

# 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

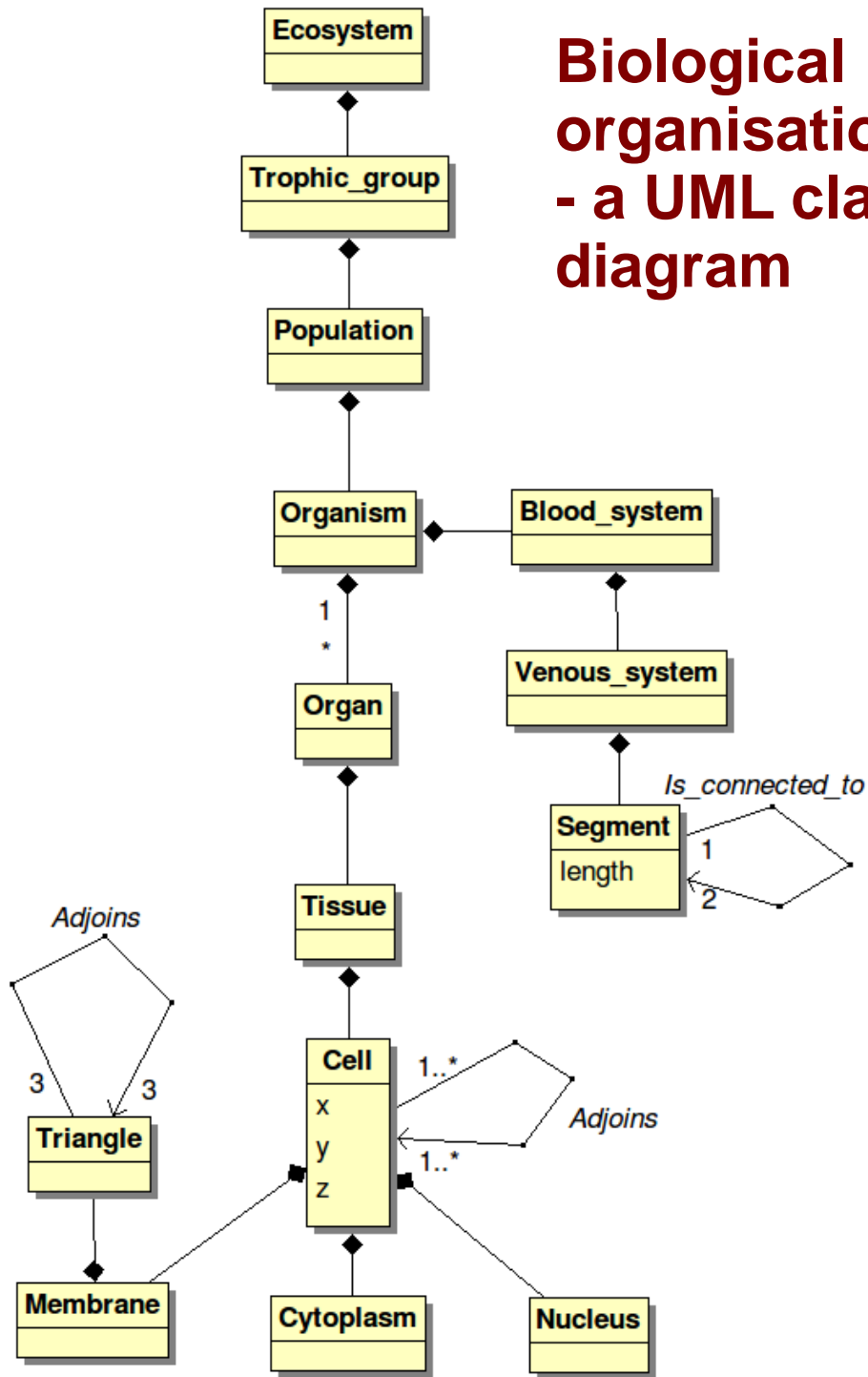
SBML

FieldML

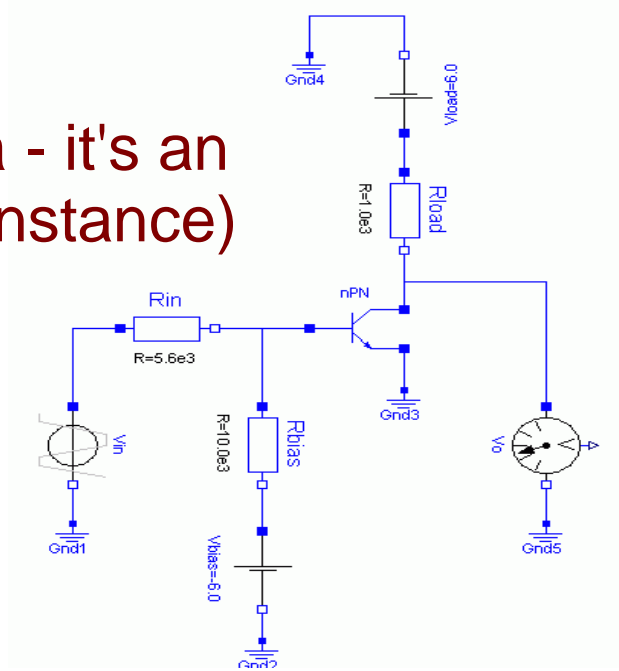
CellML



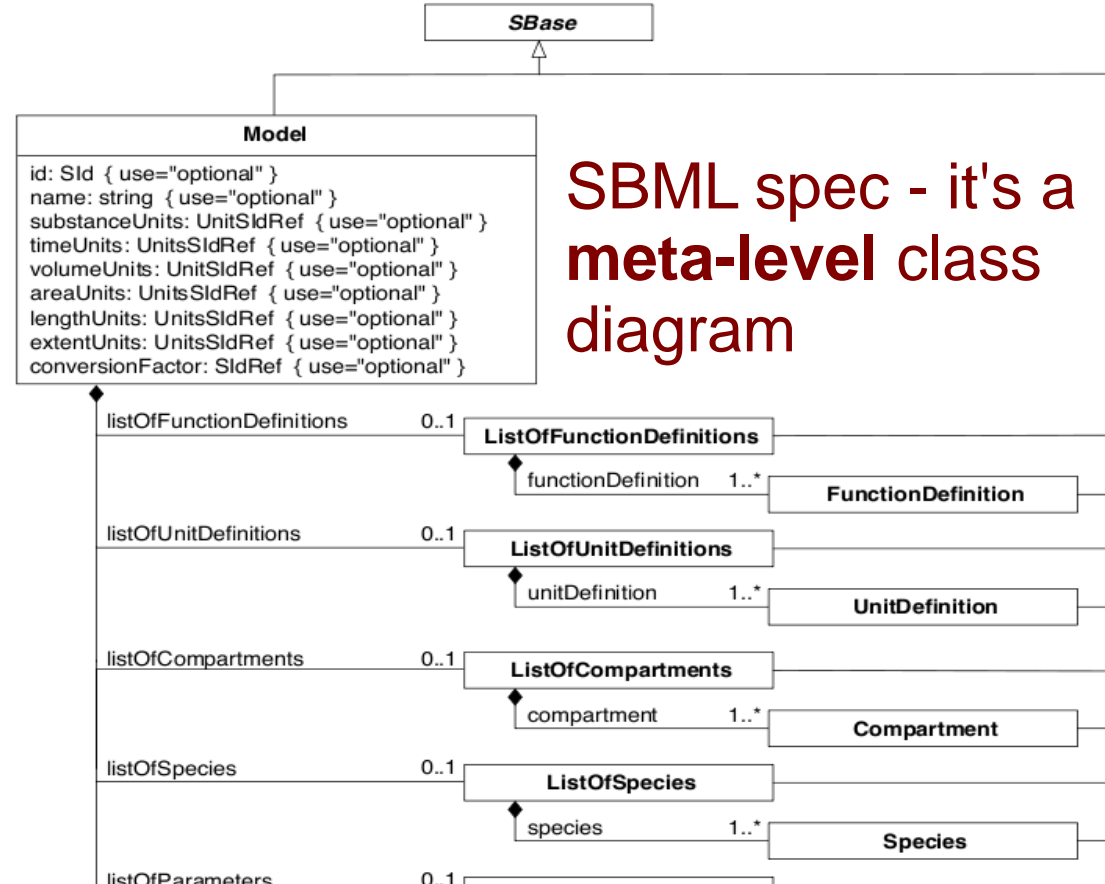
**Biological organisation - a UML class diagram**



**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**

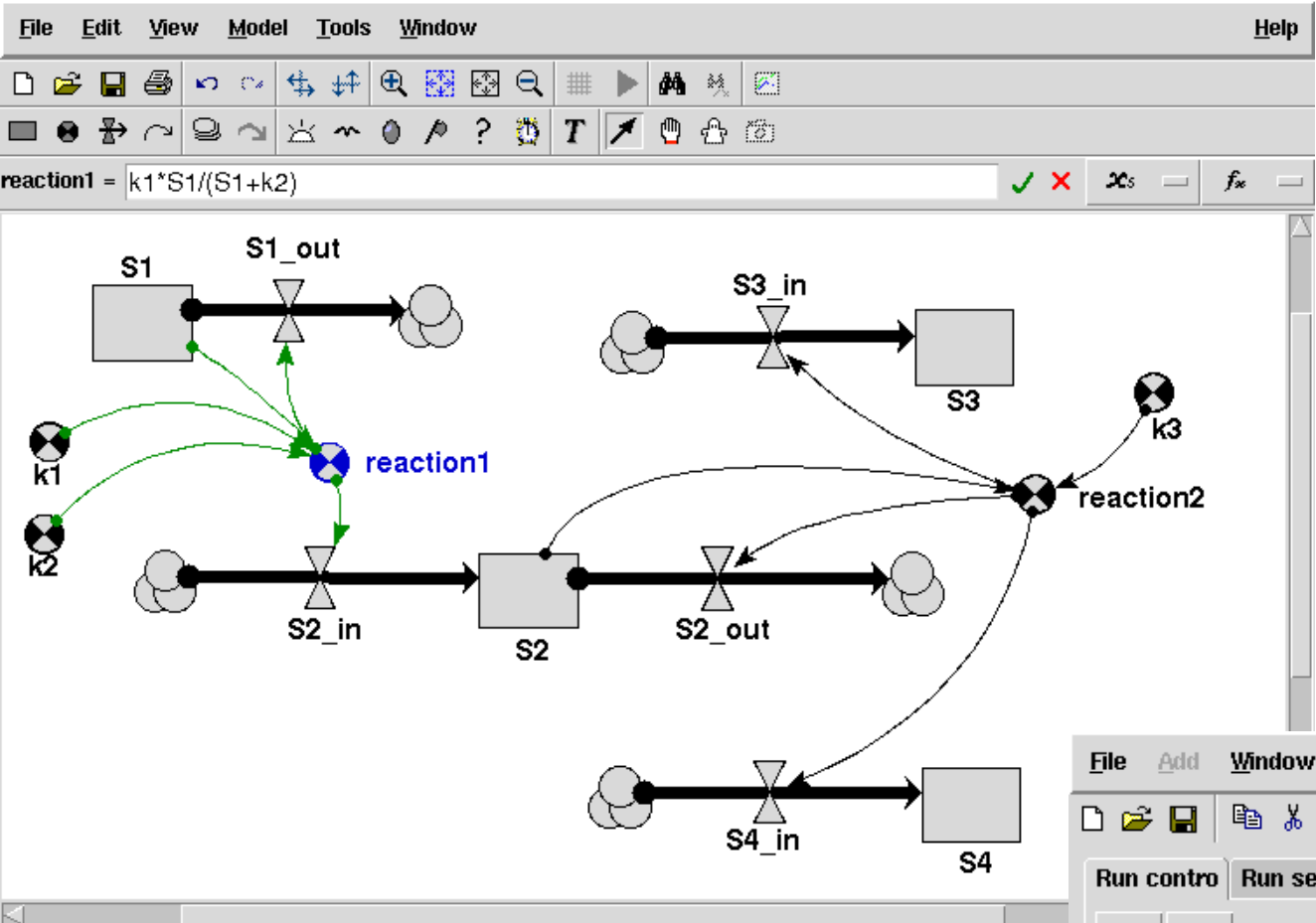
**the ability to represent lots of objects and the relationships between them**

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

**plus**

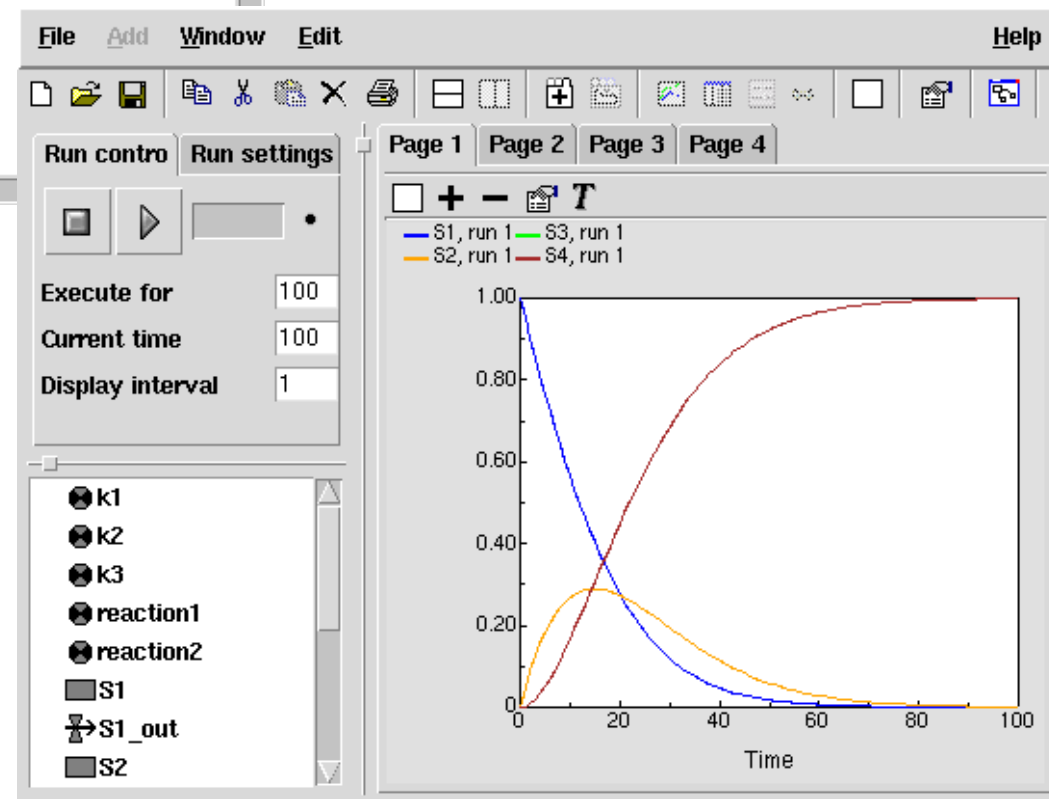
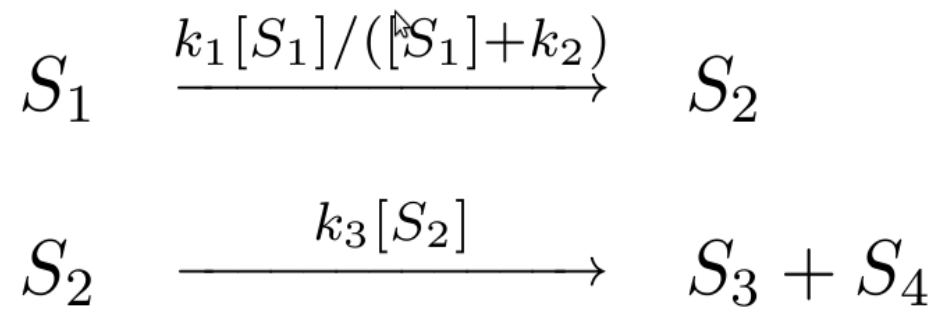
**the ability to dynamically create and destroy objects**  
(individual-based modelling, “agent-based systems”)



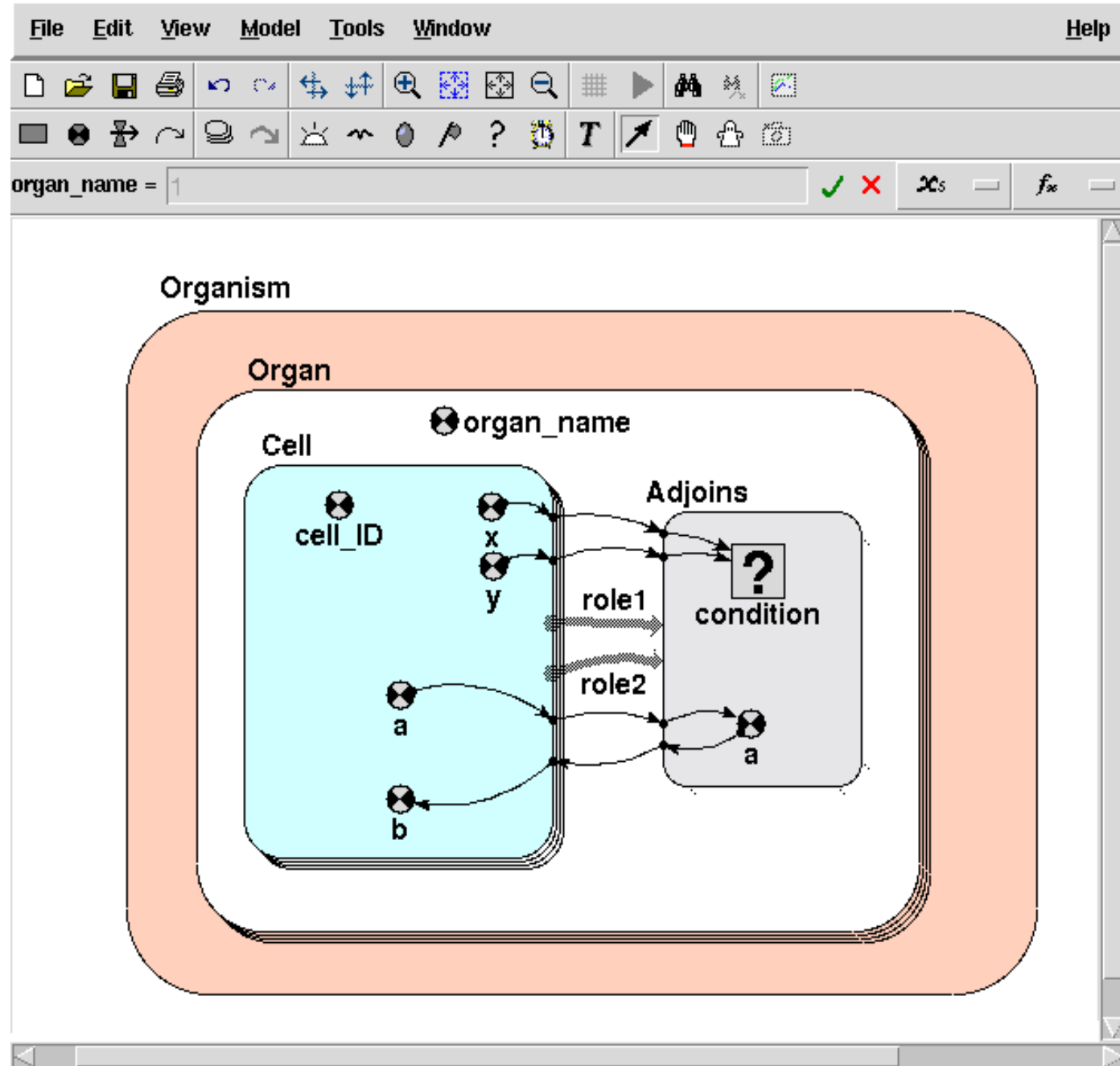
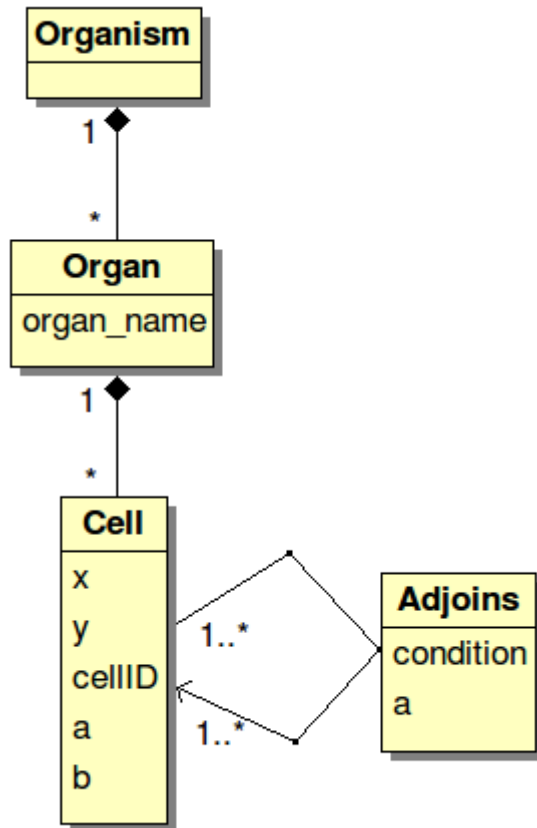


# Reactions in System Dynamics

In BBSRC Plasmo project:  
 SBML  $\longleftrightarrow$  Simile conversion

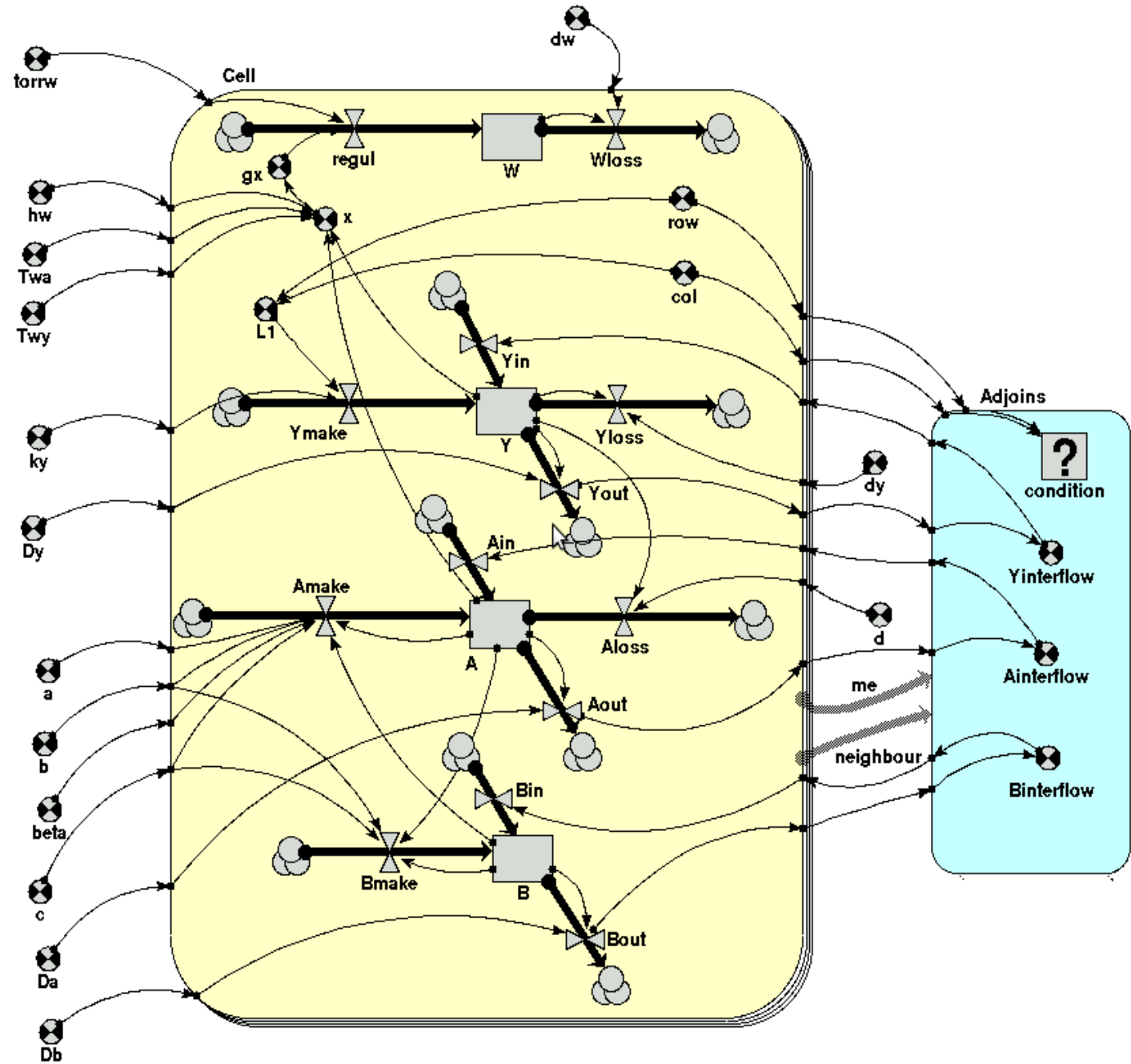
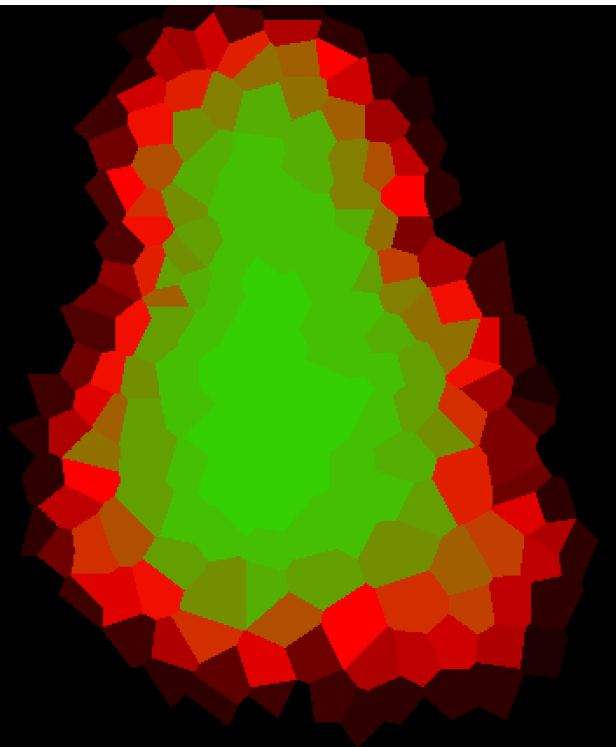
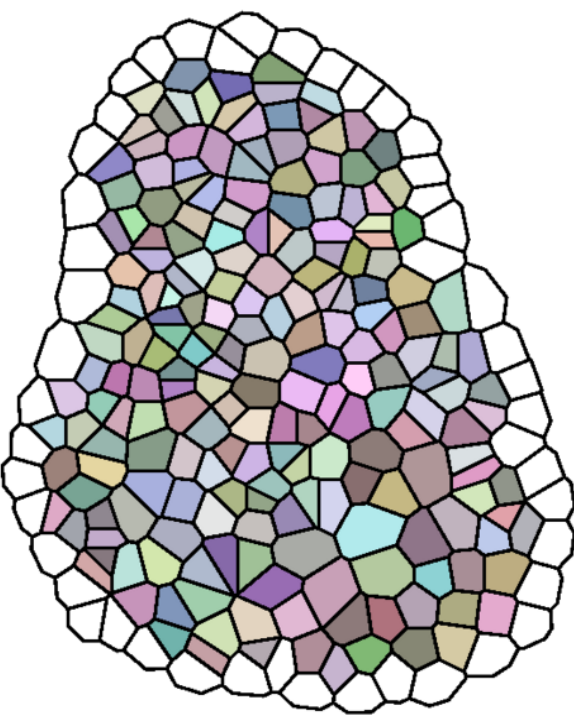


# Simple hierarchical composition

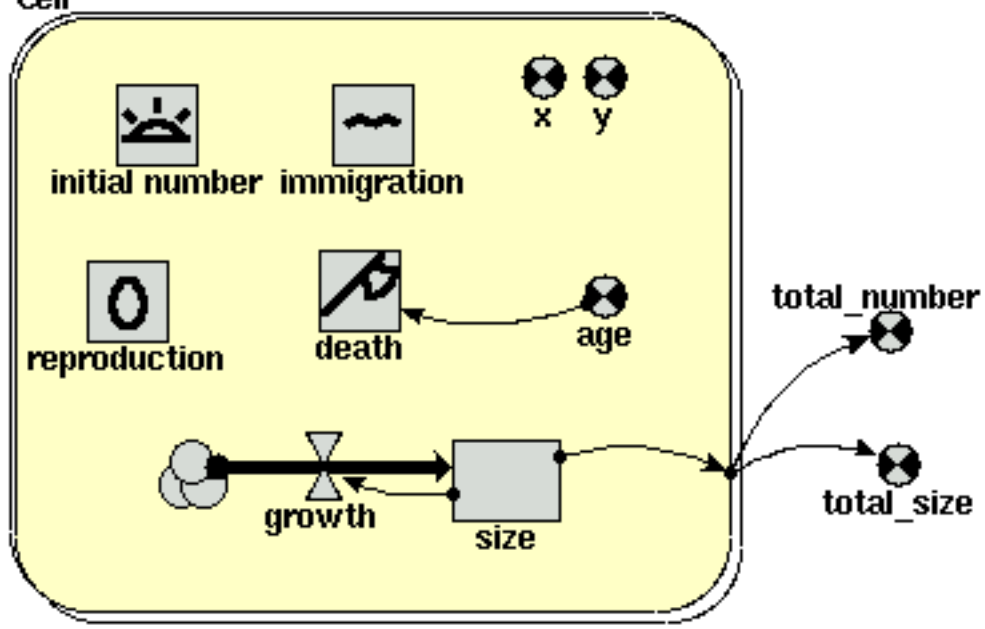


# Arrays/spatial modelling

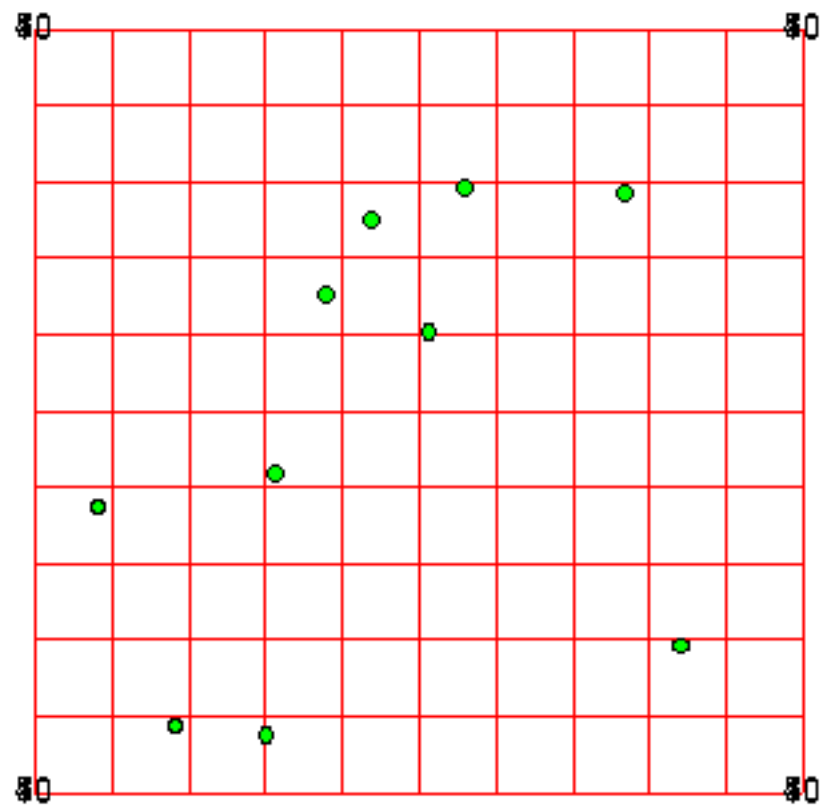
## Bruce Shapiro's 'activator' model



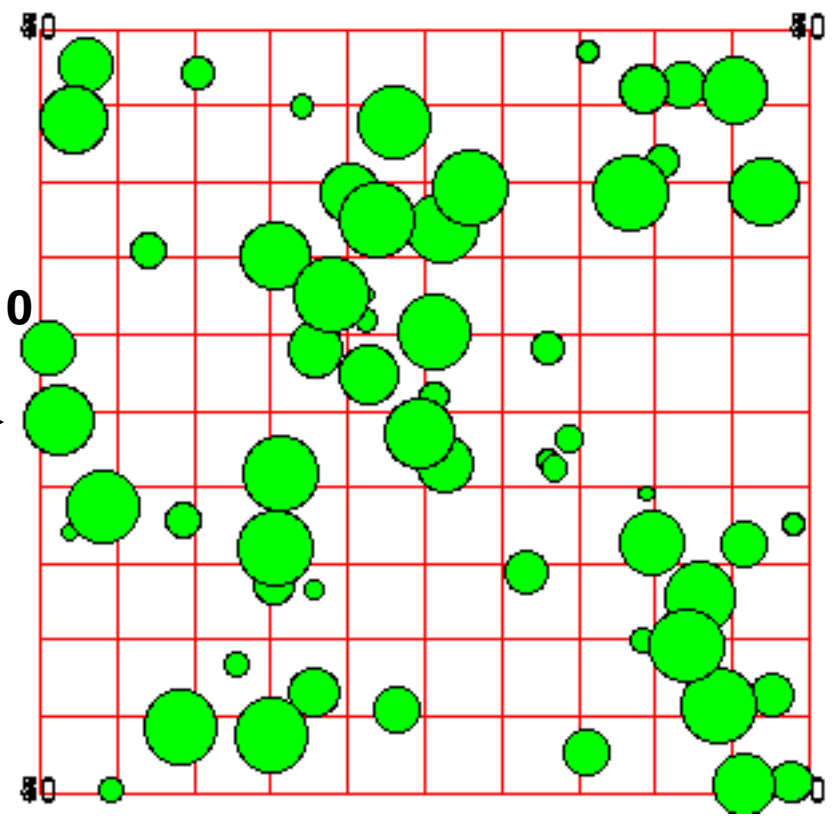
Cell



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



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



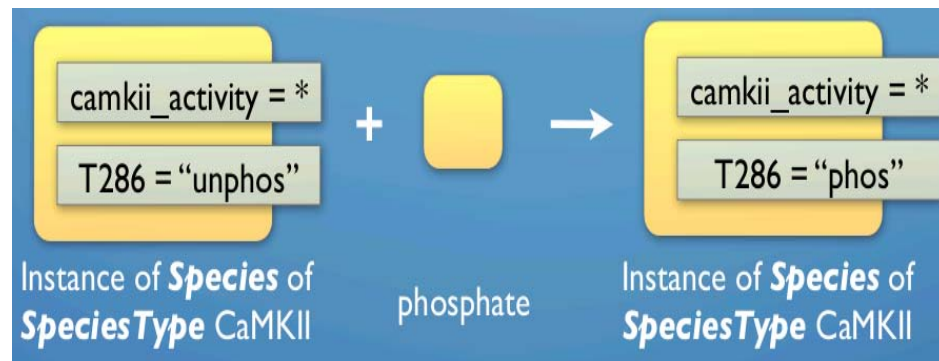
Species type CaMKII

- 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)

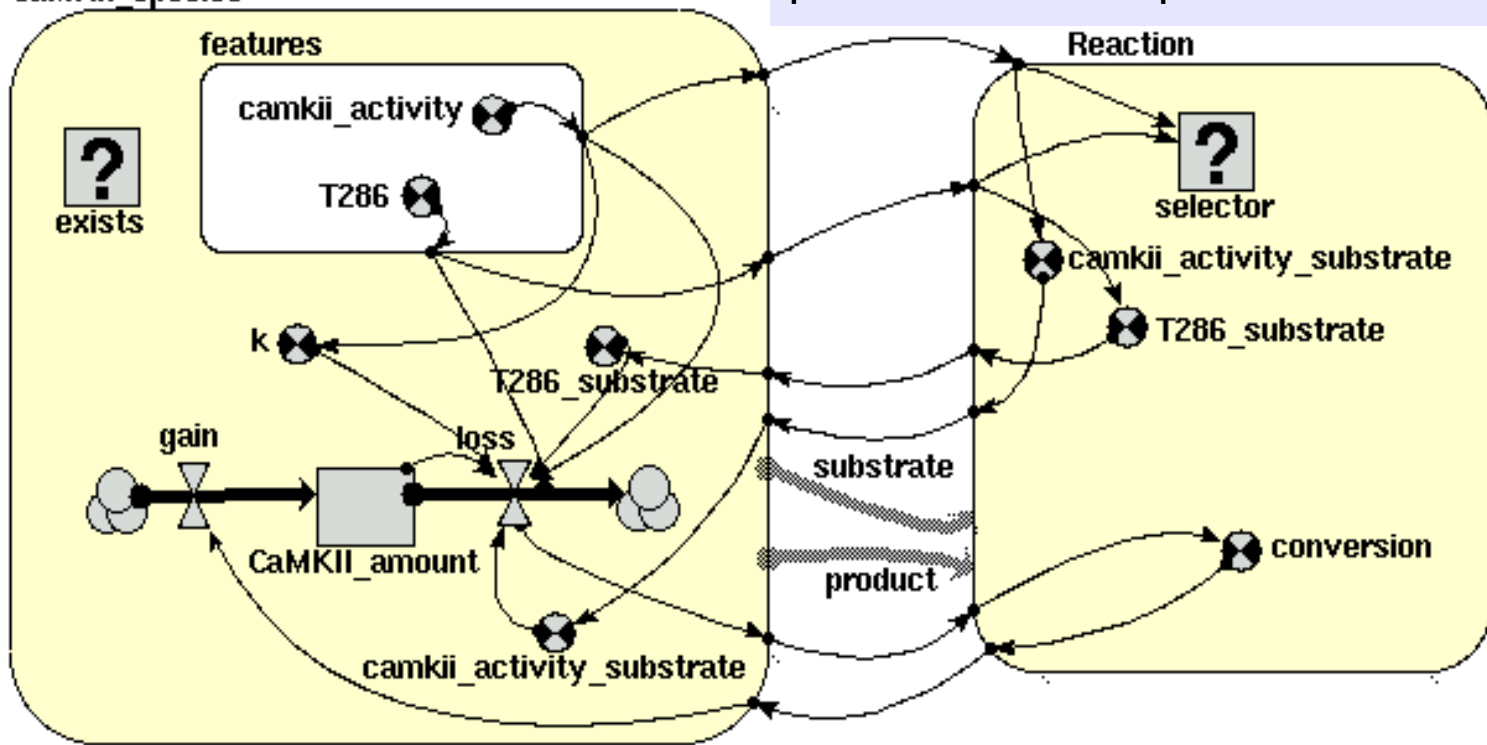
# SBML L3 'multi' package



## 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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