Interconversion Between SBML and BioPAX

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Systems Biology Markup Language (SBML)

- *Systems Biology Markup Language* (SBML) is a standard to represent quantitative, mathematical models of biological systems.
- Core constructs include compartments, species, and reactions.
- SBML supports additional features using packages.
  - Hierarchical Model Composition (comp) package
  - Qualitative Models (qual) package
  - Groups (groups) package

BioPAX

- BioPAX is a standard used to describe structural and basic qualitative behavioral aspects of a biological pathway.
- BioPAX represents metabolic, signaling, and genetic pathways.
- Each pathway consists of a set of interactions or other pathways.
- Each interaction consists of a set of entities and a description.
- Each entity can be a gene, a physical entity, or another interaction.

Motivation

Translating BioPAX pathways to SBML models:

- Enables the development of simulatable models from pathways.
- Resulting models are well annotated with BioPAX information.

Translating SBML models to BioPAX pathways:

- Makes network analysis tools available to SBML users.
- Helps visualize the structure of a biological model.

Objective

- An interconversion between BioPAX and the SBML that minimizes the loss of data in the converted form.
  - Produce BioPAX and SBML models that are structurally equivalent.
  - Make use of well define mapping by using the *Systems Biology Ontology* (SBO) terms and BioPAX elements to support roundtripping.
- Support hierarchical SBML models using the SBML comp package.
- Use packages needed to encode BioPAX elements.

Existing BioPAX to SBML Converters

	Our BioPAX2SBML	*SBVC*	*Sybill*	*BiNoM*
Authors	Tramy et al.	Büchel et al.	Rüebenacker et al.	Zinovyev et al.
Version	1.0	1.0	1.0 (Build 119)	2.0
Release date	TBD	2012-04-02	2010-02-11	2012-04-12
Input BioPAX Model	L1-L2-L3	L2-L3	L2-L3	L3
Output SBML Model	L3V1	L3V1	L2V4	L2V4-L3
Uses SBO Terms	✓	✓	–	–
Xref to MIRIAM Annot.	✓	✓	–	–
Supports SBML Comp	✓	–	–	–
Supports SBML Qual	○	✓	–	–
Supports SBML Groups	○	–	–	–
Lossless Conversion	○	–	–	–

Adapted from Büchel et al., 2013

✓ Supported by current version.

– Not supported by current version.

○ Not supported by current version, but planned for future version.

Existing SBML to BioPAX Converters

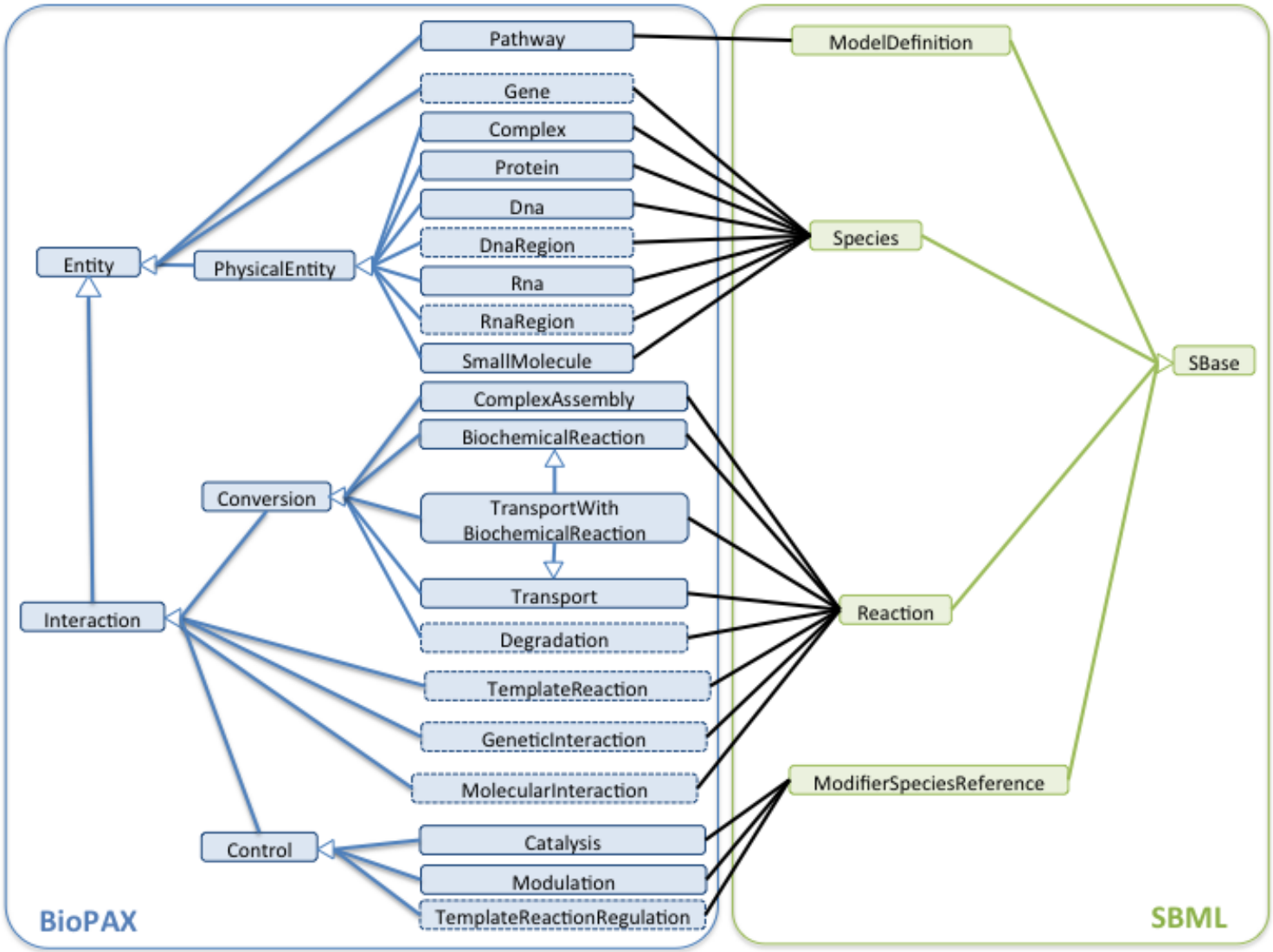
	Our SBML2BioPAX	*2014 GSOC*	*SBFC*
Authors	Tramy Nguyen et al.	Arman Aksoy et al.	Nicolas Rodriguez et al.
Version	1.0	1.0	1.3.7
Release date	TBD	2015-06-23	2015-05-27
Input SBML Model	L3V1	L3V1	L3V1
Output BioPAX Model	L3	L3	L3
Uses SBO Terms	✓	✓	–
MIRIAM Annot. to Xref	✓	✓	✓
Complete entity mapping	✓	–	✓
Supports SBML Comp	✓	–	–
Supports SBML Qual	○	–	–
Supports SBML Groups	○	–	–
Lossless Conversion	○	–	–

✓ Supported by current version.

– Not supported by current version.

○ Not supported by current version, but planned for future version.

BioPAX Entity to SBML Element Mapping



Adapted from Büchel et al., 2013

SBO Mapping for BioPAX Entity

BioPAX entity	*SBML Element*	*SBO Term*	*SBO Name*
Compartment	Compartment	SBO:0000290	Physical Compartment
Gene	Species	SBO:0000243	Gene
Complex	Species	SBO:0000253	Non-covalent Complex
Protein	Species	SBO:0000252	Polypeptide chain
Dna	Species	SBO:0000251	Deoxyribonucleic Acid
DnaRegion	Species	SBO:0000634	DNA Segment
Rna	Species	SBO:0000250	Ribonucleic Acid
RnaRegion	Species	SBO:0000635	RNA Segment
SmallMolecule	Species	SBO:0000247	Simple Chemical
TemplateReaction	Reaction	SBO:0000589	Genetic Production
GeneticInteraction	Reaction	SBO:0000343	Genetic Interaction
MolecularInteraction	Reaction	SBO:0000344	Molecular Interaction
ComplexAssembly	Reaction	SBO:0000177	Non-covalent Binding
BiochemicalReaction	Reaction	SBO:0000176	Biochemical Reaction
TransportWithBiochemicalReaction	Reaction	SBO:0000167	Biochemical or Transport Reaction
Transport	Reaction	SBO:0000185	Transport Reaction
Degradation	Reaction	SBO:0000179	Degradation
Catalysis	ModifierSpeciesReference	SBO:0000013	Catalyst
Modulation	ModifierSpeciesReference	Assigned from the ControlType	
TemplateReactionRegulation	ModifierSpeciesReference	Assigned from the ControlType	

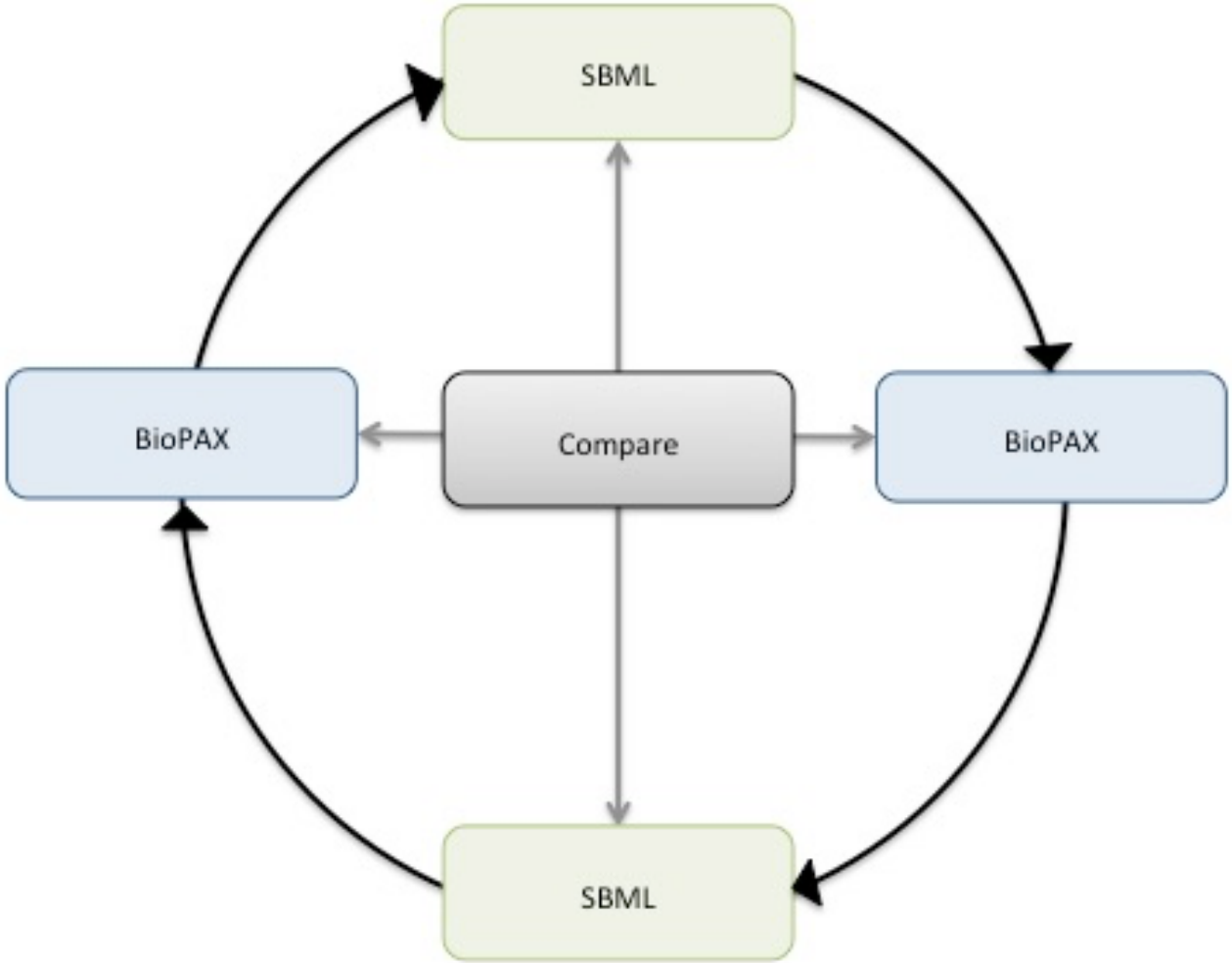
SBO Mapping for ControlType

ControlType	*SBO Term*	*SBO Name*
Activation	SBO:0000459	Stimulator
Activation allosteric	SBO:0000636	Allosteric Activator
Activation nonallosteric	SBO:0000637	Non-allosteric Activator
Inhibition	SBO:0000020	Inhibitor
Inhibition noncompetitive	SBO:0000207	Non-competitive inhibitor
Inhibition competitive	SBO:0000206	Competitive inhibitor
Inhibition irreversible	SBO:0000638	Irreversible Inhibitor
Inhibition allosteric	SBO:0000639	Allosteric Inhibitor
Inhibition other	TBD	TBD
Inhibition uncompetitive	SBO:0000640	Uncompetitive Inhibitor

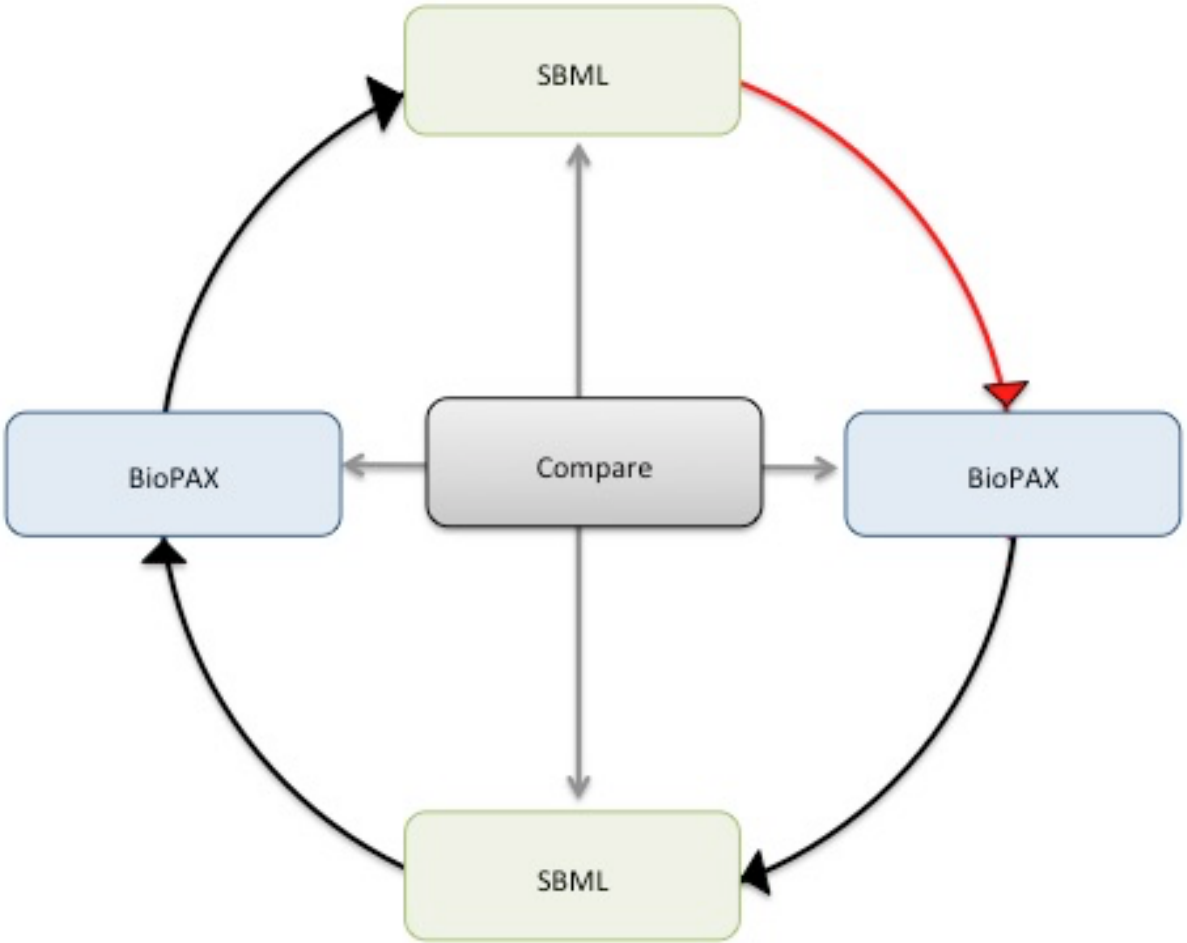
Additional SBO Mappings

BioPAX Field	*SBO Term*	*SBO Name*
deltaGPrime0	SBO:0000581	Gibbs Free Energy Change
deltaGIonicStrength	SBO:0000623	Ionic Strength
deltaGpH	SBO:0000304	pH
deltaGMg	TBD	TBD
deltaGTemperature	SBO:0000304	Thermodynamic Temperature
deltaH	SBO:0000573	Enthalpy Change
deltaS	SBO:0000577	Entropy Change
KPrime	SBO:0000281	Equilibrium Constant
KPrimeIonicStrength	SBO:0000623	Ionic Strength
KPrimepH	SBO:0000304	pH
KPrimeMg	TBD	TBD
KPrimeTemperature	SBO:0000304	Thermodynamic Temperature
cofactor	SBO:0000534	Catalytic Activator

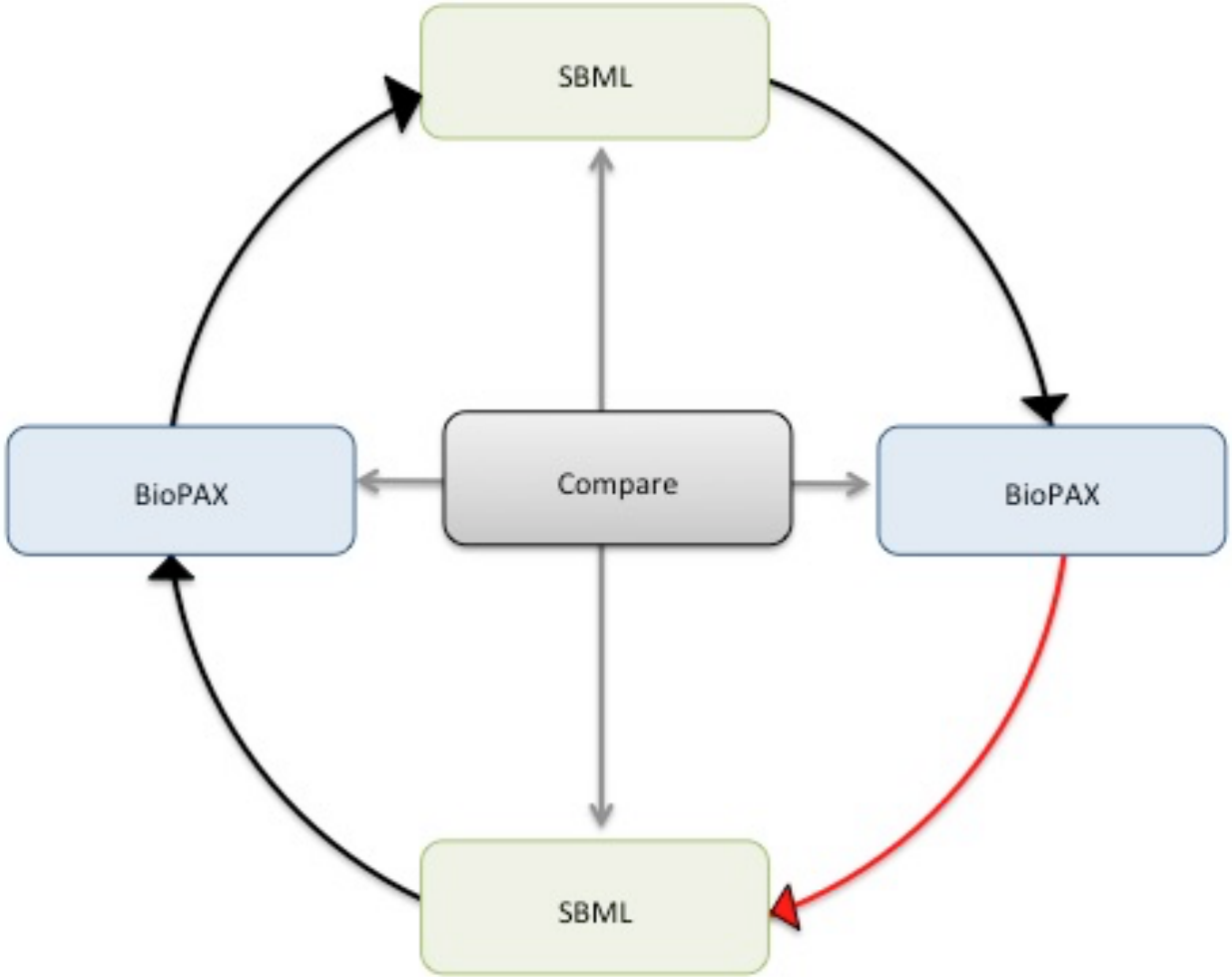
Roundtrip Testing



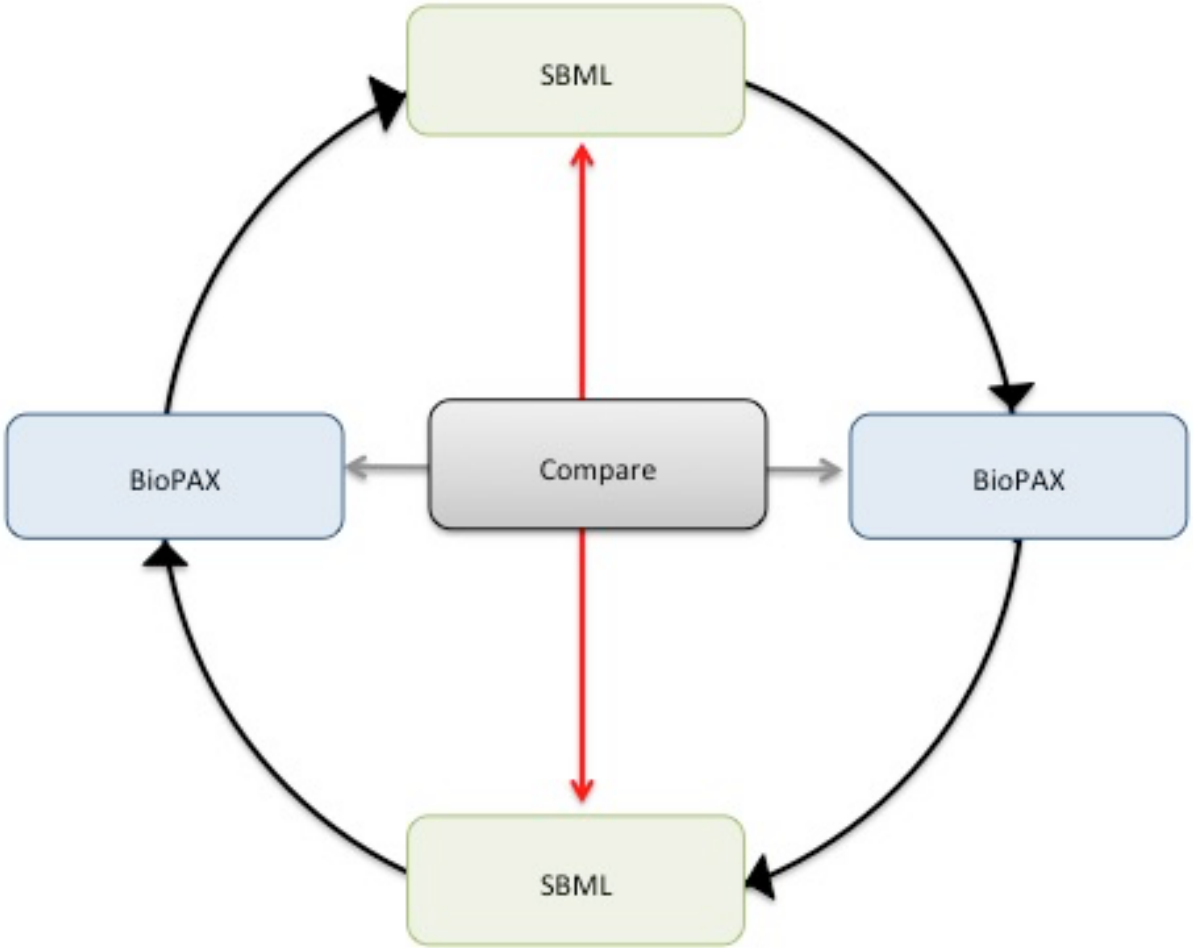
SBML to BioPAX



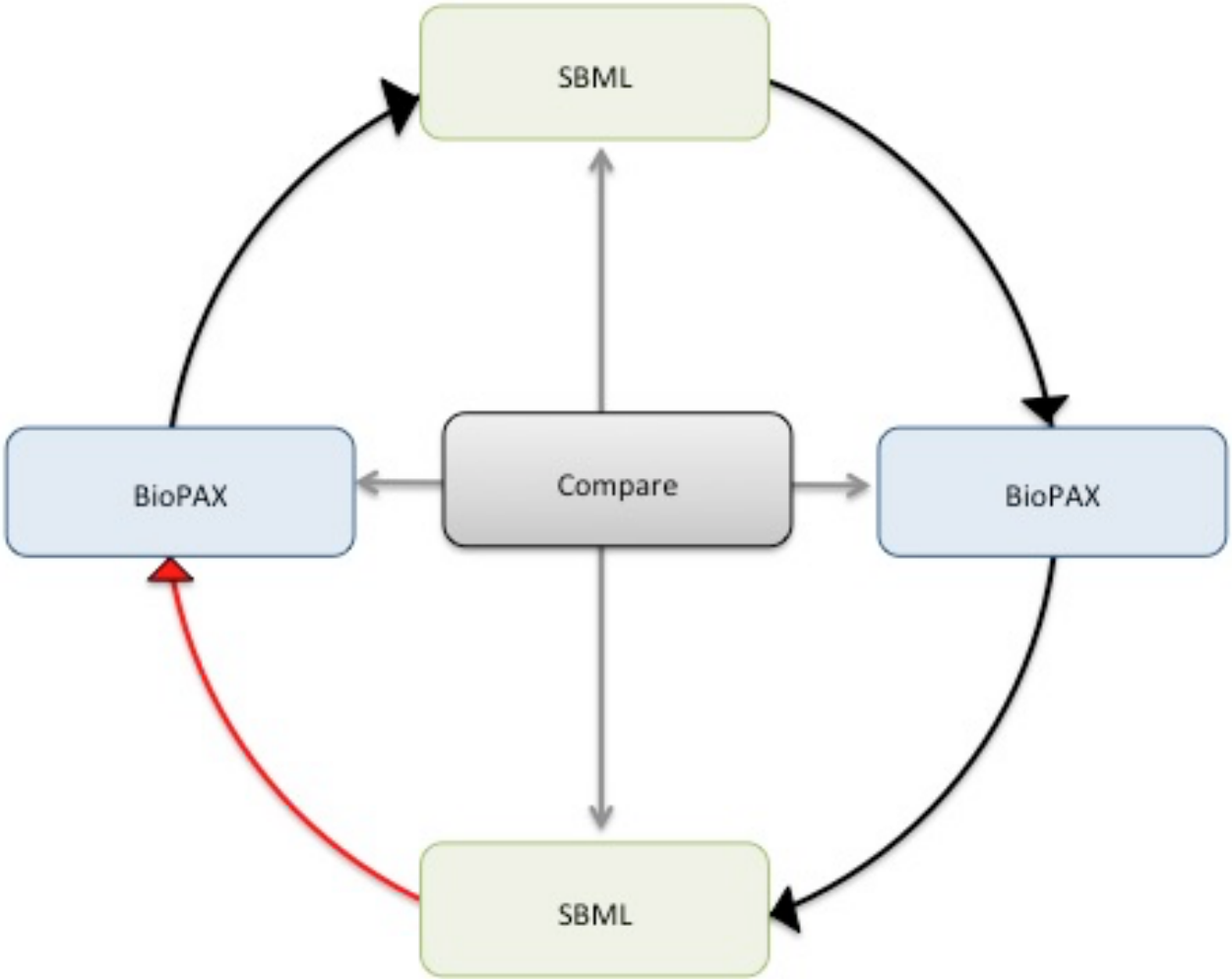
BioPAX to SBML



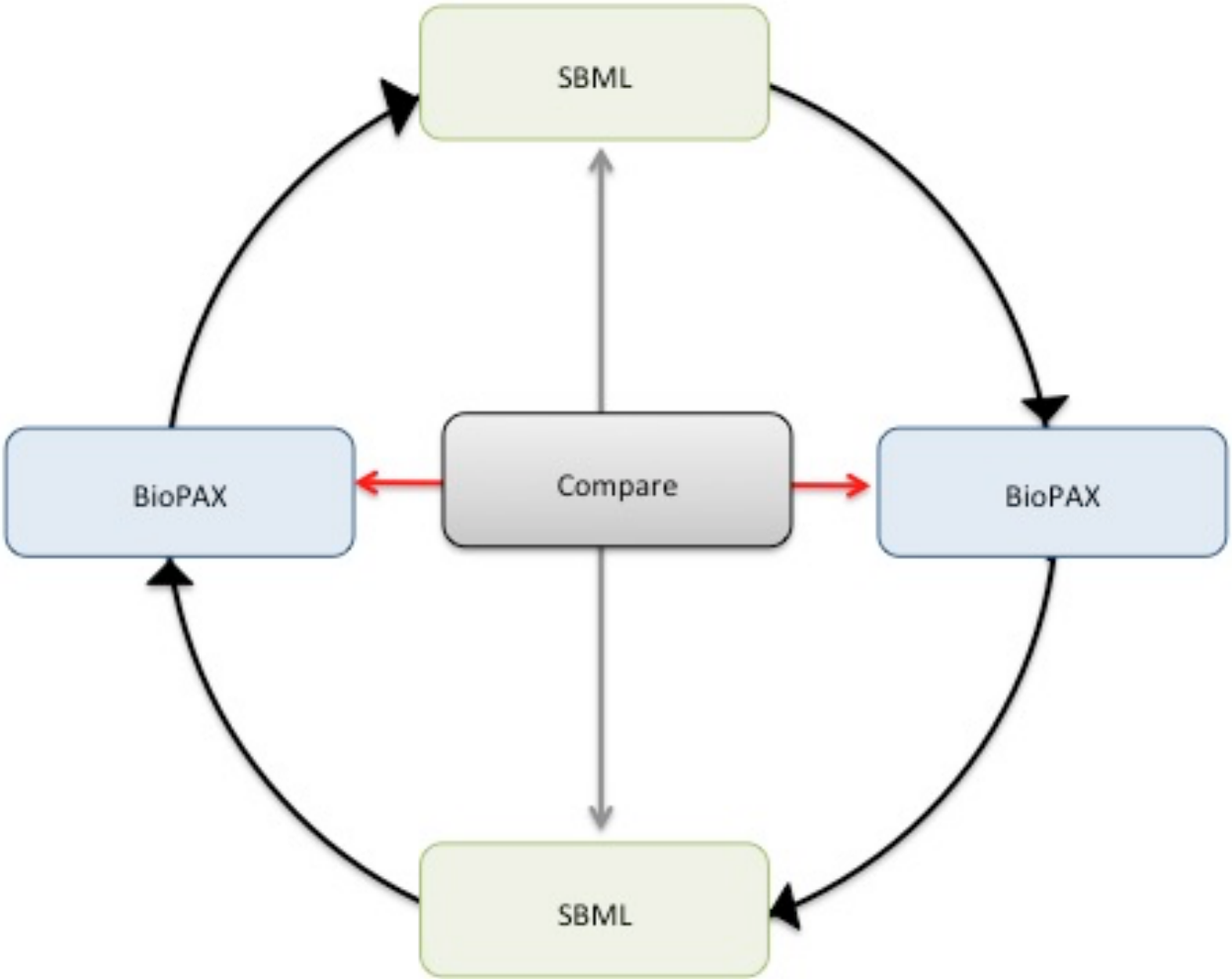
Original SBML vs. Converted SBML



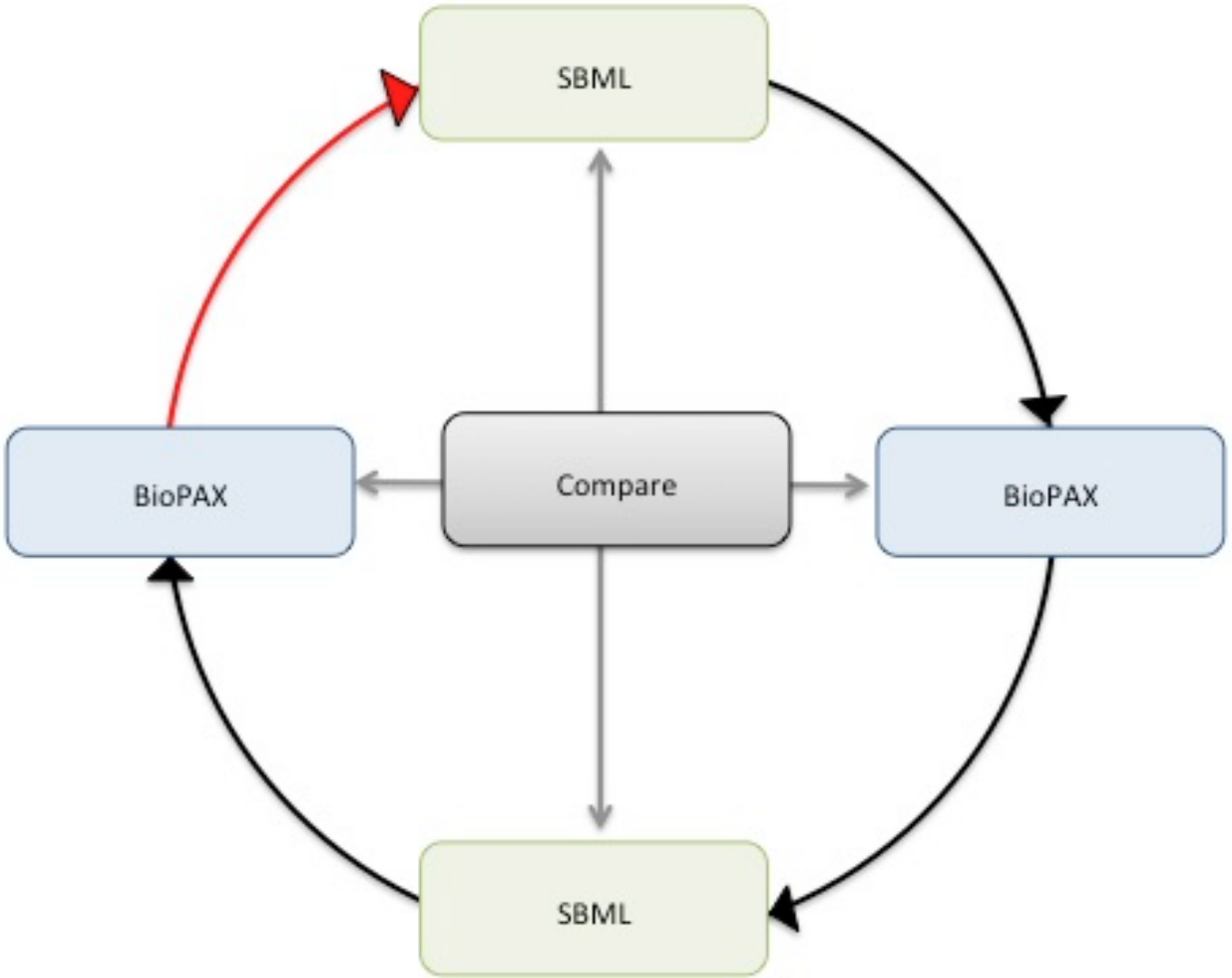
SBML to BioPAX



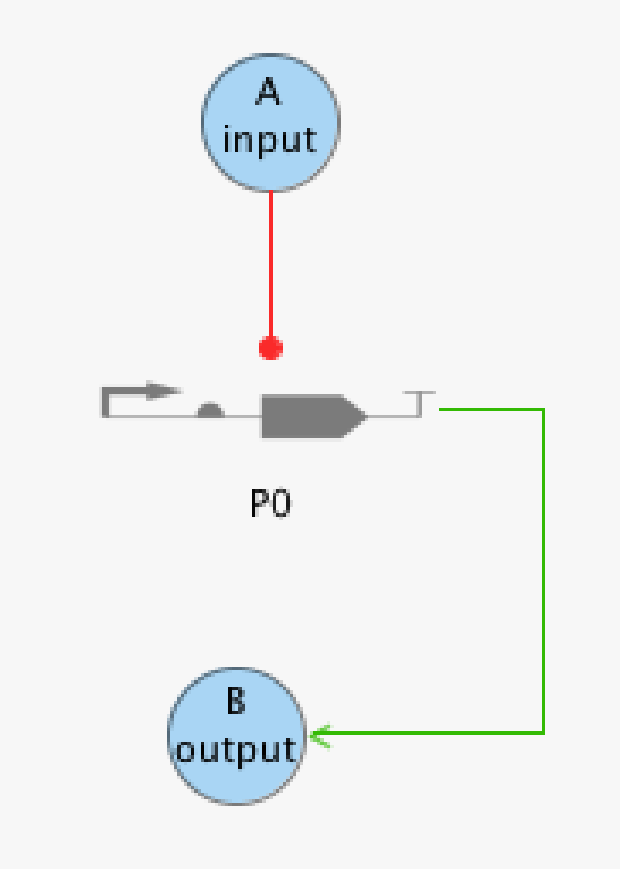
Original BioPAX vs. Converted BioPAX



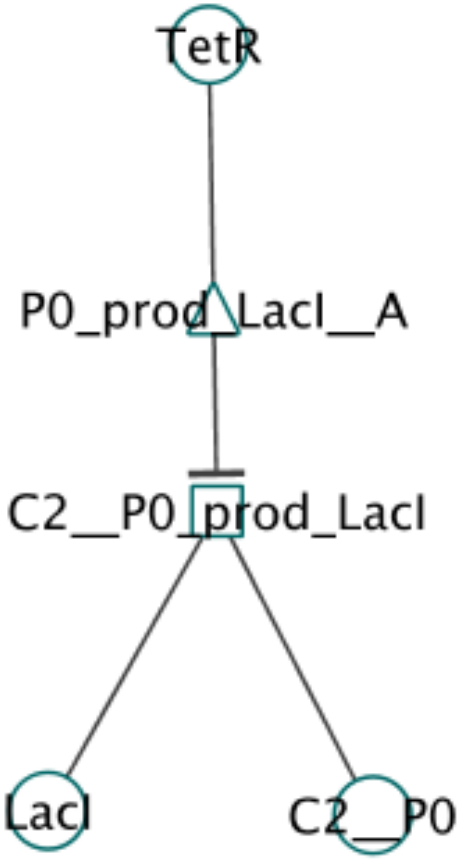
BioPAX to SBML



Original TetR Inverter Model to BioPAX

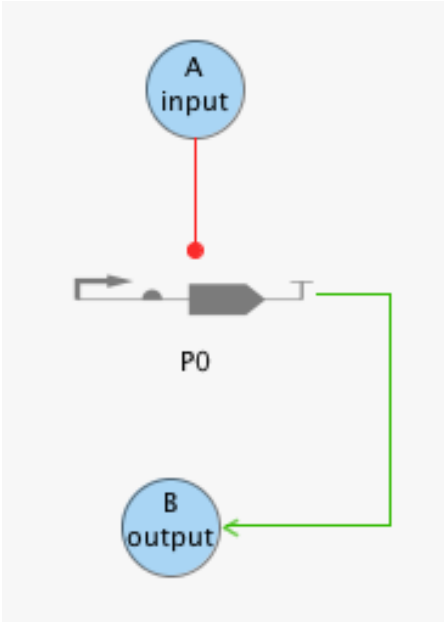


Original TetR Inverter Model

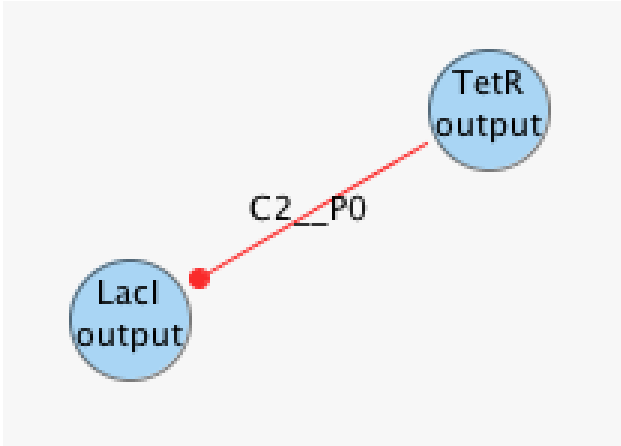


BioPAX TetR Inverter

TetR Inverter: Original vs. First SBML Conversion

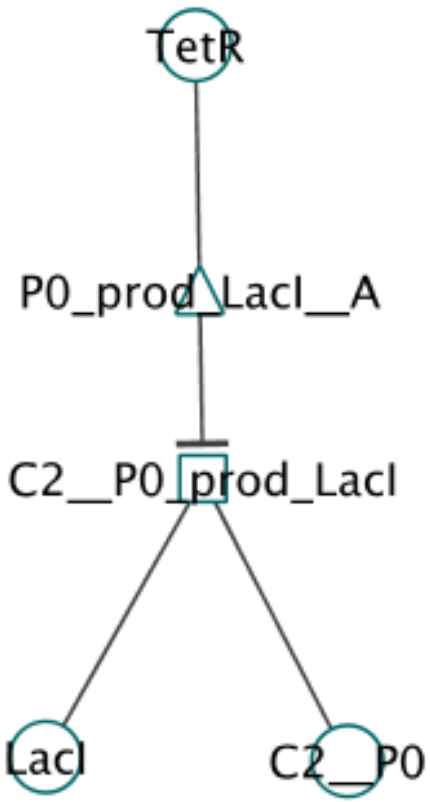


Original TetR Inverter Model

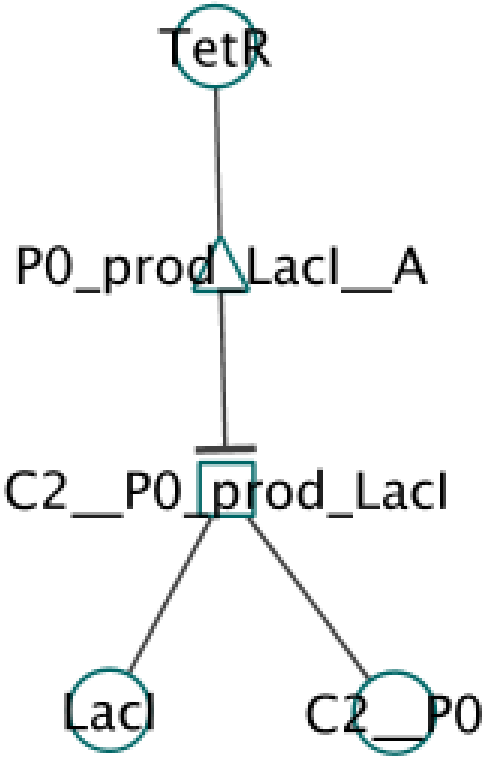


Converted TetR Inverter Model

First vs. Second BioPAX Conversion

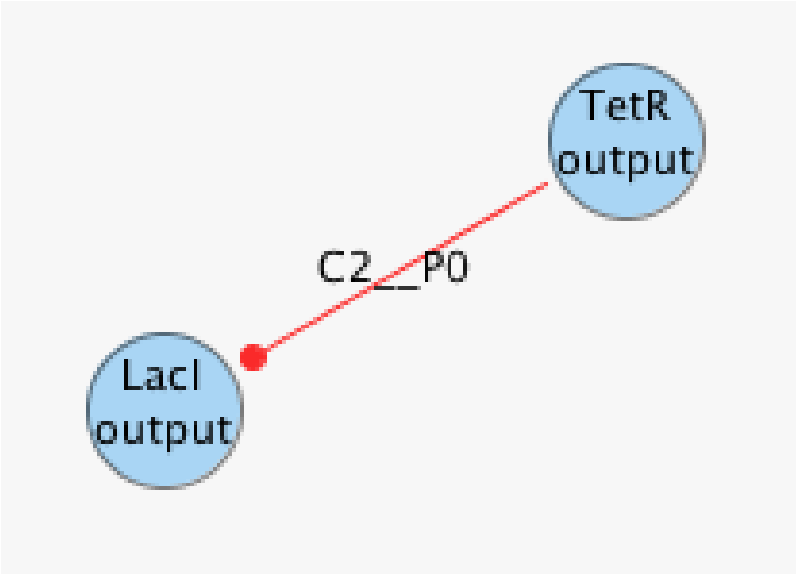


First Conversion TetR Inverter

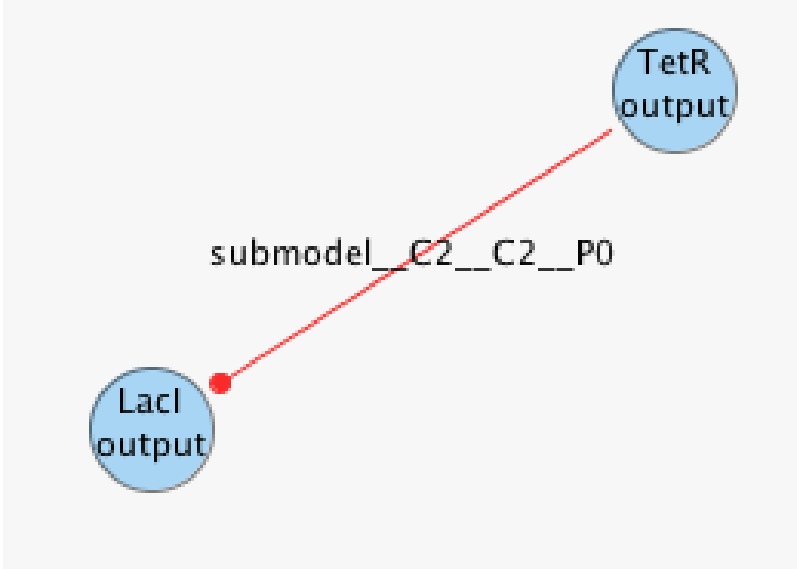


Second Conversion TetR Inverter

TetR Inverter: First vs. Second Conversion

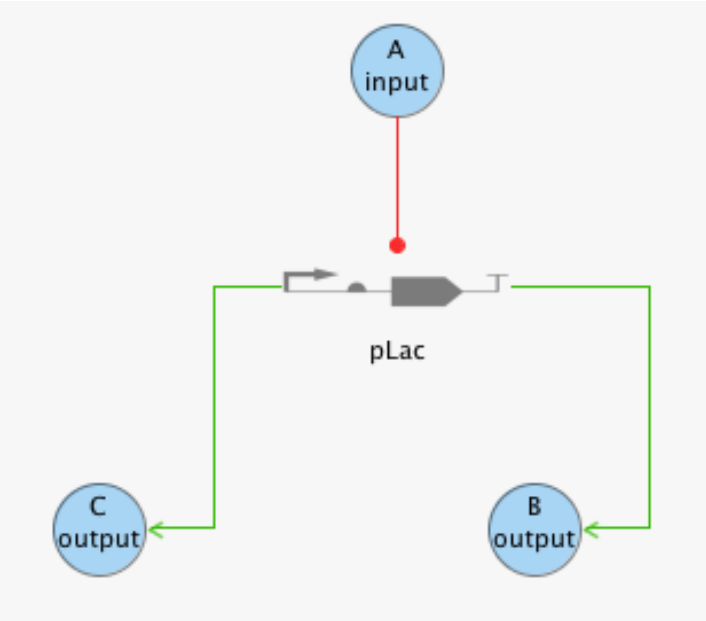


First TetR Inverter Model

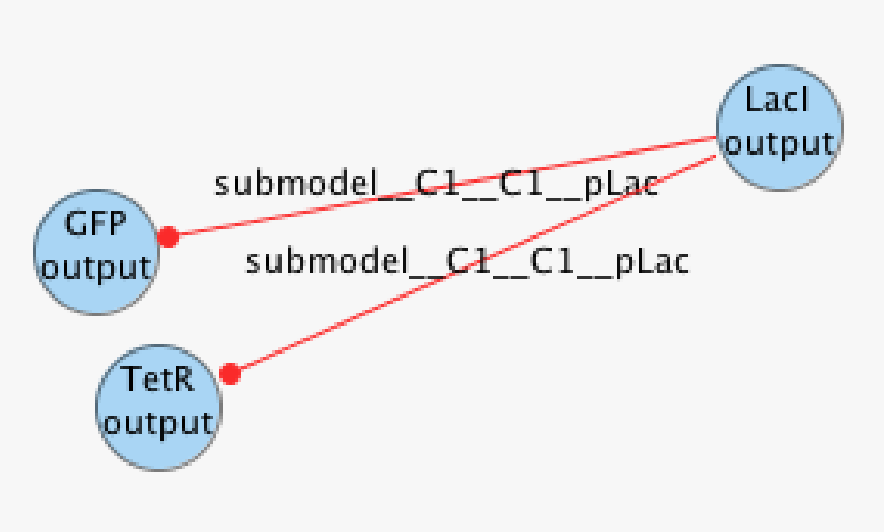


Second TetR Inverter Model

LacI Inverter: Original vs. Second Conversion

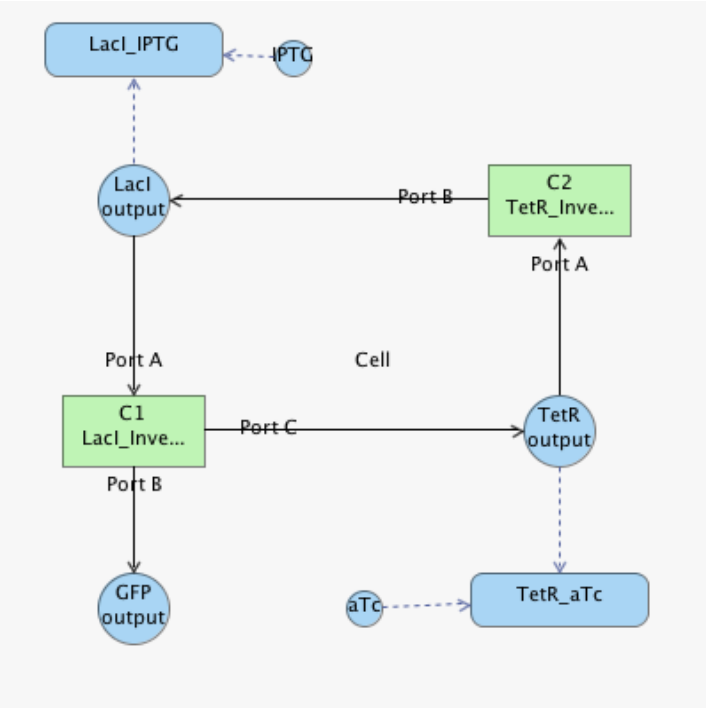


Original LacI Inverter Model

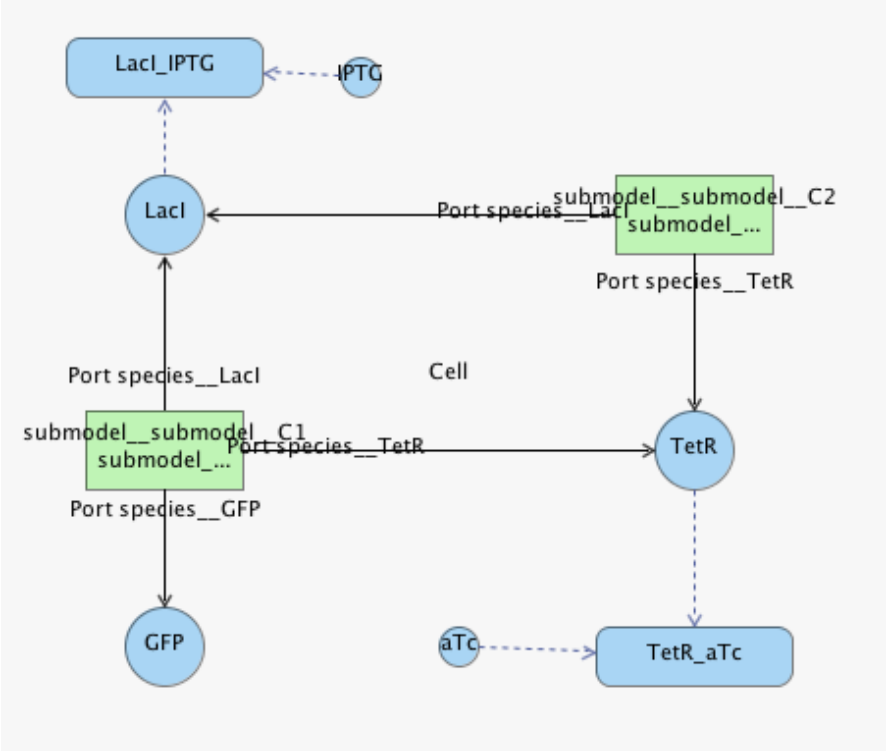


Converted LacI Inverter Model

Genetic Toggle Switch Top-Level



Original SBML Model



Converted SBML Model

Conclusion

- Current Status:
  - Completed mapping of structural elements between BioPAX and SBML.
  - Support multiple pathways using SBML comp package.
  - Interconversion supports mapping of MIRIAM Annotation and Xrefs.
- Future Work:
  - Use custom annotations to support data currently being lost.
  - Support for SBML groups package.
  - Support for SBML qual package.
  - Interconversion between *Synthetic Biology Open Language* (SBOL) and BioPAX.

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