

Dynamic Structures in SBML

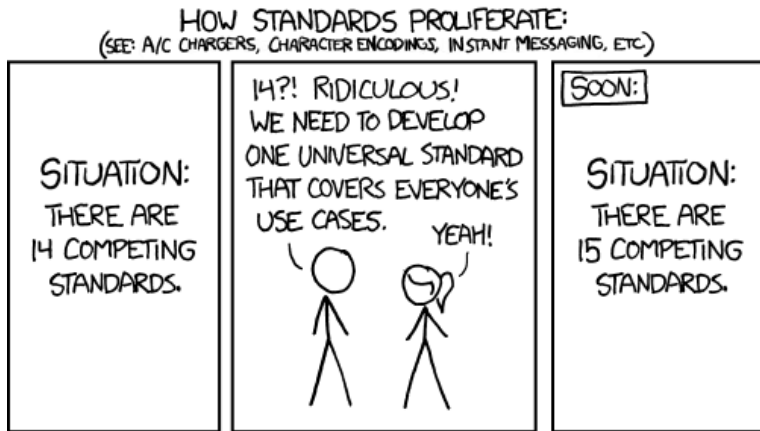
Chris J. Myers

University of Utah

COMBINE 2011

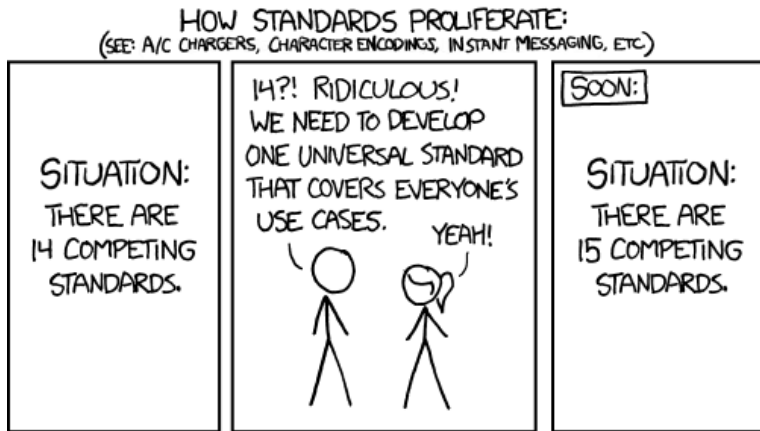
September 4, 2011

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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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.

The New York Times

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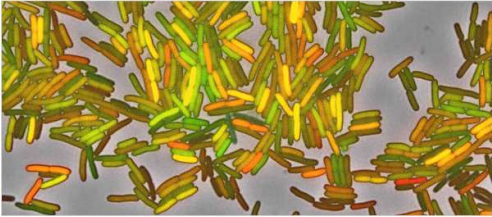
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By CARL ZIMMER
Published: April 22, 2008

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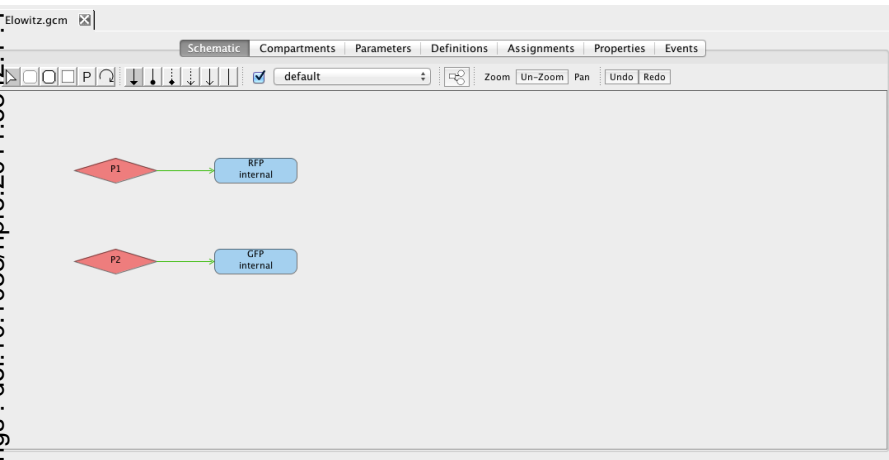
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Model for Elowitz Experiment

Precedings : doi:10.1038/npre.2011.6342.1 : Posted 5 Sep



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The screenshot shows a software window titled 'Elowitz.gcm' and 'Population.gcm'. The interface includes a menu bar with 'Schematic', 'Compartments', 'Parameters', 'Definitions', 'Assignments', 'Properties', and 'Events'. Below the menu bar is a toolbar with 'Edit Grid Size', 'Zoom', 'Un-Zoom', 'Pan', 'Undo', and 'Redo'. The main area displays a 5x9 grid of compartments, each labeled from C1 to C45 and containing the text 'Elowitz'.

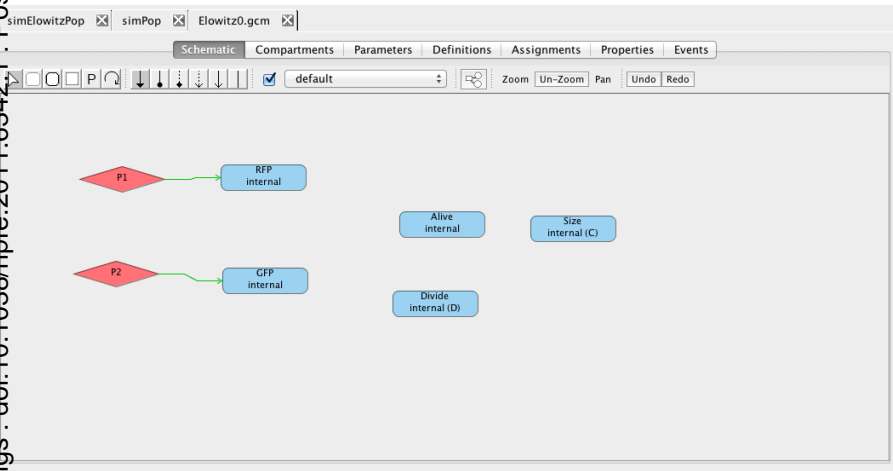
C1 Elowitz	C2 Elowitz	C3 Elowitz	C4 Elowitz	C5 Elowitz	C6 Elowitz	C7 Elowitz	C8 Elowitz	C9 Elowitz
C10 Elowitz	C11 Elowitz	C12 Elowitz	C13 Elowitz	C14 Elowitz	C15 Elowitz	C16 Elowitz	C17 Elowitz	C18 Elowitz
C19 Elowitz	C20 Elowitz	C21 Elowitz	C22 Elowitz	C23 Elowitz	C24 Elowitz	C25 Elowitz	C26 Elowitz	C27 Elowitz
C28 Elowitz	C29 Elowitz	C30 Elowitz	C31 Elowitz	C32 Elowitz	C33 Elowitz	C34 Elowitz	C35 Elowitz	C36 Elowitz
C37 Elowitz	C38 Elowitz	C39 Elowitz	C40 Elowitz	C41 Elowitz	C42 Elowitz	C43 Elowitz	C44 Elowitz	C45 Elowitz

Population Simulation for Elowitz Experiment

(Loading ElowitzSim.mov)

Dynamic Model for Elowitz Experiment

Precedings : doi:10.1038/npre.2011.6342.1 : Posted 5 Sep



Dynamic Model for Elowitz Experiment

Precedings : doi:10.1038/npre.2011.63421 : Posted 5 Sep

The screenshot shows a software window titled "Elowitz0.gcm" with three tabs: "Schematic", "Compartments", and "Parameters". The "Events" tab is active, displaying a "List of Events:" section. The list contains three entries: "Birth", "CellDivision", and "EAAAAATH". The "Birth" entry is highlighted with a blue background. At the bottom of the window, there are three buttons: "Add Event", "Remove Event", and "Edit Event".

simElowitzPop x simPop x Elowitz0.gcm x

Schematic Compartments Parameters Definitions Assignments Properties Events

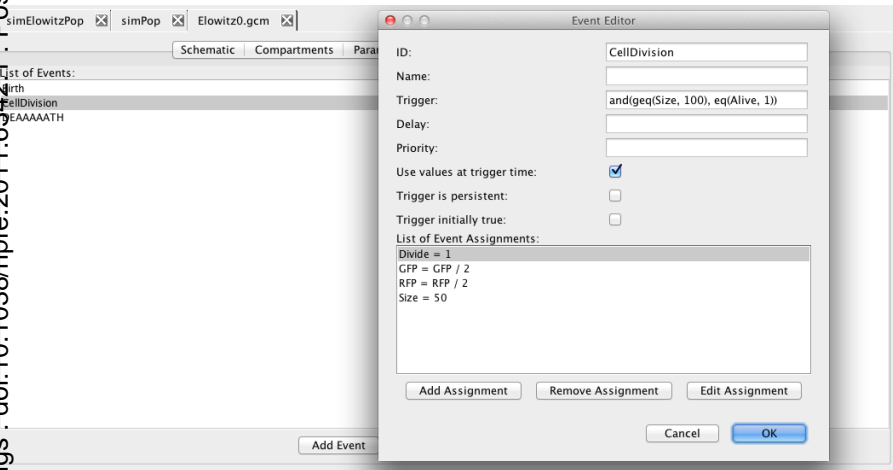
List of Events:

- Birth
- CellDivision
- EAAAAATH

Add Event Remove Event Edit Event

Dynamic Model for Elowitz Experiment

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simElowitzPop x simPop x Elowitz0.gcm x

Schematic Compartments Pa

List of Events:

- Birth
- CellDivision
- DEAAAAATH

Add Event

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:

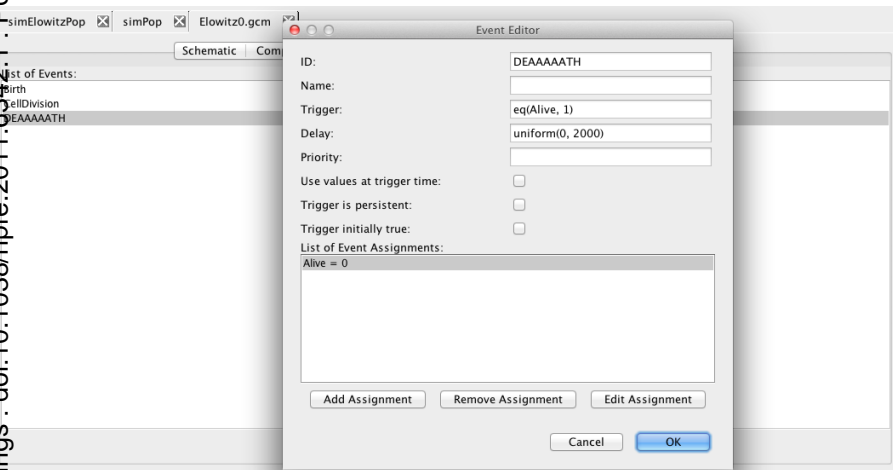
- Alive = 1
- Divide = 0
- GFP = 0
- RFP = 0
- Size = 50

Add Assignment Remove Assignment Edit Assignment

Cancel OK

Dynamic Model for Elowitz Experiment

Precedings : doi:10.1038/npre.2011.6342.1 : Posted 5 Sep



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 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.