

A generic approach for representing complex structures in biological models

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Muetzelfeldt, R. (2010) A unified approach for representing structurally-complex models in SBML Level 3. Nature Precedings. <http://bit.ly/mue27>

The Systems Biology Challenge



VPH

iPlant

Virtual X

(where X = plant, heart, liver, cell...)

NeuroML

Packages

comp

arrays

spatial

geom

dyn

multi

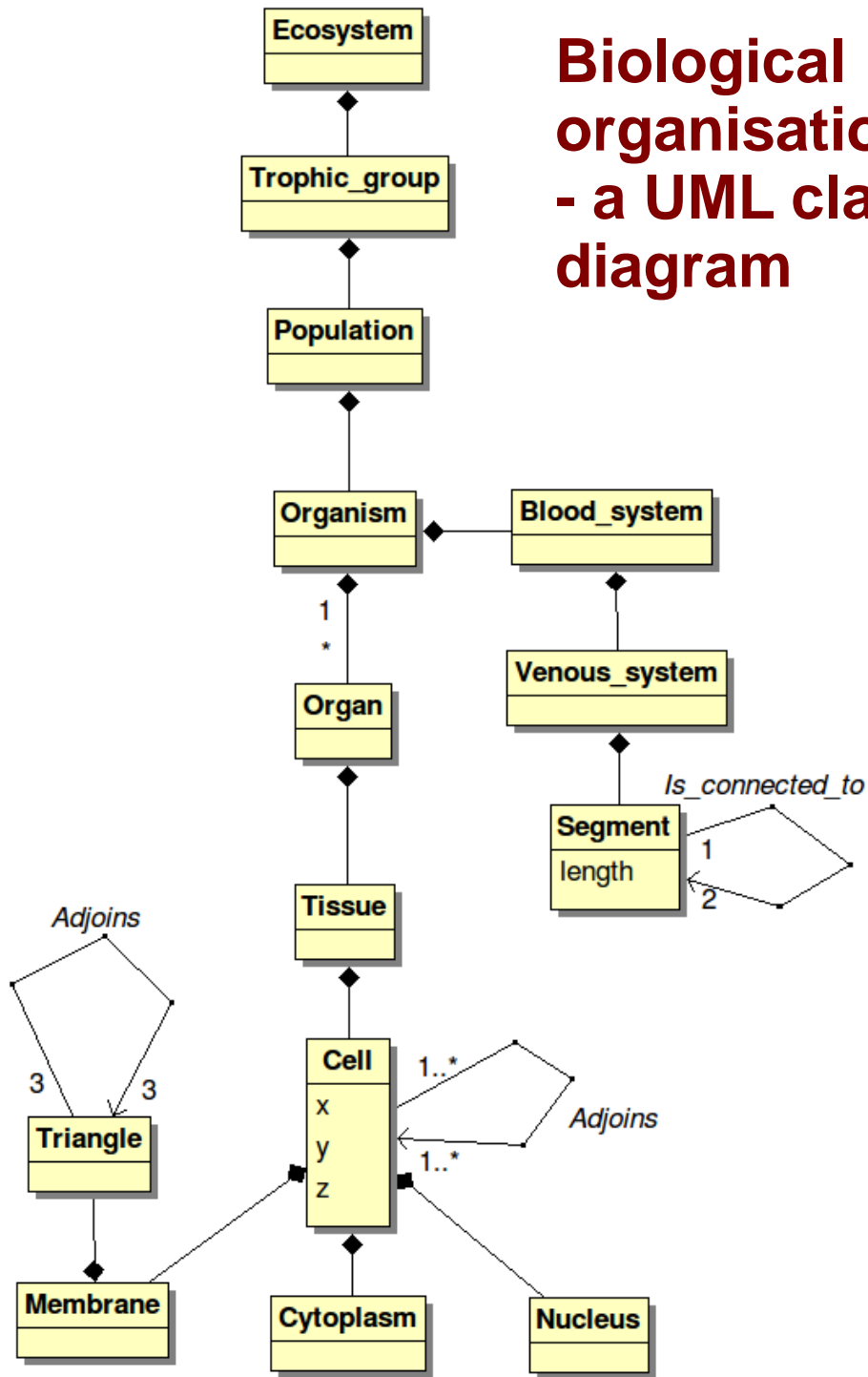
SBML

FieldML

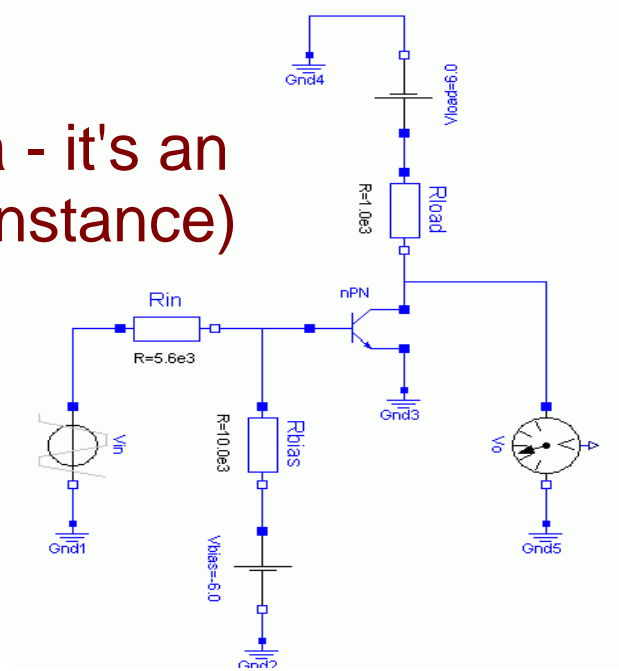
CellML



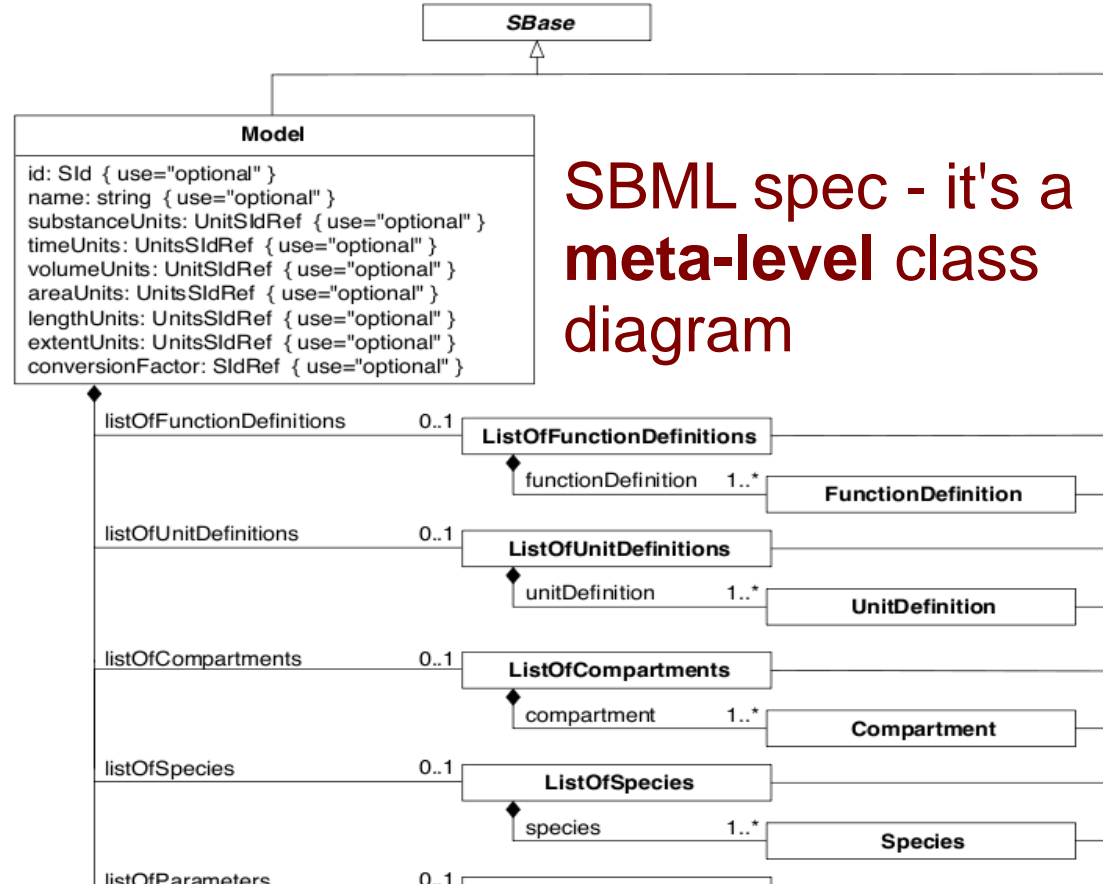
Biological organisation - a UML class diagram



Modelica - it's an object (instance) diagram



SBML spec - it's a meta-level class diagram



Simile

A visual modelling environment developed for modelling complex, disaggregated ecological and environmental systems.

System Dynamics modelling

(stock-and-flow, transport processes, continuous systems, differential equations)

plus

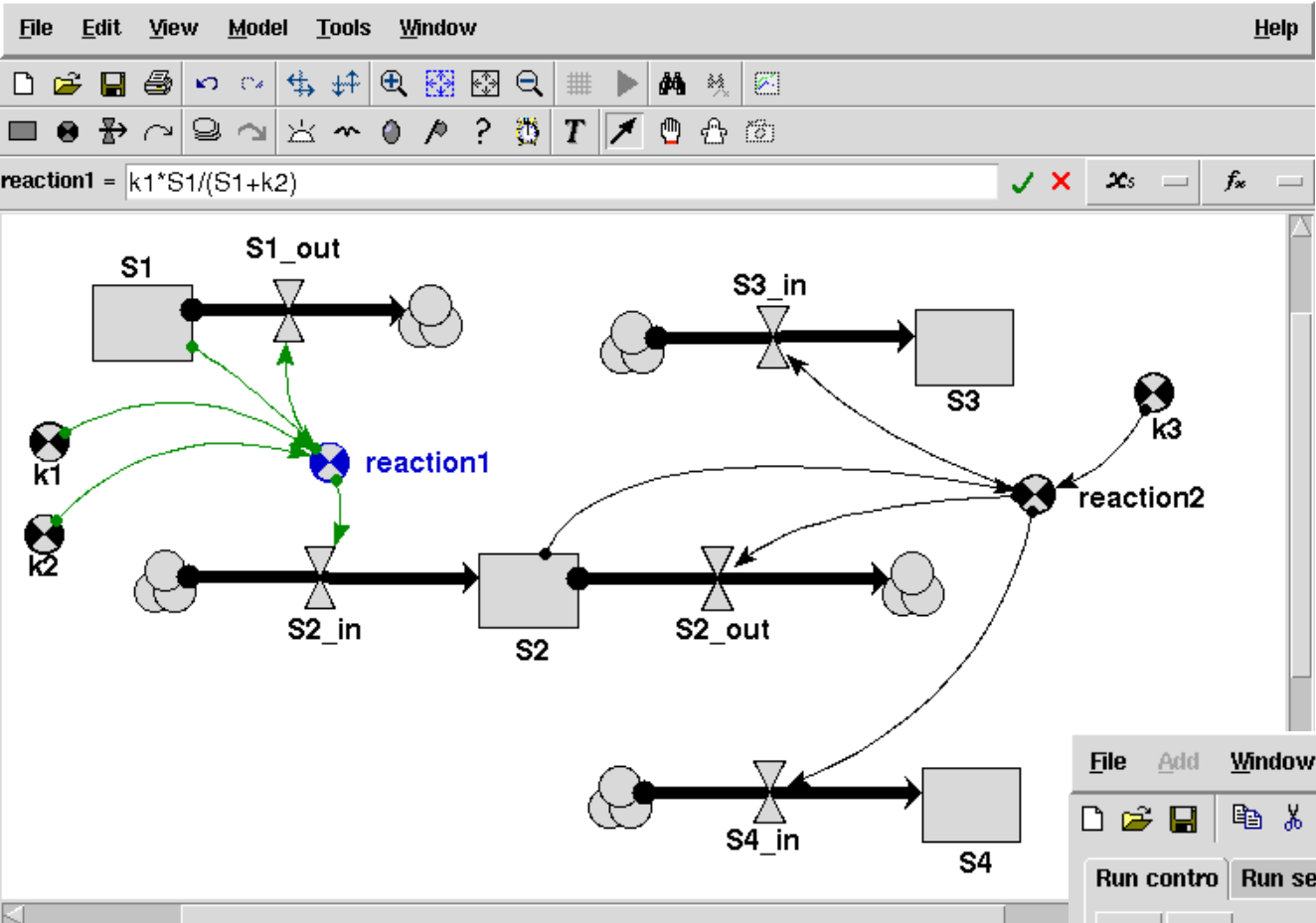
the ability to represent lots of objects and the relationships between them

(e.g. spatial grids, layers, multiple species, age-classes...)

plus

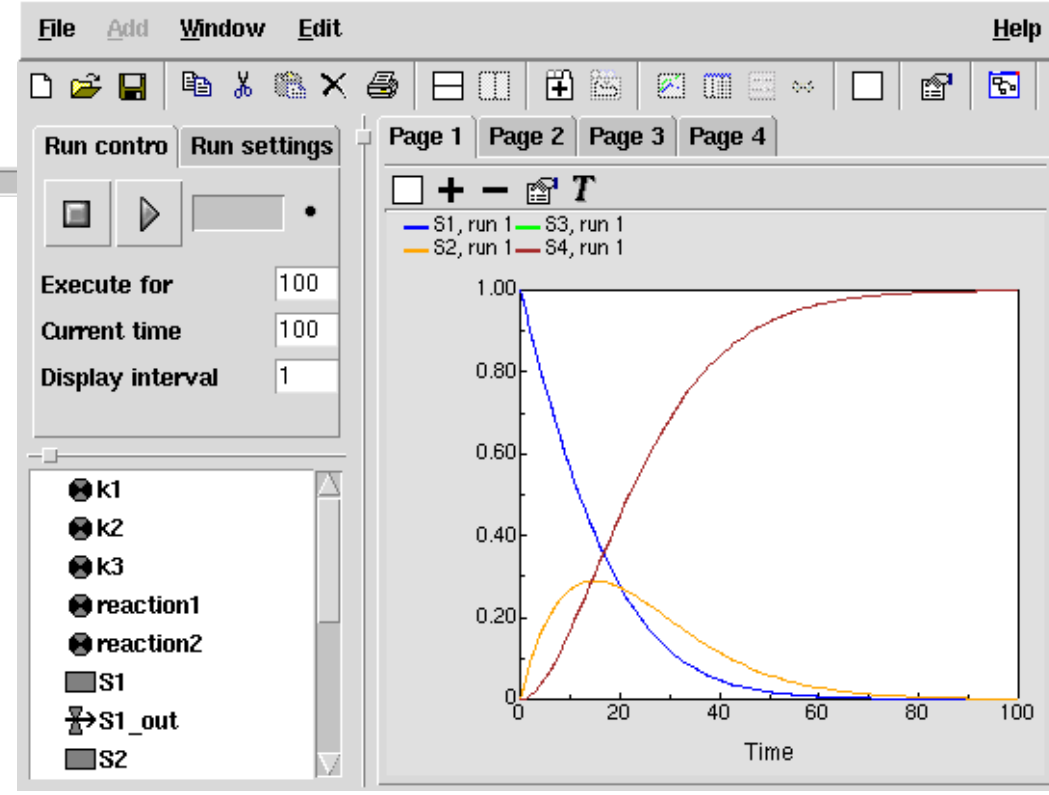
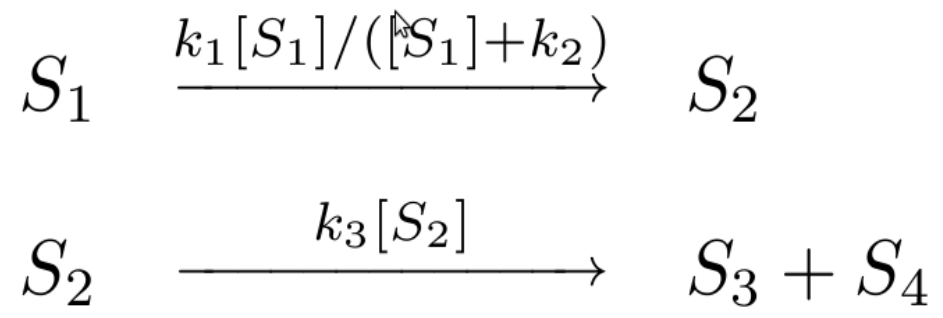
the ability to dynamically create and destroy objects
(individual-based modelling, “agent-based systems”)



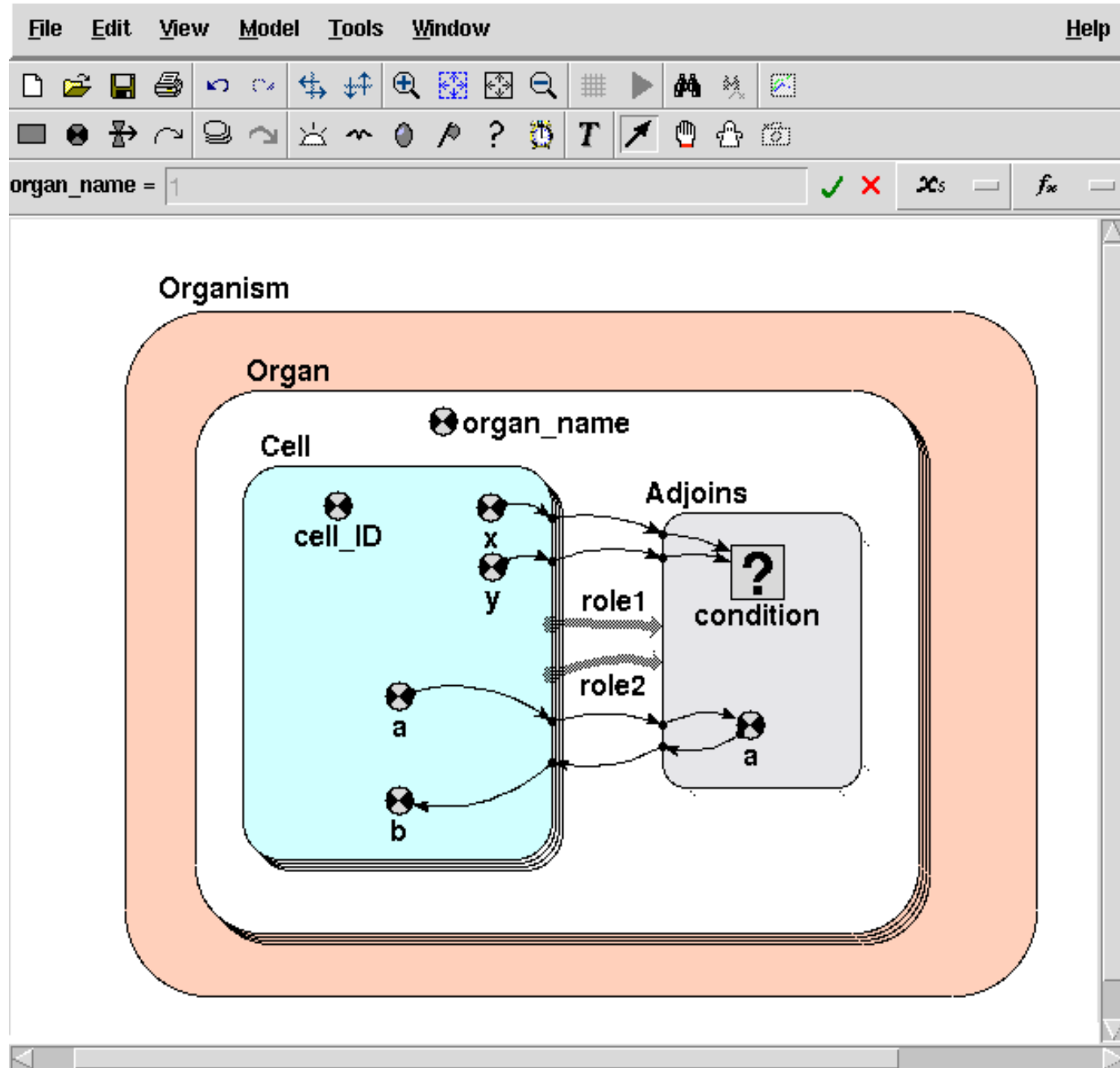


Reactions in System Dynamics

In BBSRC Plasmo project:
 SBML \longleftrightarrow Simile conversion

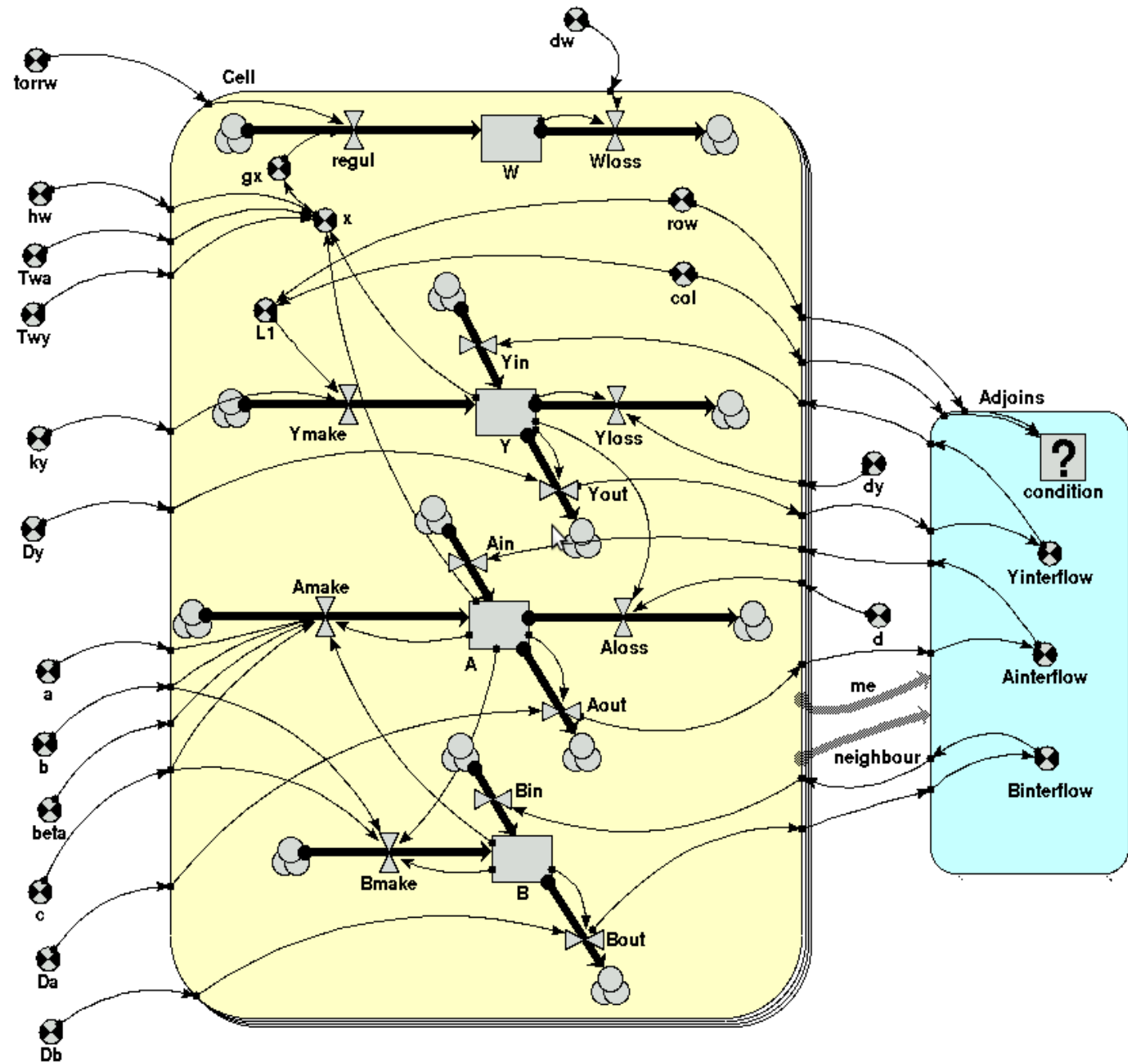
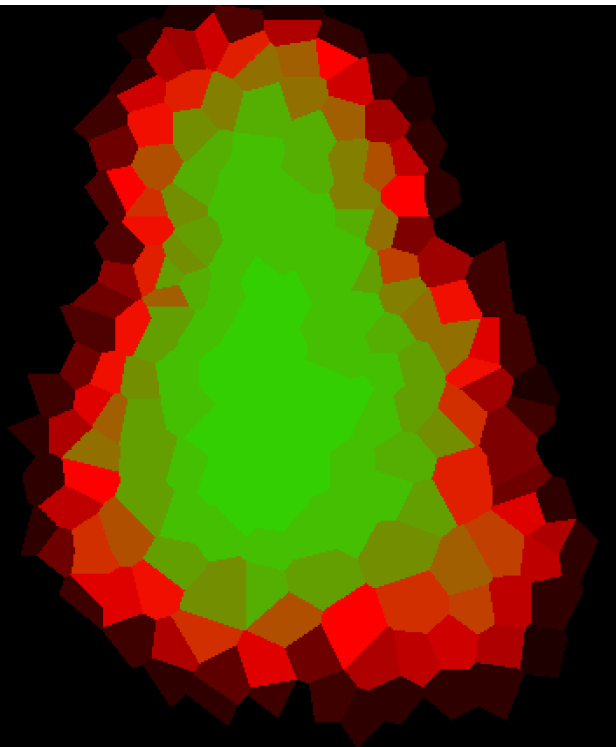
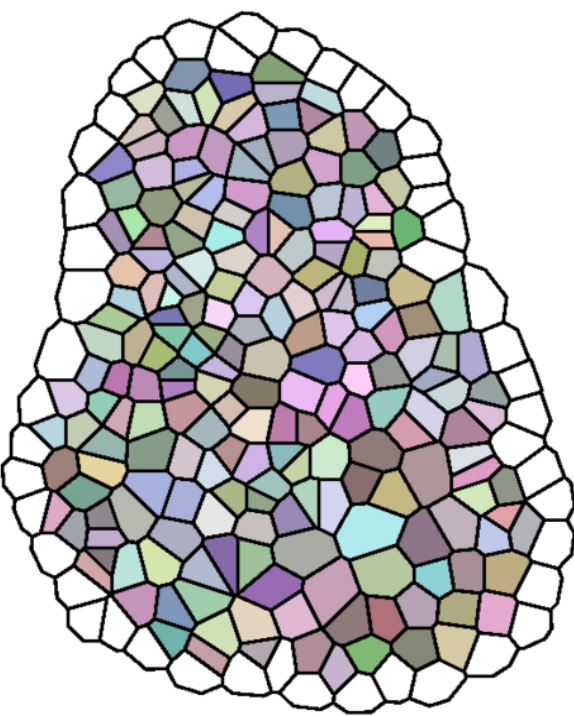


Simple hierarchical composition

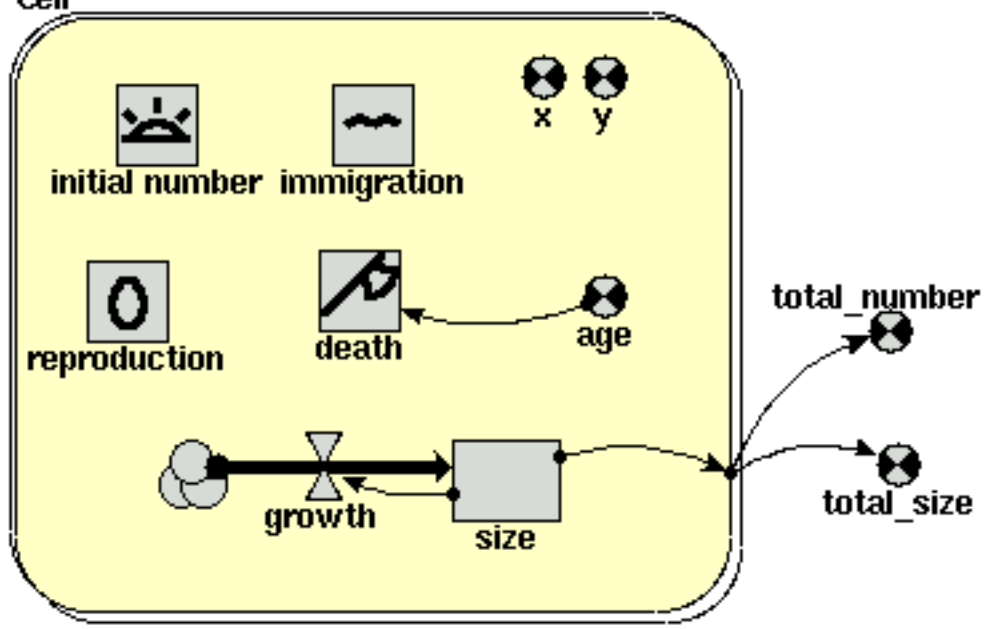


Arrays/spatial modelling

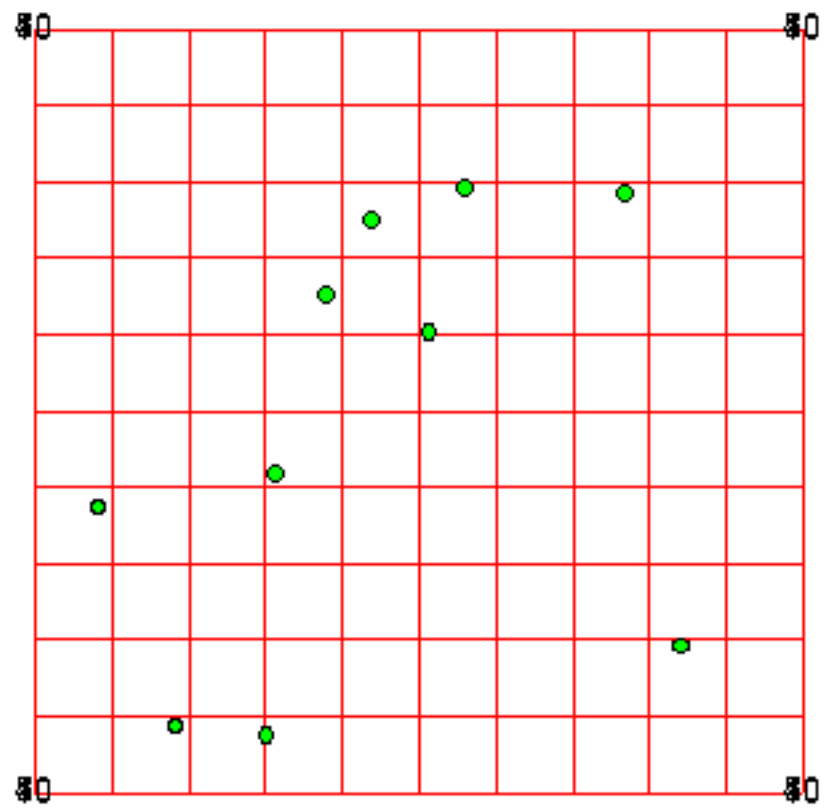
Bruce Shapiro's 'activator' model



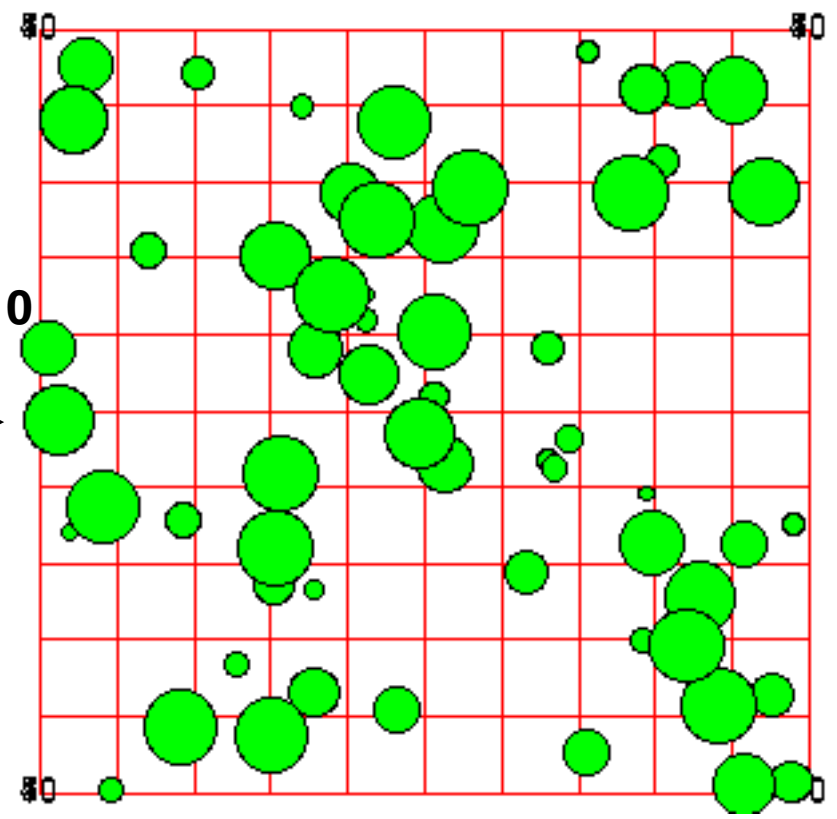
Cell



Dynamically-changing number of individuals - the SBML L3 'dyn' package



$t=0$ \longrightarrow $t=10$



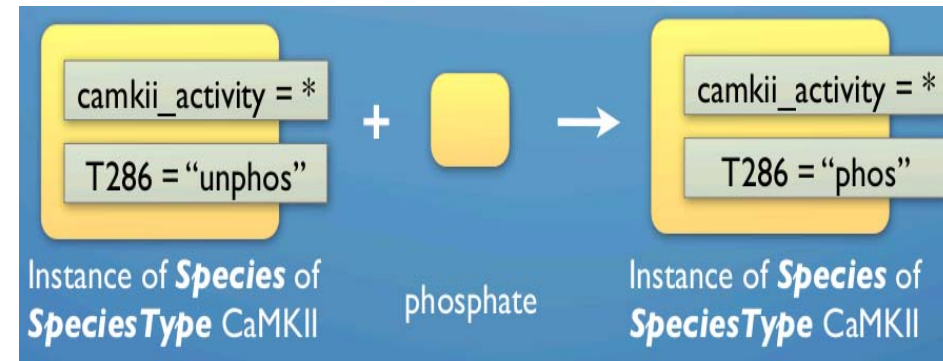
Species type CaMKII

- feature “camkii_activity” with possible values {“active”, “inactive”, “inhib”}
- feature “T286” with possible values {“unphos”, “phos”}

A species of type CaMKII could exist in 6 different states:

- (camkii_activity → inactive, T286 → unphos)
- (camkii_activity → inactive, T286 → phos)
- (camkii_activity → active, T286 → unphos)
- (camkii_activity → active, T286 → phos)
- (camkii_activity → inhib, T286 → unphos)
- (camkii_activity → inhib, T286 → phos)

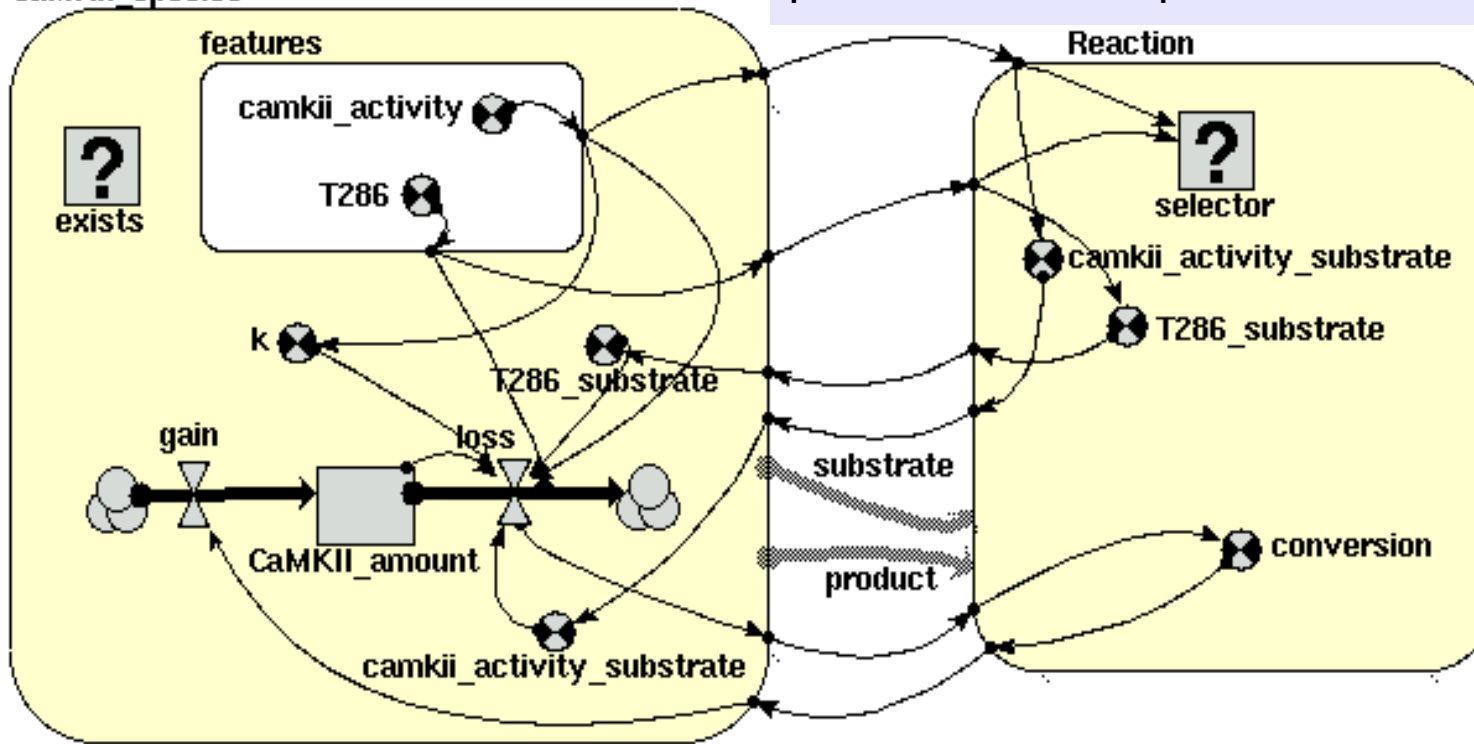
SBML L3 'multi' package



selector

substrate_camkii_activity==product_camkii_activity and
 substrate_T286=="unphos" and
 product_T286=="phos"

CaMKII_species



What is not tackled within Simile:

PDEs

Either treat as separate problem, or do the spatial discretisation yourself.

Analytical geometry

Either treat as a separate problem, or handle mathematically in the model.

Inheritance/generalisation associations

Not handled, and no plans to, since rarely needed in ecological domain.

Conclusions

- UML class-and-association (or rather, its serialisation in XMI) not enough in itself, but provides much of the expressiveness required for handling complex hierarchical structures.
- Simile not enough in itself, but demonstrates the computability of this approach.
- Is the SBML community able to re-think the idea of a set of separate L3 packages?

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