

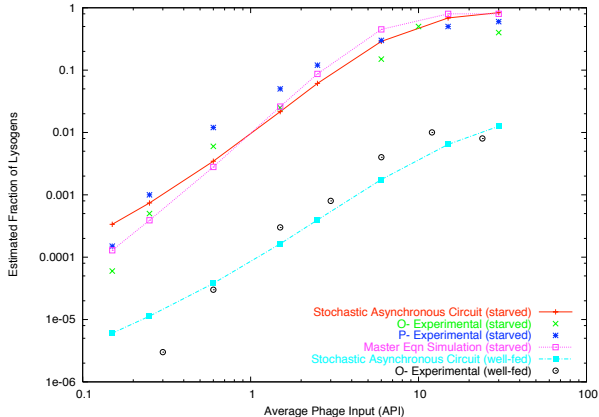
Synthetic Biology Open Language (SBOL)

Chris J. Myers

University of Utah

NormSys/ISBE Workshop
Standards for Data and Model Exchange in Systems Biology
September 18, 2014

Probability of Lysogeny in Phage Lambda



Experiments: Kourilsky et al., Mol. Gen. Genet. (1973)

Master equation: Arkin et al., Genetics (1998)

Markov chain: Kuwahara et al., Trans. on Comp. Sys. Bio. (2006)

Systems Biology Versus Synthetic Biology



Drew Endy



Potential applications:

- Produce drugs and bio-fuels.
- Consume toxic waste.
- Destroy tumors.

Synthetic Biology

- *Synthetic biology* extends *genetic engineering* by adding:
 - *Standards*
 - *Abstraction*
 - *Decoupling*

(source: Drew Endy)

Synthetic Biology

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Essential information for synthetic DNA sequences

To the Editor:

Following a discussion by the workgroup for Data Standards in Synthetic Biology, which met in June 2010 during the Second Workshop on Bidesign Automation in Anaheim, California, we wish to highlight a problem relating to the reproducibility of the synthetic biology literature. In particular, we have noted the very small number of articles reporting synthetic gene networks that disclose the complete sequence of all the constructs they describe.

To our knowledge, there are only a few examples where full sequences have been released. In 2005, a patent application¹ disclosed the sequences of the toggle switches published four years earlier in a paper by Gardner *et al.*². The same year, Basu *et al.*³ deposited their construct sequences for programmed pattern formation into GenBank³. Examples of synthetic DNA sequences derived from standardized parts that have been made available in GenBank include the refactored genome of the bacteriophage

gaps between key components are almost never reported, presumably because they are not considered crucial to the report. Yet, synthetic biology relies on the premise that synthetic DNA can be engineered with base-level precision.

Missing sequence information in papers hurts reproducibility, limits reuse of past work and incorrectly assumes that we know fully which sequence segments are important. For example, many synthetic biologists are currently realizing that translation initiation rates are dependent on more than the Shine-Dalgarno sequence⁴. Sequences upstream of the

start codon are crucial for translation rates, yet are underreported. Similarly, it has been demonstrated that intron length can affect the dynamics of genetic oscillators⁵. Many more such examples are likely to emerge.

Because full sequence disclosure is critical, we wonder why the common requirement by many journals to provide GenBank entries

for genomes and natural sequences has

and welcome contributions from the greater community.

COMPETING FINANCIAL INTERESTS

The authors declare no competing financial interests.

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1. Gardner, T.S. & Collins, J.J. US patent 6,841,376 (2005).
2. Gardner, T.S., Cantor, C.R. & Collins, J.J. *Nature* **403**, 339–342 (2000).
3. Basu, S., Gerchman, Y., Collins, C.H., Arnold, F.H. & Woicik, B. *Nature* **434**, 1125–1128 (2005).






















Synthetic Biology Open Language (SBOL)

- In 2008, a small group of researchers proposed the development of the *synthetic biology open language* (SBOL), an open-source standard for the exchange of genetic designs.
- In 2011, the first version of the SBOL core data model was released.
- In 2013, the first version of the SBOL Visual standard was released.
- Leveraging `libSBOLj`, a java-based library for SBOL's core data model, 18 software tools now support SBOL.

SBOL Community

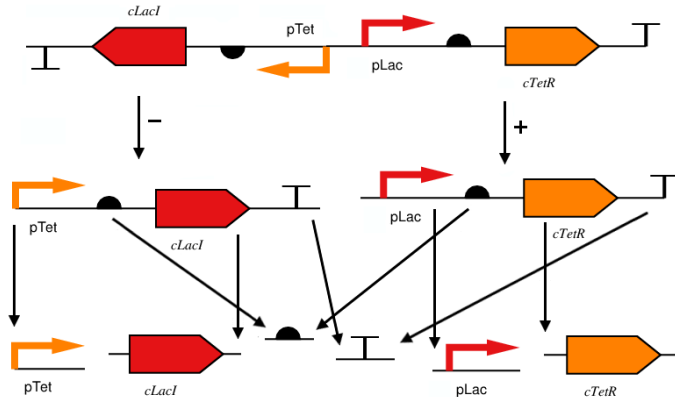
- SBOL Chair - Herbert Sauro (Washington)
- SBOL Editors - Bryan Bartley (Washington), Kevin Clancy (Life Tech.), Jacqueline Quinn (Google), Goksel Misirli (Newcastle), and Nicholas Roehner (Utah).
- Past SBOL Editors - Michal Galdzicki (U. of Washington), Ernst Oberortner (Boston), Matthew Pocock (Newcastle), Cesar Rodriguez (Autodesk), and Mandy Wilson (VBI).
- SBOL Developers Group includes 92 members from more than 30 organizations.
 - Academia - Boston, ETH Zurich, Imperial College London, Newcastle, Stanford, Berkeley, Kerala, Montreal, Utah, Washington, VBI, etc.
 - Industry - Agilent, Amyris, Autodesk, BBN, Clark & Parsia, DNA 2.0, Genome Compiler, JBEI, Life Technologies, etc.

SBOL Visual

 promoter	 origin of replication
 cds	 primer binding site
 ribosome entry site	 blunt restriction site
 terminator	 sticky restriction site
 operator	 5' overhang
 insulator	 3' overhang
 ribonuclease site	 assembly scar
 rna stability element	 signature
 protease site	 user defined
 protein stability element	

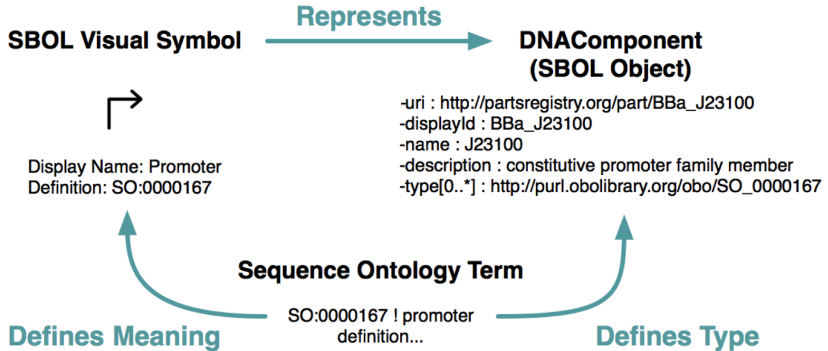
SBOL Version 1.1

- Version 1.1 specifies the hierarchical composition of *DNA components*.

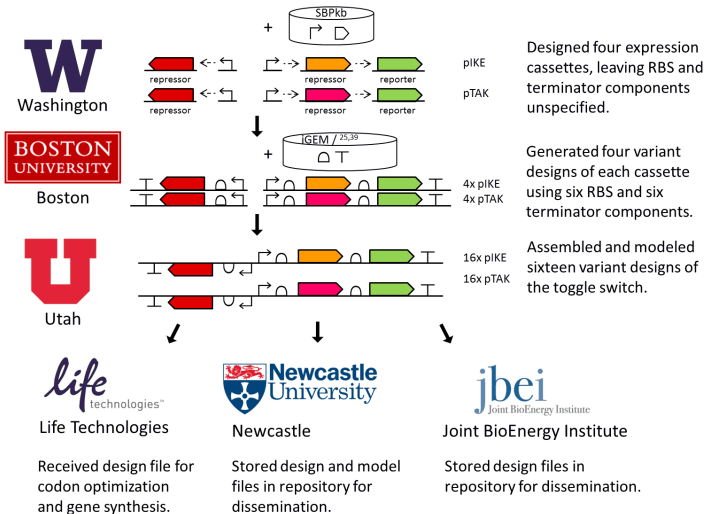


Galdzicki et al., Nature Biotechnology (2014).

Connection with SBOL Visual

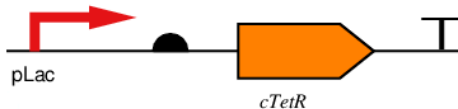


SBOL Demonstration



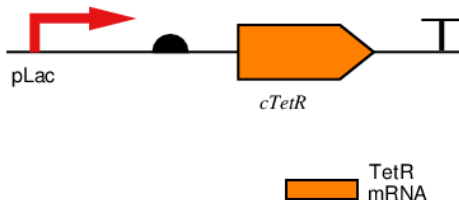
Galdzicki et al., Nature Biotechnology (2014)

Increasing SBOL's Structural Range



Roehner et al., ACS Synthetic Biology (2014)

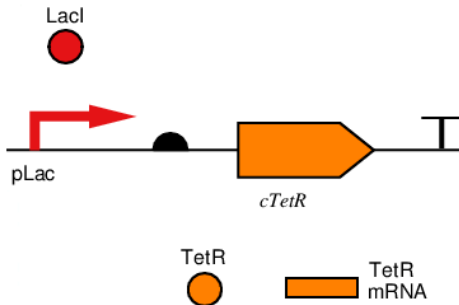
Increasing SBOL's Structural Range



- RNA components (mRNA, tRNA, siRNA)

Roehner et al., ACS Synthetic Biology (2014)

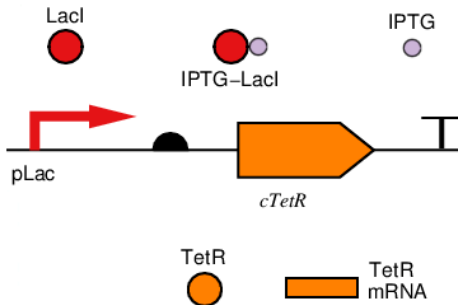
Increasing SBOL's Structural Range



- RNA components
- Protein components (TFs, enzymes)

Roehner et al., ACS Synthetic Biology (2014)

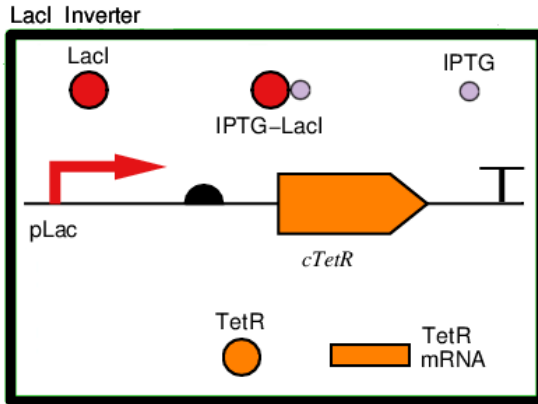
Increasing SBOL's Structural Range



- RNA components
- Protein components
- Other Components (small molecules, complexes, light, temperature, etc.)

Roehner et al., ACS Synthetic Biology (2014)

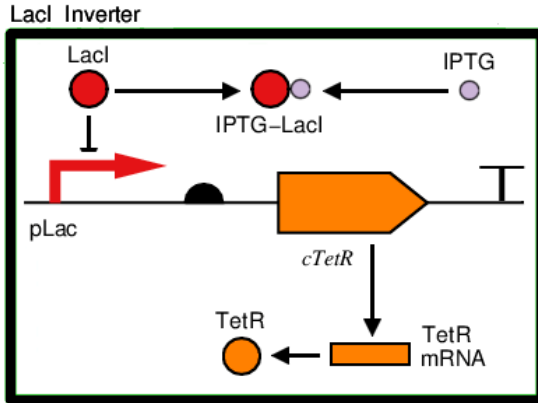
Increasing SBOL's Functional Range



- Modules (logic gates, latches, oscillators, sensors, transducers, pathways, cascades)

Roehner et al., ACS Synthetic Biology (2014)

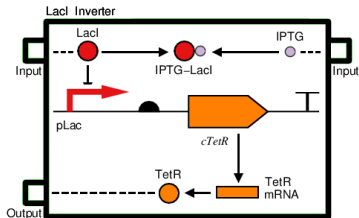
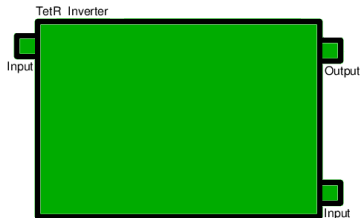
Increasing SBOL's Functional Range



- Modules
- Interactions (activation, repression, complexation, transcription, translation, phosphorylation)

Roehner et al., ACS Synthetic Biology (2014)

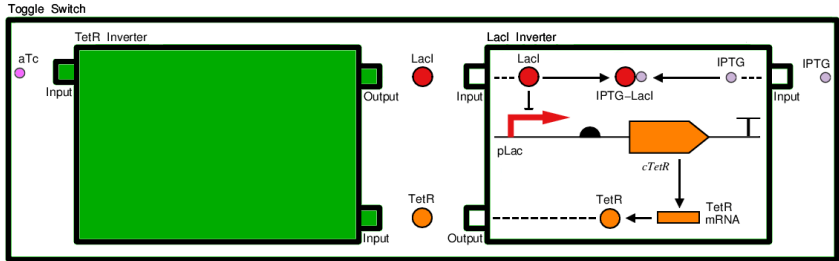
Increasing SBOL's Hierarchy Support



- Ports

Roehner et al., ACS Synthetic Biology (2014)

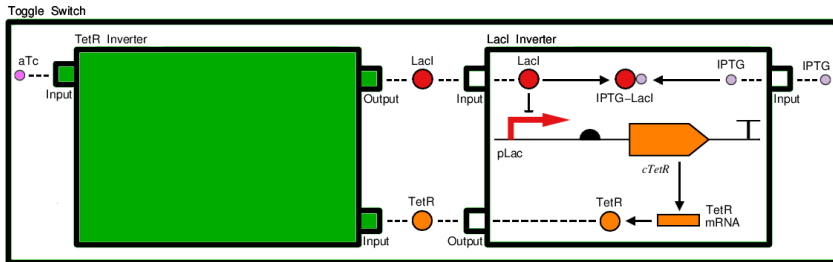
Increasing SBOL's Hierarchy Support



- Ports
- Instantiation

Roehner et al., ACS Synthetic Biology (2014)

Increasing SBOL's Hierarchy Support



- Ports
- Module Instantiation
- Port Mapping

Roehner et al., ACS Synthetic Biology (2014)

SBOL and COMBINE

- *SBOL Developers Group* meet twice a year to discuss next steps.
- SBOL recently joined the COMBINE community of standards and participated in the COMBINE Workshop at USC in August.
- There are many potential synergies between SBOL and COMBINE:
 - Specification infrastructure
 - Metadata and annotations
 - COMBINE archive
 - SBOL Visual/SBGN
 - SBOL/SBML/SED-ML
 - SBOL/BioPAX
 - Repositories
 - Journals
 - Compliance testing

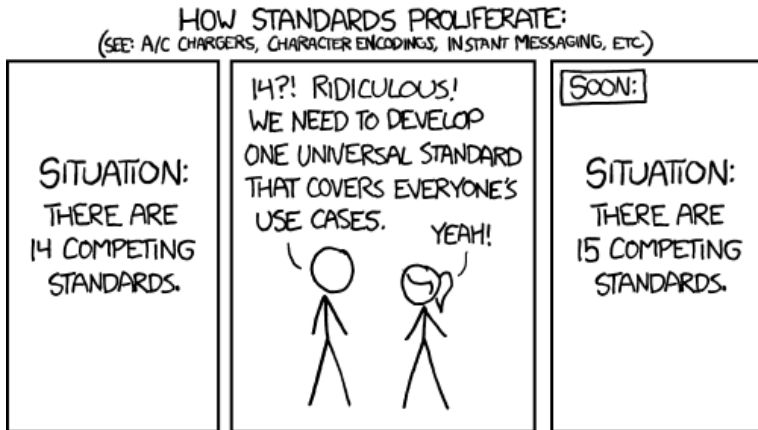
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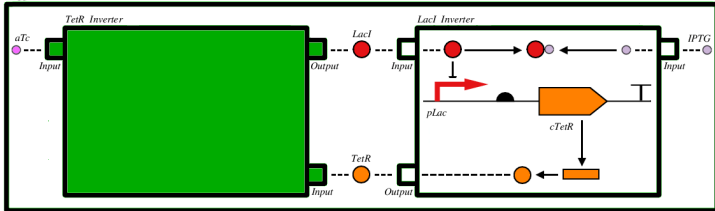
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A Word of Warning on Standards

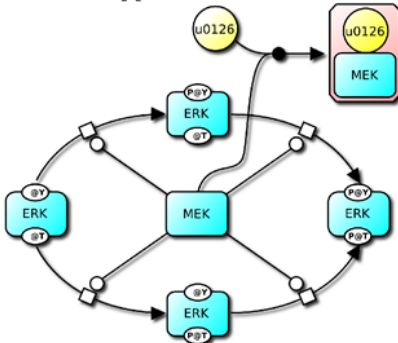


SBOL Visual/SBGN

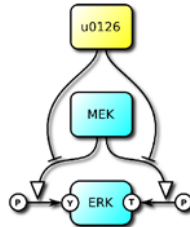
Toggle Switch



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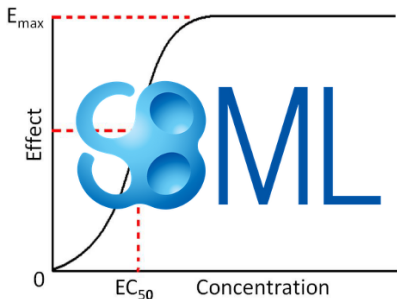
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Connecting SBML to SBOL



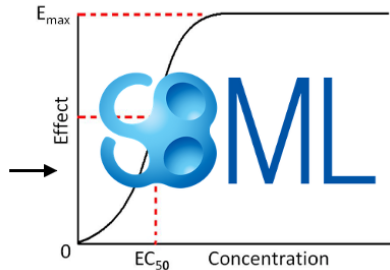
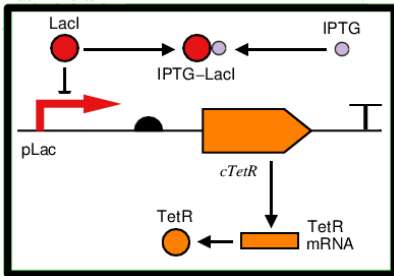
RDF/XML
Annotation



Roehner et al., ACS Synthetic Biology (2013).

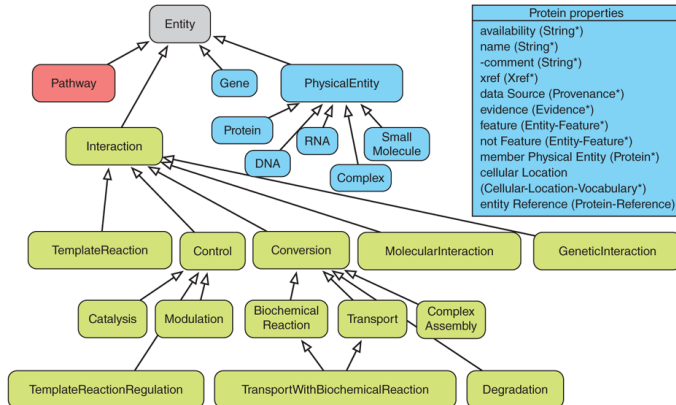
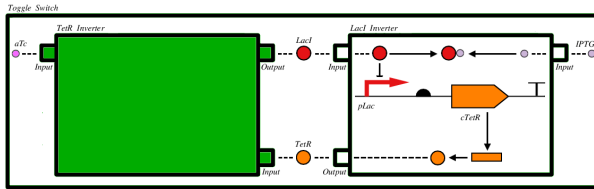
Connecting SBOL to SBML

LacI Inverter



Roehner et al., ACS Synthetic Biology (2014)

SBOL/BioPAX



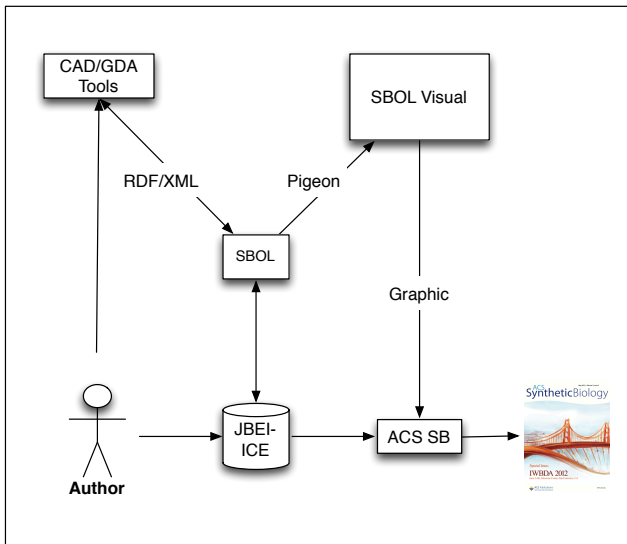
Repositories

- Many repositories for separate standards:
 - Pathway Commons (BioPAX)
 - BioModels (SBML)
 - iGEM Registry, JBEI-ICE, SBOL-Stack (SBOL)
 - Virtual Parts (SBOL/SBML)
- It would be desirable to have a single interface enabling a user to obtain all the necessary data from one information portal.

Journals

- The use of standards for DNA sequence data became commonplace when journals began to require them for publication.
- While there are journals that encourage the use of standards, such as SBML, for modeling, there are currently no journals that require it.
- In order to encourage journals to require these standard data representations, the impact on the authors must be minimized.
- We should have a user friendly portal to their repositories that enables authors to easily deposit their models and designs.
- These interfaces should allow authors to provide their information in an intuitive way while storing their information using an appropriate standard.
- This task is perhaps the one that has the potential to have the largest overall impact on the community.

SBOL and ACS Synthetic Biology



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<input type="checkbox"/>	TYPE	PART ID	NAME	SUMMARY	STATUS			CREATED
<input type="checkbox"/>	Plasmid	JPUB_001054	pET28x-Spinach2	Plasmid given by Jaffrey Lab	Complete			May 13, 2013
<input type="checkbox"/>	Strain	JPUB_000934	JBEI-6893	Ralstonia eutropha H16 strain carrying an in-frame deletion...	Complete			Mar 22, 2013
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<input type="checkbox"/>	Plasmid	JPUB_000816	pDA37	to come	Complete			Feb 7, 2013

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Feature Request

Report a Bug

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Feedback API

Dynamic Modeling of Cellular Populations within iBioSim

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Department of Electrical and Computer Engineering, University of Utah, Salt Lake City, Utah 84112, United States

Supporting

ABSTRACT:

increases, mod subsequent ex automation ce tional tools f analyzing new existing softw cell level, with address this enhanced to visualizing dyn space. This c

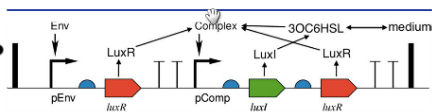


Figure 2. The genetic circuit diagram for the quorum trigger represented using SBOL visual symbols. This circuit is designed to produce a density-dependent response to an environmental signal (Env). This response is achieved using the quorum sensing molecule 3OC6HSL. The 3OC6HSL molecule can either come from LuxI generated at the basal rate of the pComp promoter, or it can come from diffusion into the cell from 3OC6HSL available in the medium that is produced by other cells.



capitalizing on iBioSim's strengths in modeling, simulating, and analyzing single-celled systems.

KEYWORDS: spatial modeling, dynamic modeling, multicellular modeling, stochastic simulation, genetic circuits, SBML

Compliance Testing

- The challenge:
 - A standard should be broad enough to support users needs.
 - A standard should not be so broad that no tools support the standard.
- If a standard is too light, users complain they cannot encode their data.
- If a standard is too heavy, users complain that tools do not interoperate.
- In both cases, the standard is blamed, but this is really a tool problem.
- A possible solution is *compliance testing*.
 - Must define what it means for a tool to support a standard.
 - Must encourage tool developers to fully support a standard.
 - Must collect and advertise data on the degree of standard support by tools.
 - COMBINE could sanction workflows known to work.

Acknowledgments



Agilent Technologies

CLARK Φ PARSIA



Raytheon

BBN Technologies

AUTODESK

life
technologies™



DNA 2.0

GENOME
COMPILER
TOOLS FOR DESIGNING LIFE



National Human
Genome Research
Institute



Supported by National Science Foundation Grants
CCF-1218095, DBI-1356041, and DBI-1355909.