Semantic Annotation with SBML and CellML Models

John Gennari & Max Neal

(and team!)

The John & Max show

Semantic Annotation & Composition of SBML and CellML models

Annotation

What is it?

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- Model-level annotation
  - Describing the whole model
  - Author, date, publication, overview, etc.
- Code-level annotation
  - Descriptions of individual species, reactions, variables
  - Proteins, chemicals, measured values, parameters & variables

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- Documentation
- Match data to models
- Merge and Reuse models

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Story time

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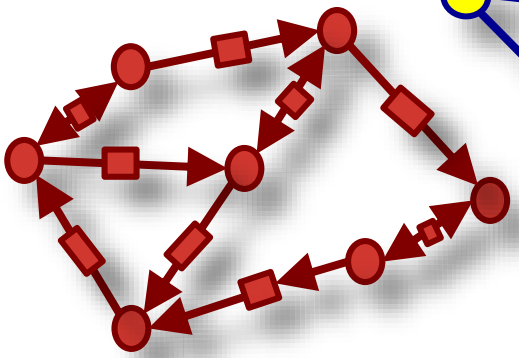
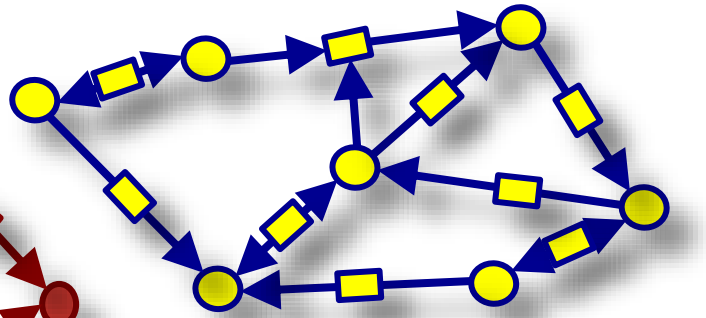
Jane's model



DeRown's model



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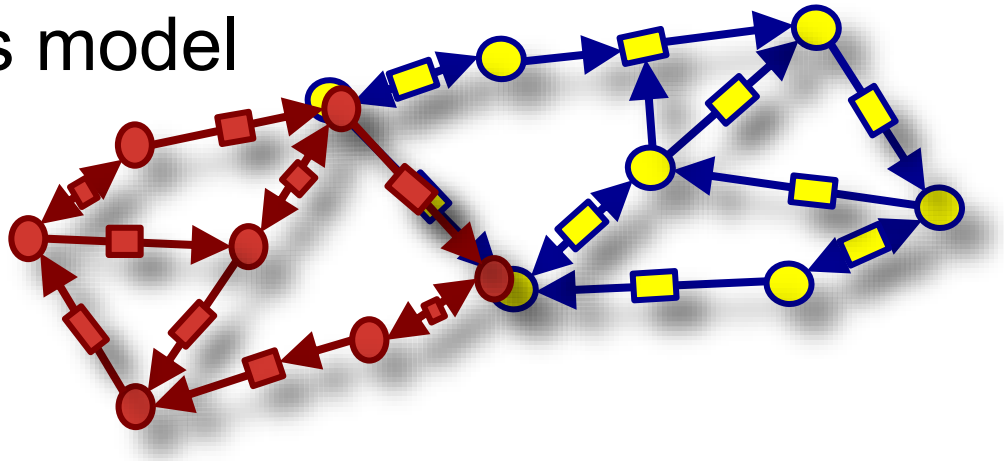
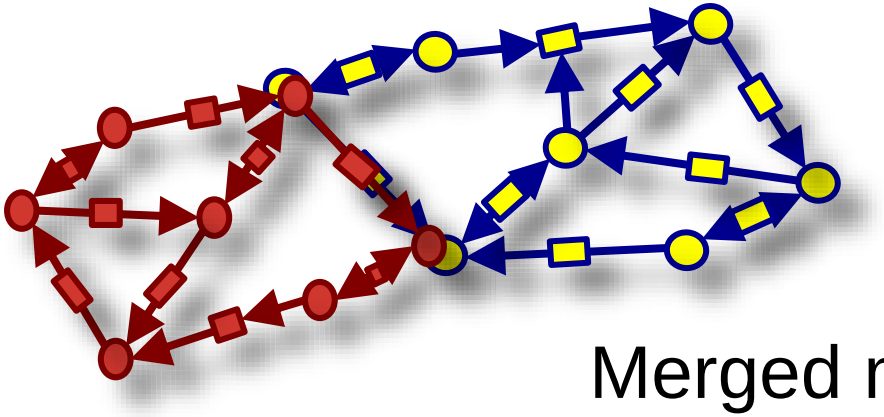


Augmented and improved model!

How?

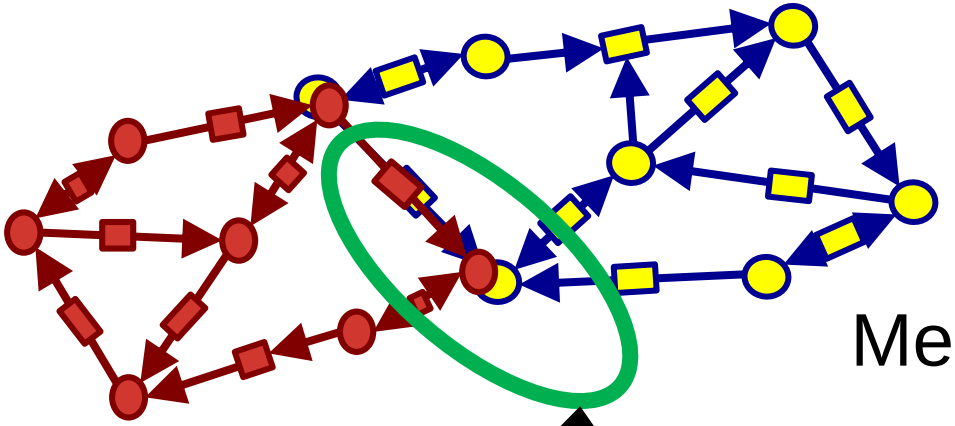


Merged model

- Rebuild DeRown's model from publication
- Retrieve's DeRown's code from GitHub
- Hire DeRown's co-author as Postdoc

Success, but…..

(semi) Automatic merging

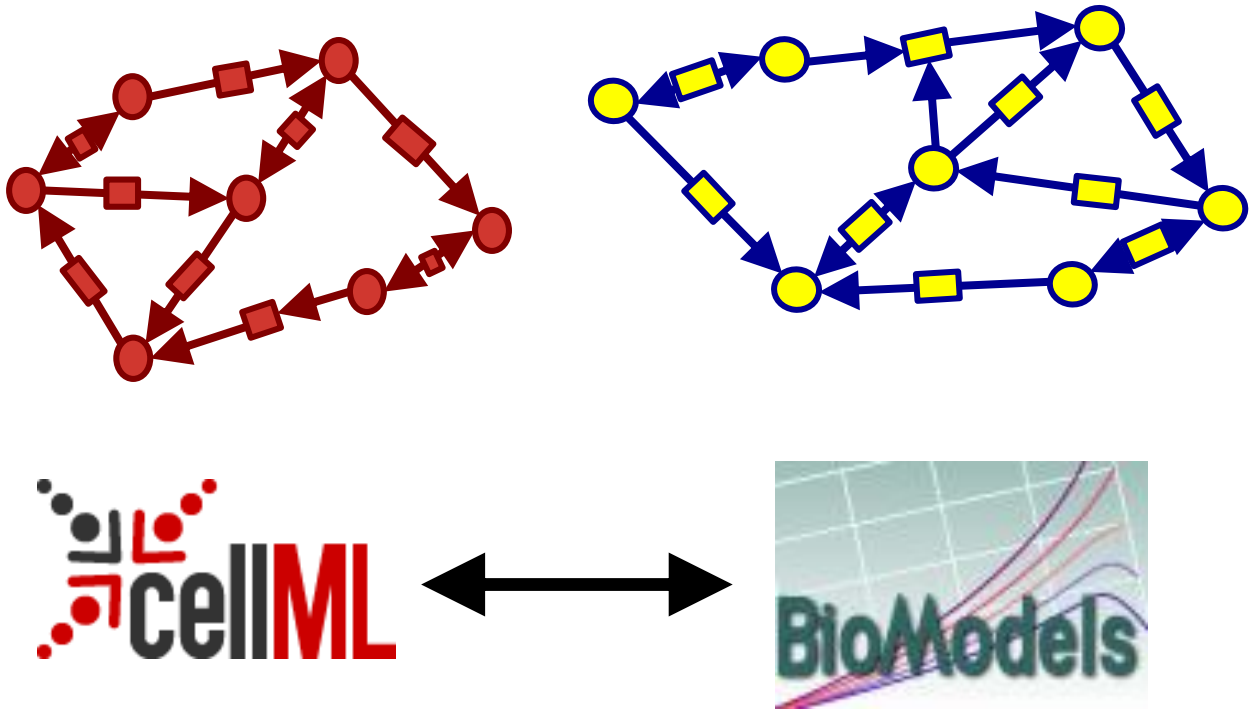


Merged model

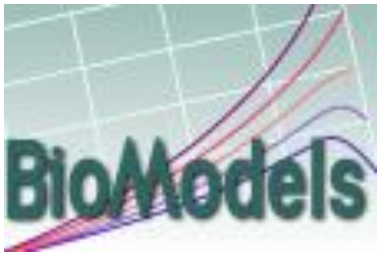
Modeler may need to match these points

- SemGen does this (next talk)
- Never can be fully automatic

Crossing the language barrier



Annotation in the repositories



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- Recent work:
  25 fully annotated models

- SBML includes code-level annotation
- However…
  Standards alone are not enough

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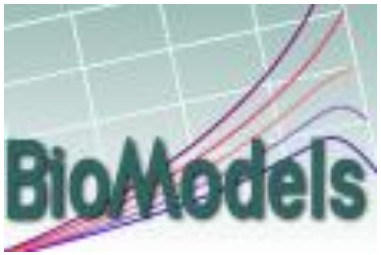

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Policies and/or a culture of best practices for annotation

Problem 1: isVersionOf

Semantics of “isVersionOf” are weak:

- Similar to “is narrower than”.
- For merging, what do we do with this?

http://co.mbine.org/standards/qualifiers: isVersionOf:

The biological entity represented by the model element is a version or an instance of the subject of the referenced resource (biological entity B). This relation may be used to represent, for example, the 'superclass' or 'parent' form of a particular biological entity.

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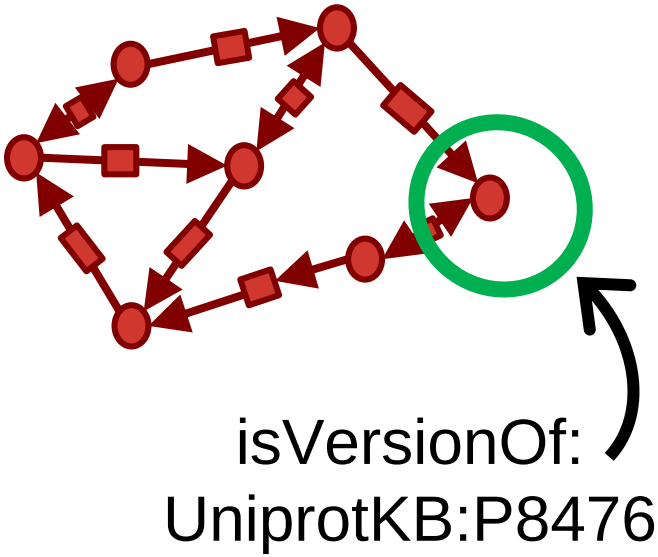

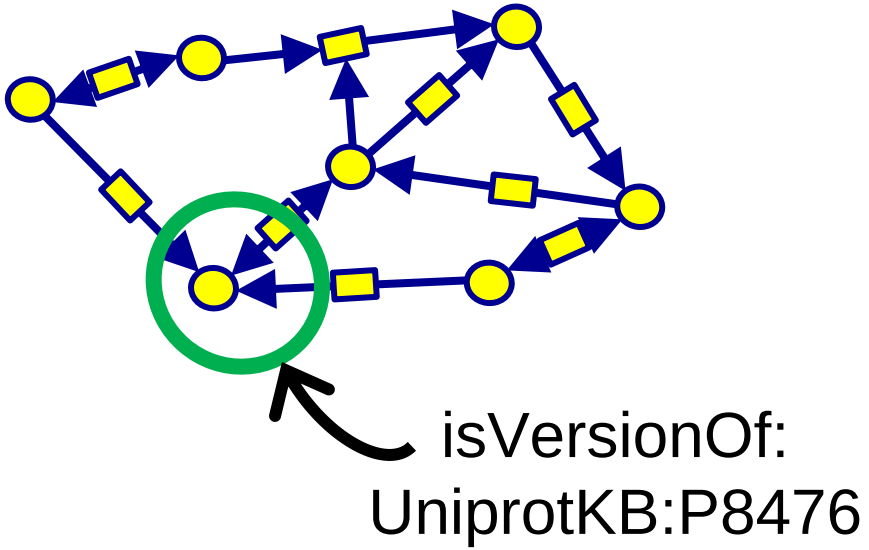

Problem 2: Ontology choices

A set of appropriate, compatible, orthogonal ontologies *(credit OBO)*

Non orthogonal example: Kegg v. Uniprot
(v. Reactome, v. InterPro, etc.)

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```
<bqbiol:isVersionOf>
    <rdf:Bag>
    <rdf:li rdf:resource="/uniprot/P35568"/>
    <rdf:li rdf:resource="/kegg.compound/C00562"/>
    </rdf:Bag>
</bqbiol:isVersionOf>
```

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Non-appropriate (?) example: UniProt

- Protein Ontology entry: PRO #000016502 "based on" three UniProt entries
  - Human: UniProtKB:P63316
  - Chicken: UniProtKB:P09860
  - Mouse: UniProtKB:P19123
- Also "isoform-1", which has different uniprotIDs…

Problem 3: Names

- What are things? What are processes?

Sometimes, PHILOSOPHY really does matter

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- What are things? What are processes?

Sometimes, PHILOSOPHY really does matter

- Example: Ion channels
  - A port?
  - A flow of ions? A flow of electricity?
  - A complex? (A set of proteins bound together)

Wait…. How do we name a complex?

Semantics of Biological Processes

To share, understand, reuse, and re-purpose biosimulation models and modules, we must..

- Share a common grounding: Biology & Physics
- Annotate models using that grounding: Semantic annotation of biological processes
- Use tools that leverage these annotations and ontologies

Ontology of Physics for Biology (OPB)

Physical continuant (things)

- Physical entity — a heart, a portion of blood, a portion of chemical
- Physical property — solid mass, fluid volume, amount of chemical
- Physical dependency — Hooke's law, Ohm's law, law of mass action

Physical processural entity (processes)

- Physical process — contracting, fluid flowing, chemicals reacting

Cook, et al. (2011). Physical Properties of Biological Entities: An Introduction to the Ontology of Physics for Biology. PLoS ONE 6(12): e28708.

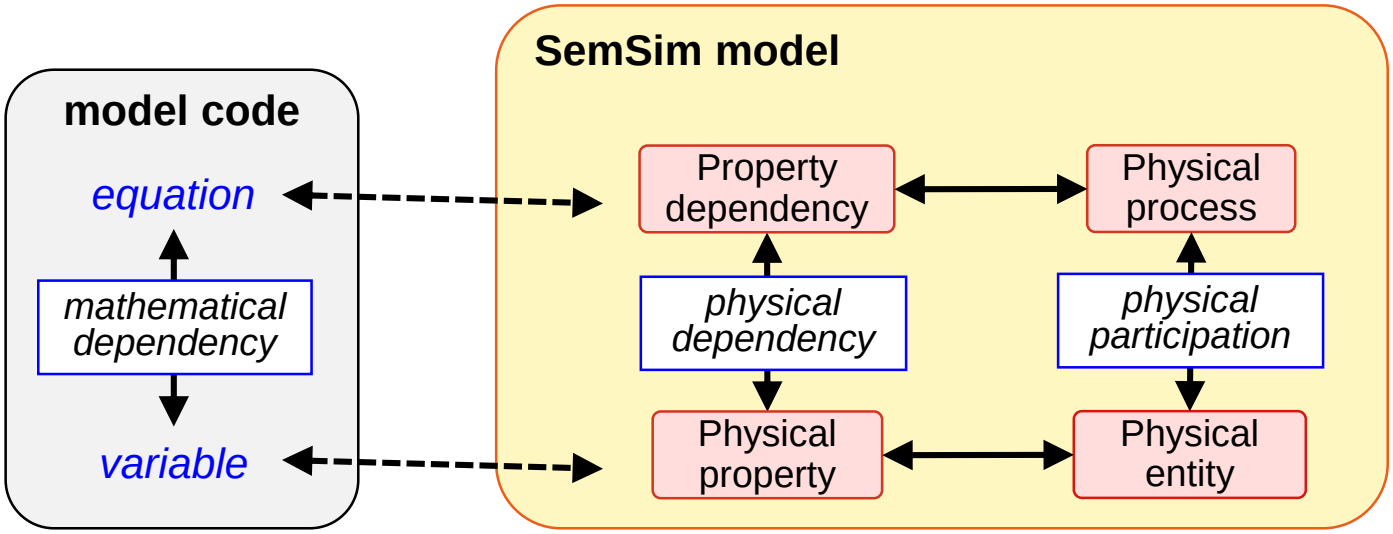
Past deeds / methods

- Merging Pandit with Hinch with Niederer:
  - Pandit: a model of cardiac electrophysiology
  - Hinch: a model of intracellular calcium dynamics
  - Niederer: a model of tension development
- How?
  - A “flat” approach to Module definitions (SAIM)
  - SemGen software
  - Composite annotations

Composite annotations

The Chemical_Concentration of Calcium(2+)
in the cytosol of the Cardiac myocyte

Composite annotations



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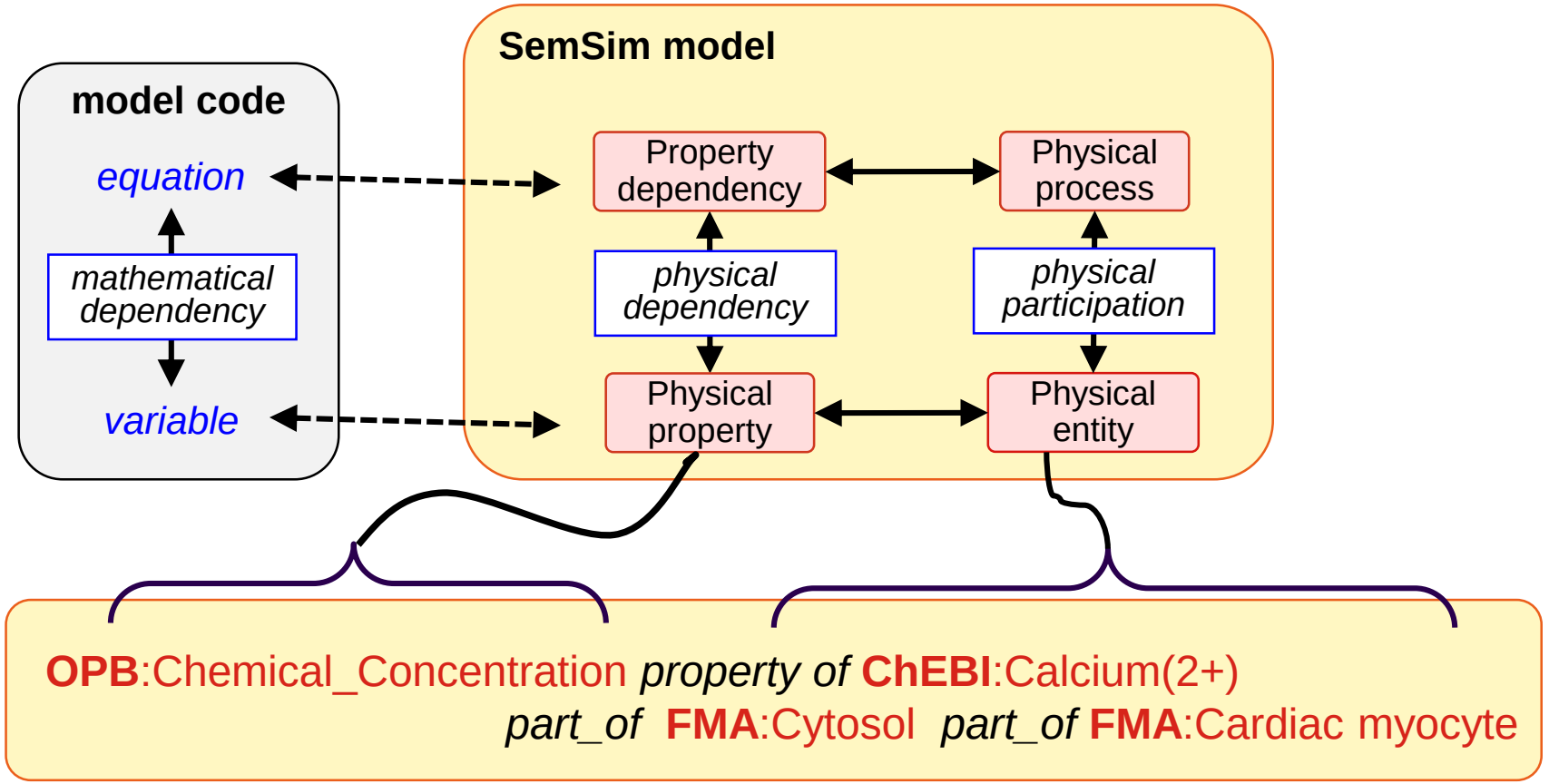
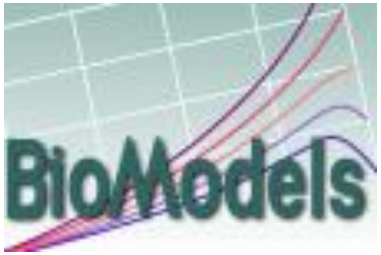


Current results

With



Niederer:
Intracellular tension

Abel 2011:
Calcium signaling
(bioMD#00355)

- Next talk!

Thank you!

Questions / Suggestions?

Acknowledgements:

- Team: Brian Carlson, Dan Cook, Ryan James, Graham Kim, and Chris Thompson
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