

**METHODOLOGY ARTICLE**

**Open Access**

# The systems biology simulation core algorithm

Roland Keller<sup>1†</sup>, Alexander Dörr<sup>1†</sup>, Akito Tabira<sup>2</sup>, Akira Funahashi<sup>2</sup>, Michael J Ziller<sup>3</sup>, Richard Adams<sup>4</sup>, Nicolas Rodriguez<sup>5</sup>, Nicolas Le Novère<sup>6</sup>, Noriko Hiroi<sup>2</sup>, Hannes Planatscher<sup>1,7</sup>, Andreas Zell<sup>1</sup> and Andreas Dräger<sup>1,8\*</sup>

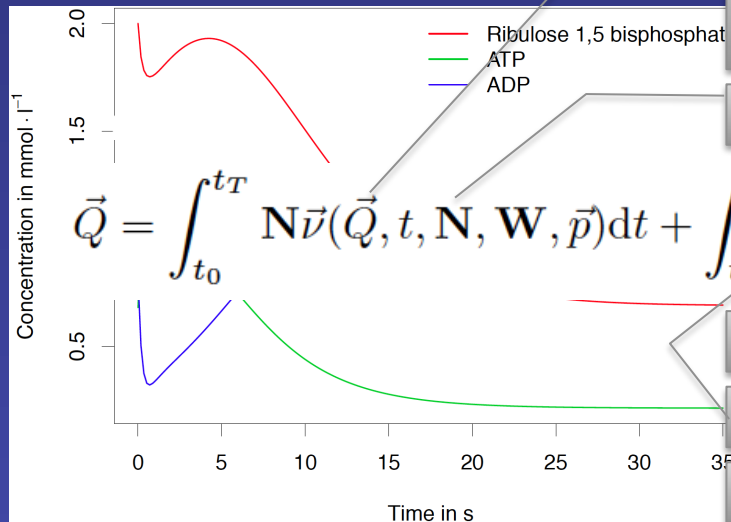
# The mathematics behind SBML

Metabolic network:

$$\frac{d}{dt}\vec{S} = \mathbf{N}\vec{v}(\vec{S}, t, \mathbf{N}, \mathbf{W}, \vec{p})$$

Integration yields:

$$\vec{S} = \int_{t_0}^{t_T} \mathbf{N}\vec{v}(\vec{S}, t, \mathbf{N}, \mathbf{W}, \vec{p})dt$$



Amounts/concentrations of species

Stoichiometric matrix (constant)

Parameter vector (constant)

Modulation matrix (constant)

Current time

Reaction velocities function

Values of model quantities  
(compartments, species, variable  
parameters)

Stoichiometric matrix (variable)

$$\vec{Q} = \int_{t_0}^{t_T} \mathbf{N}\vec{v}(\vec{Q}, t, \mathbf{N}, \mathbf{W}, \vec{p})dt + \int_{t_0}^{t_T} \vec{g}(\vec{Q}, t)dt + \vec{f}_E(\vec{Q}, t) + \vec{r}(\vec{Q}, t)$$

Event functions

Rate rule functions

Assignment rules functions

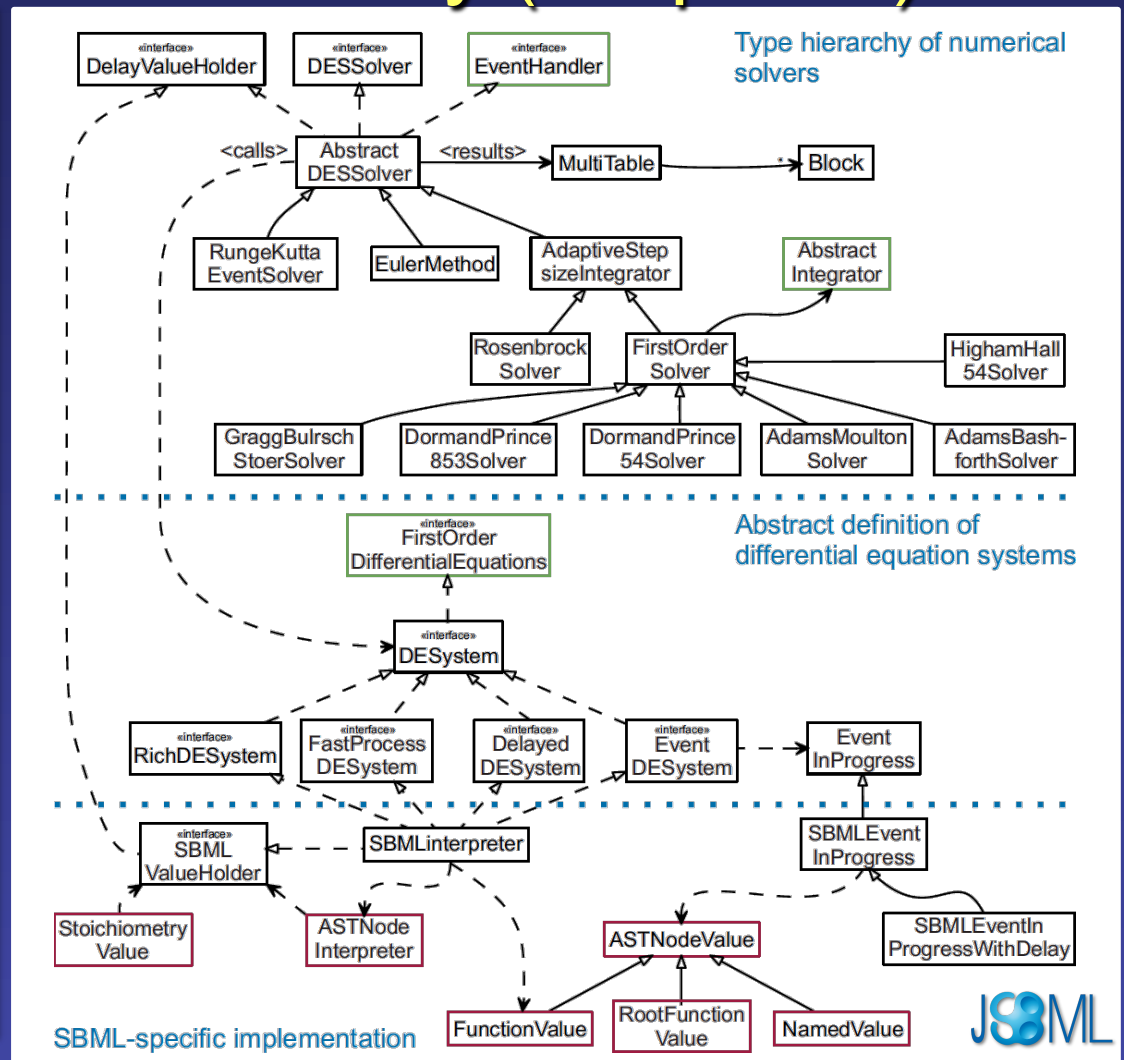
Further SBML  
elements:

- Delay functions and delayed events
- Fast and slow time scales
- Algebraic equations
- Function definitions

# Architecture of the Systems Biology Simulation Core Library (simplified)

## Design principles

- Strict separation between numerical integration method and differential equation system
- General, multi-layered abstract definition of differential equation system, independent from any application
- Implementation of these data structures for the interpretation of SBML, based on library JSBML
- In this way, further applications possible, e.g., an interpreter for the modeling language CellML



# SED-ML in Simulation Core Library

- Support for SED-ML in Simulation Core Library (mainly implemented by Richard Adams)
  - Integration of existing libraries (reading, writing of SED-ML)
  - Some wrapper classes
- Successfully tested with SED-ML files contained in the SBML Test Suite
- Direct simulation with information from SED-ML possible, but
  - information whether to calculate the **amount** or the **concentration** of a species has to be given to the simulator in advance (via a map)

```
SEDMLDocument doc =  
    Libsedml.readDocument(new  
        File(sedmlfile));  
  
SedML sedml = doc.getSedMLModel();  
  
Output wanted = sedml.getOutputs().get(0);  
  
SedMLSBMLSimulatorExecutor exe =  
    new SedMLSBMLSimulatorExecutor(sedml,  
        wanted, amountConcentrationMap);  
  
Map<Task,IRawSedmlSimulationResults> res =  
    exe.runSimulations();  
  
MultiTable mt = null;  
for (Task t: res.keySet()) {  
    mt = ((MultiTableSEDMLWrapper)  
        res.get(t)).getMultiTable();  
    break;  
}
```

# Thanks

## People:

- Roland Keller<sup>1</sup>
- Alexander Dörr<sup>1</sup>
- Akito Tabira<sup>2</sup>
- Akira Funahashi<sup>2</sup>
- Michael Ziller<sup>1,3</sup>
- Richard Adams<sup>4</sup>
- Nicolas Rodriguez<sup>5</sup>
- Nicolas Le Novère<sup>6</sup>
- Hannes Planatscher<sup>7</sup>
- Andreas Zell<sup>1</sup>



## Institutions:

- <sup>1</sup>Center for Bioinformatics Tuebingen (ZBIT), Tübingen, Germany
- <sup>2</sup>Graduate School of Science and Technology, Keio University, Yokohama, Japan
- <sup>3</sup>Dept. of Stem Cell and Regenerative Biology, Harvard University, Cambridge, USA
- <sup>4</sup>SynthSys Edinburgh, University of Edinburgh, UK
- <sup>5</sup>European Bioinformatics Institute, Hinxton, UK
- <sup>6</sup>Barbraham Institute, Cambridge, UK
- <sup>7</sup>Natural and Medical Sciences Institute at the University of Tuebingen, Reutlingen, Germany
- <sup>8</sup>University of California, San Diego, La Jolla, USA

## Availability:

<http://simulation-core.sourceforge.net>

## Mailing list:

[simulation-core-development@lists.sourceforge.net](mailto:simulation-core-development@lists.sourceforge.net)

## Bug tracker:

<http://sourceforge.net/p/simulation-core/tickets/>

## Main funding:

