Dynamic Structures in SBML

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COMBINE 2011

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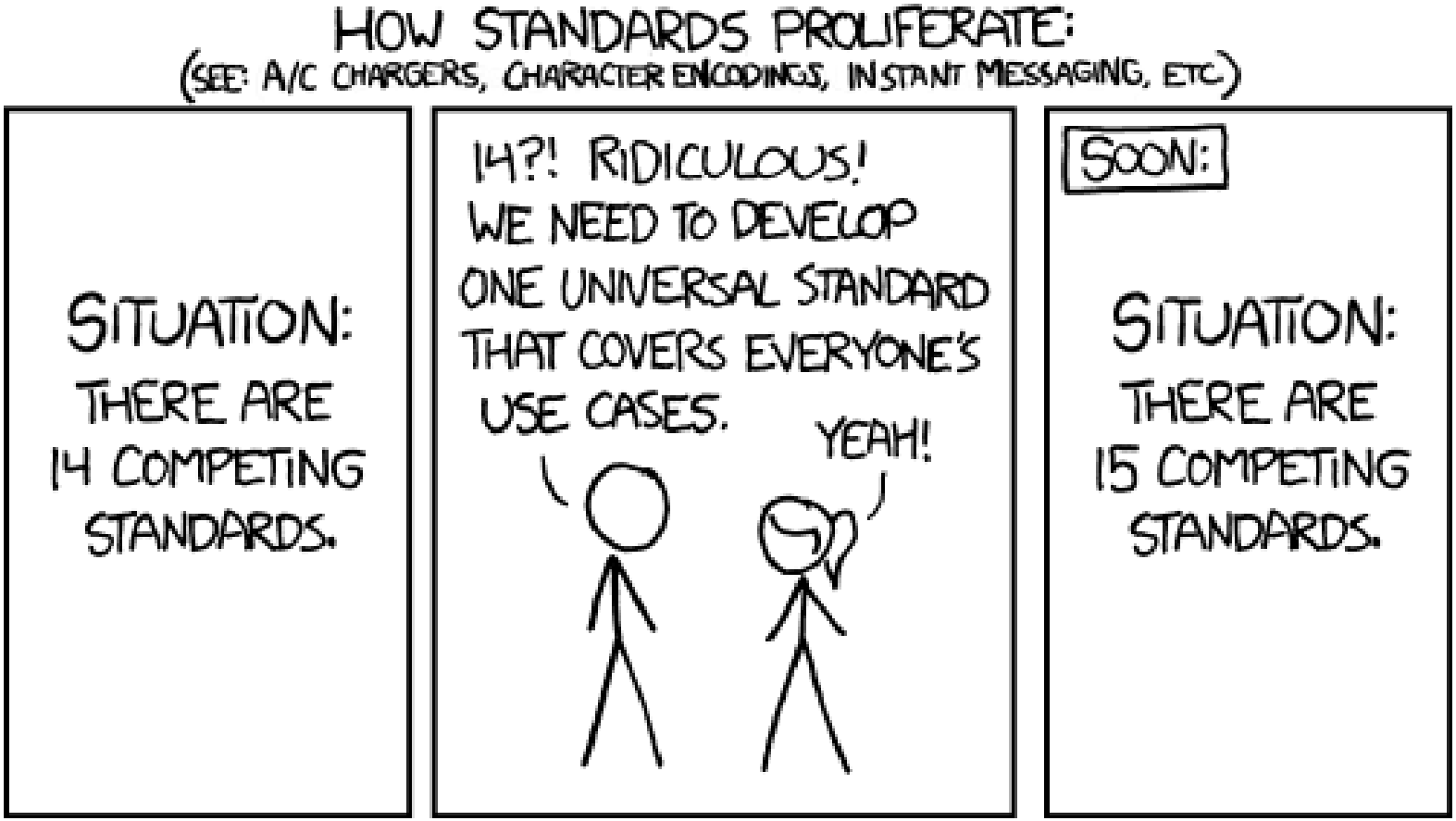
Motivation



- Standardized Model Description Language for Multi-Cellular Simulations:
  - Several workshops including one last week at ICSB.
- Synthetic Biology Open Language (SBOL):
  - Emerging standard for synthetic biology (more on this tomorrow).

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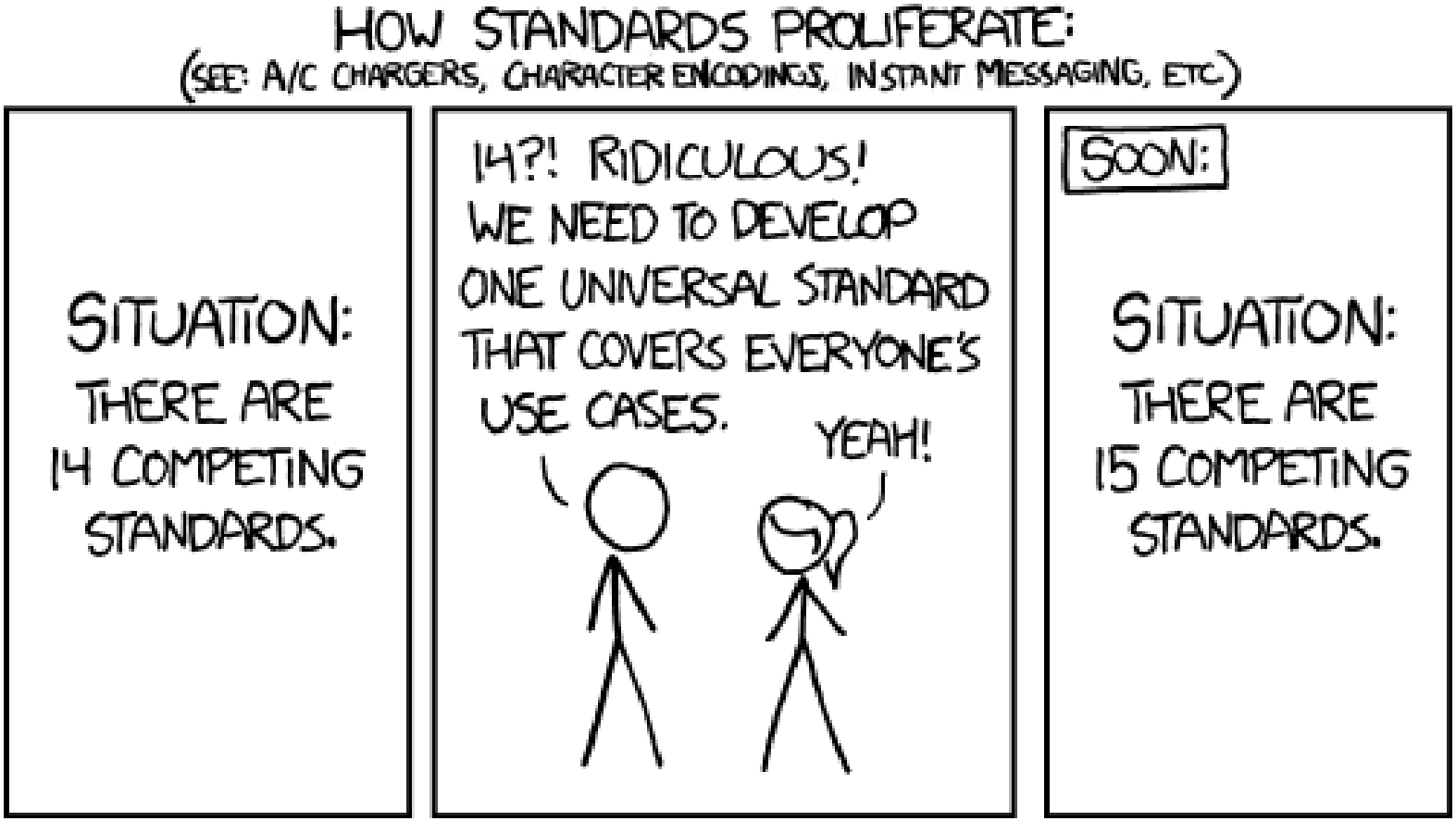

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Cell Behavior Ontology

- *Cell Behavior Ontology* (CBO):
  `http://cbo.biocomplexity.indiana.edu/cbo`
- *Property Processes* (object structure remains static):
  - Movement
  - Growth
  - Secretion
  - Absorption
  - Diffusion
  - Decay
  - Advection
- *Entity Processes* (object structure changes):
  - Polarization
  - Differentiation
  - Division
  - Death

How far can we get with existing SBML core?

- Performed this experiment using Version 2.0 of our `iBioSim` tool:
  `http://www.async.ece.utah.edu/iBioSim/`
- `iBioSim` adds the following syntactic sugar:
  - Constructs for genetic regulation.
    (i.e., promoters that can be activated and repressed)
  - Support for hierarchical models.
  - Notion of grids.
  - Diffusible species.
- Creates a single flattened SBML model using L3V1 core for simulation.

NYTimes: Expressing Our Individuality, the Way E. Coli Do

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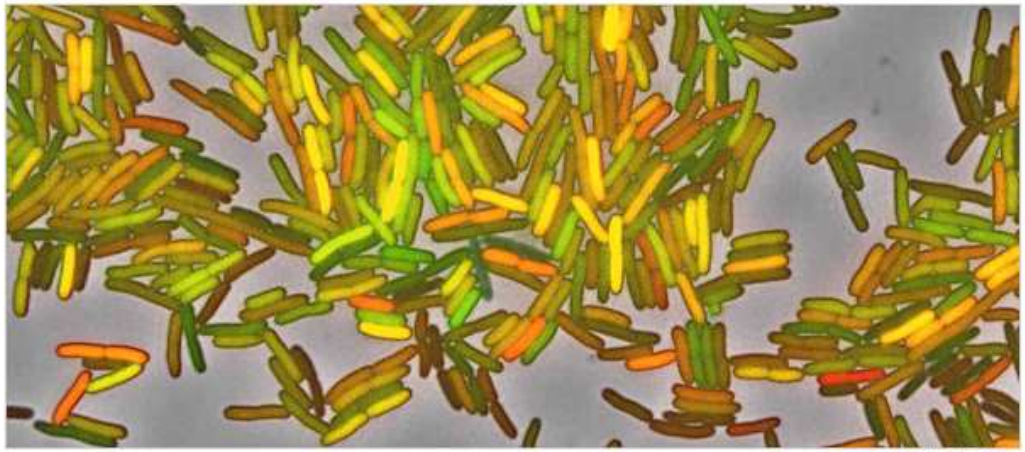
Expressing Our Individuality, the Way E. Coli Do



Dr. Michael Elowitz

A colony of genetically identical E. coli is actually a mob of individuals. Under identical conditions, they behave in different ways.

By CARL ZIMMER
Published: April 22, 2008

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Well
Tara Parker-Pope on Health

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  June 4, 2008, 12:34 PM
- **Colon Cancer in Family Predicts Better Survival**
  June 3, 2008
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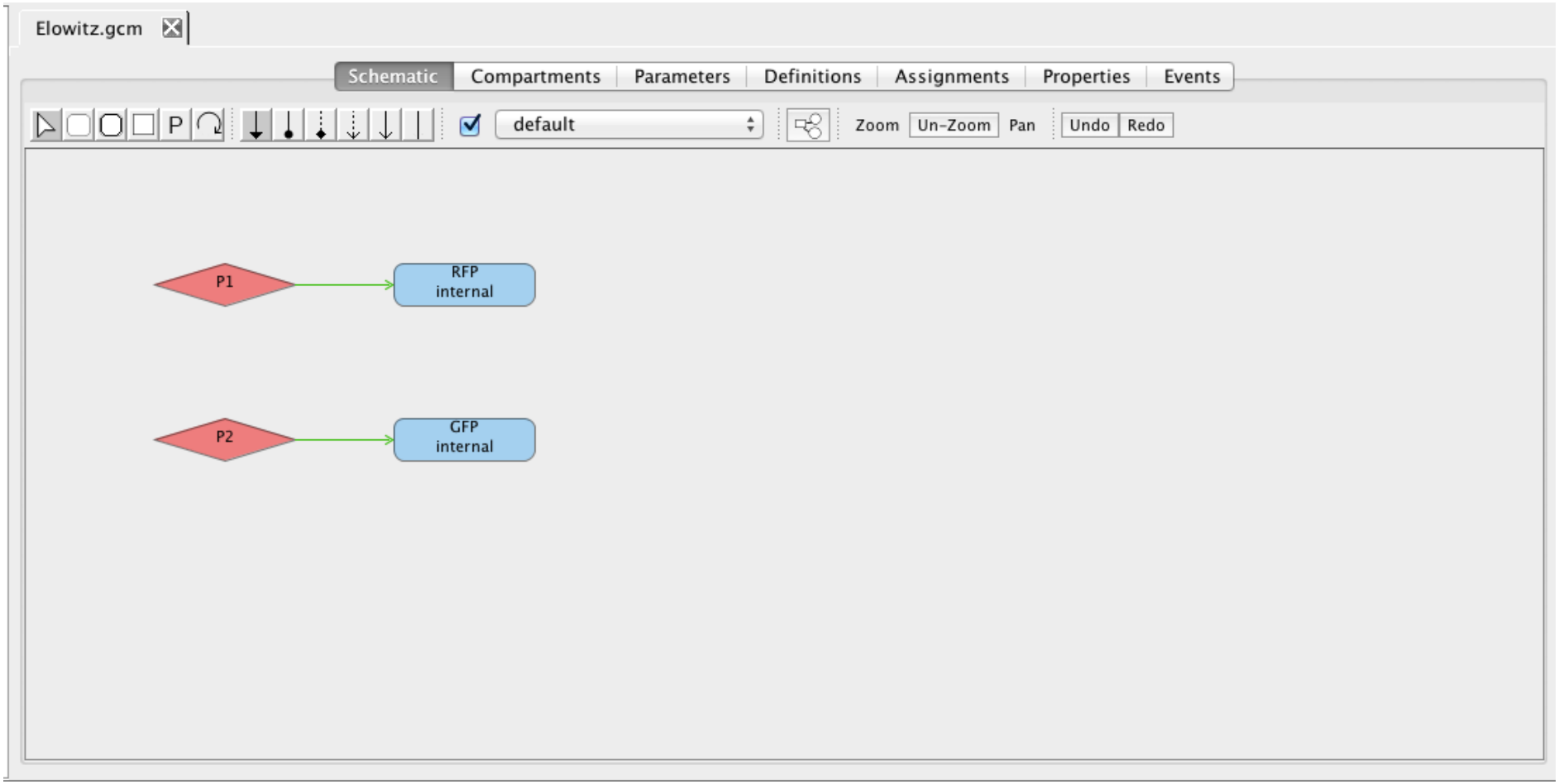
Model for Elowitz Experiment



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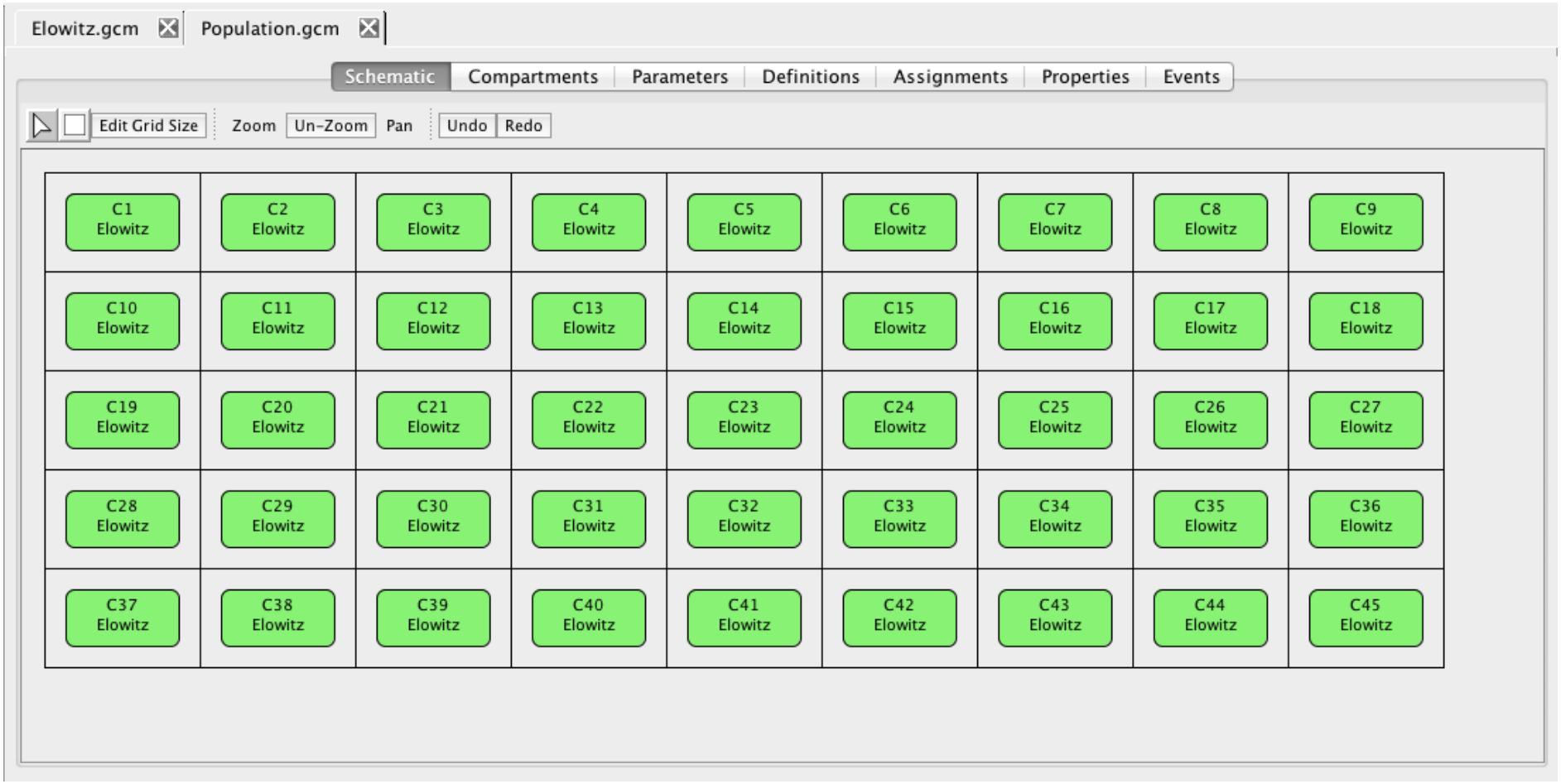

Population Simulation for Elowitz Experiment

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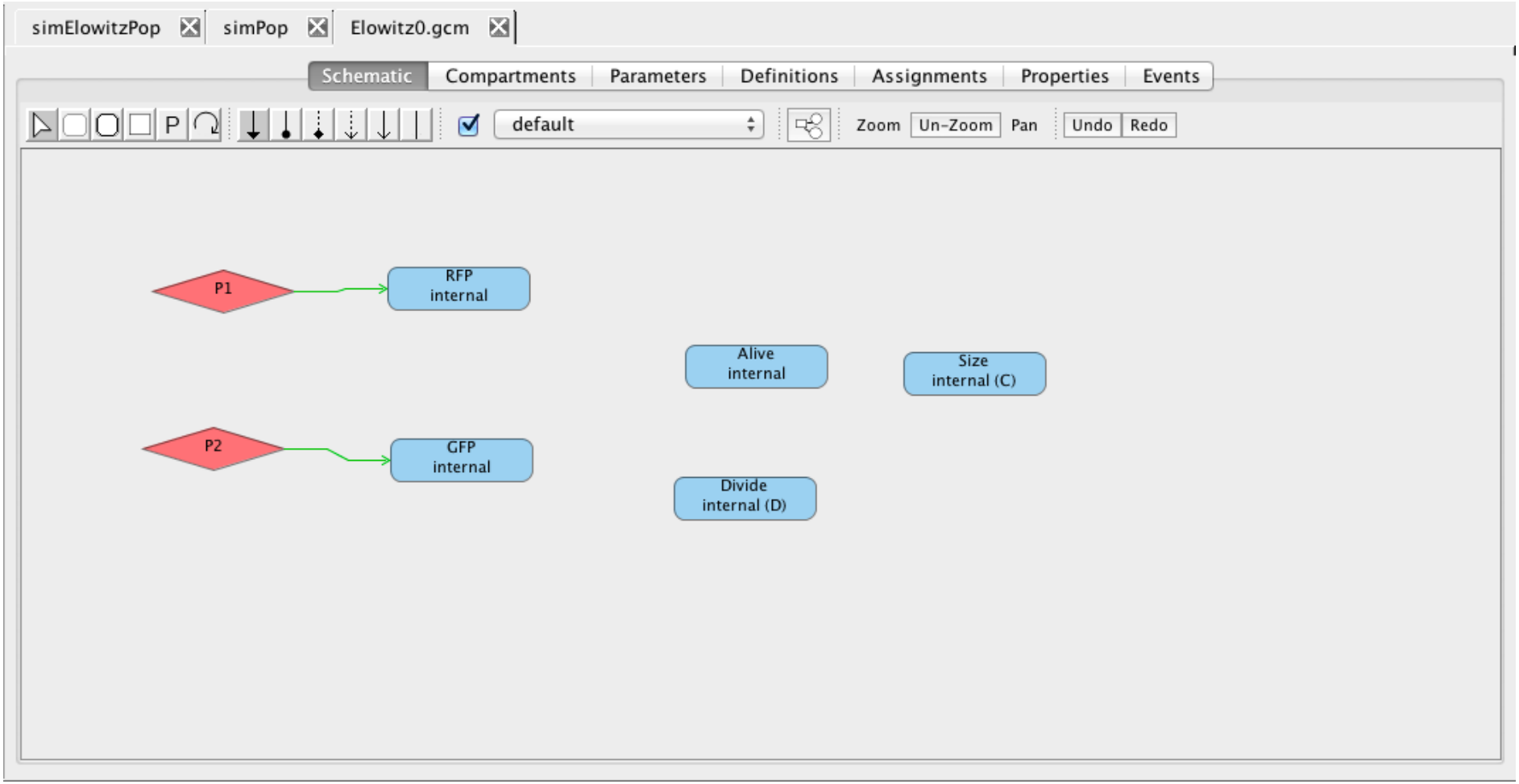
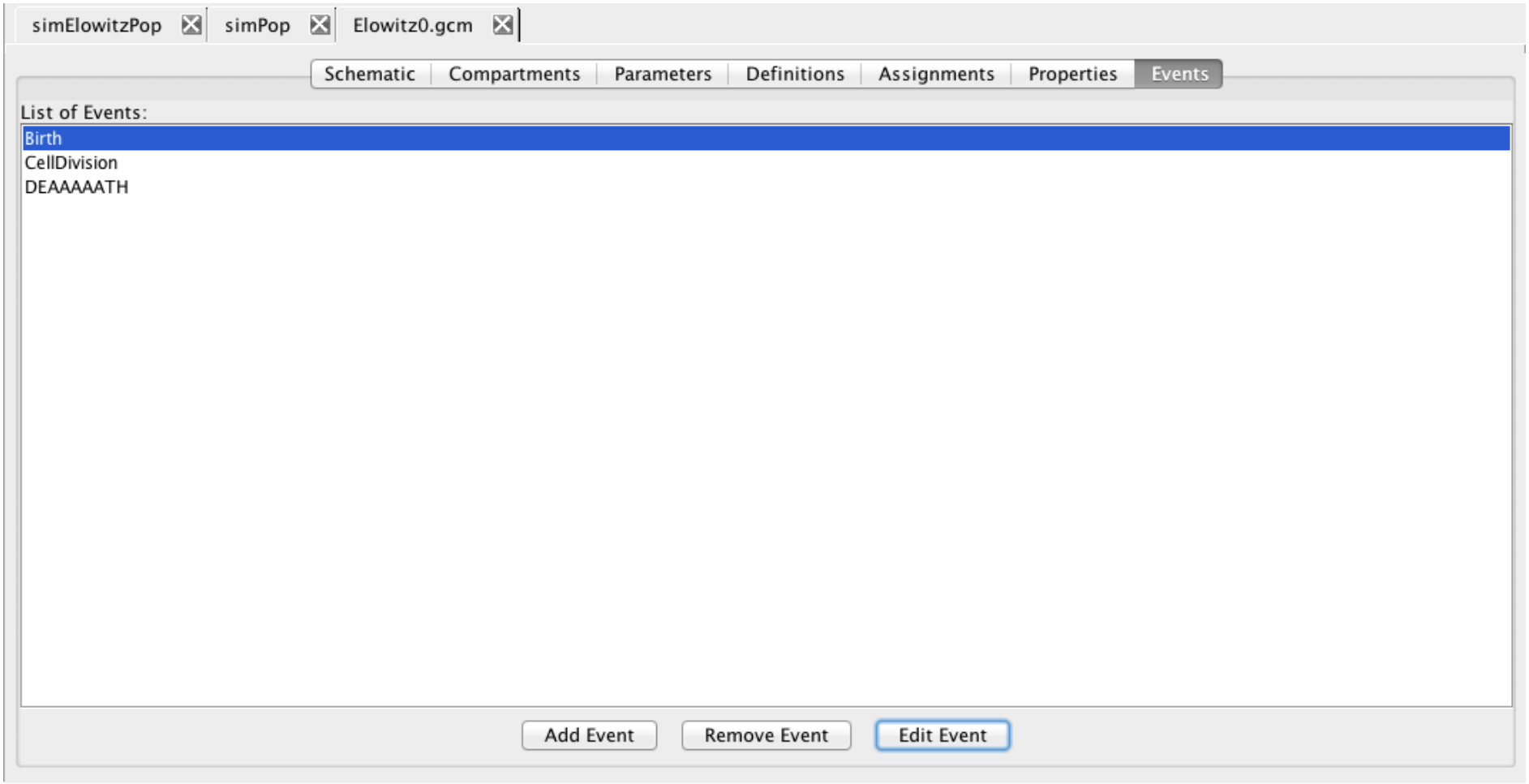
Dynamic Model for Elowitz Experiment



Dynamic Model for Elowitz Experiment



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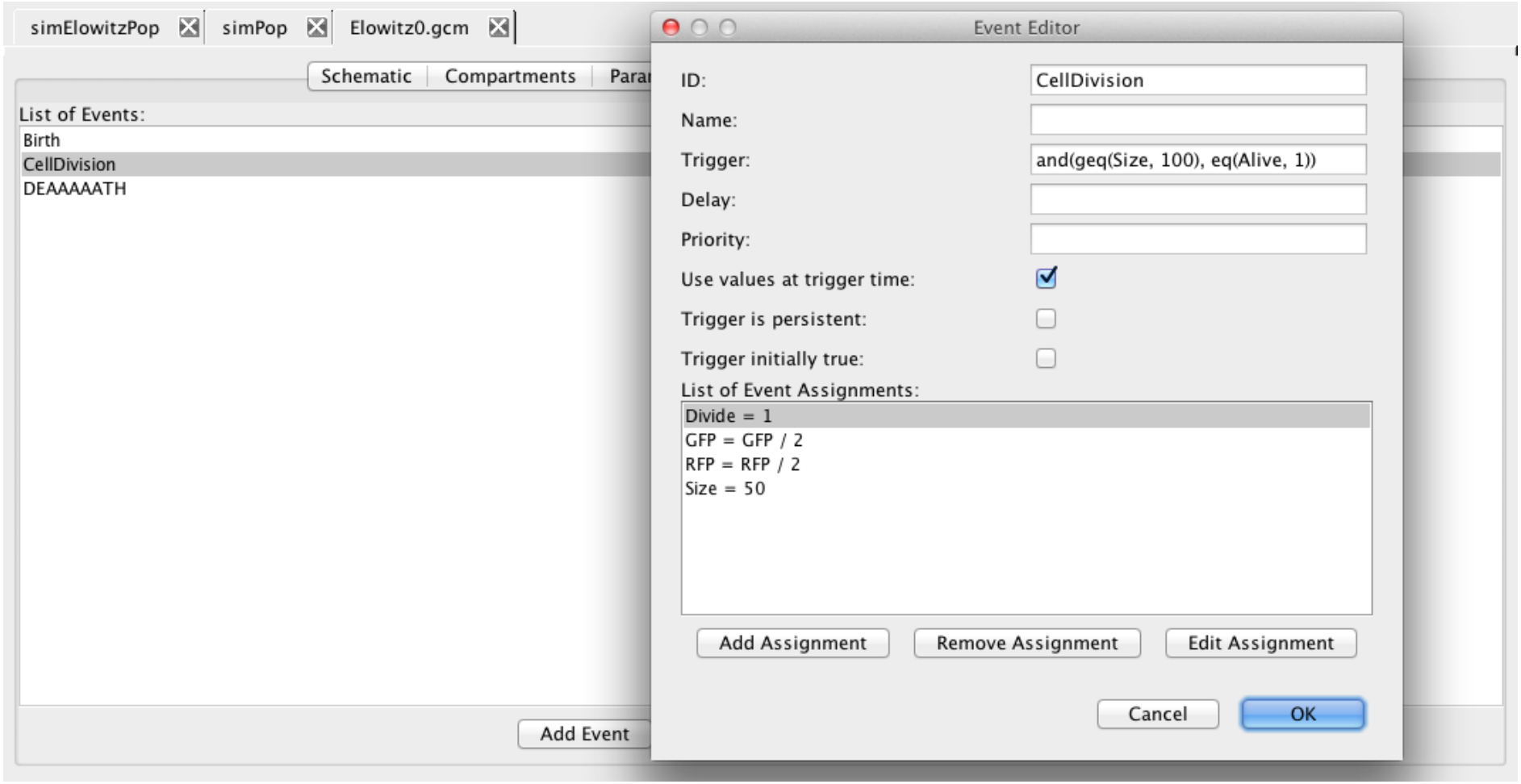

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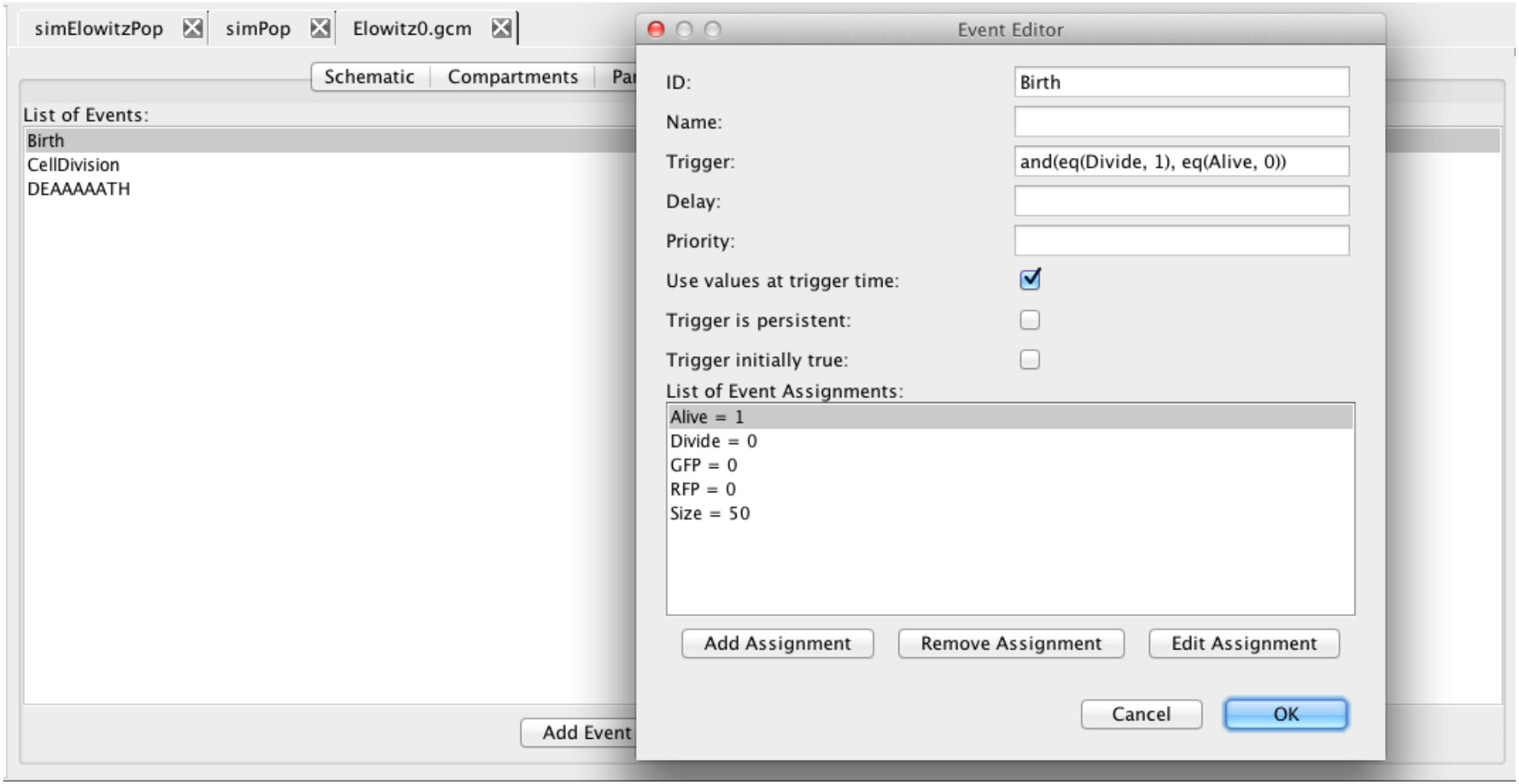

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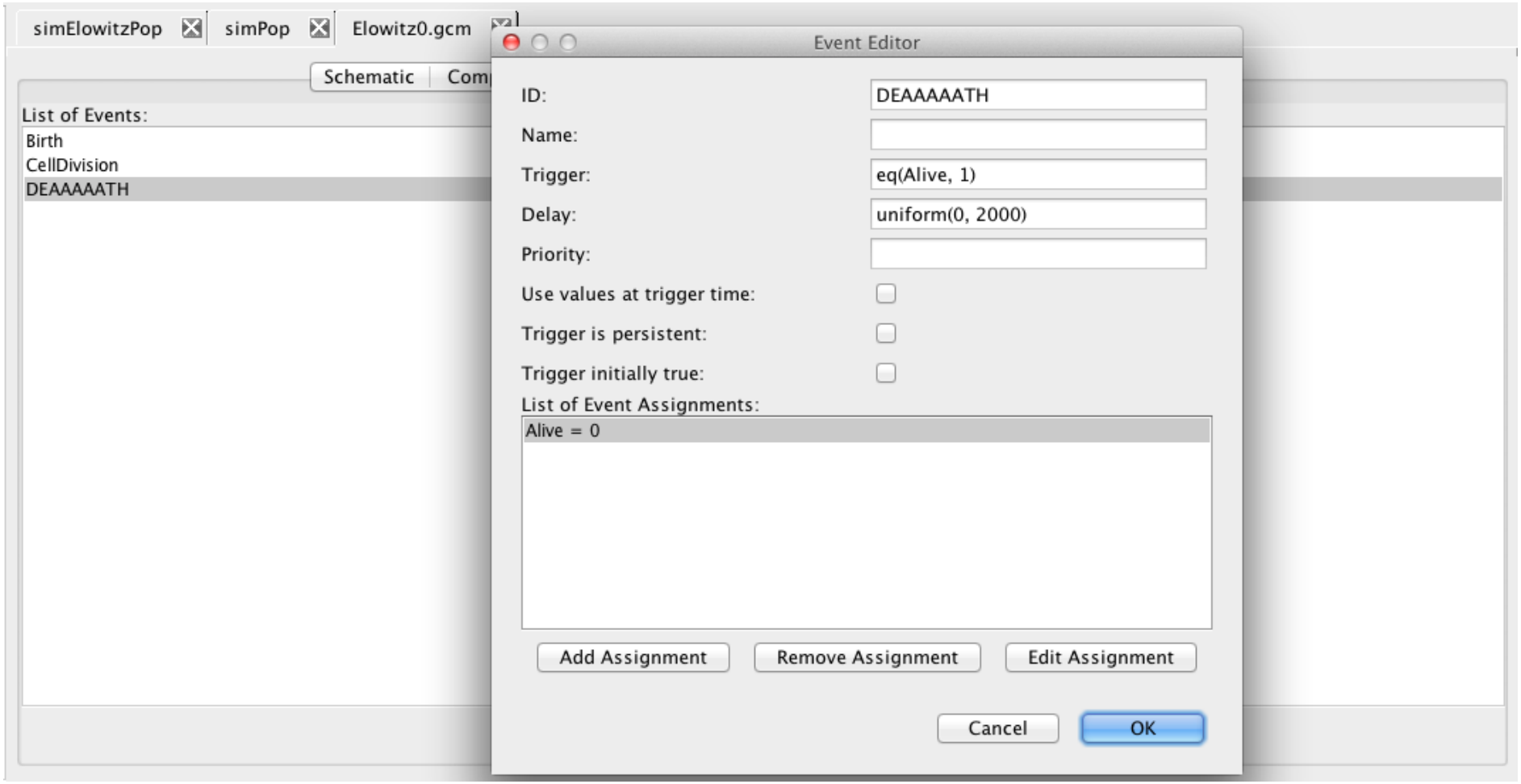

Dynamic Population Simulation for Elowitz Experiment

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Evaluation

- Support for property processes is not too difficult:
  - Growth is easy.
  - Secretion, absorption, and diffusion facilitated with diffusible species.
  - Movement is possible with specialized species.
- Support for entity processes is possible, but it is a hack:
  - All possible objects that may be needed must be statically instantiated.
  - Cell death is easy, but model objects remain, making simulation inefficient.
  - Cell differentiation is easy, but all needed objects always present.
  - Cell division sort of works, but it is difficult to get just right.

Dynamic Structures Package

- Add new event actions:
  - Create (new) object
  - Destroy (delete) object
- Enables adding new objects needed for cell differentiation or division.
- Allows objects to be removed such as when a cell dies.
- Could replace models on the fly to perform better abstraction.
- **Challenge**: substantial change to simulation paradigm as well as significant added complexity.

Technical Issues

- Can be tedious to create complete models.
  - Utilize the hierarchal model composition package.
- Must keep identifiers unique and handle model interconnections.
  - Utilize arrays and sets package.
- Requires some way to initialize the instantiated object.

Non-Technical Issues

- Approximate quotes overheard at the Multi-Cellular Workshop:

  SBML is only for modeling reaction networks.

  SBML must adapt to us, we will not adapt to it.

  SBML is too big and complicated to deal with.

- How should we respond and deal with these types of concerns?

Additional Discussion

- Come to break out session on Tuesday at 9:00am.