic reactions, and 3,173,238 proteins from 3,908 organisms

Sequence Editor: Benchling

Projects

SynBioHub Transfers

NOTEBOOK INVENTORY NAME

A1_AmtR Last modified 2 days ago

AmtR Last modified 5 hours ago

Test Last modified 2 days ago

The Best Last modified 3 days ago

SEQUENCE MAP

The Best A1_AmtR aadA.ref pJ163mRm_EF pJ033mRm_EF

LINEAR MAP DESCRIPTION METADATA PDF

The Best (899 bp)

BlpI BstAPI MfeI FokI HpaII BspI NlaIII CviaII FatI KpnI BanI Acc65I

MlyI PleI HinFI DrdI AcuI BsmAI SmlI TspRI TscAI BtsIMutI XbaI BspMI BpuAI BglII PvuII XbaII BsaI BspMI BpuAI BglII PvuII BceAI PflBaeGI AluI BcoDI BfaI BsgI AmtR

100 200 300 400 500 600 700 800

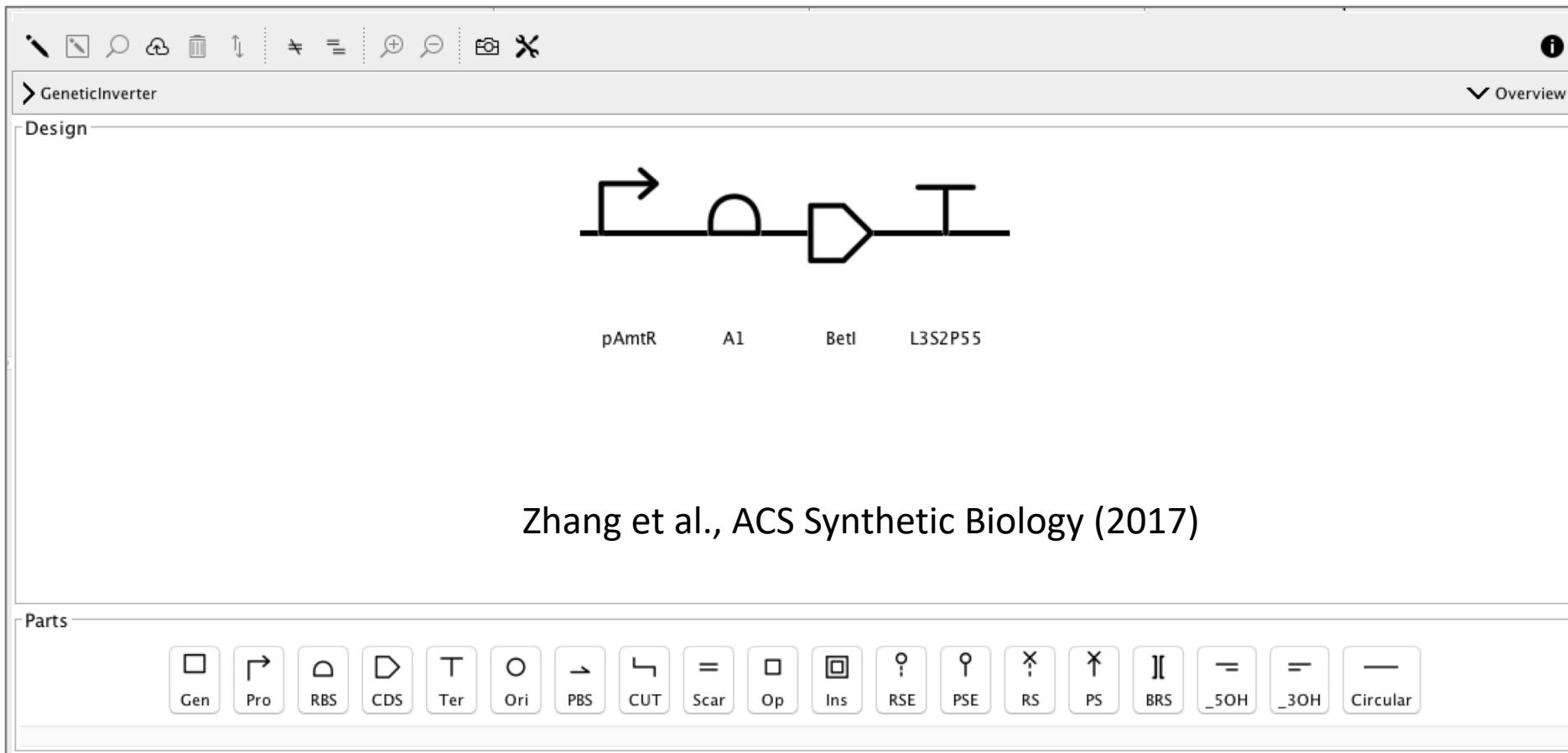
Linear Map: AmtR (899 bp) restriction sites: BlpI, BstAPI, MfeI, FokI, HpaII, BspI, NlaIII, CviaII, FatI, KpnI, BanI, Acc65I, MlyI, PleI, HinFI, DrdI, AcuI, BsmAI, SmlI, TspRI, TscAI, BtsIMutI, XbaI, BspMI, BpuAI, BglII, PvuII, BceAI, PflBaeGI, AluI, BcoDI, BfaI, BsgI.

SEQUENCE MAP: The sequence map shows the linear arrangement of restriction sites and promoter regions. The top panel shows the OR2-OR1 Promoter (green arrow) and BydvJ (grey arrow). The middle panel shows the BydvJ gene (grey arrow). The bottom panels show the A1 (purple arrow) and Amtr (blue arrow) genes. The x-axis represents base positions from 10 to 330.

Linear Map: The linear map shows the AmtR gene (899 bp) with its restriction sites. The x-axis represents base positions from 100 to 800.

BASES 899 ASSEMBLY WIZARD ▾ SPLIT WORKSPACE

Sequence Editor: SBOLDesigner



Zhang et al., ACS Synthetic Biology (2017)

Other sequence editors that support SBOL: DeviceEditor, J5, VectorEditor (JBEI), DNAPlotLib (MIT/UW/Bristol), Eugene (Boston), GenoCAD (VBI), BOOST (JGI), etc.

Circuit Design & Modelling: Cello

The screenshot shows the Cello web application interface. At the top, there are tabs for Cello, Verilog, Options, Results, and About. The user is logged in as 'myers'.

Verilog: A dropdown menu is set to "choose". Below it is the Verilog code for a module A:

```
1 module A(output out1,  input in1, in2);
2   always@(in1,in2)
3   begin
4     case({in1,in2})
5       2'b00: {out1} = 1'b0;
6       2'b01: {out1} = 1'b0;
7       2'b10: {out1} = 1'b0;
8       2'b11: {out1} = 1'b1;
9     endcase
10   end
11 endmodule
12
```

Inputs: A dropdown menu is set to "choose". Below it is a table with columns: index, name, low RPU, high RPU, and DNA sequence.

index	name	low RPU	high RPU	DNA sequence
1	pTac	0.0034	2.8	AACGATCGTGGCTGTGTTGACAA
2	pTet	0.0013	4.4	TACTCCACCGTTGGCTTTTCCC

Outputs: A dropdown menu is set to "choose". Below it is a table with columns: index, name, and DNA sequence.

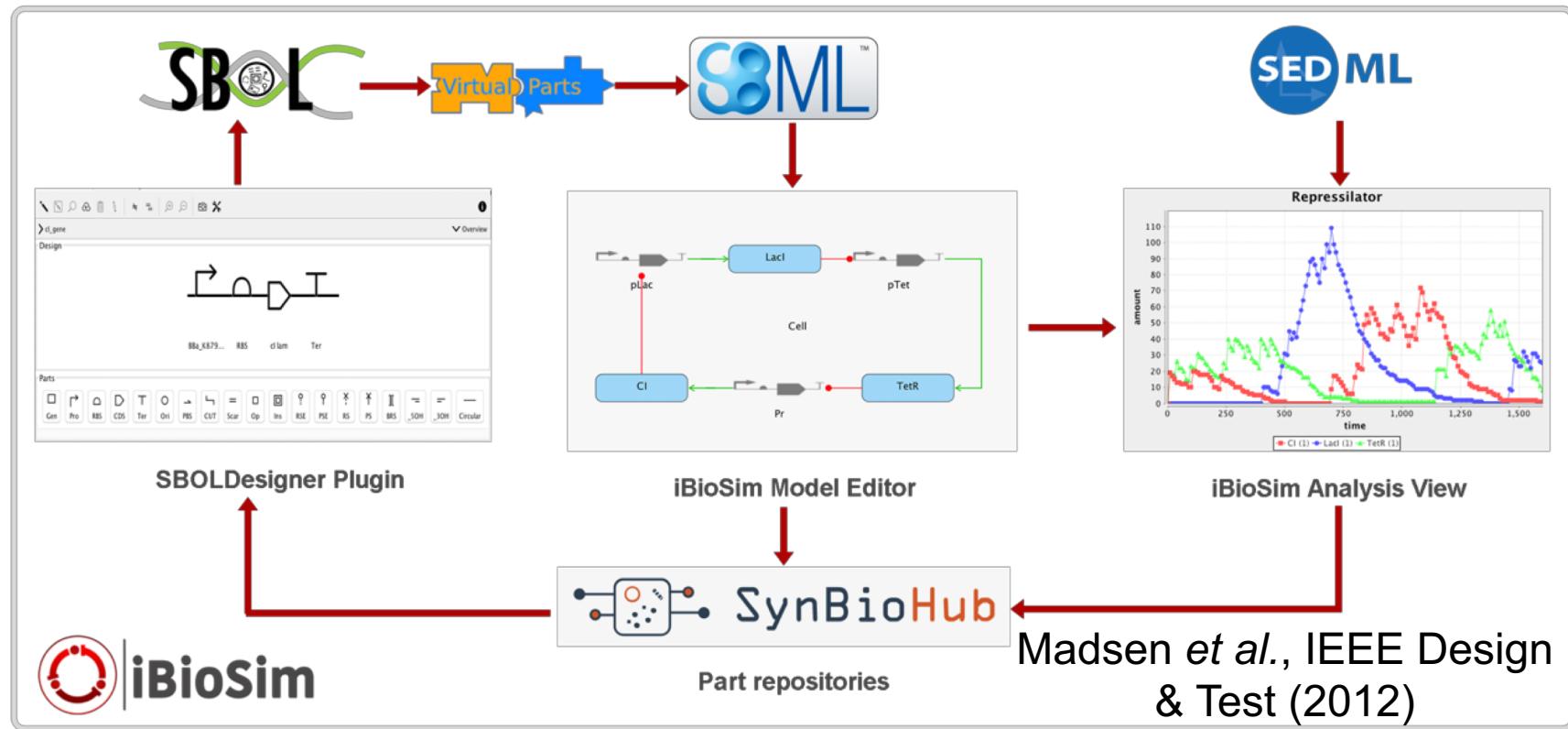
index	name	DNA sequence
1	YFP	CTGAAGCTGTCACCGGATGTGCTTCCGGCTGATGAGTCCGT

At the bottom left, there is a "design name" input field and a green "Run" button.

Nielsen *et al.*,
Science (2016)

- Compiles combinational designs described in Verilog into genetic circuits
- Uses a gate library of 2-input NOR gates and inverters

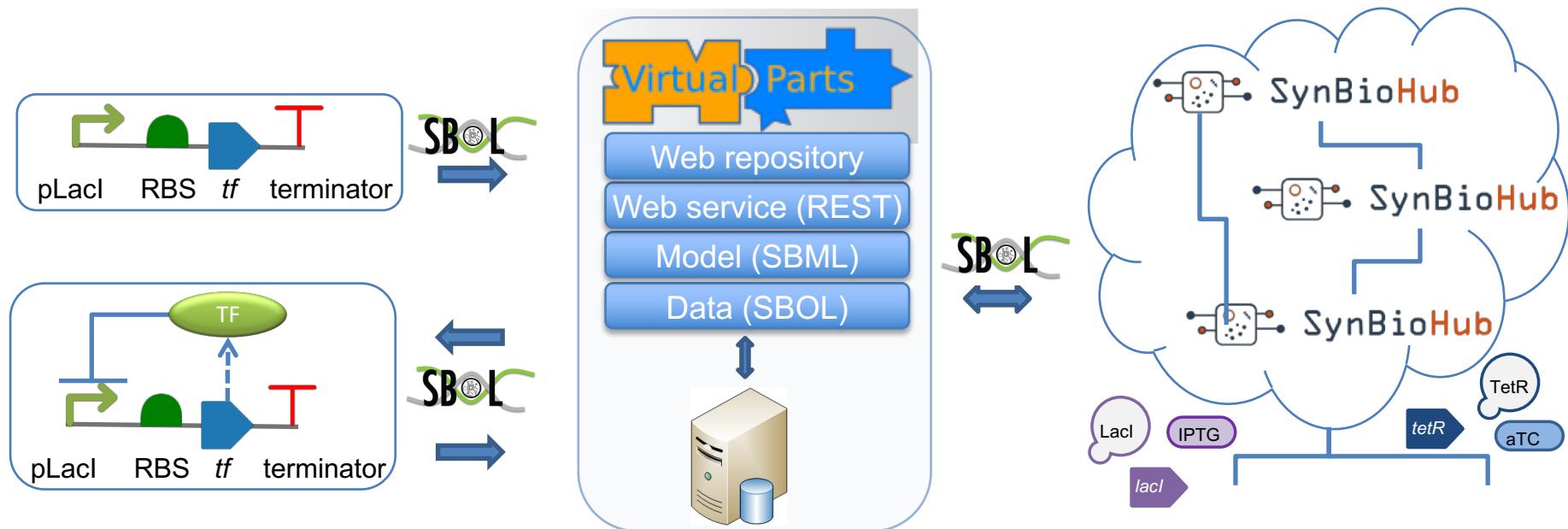
Circuit Design & Modelling: iBioSim



- Supports modeling, analysis, and design of genetic circuits
- Modelling uses SBML, analysis uses SED-ML, and design uses SBOL
- Includes SBOLDDesigner as plugin providing a connection to SBOL Stack
- Provides converters between SBML and SBOL

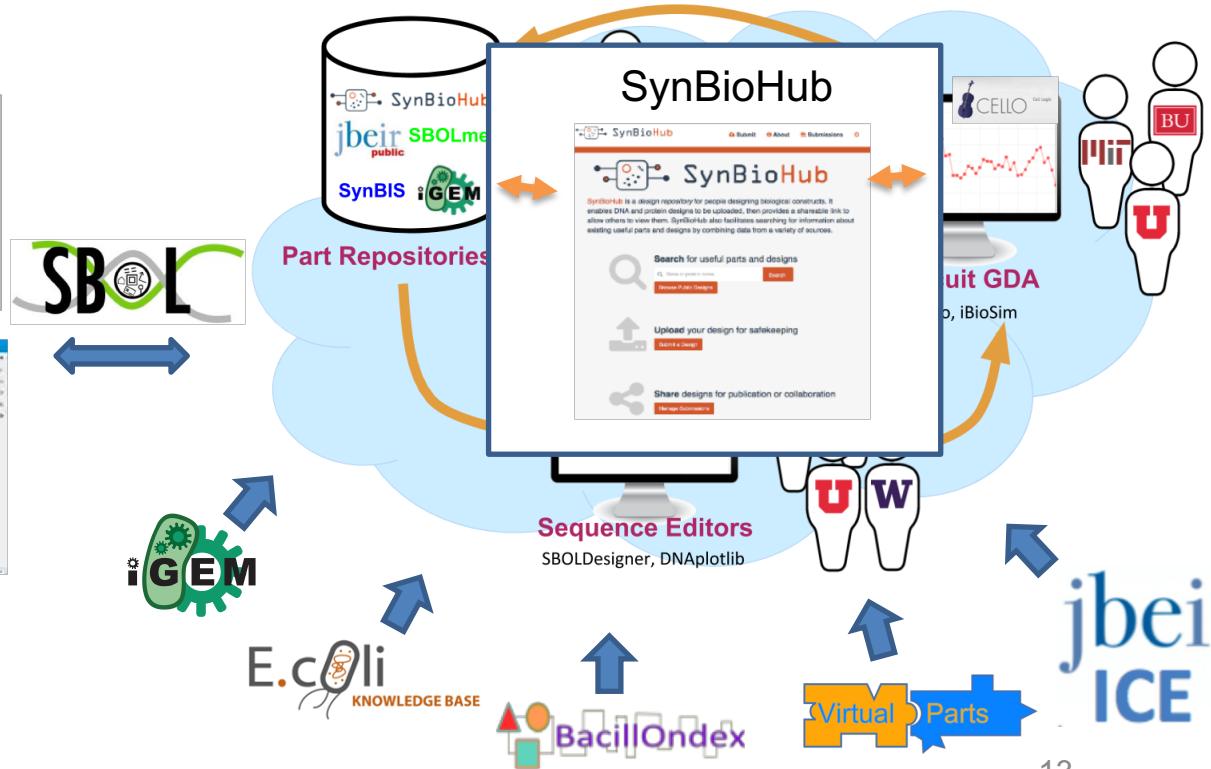
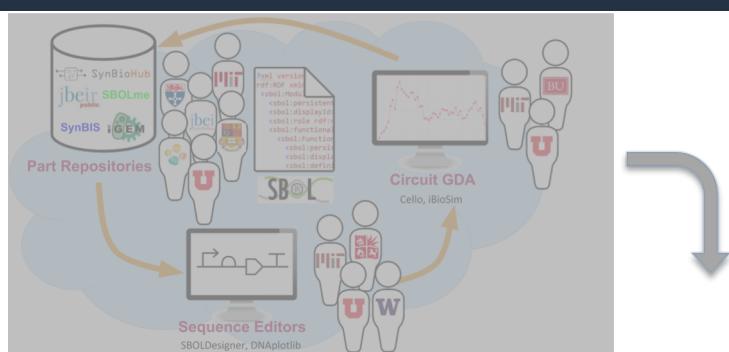
Circuit Design & Modelling: Virtual Parts Repository

- A repository of modular and composable models of biological parts and interactions
- Provides a modelling abstraction for genetic circuit designs specified in SBOL files

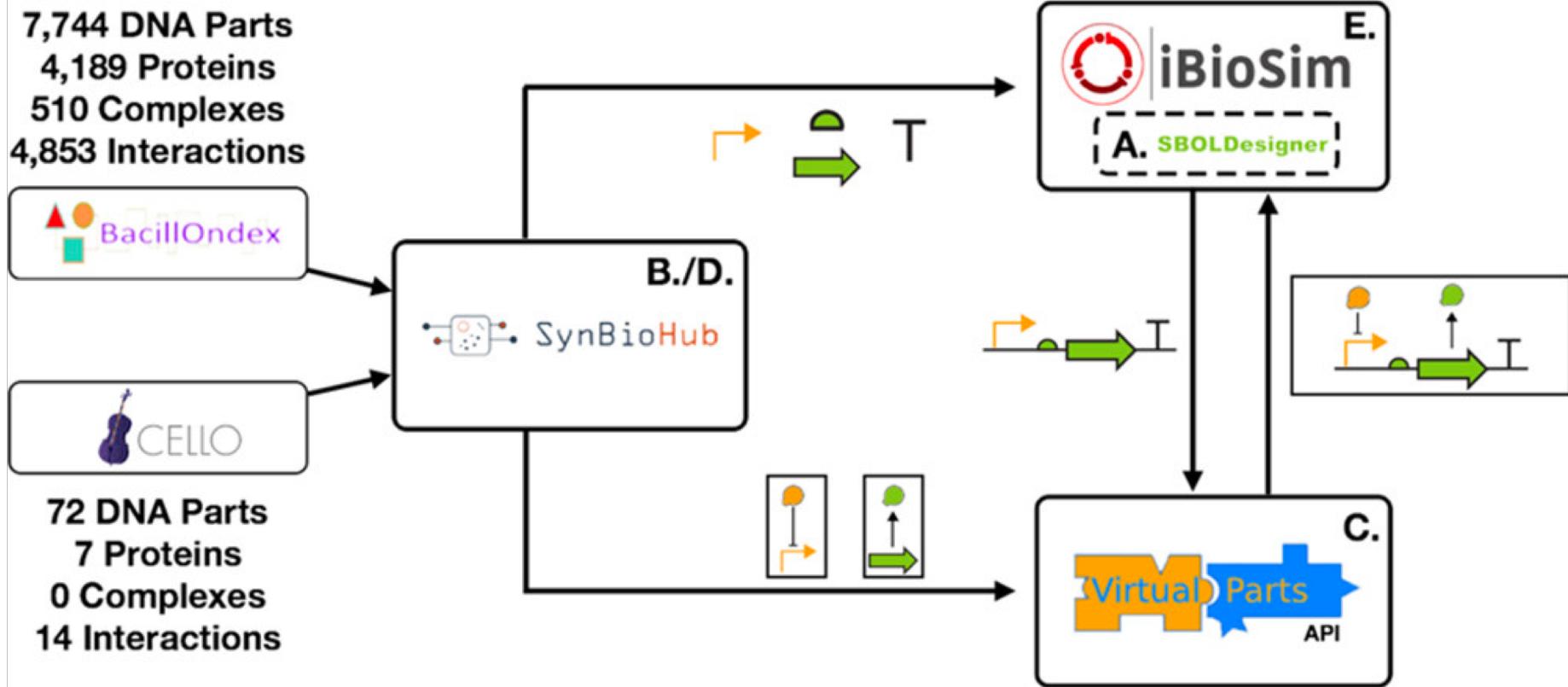


Misirli *et al.*, JETC (2014)
Misirli *et al.*, IWBDA (2019)

Workflows: SynBioHub as a central hub for synbio data management and workflows



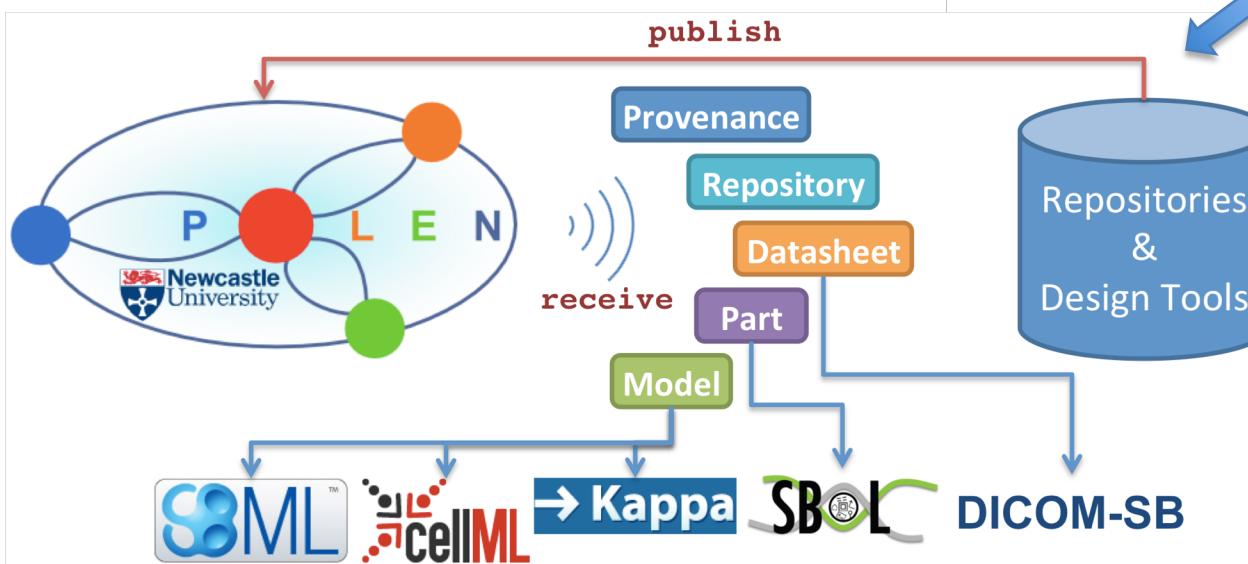
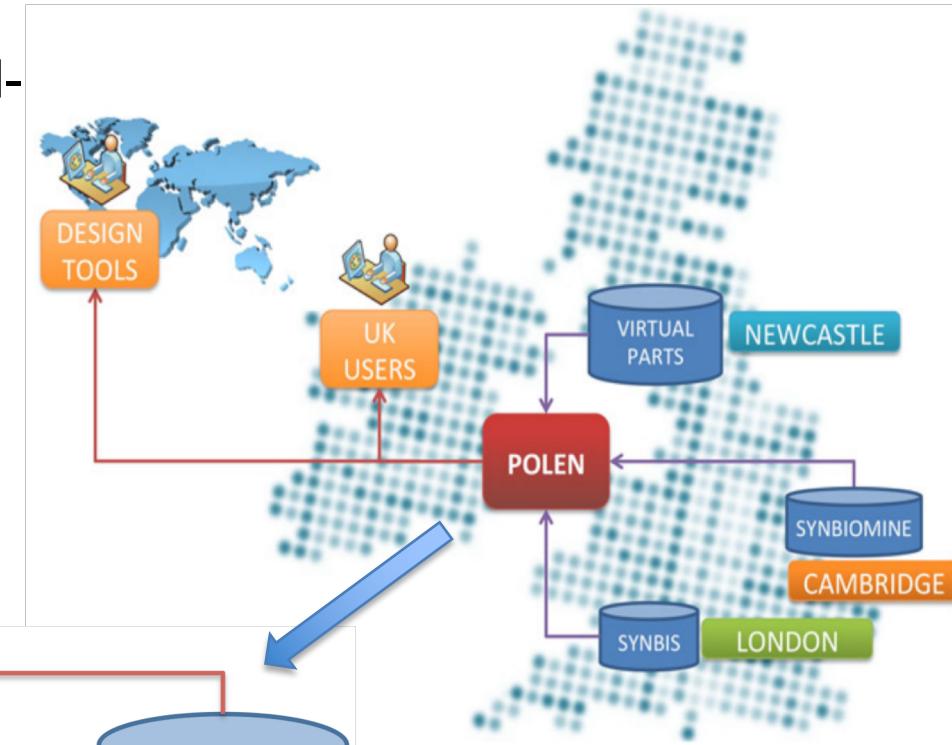
Workflows: Automated generation of models of genetic designs



Misirli & Nguyen *et al.*, 2018
ACS Synthetic Biology

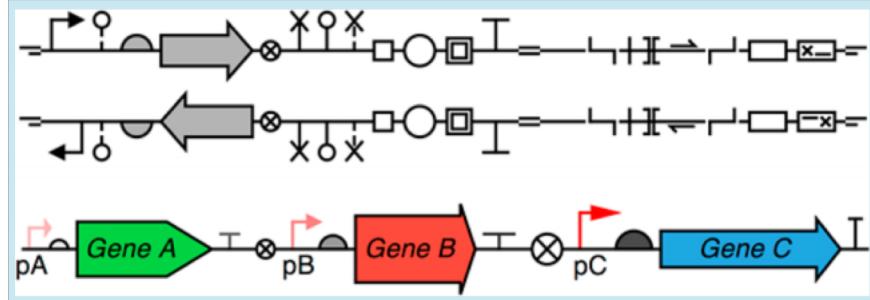
Workflows: POLEN - PrOtocol for Linking External Nodes

- Light-weight, asynchronous, Cloud-based messaging system
- Messages can be published/received for a particular topic
- Messages include URIs that point to actual resources in standard formats



Misirli et al., 2017
IET Engineering Biology

Visualisation examples



DNAplotlib

VisBOL is a web-based tool for visualizing synthetic biology designs. It includes a design interface with tabs for SBOL, PIGEON, and GENBANK, and a display list. It also features a font and scale selector. Below the interface, there are examples of genetic constructs like LacI Inverter, LacI/TetR Toggle Switch, and TetR Inverter, each with their respective DNA sequences and part IDs (e.g., ECK120003736).

PartsGenie is a tool for designing genetic parts. It shows a library of parts (represented by icons) and a detailed view of Part 1: hexokinase-encoding part. This view includes a schematic diagram of the part's structure with labels for the promoter, coding sequence, and terminator.

PartsGenie

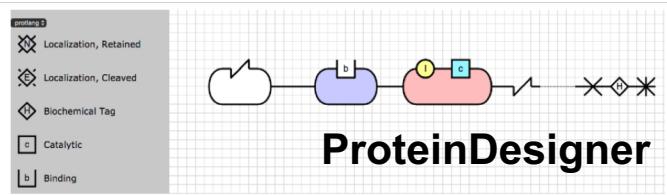
pigeoncad.org is a design visualizer for synthetic biology. It features a drawing of a pigeon and the text "Pigeon". Below it is the subtitle "Design Visualizer for Synthetic Biology". The interface includes a color palette for labels and a legend for codes.

Color palette: A list of type [name] [color] [n] where type is one of p, P, c, r, t, T, s, o, >, <, | or -; a blank line; followed by name ind | rep name There are 14 colors labeled as the third item in each line. Even numbers are darker versions of the odd numbered colors in the following order of hues: blue, green, red, orange, purple! as a fourth item removes the label for that element. Characters < and > before p and c give inverse p and c.

Color codes:



Label codes:



ProteinDesigner

Open Source Libraries

Software libraries which import and export SBOL files are freely available at the [Synthetic Biology Data Exchange](#) on GitHub under the Apache 2.0 license.

Library	Programming Language
libSBOLj	Java
sboljs	JavaScript
libSBOL	C++
pySBOL	Python
semanticSBOL	OWL
SBOL-Validator	Online validation

- Developer support
- Online documentation
- Getting started tutorials
- Sample projects
- Code examples

<http://sbolstandard.org/software/libsbol>
<https://github.com/SynBioDex/>

Acknowledgments

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SBOL Libraries

<http://sbolstandard.org/software/libsbol>

Synthetic Biology Data

Exchange Group

<https://github.com/SynBioDex/>

<http://sbolstandard.org>

