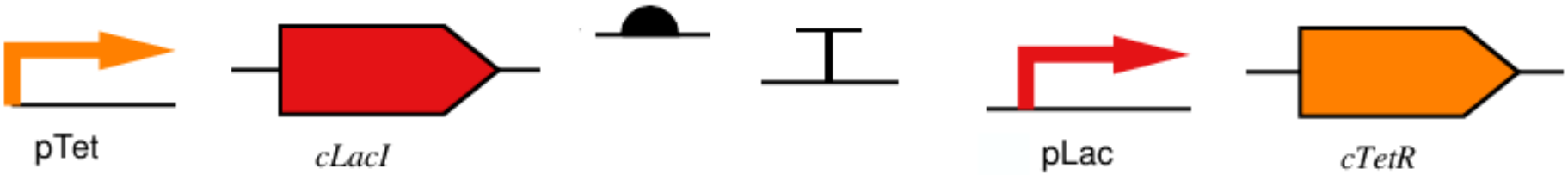
Generating SBML Models from SBOL

Nicholas Roehner

University of Utah

August 20, 2014

SBOL Version 1.1: Genetic Structure



- Specification of DNA components.
- Hierarchical composition of DNA components.

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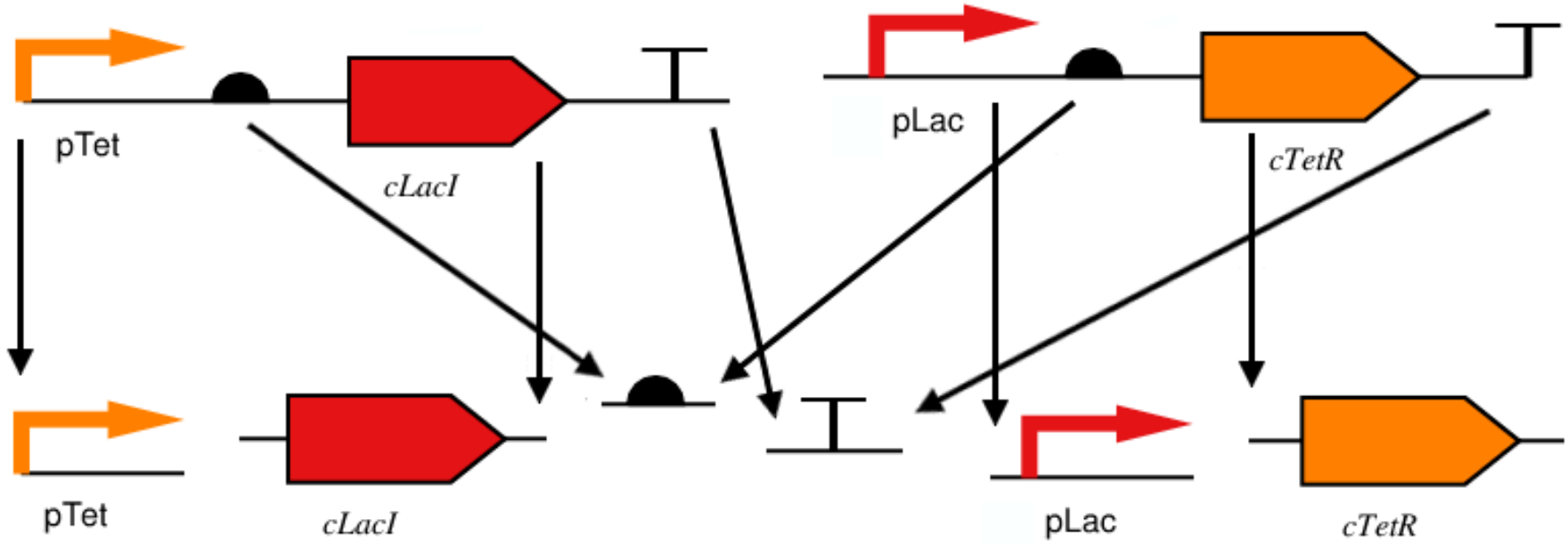

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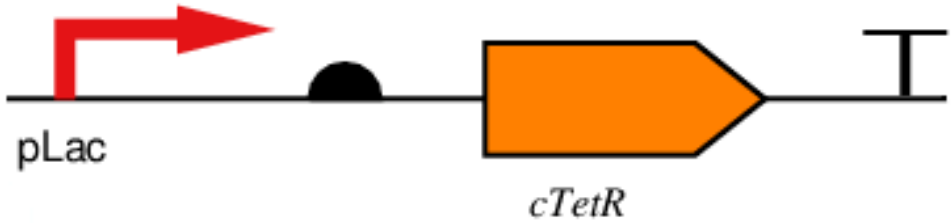
Proposal for SBOL Version 2.0: Genetic Structure



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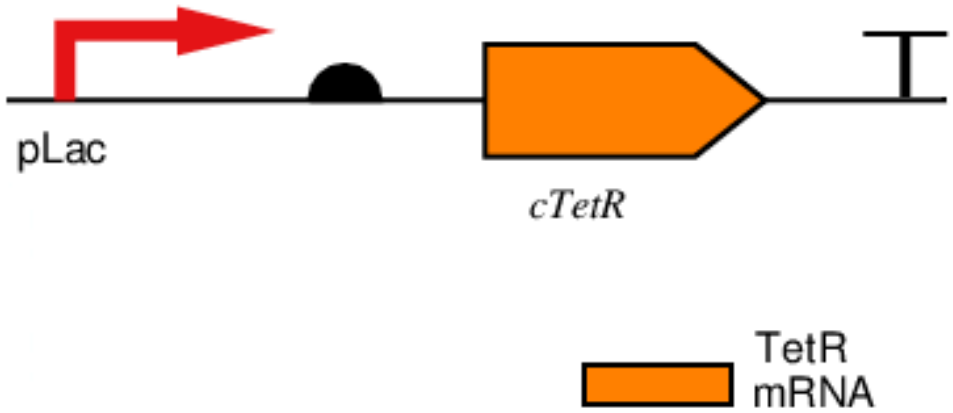
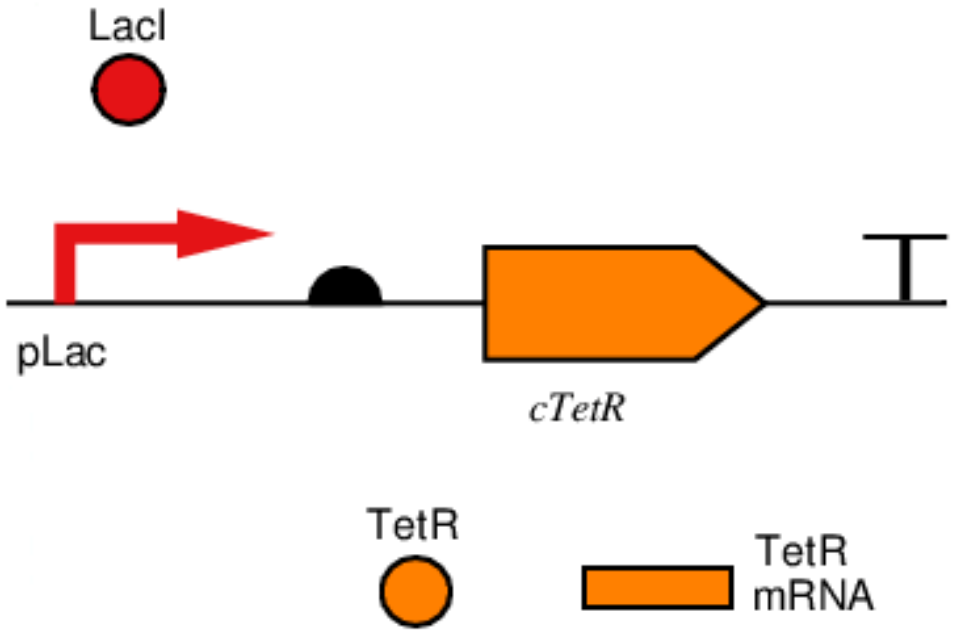


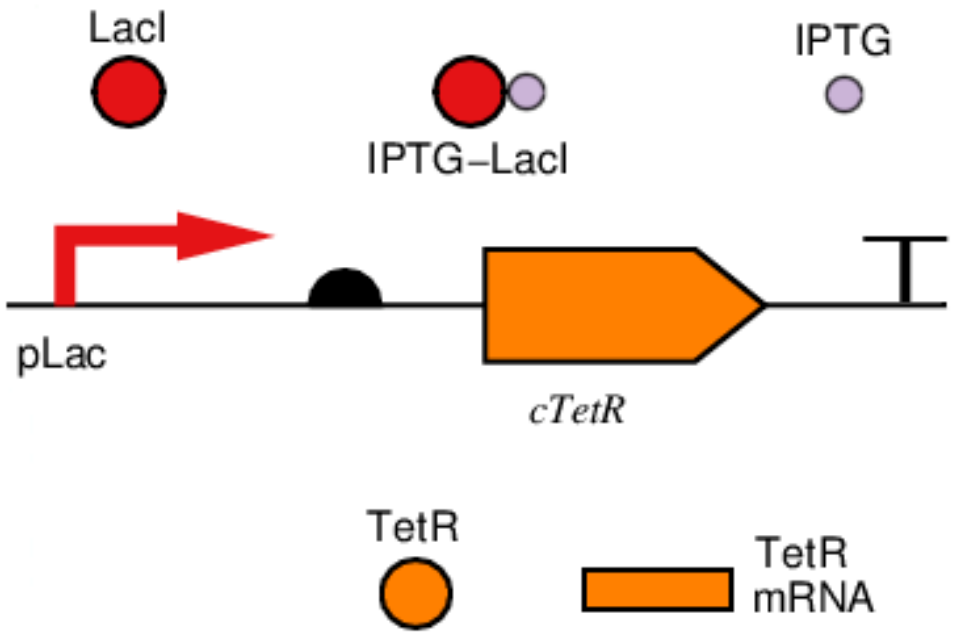
- RNA components (mRNA, tRNA, siRNA)
- Protein components
- Other Components

Proposal for SBOL Version 2.0: Genetic Structure



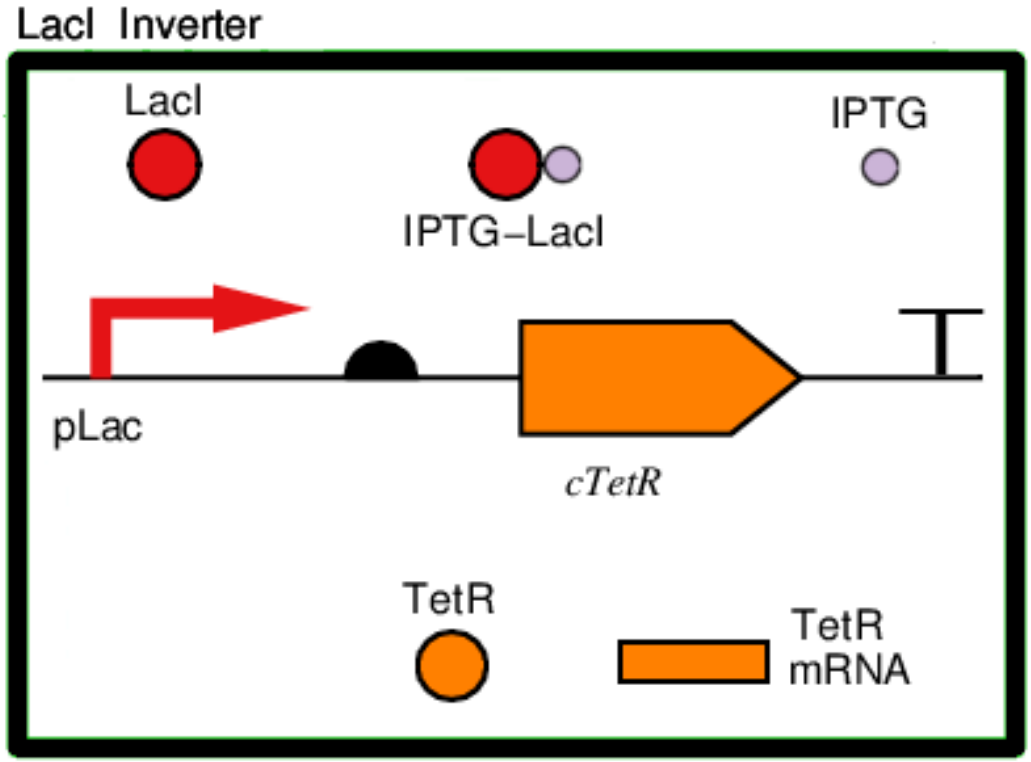
- RNA components
- Protein components (transcription factors, enzymes)
- Other Components

Proposal for SBOL Version 2.0: Non-Genetic Structure



- RNA components
- Protein components
- Other Components (small molecules, molecular complexes, light)

Proposal for SBOL Version 2.0: Qualitative Function



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

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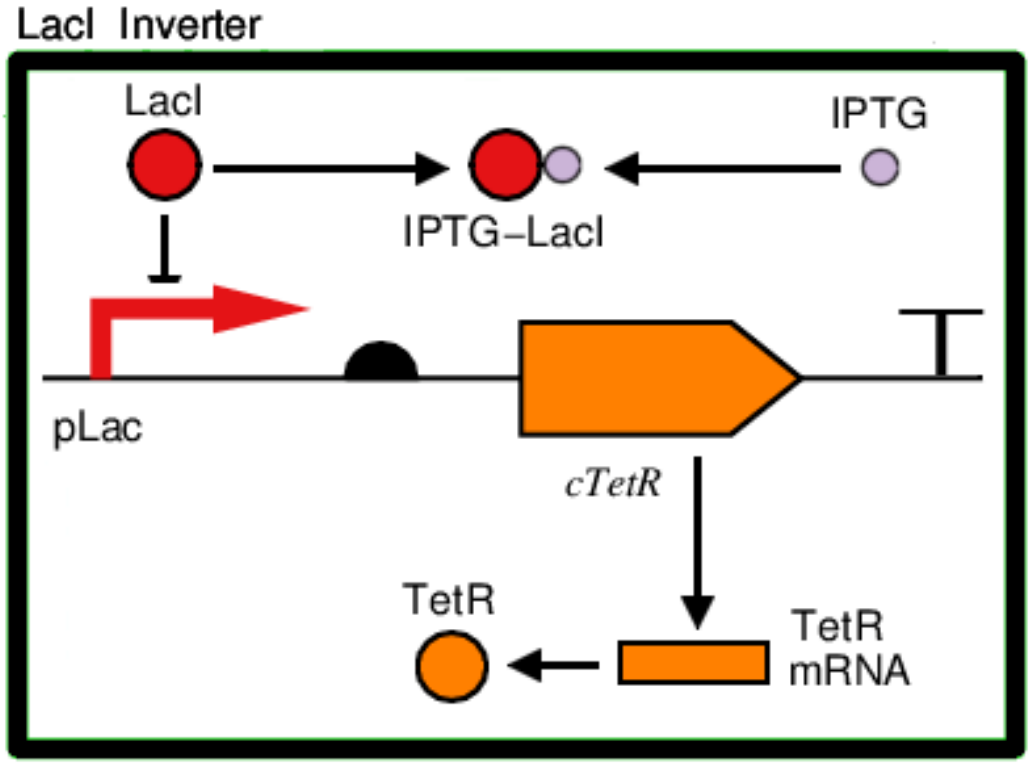
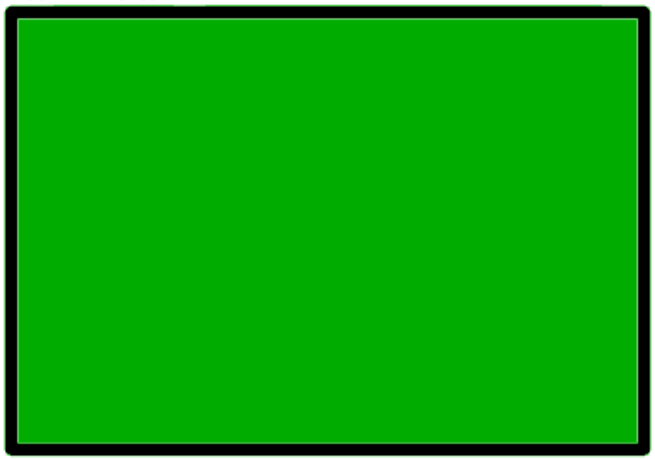


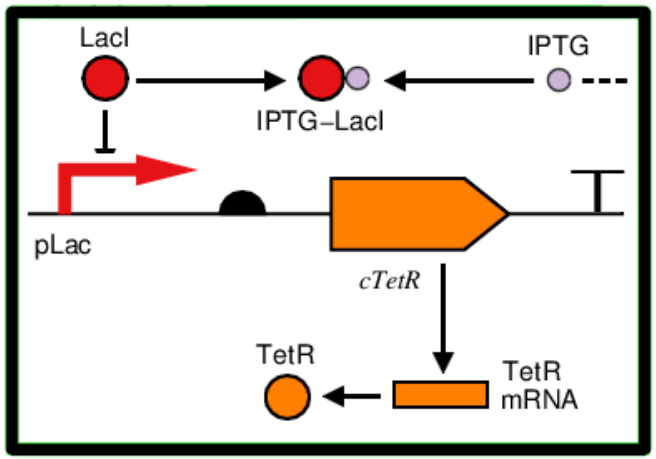
- Modules
- Interactions (activation, repression, complex formation, transcription, translation, phosphorylation)

Proposal for SBOL Version 2.0: Hierarchical Composition

TetR Inverter



LacI Inverter



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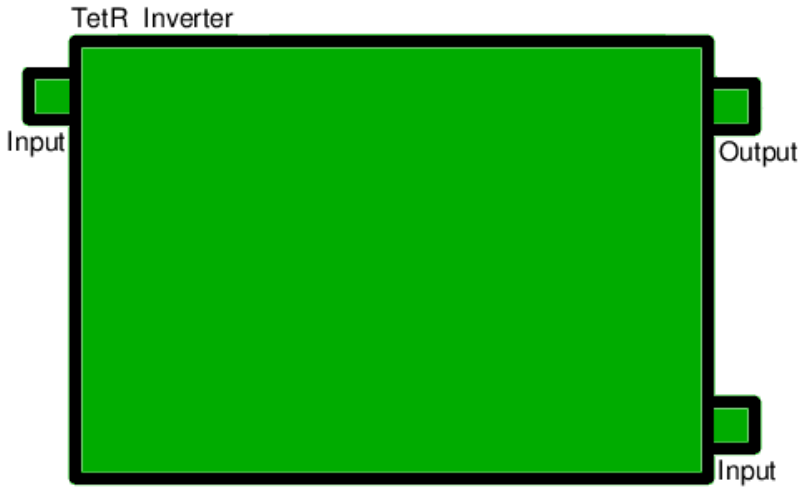

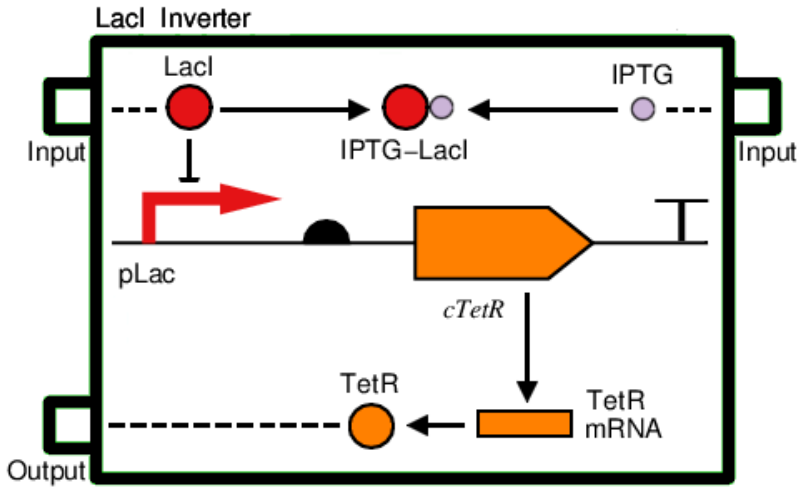

- Ports
- Instantiation
- Port Mapping

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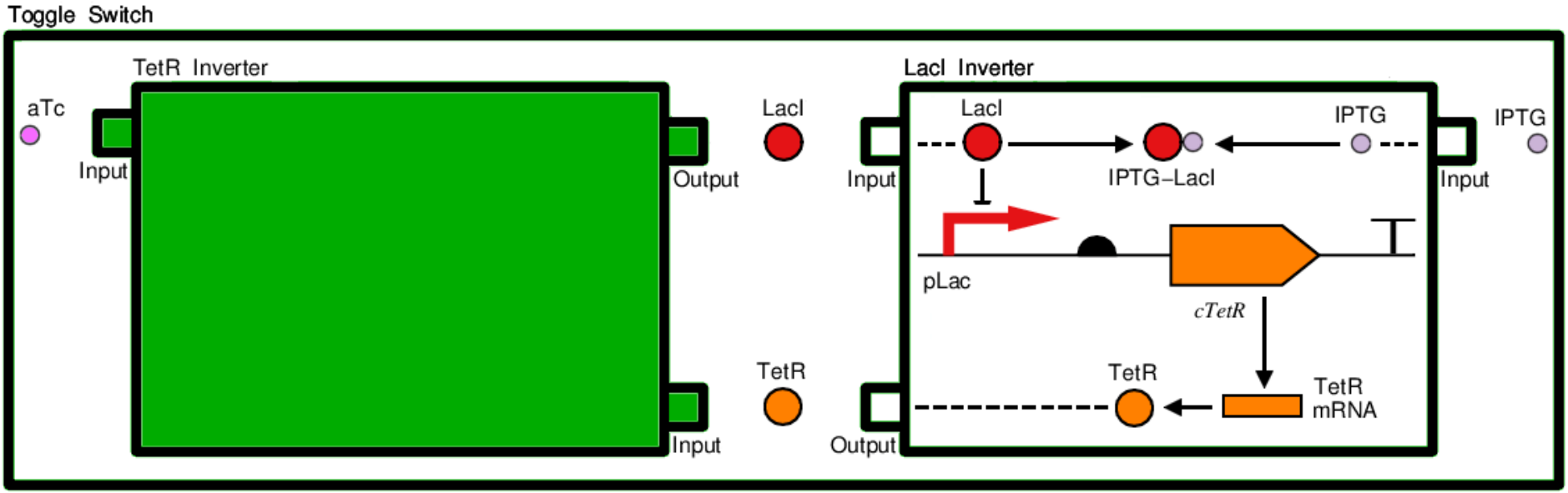

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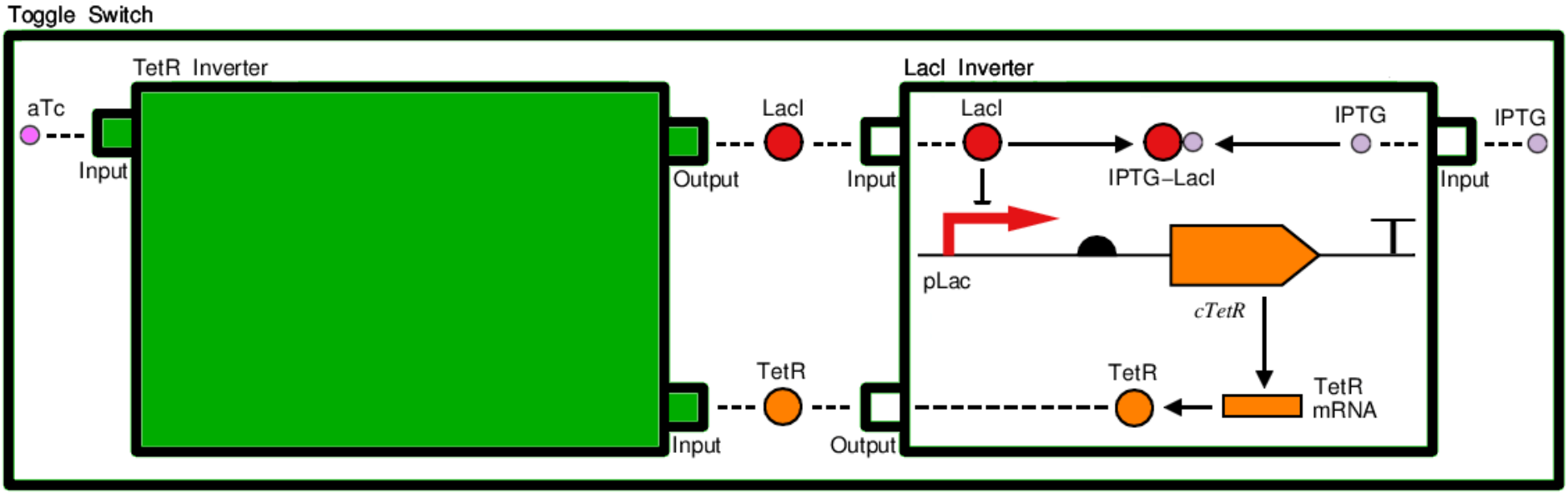

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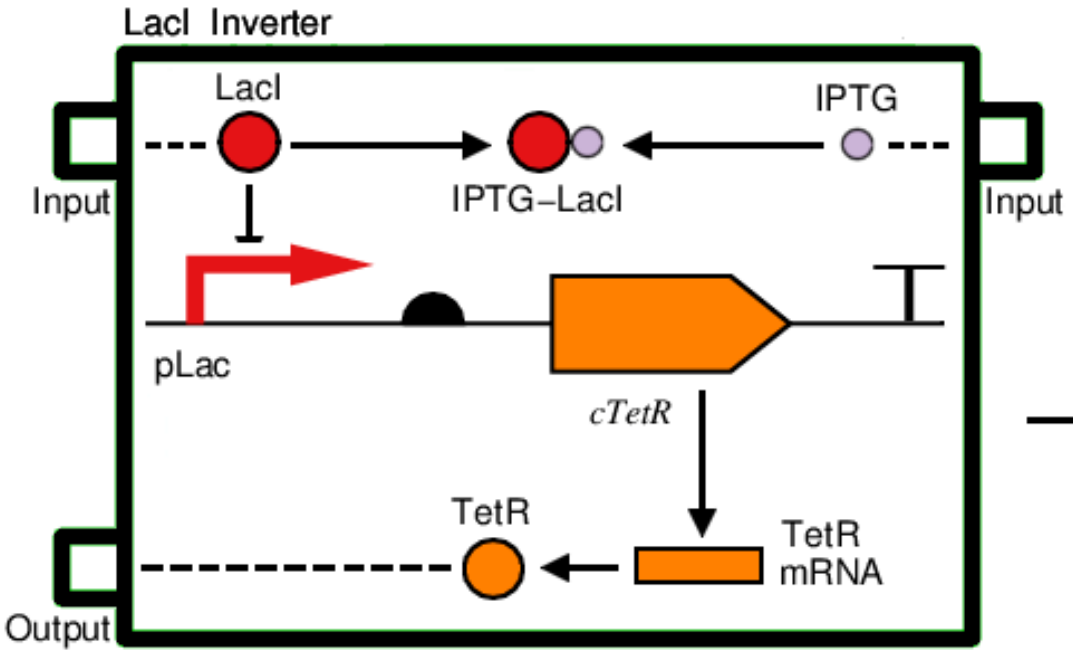
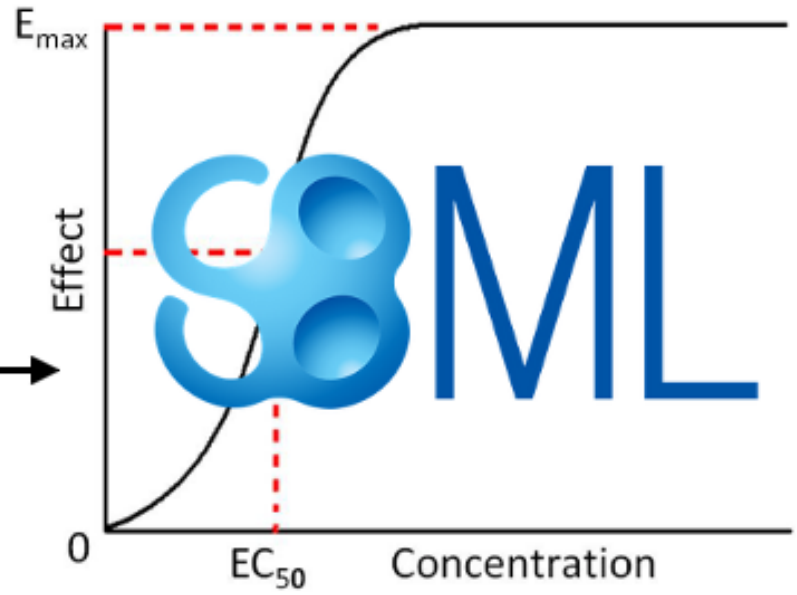
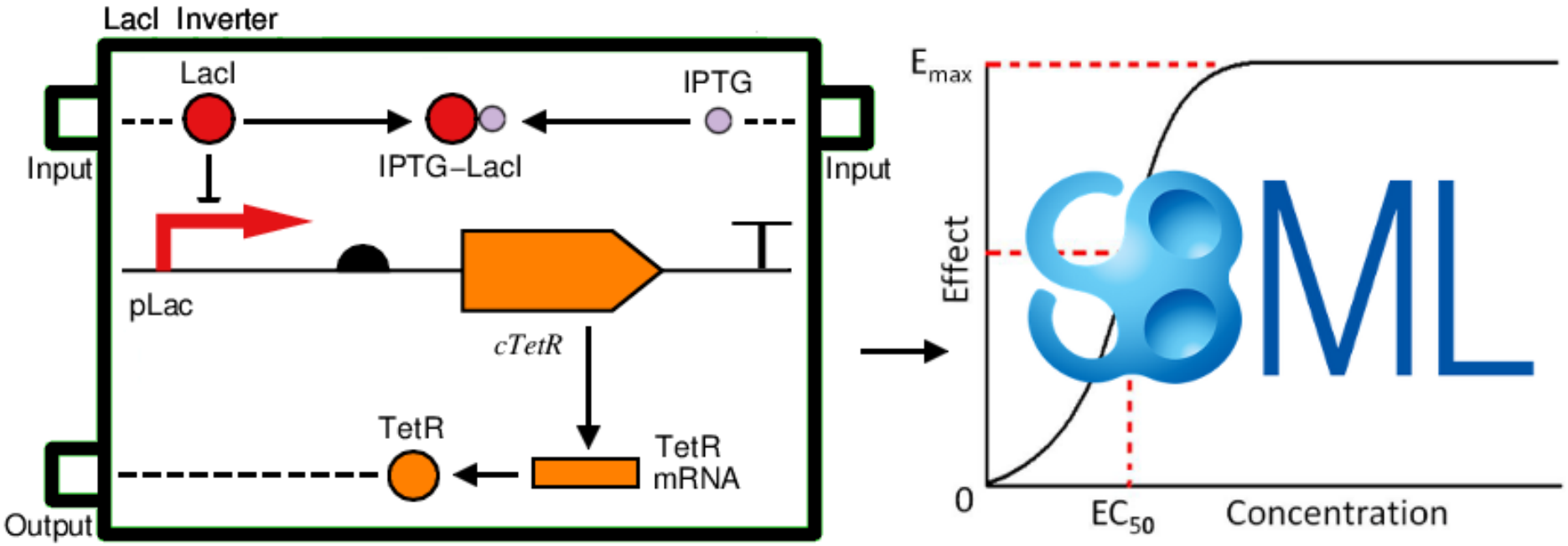
Proposal for SBOL Version 2.0: Quantitative Function





- Models (SBML, CellML, MATLAB)

Model Generation



- Supplies quantitative models for analysis of synthetic genetic designs.
- Facilitates collaboration between biologists and engineers.
- Enables comparison of different models backed by same SBOL module.

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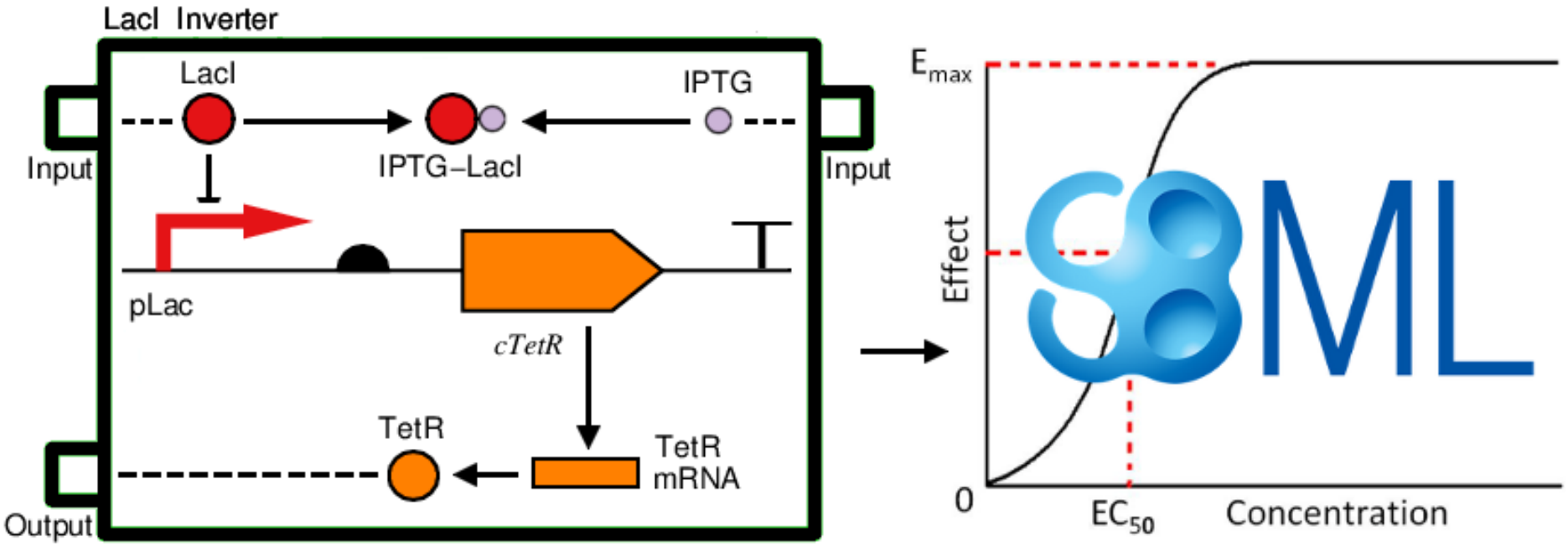

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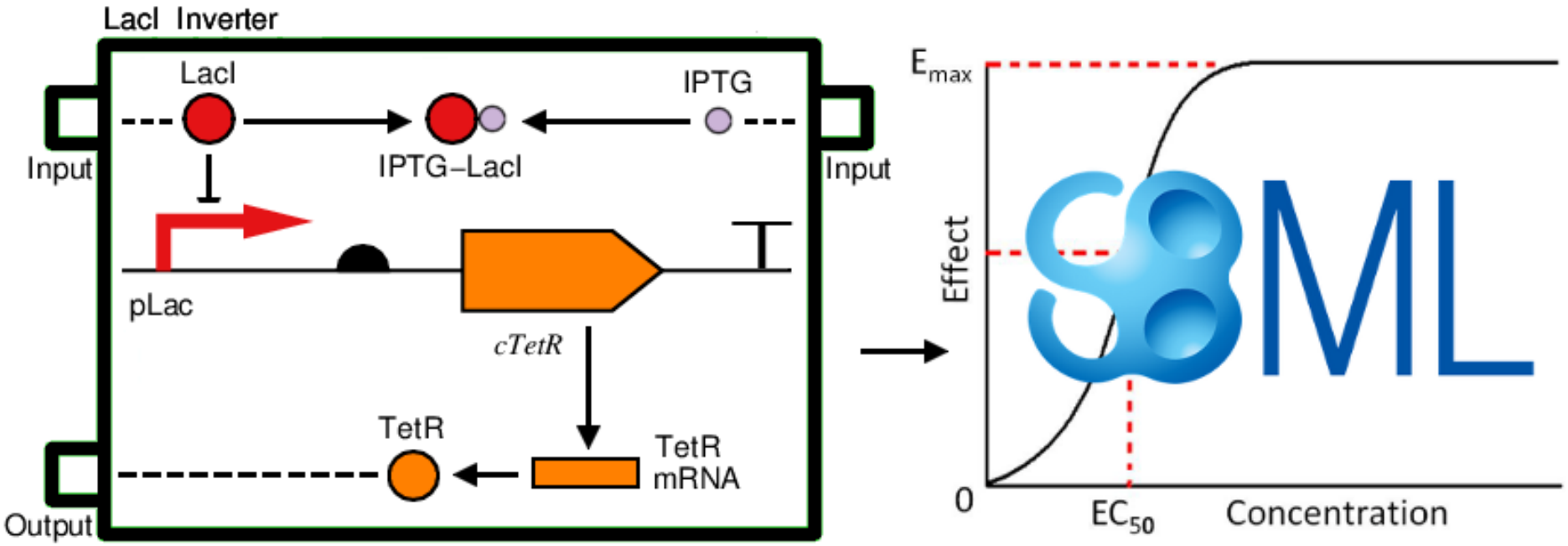

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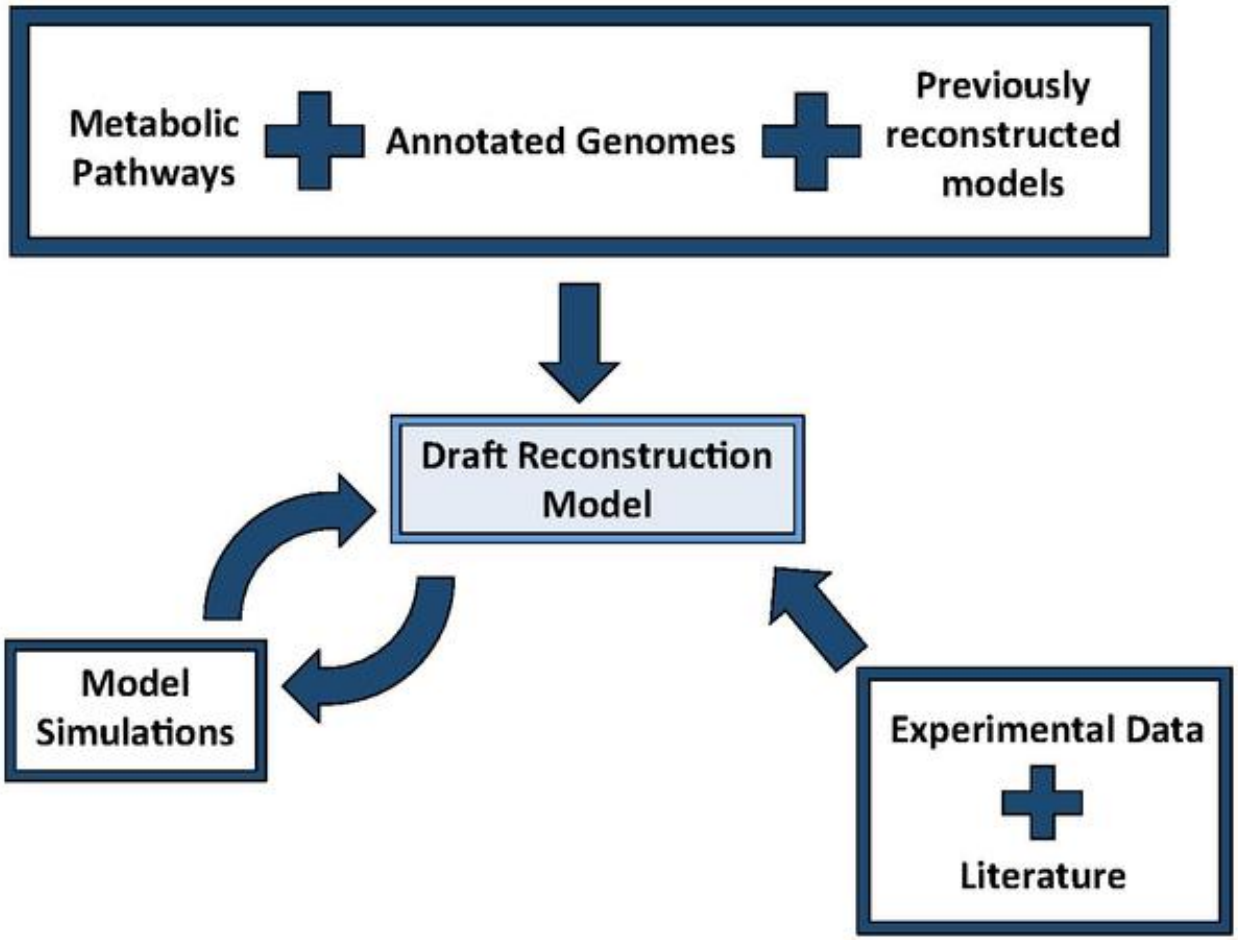
Metabolic Reconstruction



Metabolic Reconstruction vs. Model Generation

- Primary applications for metabolic reconstruction include:
  - Refinement of data on metabolic and signaling pathways in natural biological systems.
  - Forward engineering of metabolic and signaling pathways in synthetic biological systems.
- By contrast, our approach to model generation for synthetic biology:
  - Places greater emphasis on engineering genetic regulatory networks.
  - Operates on SBOL, a standard expressly developed for representing synthetic biological designs.

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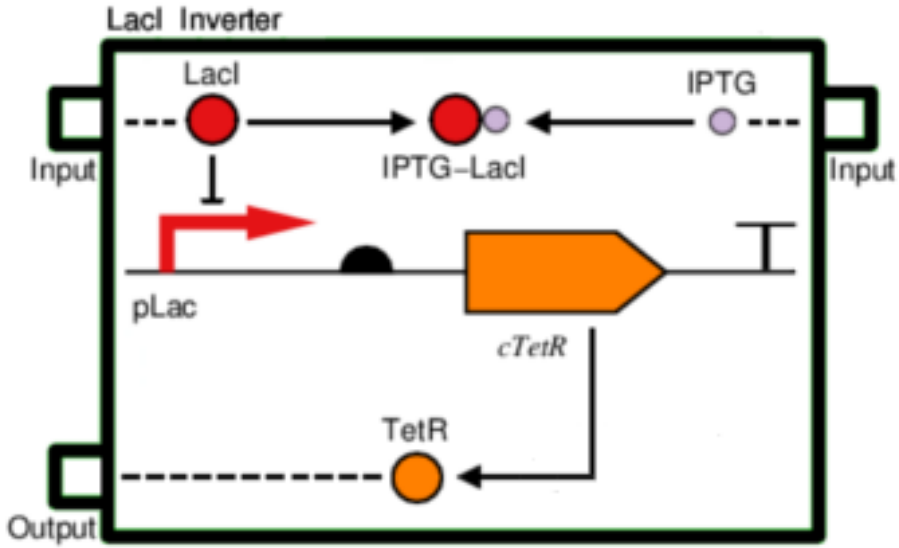

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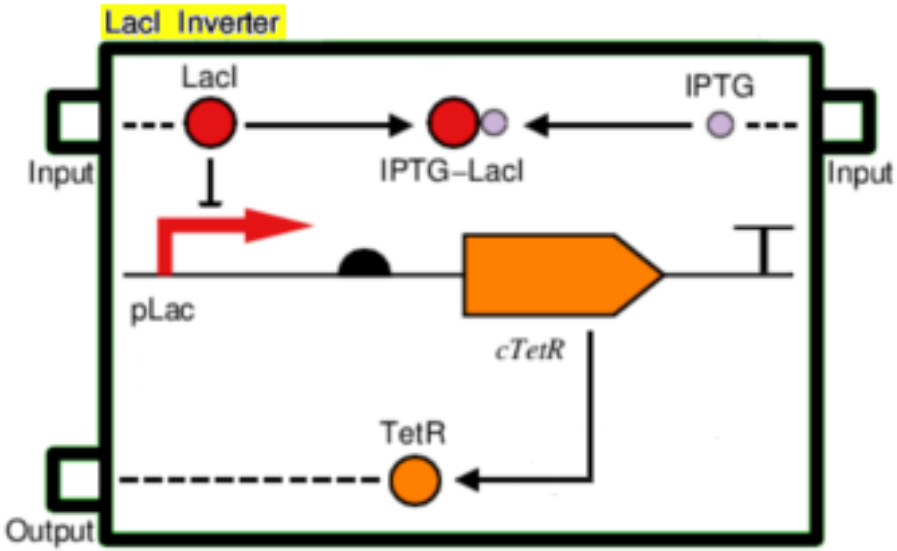

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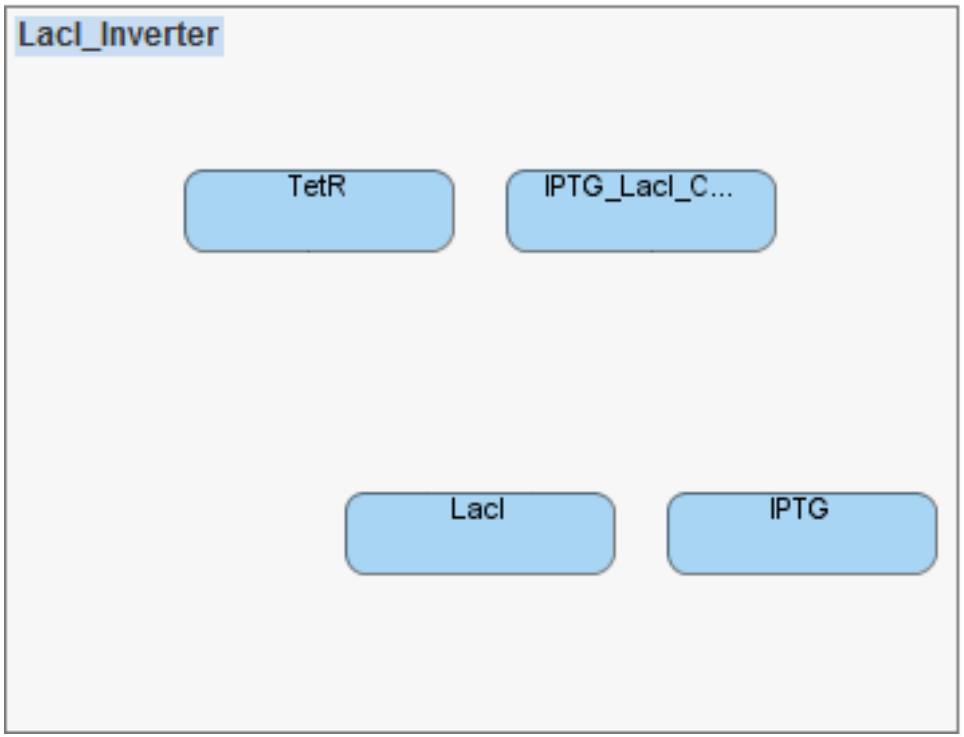

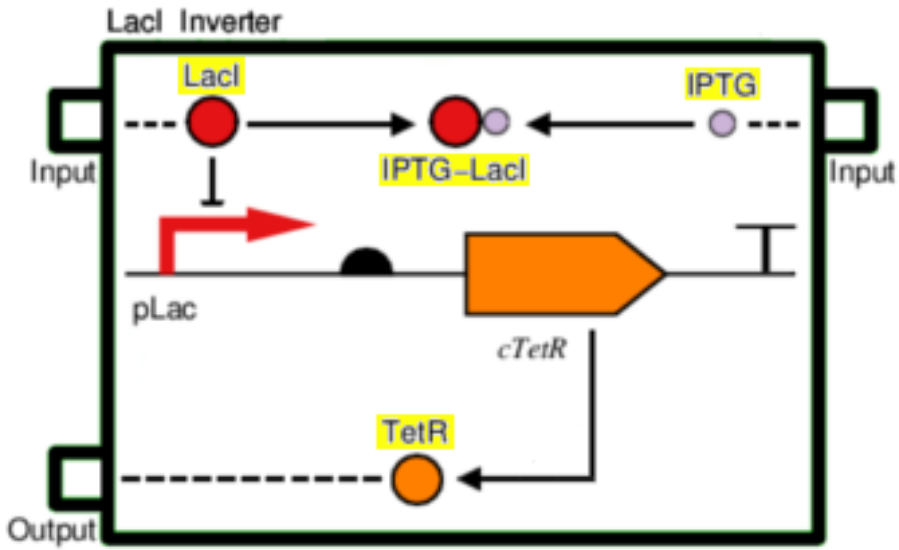

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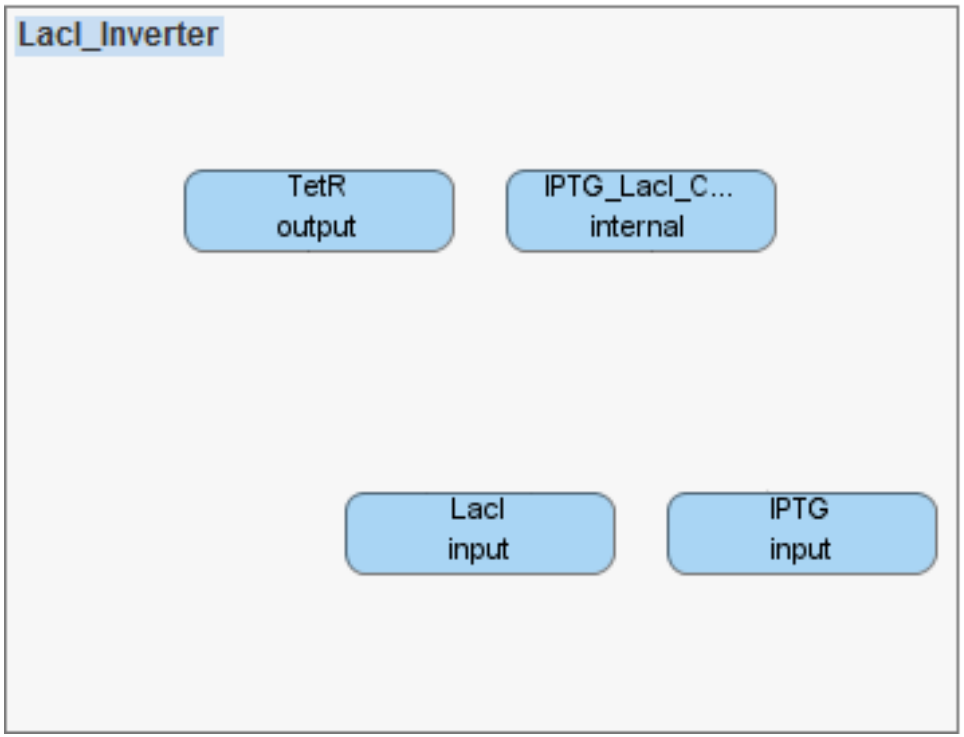

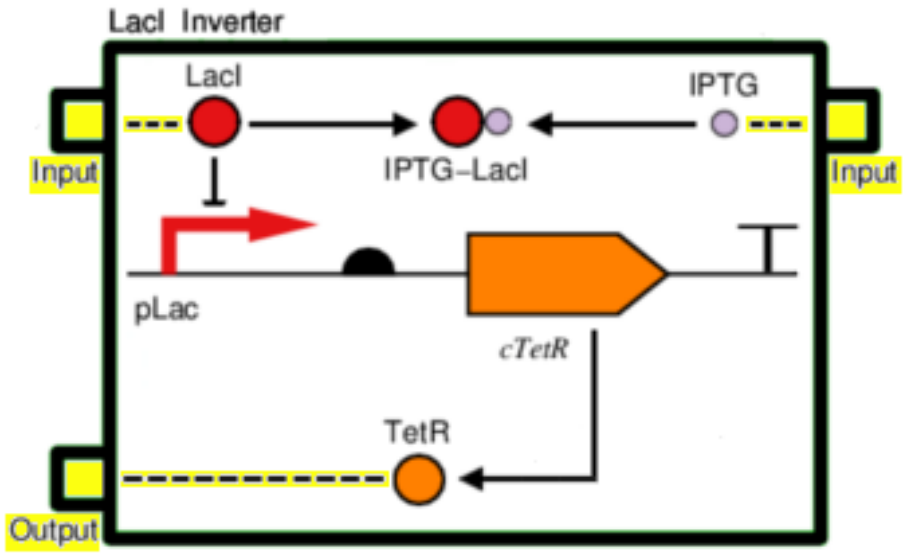

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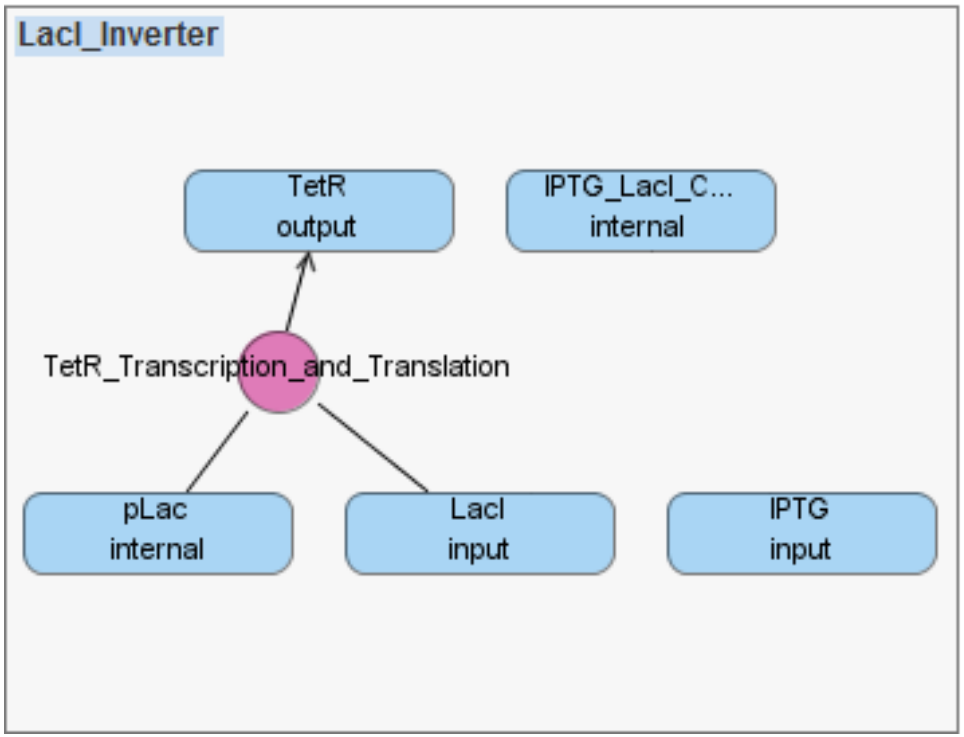

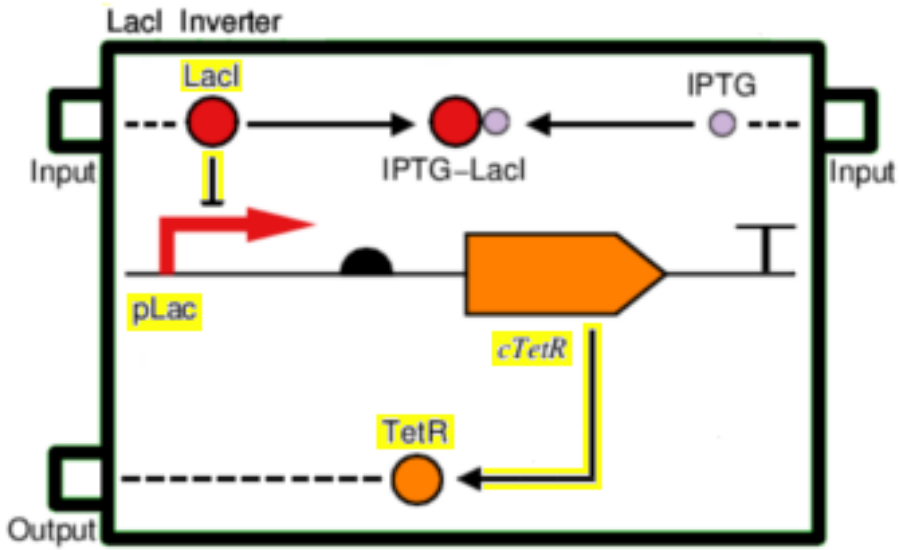

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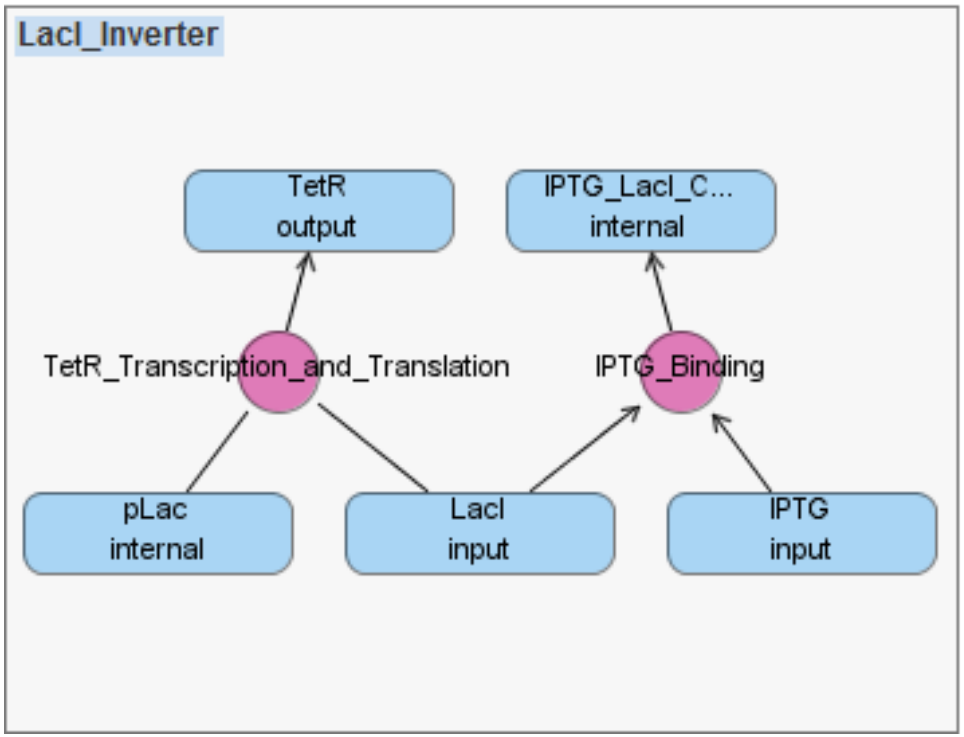

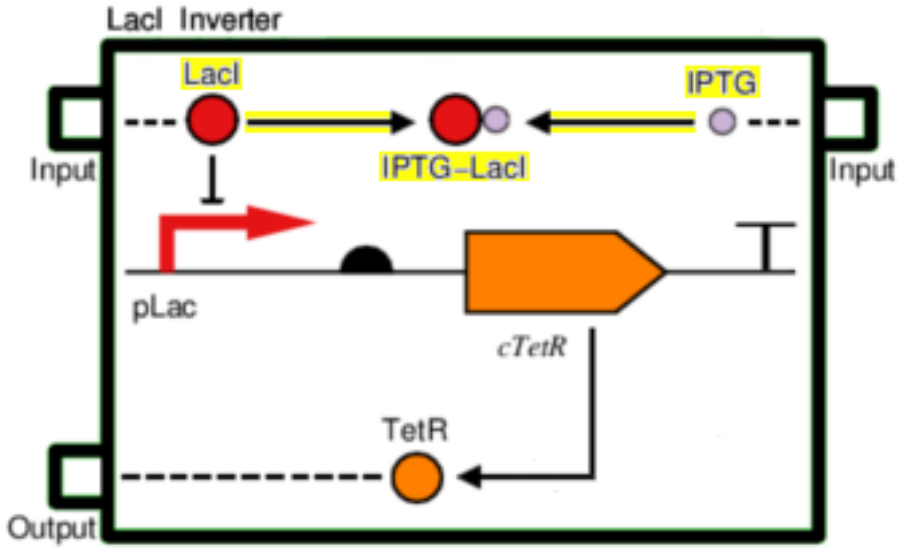

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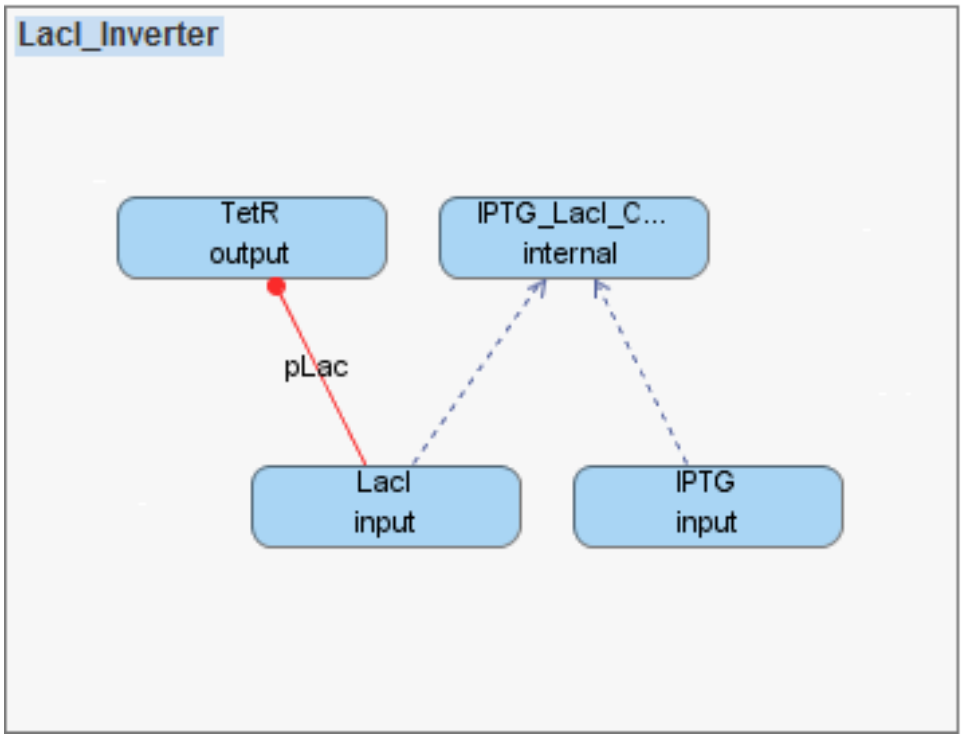

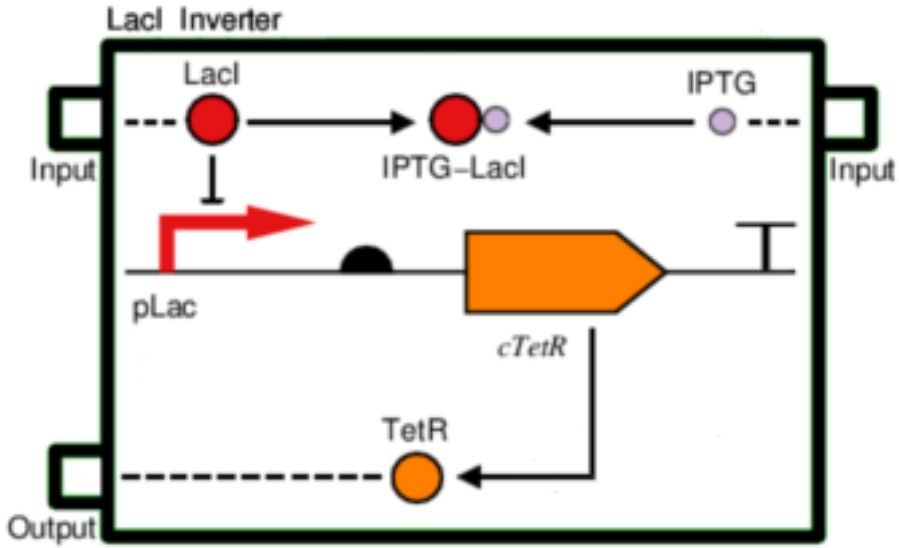

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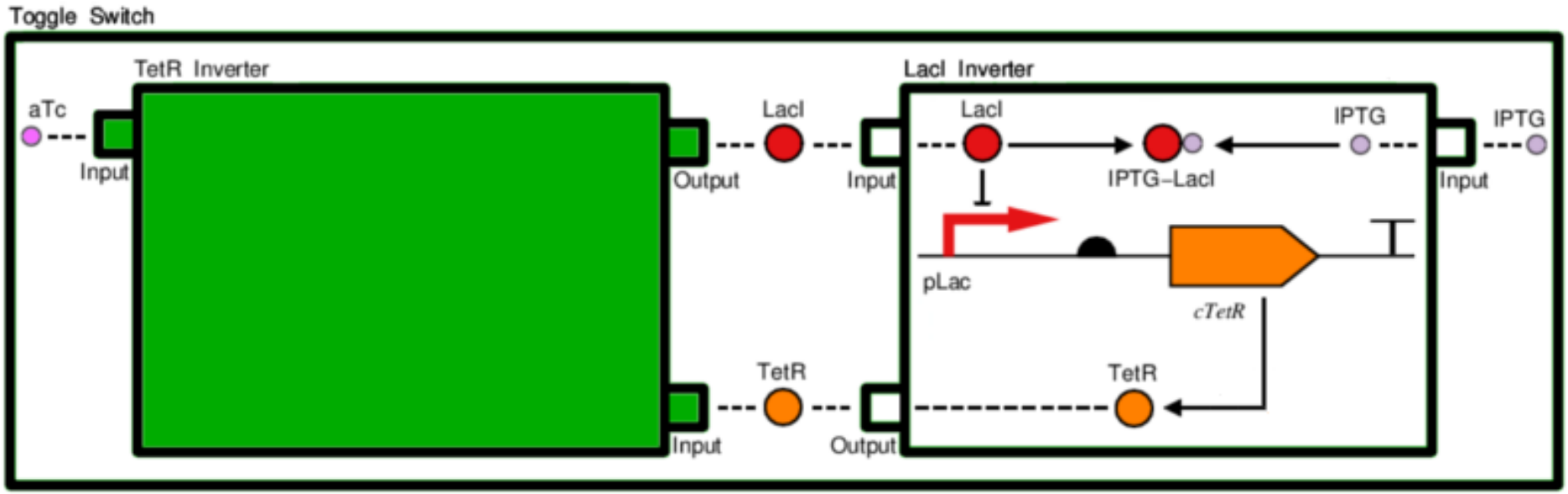

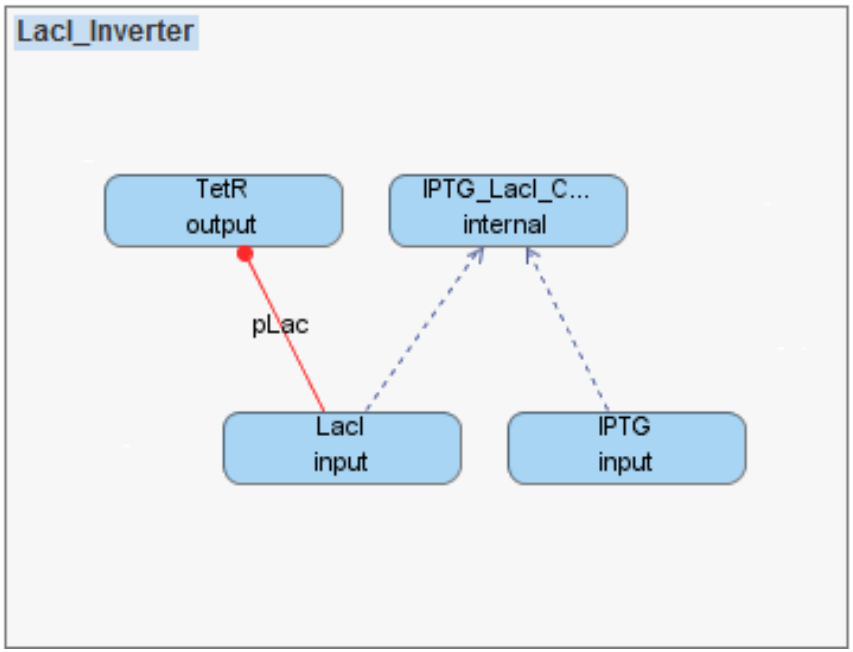

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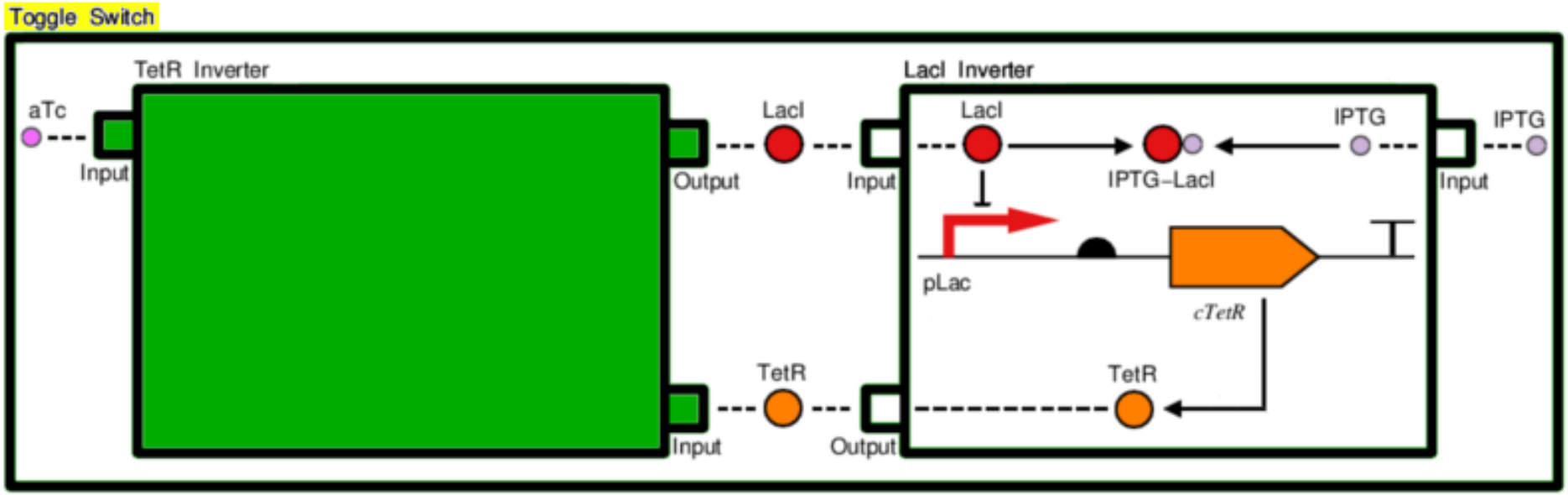

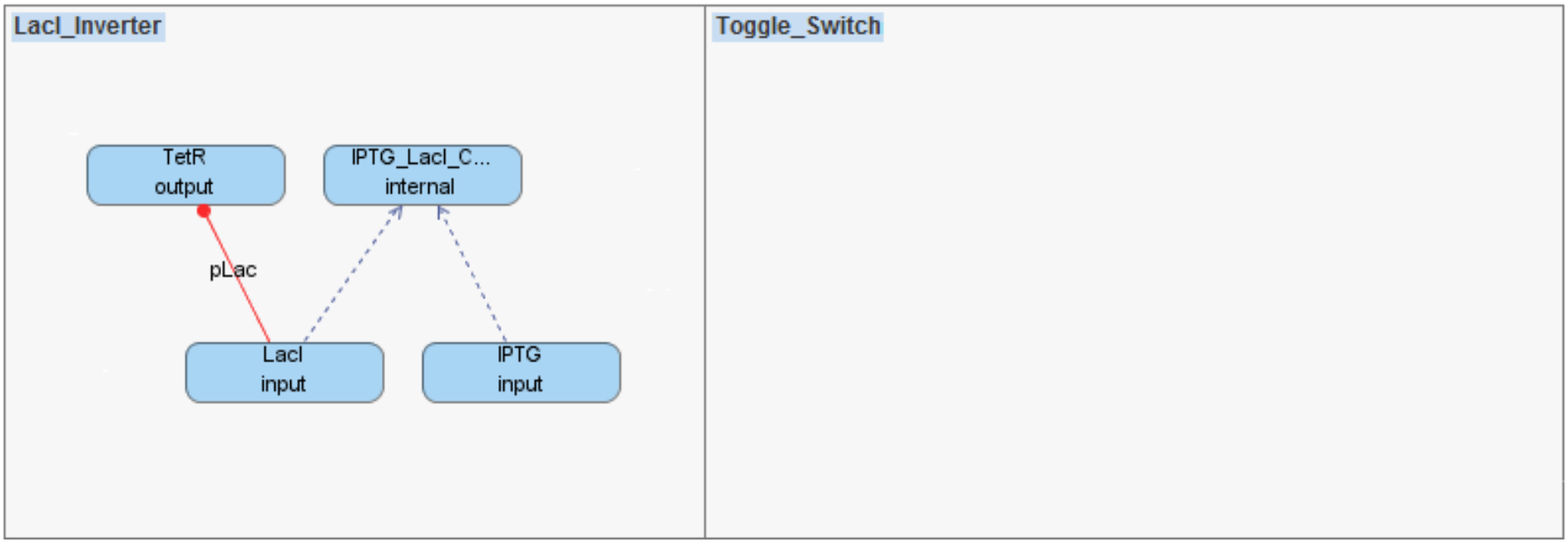

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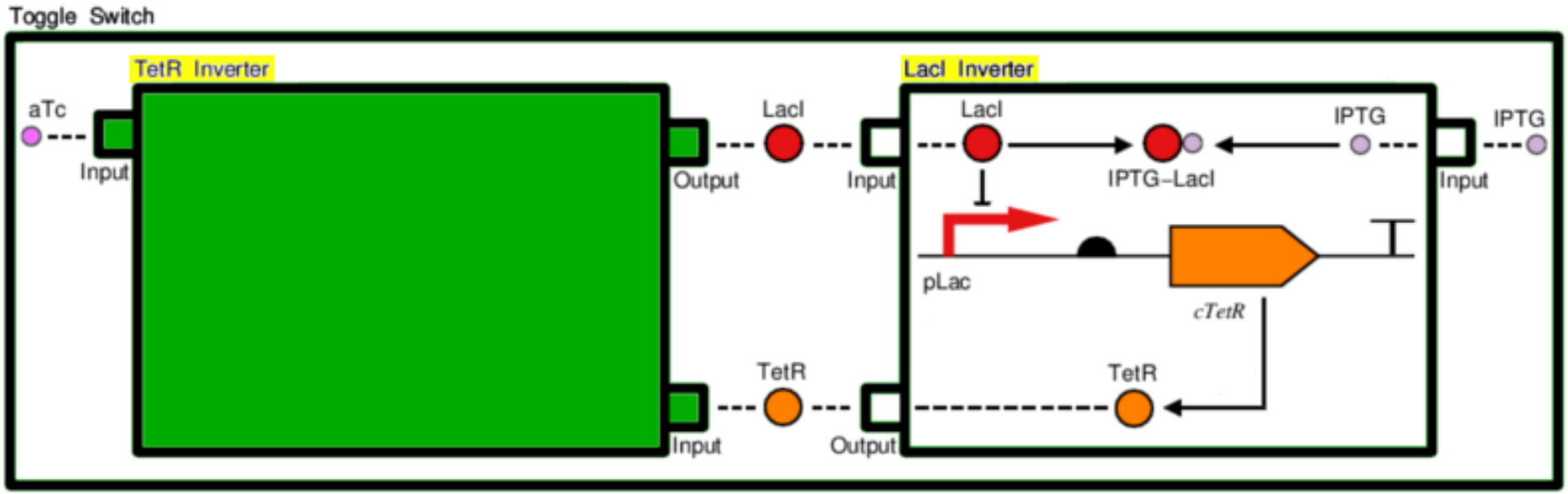

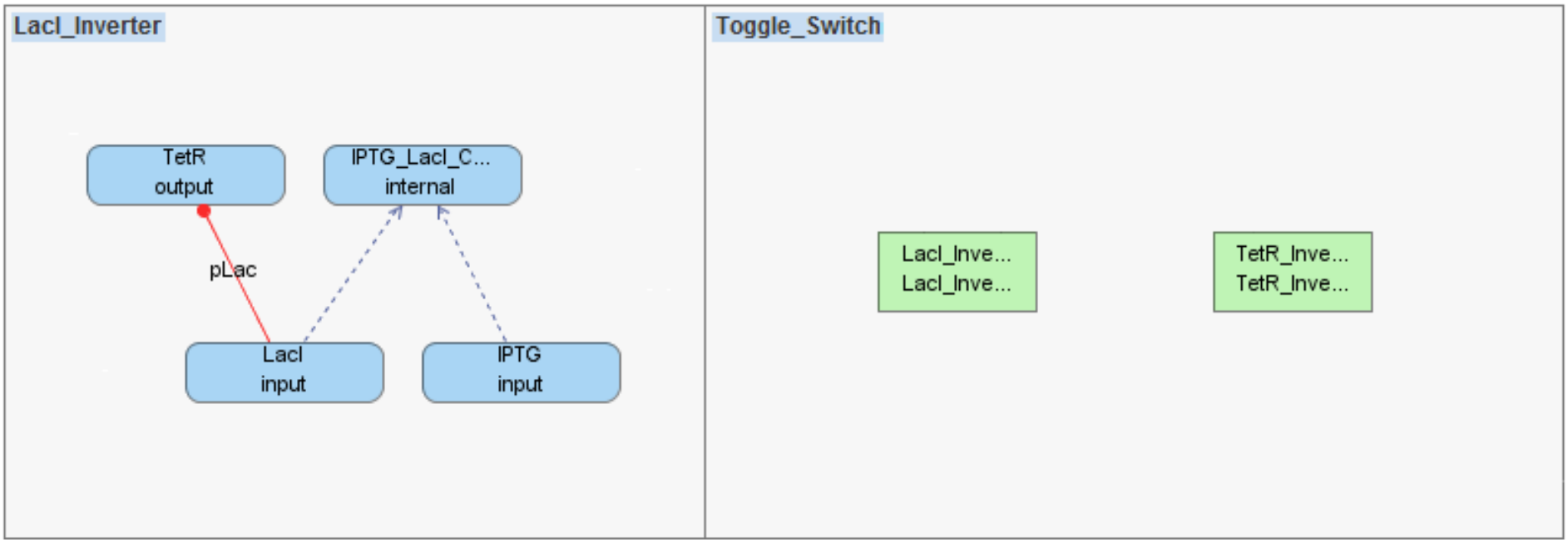

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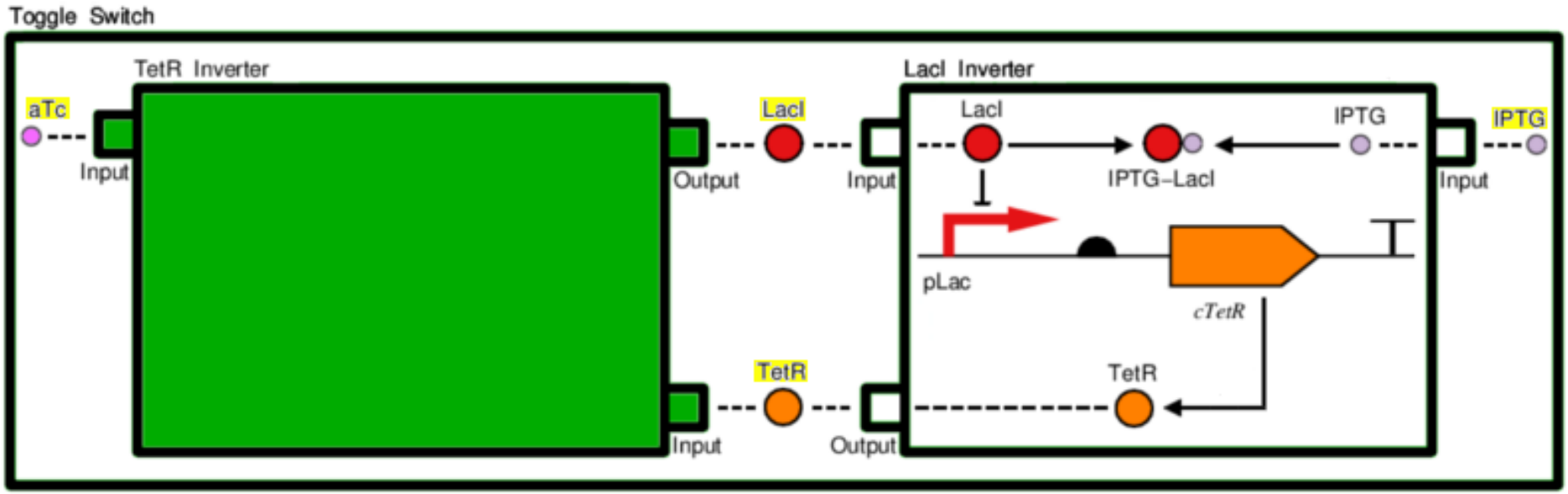

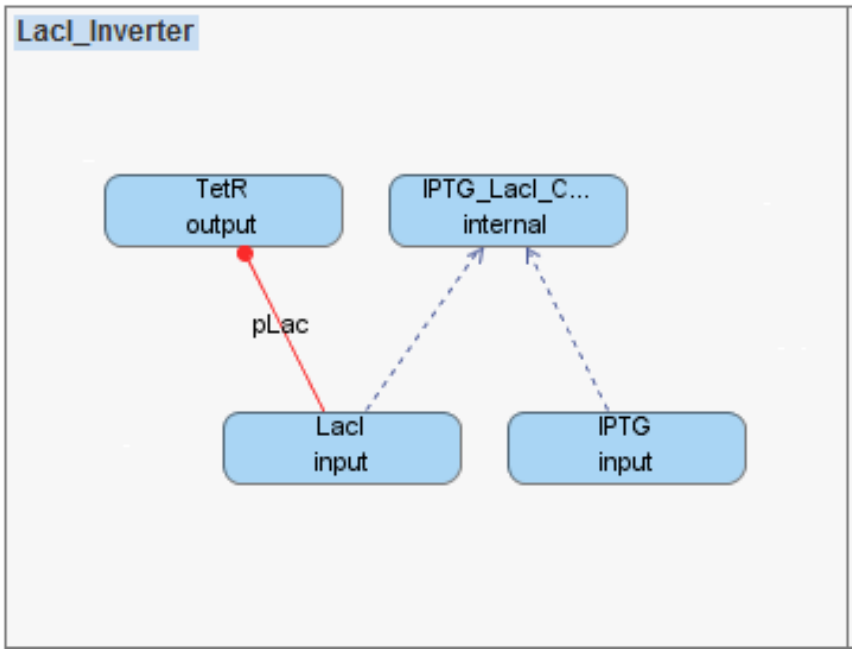

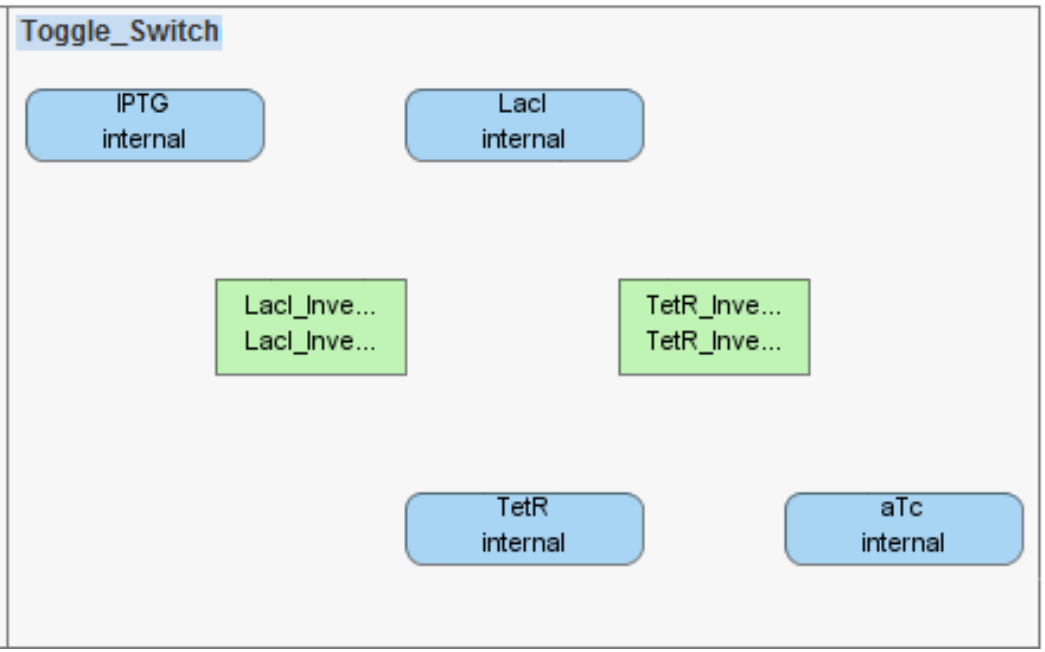

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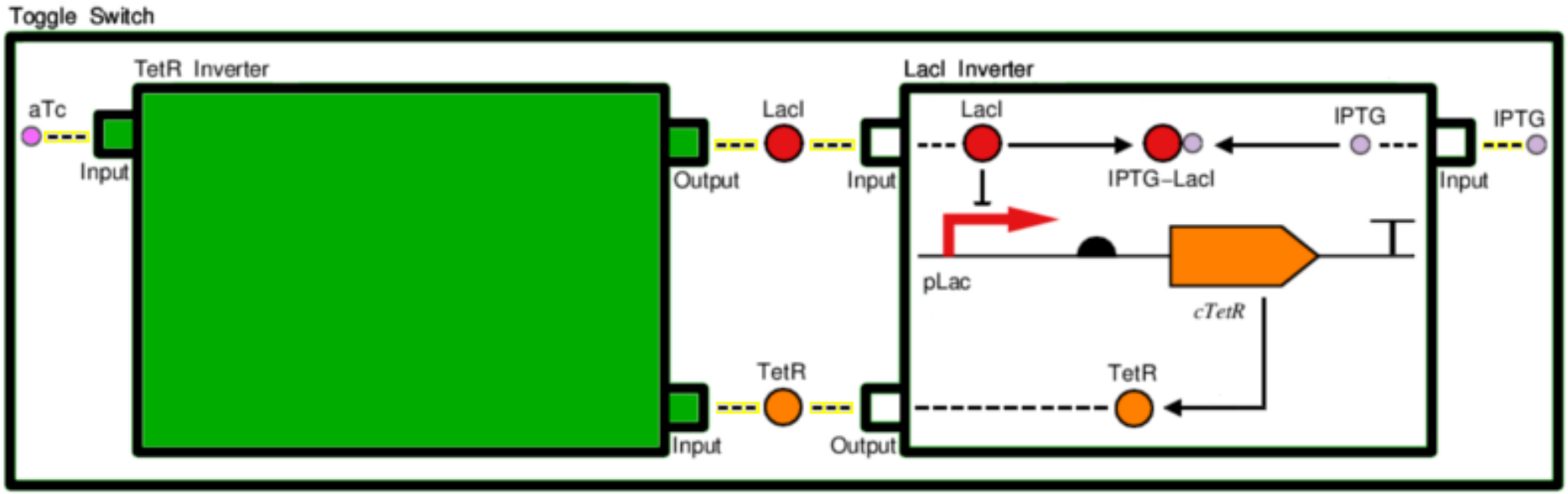

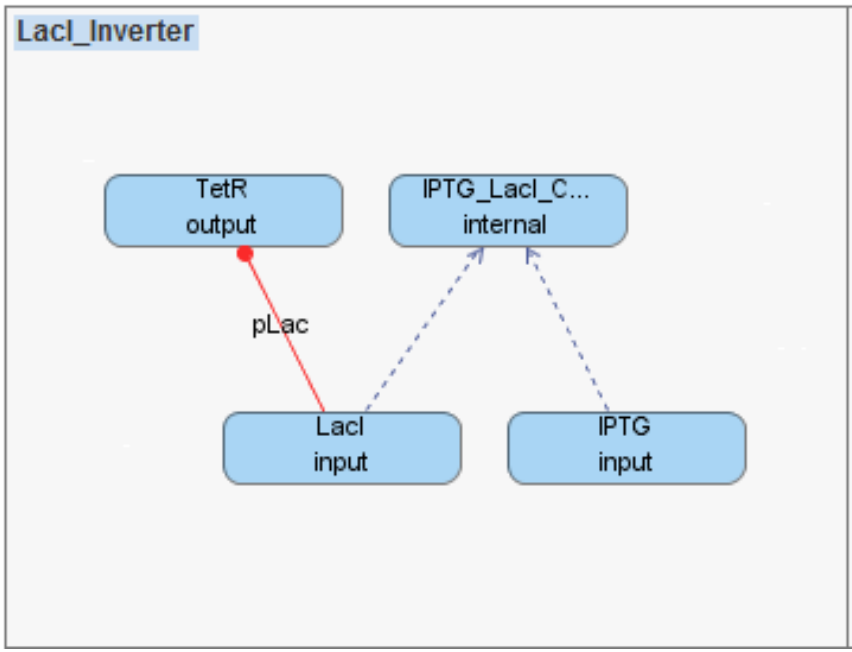

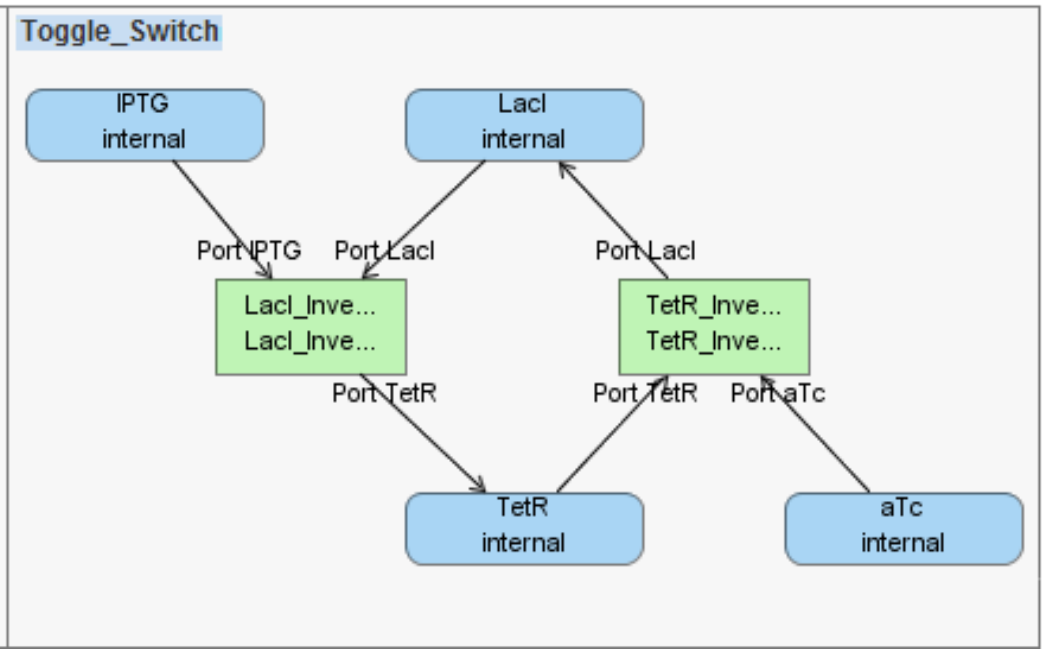

Kinetic Laws: Degradation

$$\text{rate}(r_s) = k_d s$$

Kinetic Laws: Complex Formation

$$\text{rate}(r_s) = k_{c_f}\left(K_c{}^{|\text{React}(s)|-2}\prod_{s' \in \text{React}(s)} s'\right) - k_{c_r} s$$

Kinetic Laws: Genetic Production

$$\text{rate}(r_p) = \begin{cases} \dfrac{n_p k_o n_g K_o n_r}{1 + K_o n_r + \sum\limits_{s_r \in \text{Rep}(p)} (K_r s_r)^{n_c}} & |\text{Act}(p)| = 0 \\ \dfrac{n_p k_b n_g K_o n_r + n_p k_a n_g K_{oa} n_r \sum\limits_{s_a \in \text{Act}(p)} (K_a s_a)^{n_c}}{1 + K_o n_r + \sum\limits_{s_r \in \text{Rep}(p)} (K_r s_r)^{n_c} + K_{oa} n_r \sum\limits_{s_a \in \text{Act}(p)} (K_a s_a)^{n_c}} & \text{otherwise} \end{cases}$$

Kinetic Parameters

Parameter	Symbol	Value	Units
Rate of degradation	k_d	0.0075	$\frac{1}{sec}$
Stoichiometry of production	n_p	10	*unitless*
Open complex production rate	k_o	0.05	$\frac{1}{sec}$
Basal production rate	k_b	0.0001	$\frac{1}{sec}$
Activated production rate	k_a	0.25	$\frac{1}{sec}$
Promoter count	n_g	2	*molecule*
RNA polymerase binding equilibrium	K_o	0.033	$\frac{1}{molecule}$
Activated RNA pol. binding equilibrium	K_{oa}	1	$\frac{1}{molecule}$
RNA polymerase count	n_r	30	*molecule*
Repression binding equilibrium	K_r	0.5	$\frac{1}{molecule}$
Activation binding equilibrium	K_a	0.0033	$\frac{1}{molecule}$
Stoichiometry of binding	n_c	2	*unitless*
Forward non-covalent binding rate	k_{c_f}	0.05	$\frac{1}{molecule*sec}$
Non-covalent binding equilibrium	K_c	0.05	$\frac{1}{molecule}$
Reverse non-covalent binding rate	k_{c_r}	1	$\frac{1}{sec}$

Future of Model Generation

- Mappings from SBOL to other model languages and frameworks will be developed for different design tasks.
- Development can be democratized with software tools for creating new mappings between qualitative SBOL and quantitative modeling standards.

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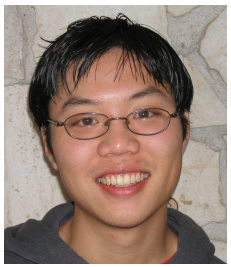

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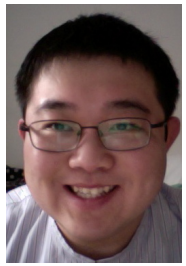

Zhen Zhang

This work is supported by the National Science Foundation under Grants No. 0331270, CCF-07377655, CCF-0916042, and CCF-1218095.

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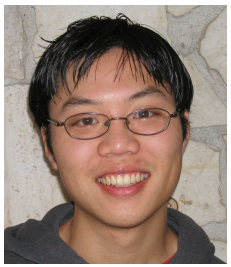

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Jason Stevens

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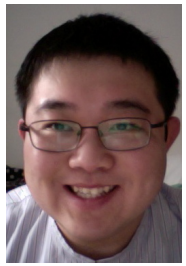

Zhen Zhang

This work is supported by the National Science Foundation under Grants No. 0331270, CCF-07377655, CCF-0916042, and CCF-1218095.