

Dynamic Structures in SBML

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University of Utah

COMBINE 2011
September 4, 2011

Motivation

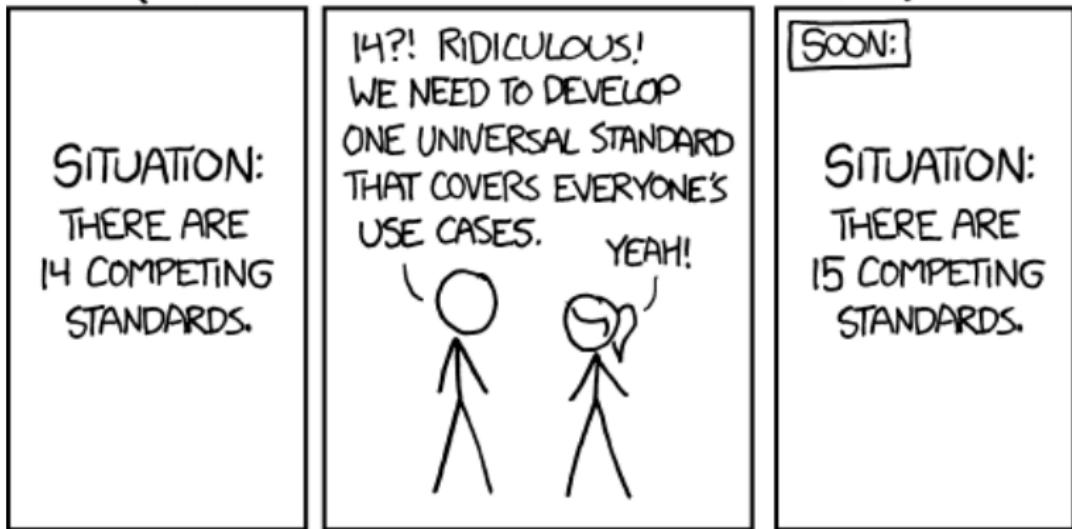
HOW STANDARDS PROLIFERATE:
(SEE: A/C CHARGERS, CHARACTER ENCODINGS, INSTANT MESSAGING, ETC.)



- 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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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

The New York Times

Research

Health All NYT Search

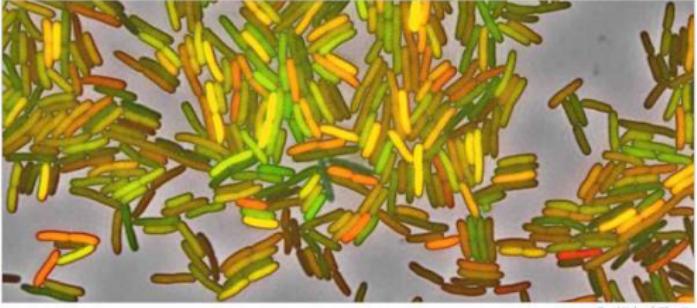
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Expressing Our Individuality, the Way E. Coli Do



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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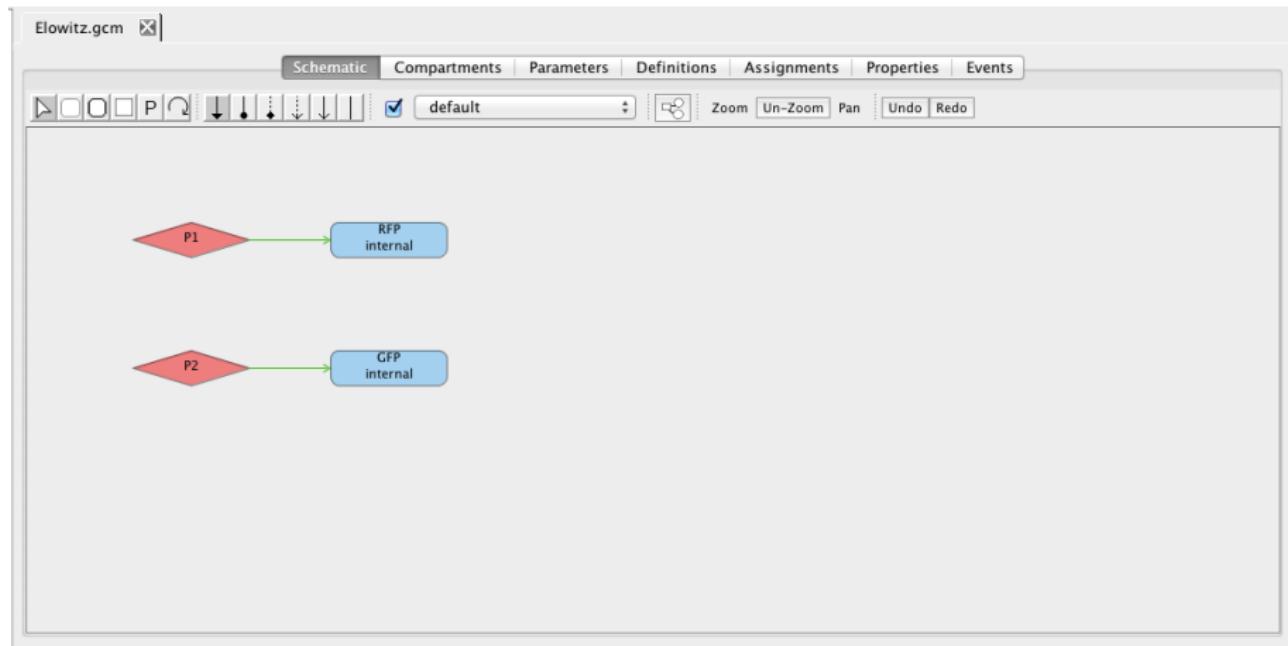
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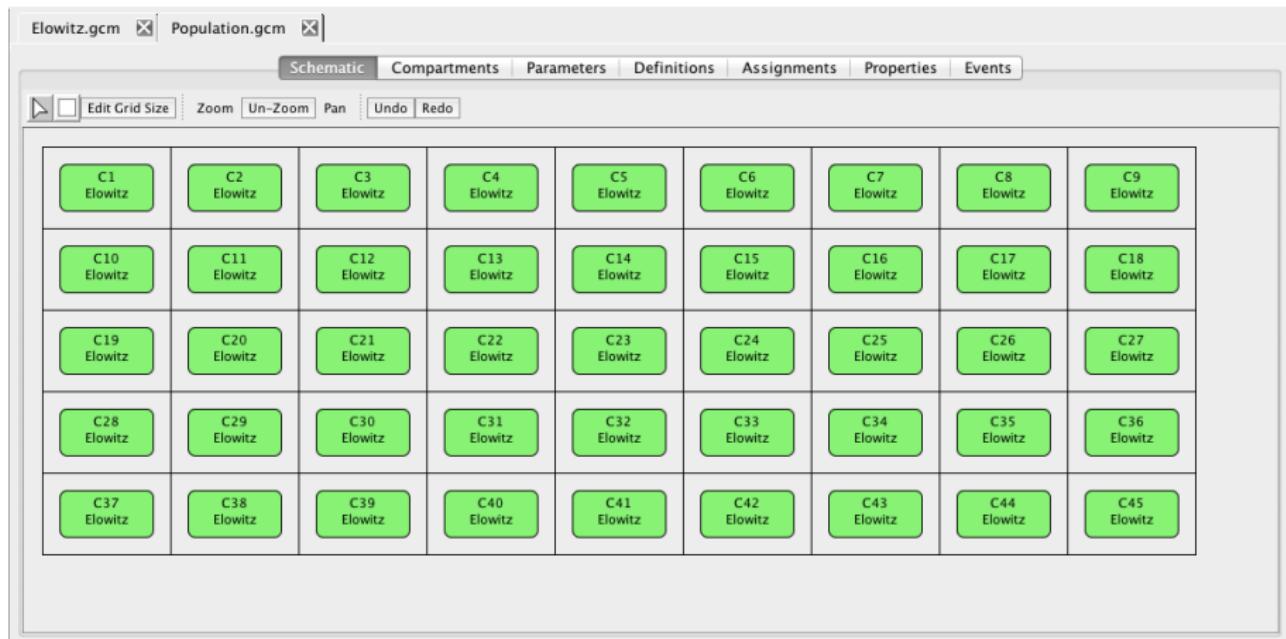
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Model for Elowitz Experiment



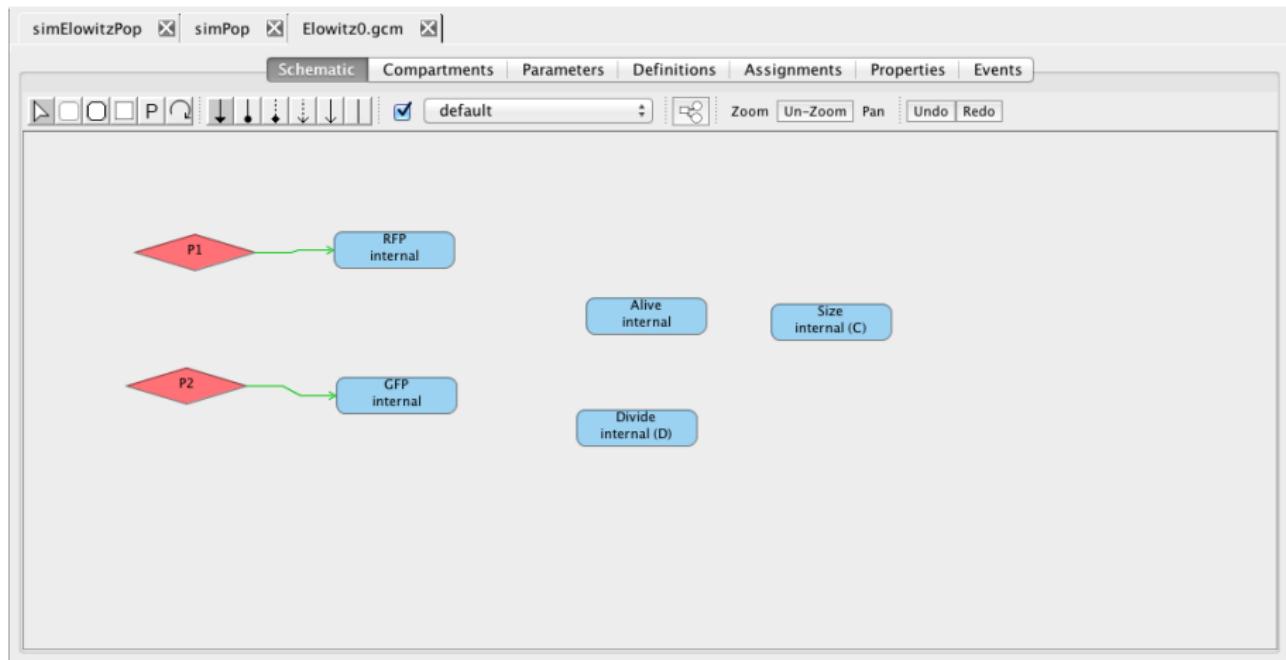
Model for Elowitz Experiment



Population Simulation for Elowitz Experiment

(Loading ElowitzSim.mov)

Dynamic Model for Elowitz Experiment



Dynamic Model for Elowitz Experiment

simElowitzPop simPop Elowitz0.gcm

Schematic Compartments Parameters Definitions Assignments Properties Events

List of Events:

- Birth
- CellDivision
- DEAAAAAATH

Add Event Remove Event Edit Event

Dynamic Model for Elowitz Experiment

simElowitzPop simPop Elowitz0.gcm

Schematic Compartments Parameters

List of Events:

Birth
CellDivision
DEAAAAATH

Event Editor

ID: CellDivision

Name:

Trigger: and(geq(Size, 100), eq(Alive, 1))

Delay:

Priority:

Use values at trigger time:

Trigger is persistent:

Trigger initially true:

List of Event Assignments:

Divide = 1
GFP = GFP / 2
RFP = RFP / 2
Size = 50

Add Assignment Remove Assignment Edit Assignment

Cancel OK

Add Event

Dynamic Model for Elowitz Experiment

simElowitzPop simPop Elowitz0.gcm

Schematic Compartments Parameters

List of Events:

- Birth
- CellDivision
- DEAAAAATH

Event Editor

ID: Birth

Name:

Trigger: $\text{and}(\text{eq}(\text{Divide}, 1), \text{eq}(\text{Alive}, 0))$

Delay:

Priority:

Use values at trigger time:

Trigger is persistent:

Trigger initially true:

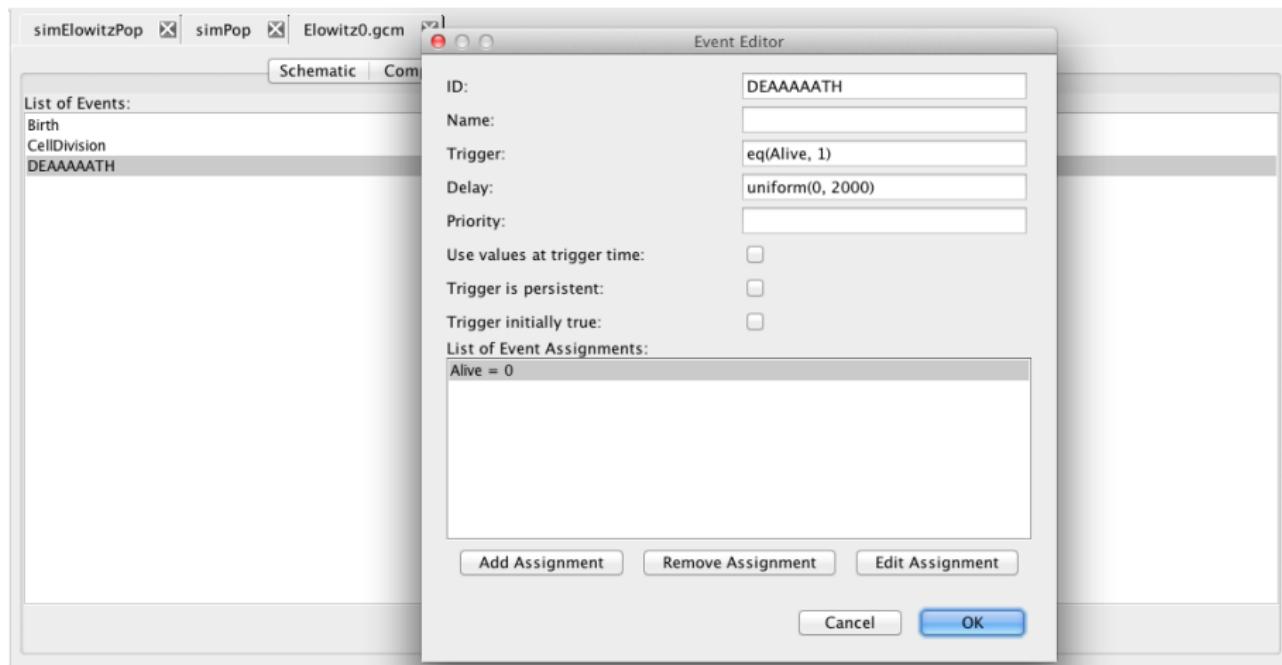
List of Event Assignments:

- Alive = 1
- Divide = 0
- GFP = 0
- RFP = 0
- Size = 50

Add Assignment Remove Assignment Edit Assignment

Add Event Cancel OK

Dynamic Model for Elowitz Experiment



Dynamic Population Simulation for Elowitz Experiment

(Loading ElowitzSimDyn.mov)

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 hierachal 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.