# Standard Enabled Workflow for Synthetic Biology

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## Introduction

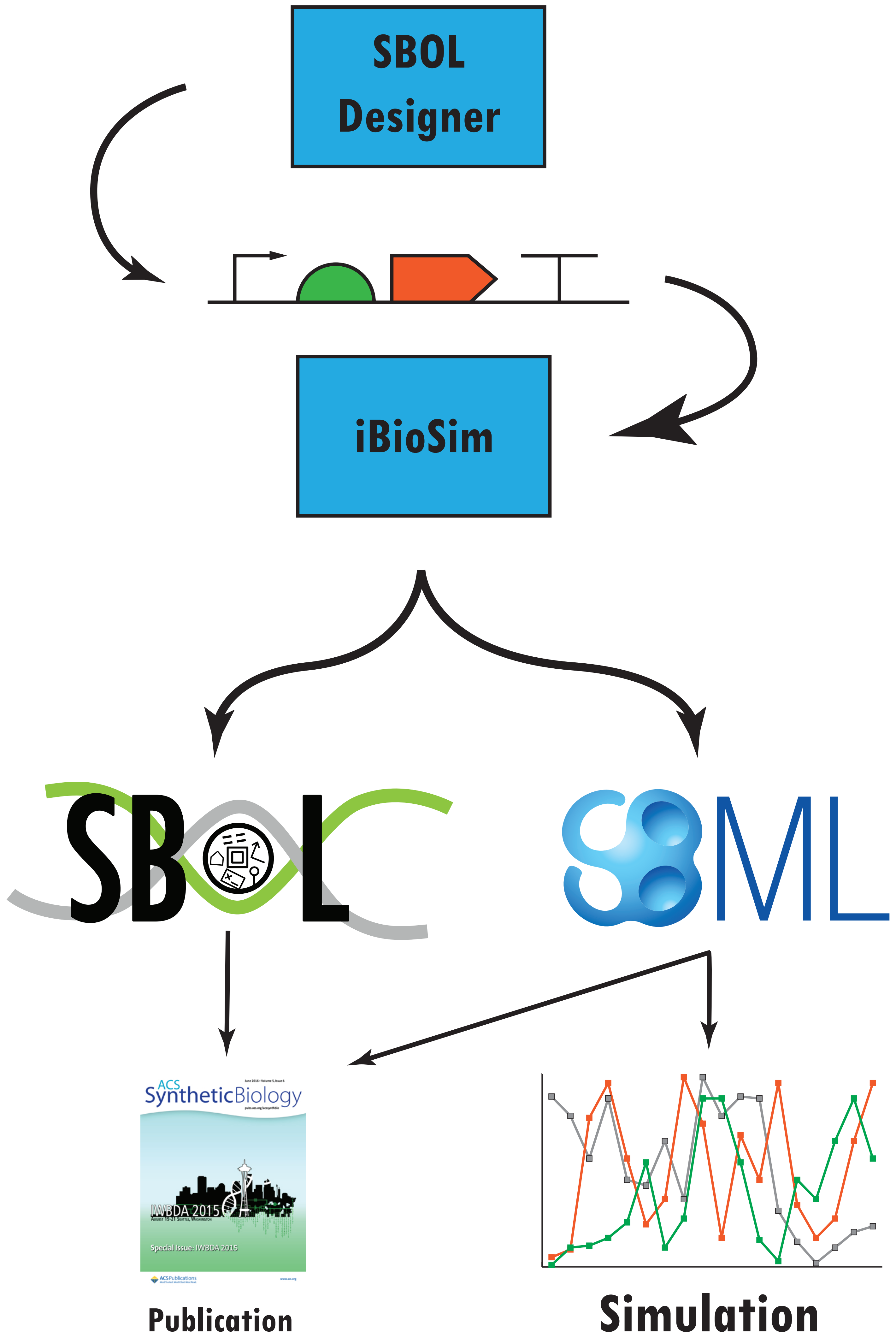
- Standards are key to the success of systems and synthetic biology
- Allow for easy exchange and standard expression of data across labs and projects
- SBOL (Synthetic Biology Open Language) [1] is an evolving standard for the exchange of genetic constructs
- SBOL allows creation of hierarchical, modular representations of genetic structure and function
- SBML allows creation of behavioral models of biological systems at the molecular level.
- Many different tools handle different components of the SBOL and SBML creation process
- Current tools must be examined to determine a usable workflow for creating SBOL and SBML
- A widely-applicable workflow would facilitate adoption of SBOL and SBML by the larger community
- Additionally, a workflow would be useful if it could also allow for the *in silico* simulation of biological constructs.
- There is a clear need for a standard to ensure that uniform data is expressed
- This standard should be open-source and allow for free exchange of data
- Reduces the load for researchers who may be approached by those replicating their work
- End goal is SBOL and SBML adoption by journals so all publications have supplemental annotated models

## Current Issues

- No standard way of expressing data in synthetic biology publications
- Variation here often leads to missing valuable pieces of information
- Information that is present could be present in an obtuse or difficult-to-use form
- Oftentimes, crucial information is missing all together
- Data is often difficult to obtain from researchers after publication
- When given, data is not always formatted in a standard manner
- Even when a standard is used, it is not always possible to ensure that implied homologues are valid
- Lack of requirements for publication allows many of these issues to continue

## Test Case Analysis

- To exemplify the workflow, a test case was created corresponding to the result of each step in the workflow.
- The example genetic construct created is a Combinatorial Logic Circuit.
- First, four inputs are detected using sensors:
  - Ara is detected by combining with araC
  - IPTG is detected by combining with lacI
  - 3OC6 is detected by combining with luxR
  - aTc is detected by combining with tetR
- Next, these inputs are combined in AND-gate-equivalent circuits:
  - *araC* and *Ara* activate *pBAD*, which enables production of *ipgC*
  - *lacI* and *IPTG* activate *pTac*, which enables production of *mxiE*
  - *luxR* and *3OC6* activate *pLux*, which enables production of *exsC*
  - *aTc* and *tetR* activate *pTet*, which enables production of *exsD* and *exsA*
  - *ipgC* and *mxiE* combine to activate *pipaH*, which enables production of *sicA*
  - *exsC*, *exsD*, and *exsA* combine to activate *pexsC*, which enables production of *invF*
  - *invF* and *sicA* combine to activate *psicA*, which enables production of *rfp*
- Thus, rfp will only be produced if Ara, IPTG, 3OC6, and aTc are present in the cell



SBOL Designer

iBioSim

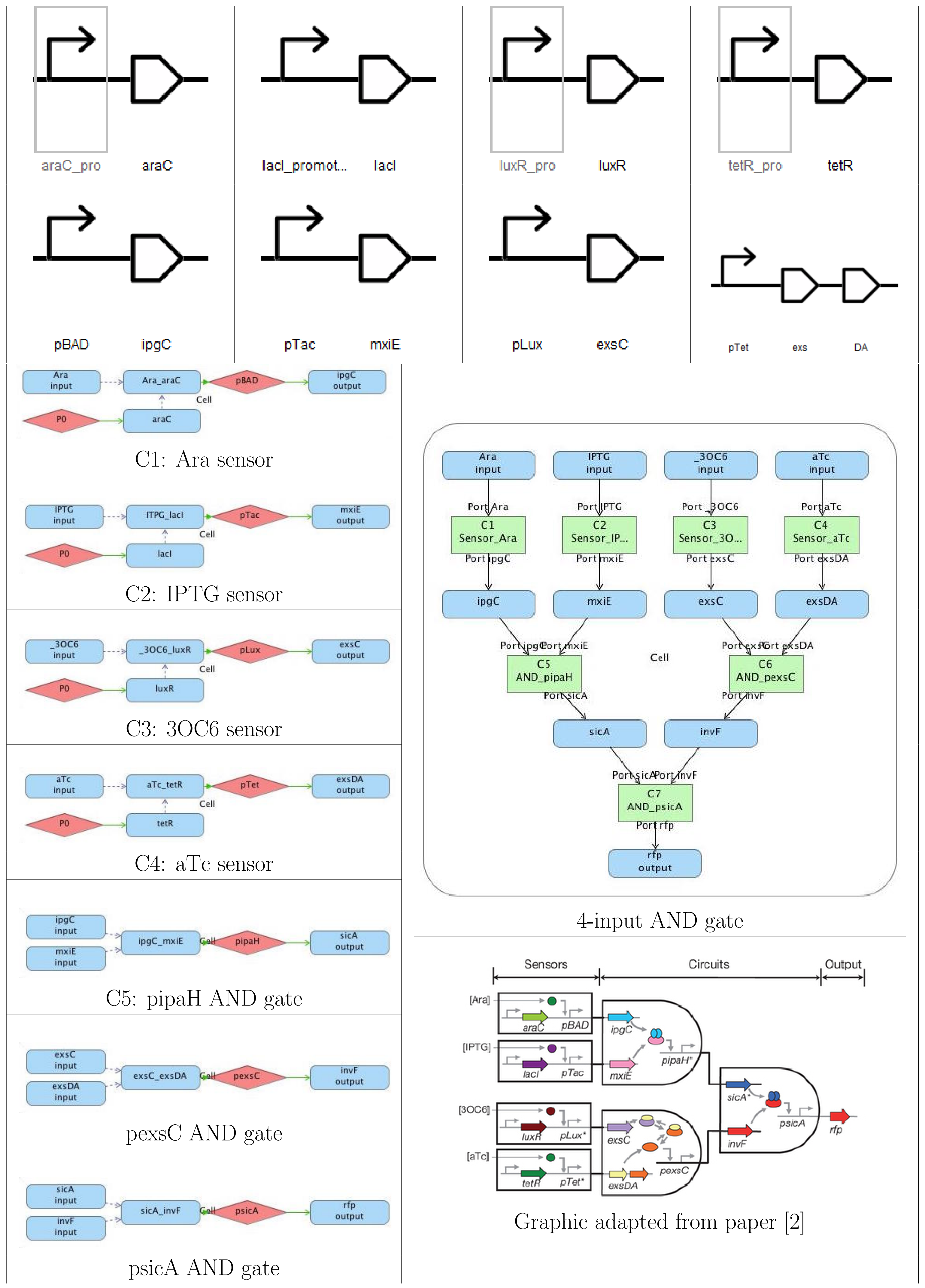
Publication

Simulation

## Specific Workflow

1. The user begins by using SBOL Designer to connect to various parts repositories and compose individual parts into structural units. These structural units can then be composed into larger SBOL documents for ease of sharing and exchanging.
2. These SBOL files can then be imported into iBioSim, where users can describe the functional interactions of the structural composites.
3. In iBioSim, the user can also encode data about small molecules involved in the genetic circuit.
4. Once the user has encoded information about small molecule interactions and interactions between genetic structures, they must associate mathematical models with each interaction to describe the mathematical relationship between components.
5. The user can then use those mathematical models to run *in silico* simulations of the behavior of the genetic circuit.
6. SBOL and SBML can be exported from iBioSim for publication and verification by peer review or other third-parties.

## Creating a Test Case



C1: Ara sensor

C2: IPTG sensor

C3: 3OC6 sensor

C4: aTc sensor

C5: pipaH AND gate

pexsC AND gate

psicA AND gate

4-input AND gate

Graphic adapted from paper [2]

## Acknowledgements

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## References

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