

8th Forum on Software Platforms for Systems Biology

10 November 2003, Chase Park Plaza Hotel, Saint Louis, MO, USA

Delegates present

Mirit Aladjem	NCI/NIH, Bethesda, MD, USA
Nicolas Allen	Virgia Tech, Blacksburg VA, USA
Benjamin Bornstein	NASA JPL, Pasadena CA, USA
Fabien Campagne	Mt Sinai School of Medicine, New York NY, USA
Vijay Chickarmane	Keck Graduate Institute, Claremont CA, USA
Autumn Cuellar	University of Auckland, Auckland, New Zealand
Marco Donizelli	EBI, Cambridge, UK
Jens Doutheil	Dechema, Frankfurt, Germany
Rashad El-Badrawi	UCHC, Farmington CT, USA
Andrew Finney	STRC, University of Hertfordshire, Hatfield, UK
Akira Funahashi	ERATO Kitano Symbiotic Systems Project, Tokyo, Japan
Warren Hedley	San Diego Supercomputer Center, San Diego CA, USA
Michael Hucka	Caltech, Pasadena CA, USA
Sarah Keating	STRC, University of Hertfordshire, Hatfield, UK
Tom Kiehl	GE Global Research, Schenectady NY, USA
Ben Kovitz	Caltech, Pasadena CA, USA
Nicolas Le Novère	EBI, Cambridge, UK
Zhang Li	TeraNode, Seattle, WA, USA
Rolf Lohaus	German Cancer Research Centre, Heidelberg, Germany
Joanne Matthews	STRC, University of Hertfordshire, Hatfield, UK
Pedro Mendes	Virginia Tech, Blacksburg VA, USA
Ute Platzer	(formerly) German Cancer Research Centre, Heidelberg, Germany
Stephen Ramsey	ISB, Seattle, WA, USA
Wayne Rindone	Harvard University, Cambridge MA, USA
Shai Sachs	Akaza Research, Cambridge MA, USA
Sven Sahle	European Media Laboratory, Heidelberg, Germany
Takeshi Sakurada	Keio University, Tokyo, Japan
Herbert Sauro	Keck Graduate Institute, Claremont CA, USA
James Schaff	UCHC, Farmington CT, USA
Maria Schilstra	STRC, University of Hertfordshire, Hatfield, UK
Bruce Shapiro	NASA JPL, Pasadena CA, USA
Jacky Snoep	Stellenbosch University, Matieland, South Africa
Koichi Takahashi	Keio University, Tokyo, Japan
Mark Vass	Virginia Tech, Blacksburg VA, USA

Notes

(Compiled on the basis of notes made during the meeting by Maria Schilstra)

9:00 **Mike Hucka, Andrew Finney** (SBML Editors)

Welcome; agenda; announcements.

9:05 **Ben Kovitz** (SBML team)

New SBML website with easy to remember url: www.sbml.org. SBML will be registered as a MIME media type (so that the url must be persistent). Demo of the use of the wiki on the website. Wiki best practice recommendation.

9:20 **Jo Matthews** (SBML team)

Plans for and development stage of new online tools: 1) SBML validator (part of Ben Bornstein's libSBML); 2) SBML model visualization tool (based on AT&T's GraphViz). Live demo of validator and visualization tools. Online tools will reside on SBML server. Planned: online SBML L1 → L2 converter; online utilities from mathSBML (Bruce Shapiro).

9:30 **Sarah Keating** (SBML team)

SBML toolbox for MATLAB: toolbox reads SBML, converts SBML into MATLAB structures, returns lists of species, reactions, etc, through simple interactive GUIs. Toolbox development incidental to main project: using SBML to make Caltech's Dynamical Systems Group SOS-tools (MATLAB application) accessible to non-specialists. Short discussion of the fundamentals of the SOS-Tools.

9:40 **Ben Bornstein** (SBML team)

LibSBML: short announcement of new features (Expat port, Formula Eval, Windows Build) and future directions (C++ rather than C object model; Java and Python APIs; semantic validation tool). In answer to a question (Sauro): SBW NOM could be considered, but is not a priority.

9:50 **Stephen Ramsey** (Dizzy)

Dizzy is a simulation package for modelling the kinetics of complex reactions, integrated with SBW and Cytoscape. Written in Java (with Swing library); provides several ODE solvers and stochastic simulators. See workshop documentation

10:05 **Ute Platzer** (Gene-O-Matic)

Gene-O-Matic, a discrete Boolean gene network simulator. Would like to use SBML to store models, but would need extra features (information about interaction strength or Boolean formulas, cell positions and radii, species location, cell division). Announced she has now finished writing her thesis, and is looking for a post-doc position in Systems Biology.

10:15 **Bruce Shapiro** (SBML team)

MathSBML: a Mathematica notebook that allows interaction between Mathematica and SBML. Features: SBML file viewer; SBML → Xpp and SBML → Fortran converters; web page generator (with tables of species, reactions, and other SBML structures, but also full ODEs); ODE solvers; SBML model generator. Complete documentation available via www.sbml.org/mathsbml.html.

10:45 **Zheng Li** (TeraNode)

TeraLab (TL) and TeraSim (TS) are part of a commercial package for modelling and simulation of biochemical networks (various ODE-based and stochastic simulators). TL provides integration of experimental results with its modelling and simulation facilities. TS can import and export and export its models in SBML (import L1v2 and L2v1; export L2v1). TS has interactive graphical facilities for model building. Models are hierarchical, and support for interaction with several databases is provided. As yet, TS does not support events, not user-defined functions, and units must be fully defined. Live demonstration of the use of TS.

11:05 **Shai Sachs** (Akaza, STKE)

Akaza and STKE Research are adopting SBML for signal transduction pathway model storage. STKE Connections Map (CM) concepts can be mapped relatively easily onto SBML structures: CM Pathway \equiv SBML Model; CM Components and Nodes \equiv SBML Species; CM Relations \equiv SBML Reactions. 'Specific' CM pathways (specific to particular biological species; as opposed to 'canonical' pathways, which are present in multiple, or all, species) will be associated with SBML Compartments that have the name of the biological species in which the specific pathway is found.

Put forward implementation for controlled vocabularies. Proposed that an SBML L3 contains a `listOfControlledVocabularies`, containing zero or more `controlledVocabulary` elements. These would reference externally defined controlled vocabularies.

CM concepts that cannot be mapped onto SBML yet: qualitative descriptions for modifier effects, homologs/ synonyms, reaction groups. Suggestion (Finney) that Complex Species and other L3 concepts whose definition and implementation are currently being discussed in the Working Groups may prove to be useful in these respects.

11:25 **Autumn Cuellar** (CellML)

Update on recent CellML developments. 1) Facility for importing model components rather than whole model has been implemented; 2) a Python library is now available; 3) there are now usage cases for ontologies; will be possible to use the same XML ontologies for CellML and SBML, which will make transformations between SBML and CellML easier.

11:30 **Ben Kovitz** (SBML team)

Short update on the progress made by the various SBML Working Groups, and on recent proposals and draft implementations. Complete information can be found on the wiki pages.

11:35 **Herbert Sauro** (Keck Graduate Institute; SBW)

Discussion of work with group at Thomas Jefferson University on transcription networks, new developments in JDesigner, and current efforts on SBW (BioSpice bridge; additional MATLAB, bifurcation, and optimization modules). Mentioned problems with implementation of SBML diagrams proposal: there are now two (competing?) proposals, which one should be implemented?

11:45 **Sven Sahle** (EML Heidelberg)

Diagram layout proposal: illustration of requirements; reasons for not using existing solution (such as SVG or GraphML). Decisions: 1) zero or more layouts can be associated with single model; 2) No 1:1 relationship between model components and graphical representation; 3) Layout separate from rendering information (but decisions still to be taken about which elements are part of the layout, for instance: font size?). Proposed `listOfLayouts`, containing layout elements; layout element contains `listOfSpeciesGlyphs` and `listOfReactionGlyphs`. `SpeciesGlyph` and `reactionGlyph` each have an id, a name, a reference to a species or reaction, and a description of the glyph (currently a box whose dimensions are determined by 2 parameters). Inheritance tree for graphical objects proposed. Further information on wiki pages, and in Forum documentation.

Discussion: should text (e.g. name) be placed inside the box that symbolizes the species/reaction or should species/reaction glyphs define separate boxes for text. Important consideration when avoiding lines crossing. No firm decision taken, arguments in favour of each were brought forward. It was mentioned that in the current proposal box size is specified, and clipping or resizing of text is left to tool (as opposed to specifying text size, and generation of bounding box by tool).

General feeling was that reactionGlyph should be optional (laying out simple reactions such as $A \rightarrow B$ may not require separate symbol for the reaction).

13:00 **Lunch**

14:10 **Mike Hucka** (SBML Editor)

Introduction to afternoon program.

14:15 **Jacky Snoep** (JWS Online Cellular Systems Modelling)

Models in the interactive JWS Online database (jjj.biochem.sun.ac.za/index.html or www.jjj.bio.vu.nl/database) can be simulated online. List of models in SBML model repository contains links to corresponding models in the JWS database.

14:20 **Sven Sahle** and other delegates to the Forum

Further discussion of diagram layout proposal.

'Competing' layout proposal by Jonathan Webb (not present): SBML Editors feel that JW's proposal was makeshift solution in absence of more complete proposal, and that BioSpice are likely to support the current EML proposal.

GraphML: proposed layout description is not based on GraphML, because the EML team felt that only a limited range of diagrams can be generated on the basis of an SBML model. The application range of GraphML (and SVG) is too wide, so that the EML team opted for a tailor-made solution.

Layout vs rendering: layout description contains the minimum information necessary to generate a diagram; rendering is tool-specific.

Summary of consensus: 1) use the EML proposed approach; 2) focus on layout description, leave rendering to future implementations; 3) omit glyph grouping (too complicated).

Core language: In current proposal layout info has its own, separate namespace, which makes it easy to ignore for applications that cannot handle it. Thus, diagram layout not a part core language definition.

Way forward: EML team will produce an amended diagram layout proposal, reflecting the current consensus (suggested submission before the end of November 2003).

Trials and tests: Campagne, Sauro, Mendes, Lohaus, Matthews, and Schaff volunteered to involve themselves or their team with trying out and testing the amended layout proposal. First implementations to be finished by the end of 2003. Hackathon-style event after first implementation round?

14:45 **Andrew Finney** (SBML Editor)

Requests for additional features in SBML. Issues with SBML L1 and L2 and solutions summarized on wiki pages.

Sets, Arrays, and Model Composition proposals: The previous Forum felt that there are several difficulties with the Arrays proposal. Biological systems are not often bounded, fixed, or ordered, whereas arrays-based solutions necessarily are. A more 'natural' solution would use sets in combination with database-style queries to select or address specific set members. Set membership must be probably constrained to limit implementation cost and model complexity (in addition to the most basic constraint that all members be of the same type). Example constraint: species can only belong to one set.

Prototype Reference Implementation: A reference implementation is being developed for the Arrays and Model Composition proposals. This is composed from 2 components: one which translates a humanly readable text form into provisional level 3 and another which translates, where possible, provisional level 3 into level 2.

15:40 **Andrew Finney** (SBML Editor)

SBML L2 errata: see wiki pages.

On 'outside' attribute to SBML compartment: (Schaff) should not adjacency be defined as well? (Hucka) Adjacency will probably be defined under spatial properties proposal.

15:50 **Andrew Finney** and other delegates to the Forum

Software tools and SBML model exchangeability.

Test and validation suite: should suite consist of test models *plus* corresponding simulation results? Not all tools that use SBML are simulators – simulation results may in fact 'test' algorithms used by simulators, which are of no concern to SBML. Validation suite should provide models that can be used to test whether tools extract and handle SBML correctly. Campagne, Mendes, Zheng, Vass, Schaff, LeNovère, and Donizelli will collaborate in the assembly of the suite. Mike Hucka and Andrew Finney will lead this effort.

Compliance levels: Most tools that read and/or write SBML are only partially SBML compliant (can only handle a subset of all SBML features). Compliance levels have not yet been defined, but it was agreed to define a suite of tests grouped by SBML features. The feature groups could then be used to summarize tool compliance for users.

16:30 **Andrew Finney** (SBML Editor)

Plans and suggestions for further SBML development.

Changes to core must be implemented to accommodate layout definition (and other possible additions such as controlled vocabularies).

CellML metadata can be used to provide accession codes for entrance into databases.

Campagne will look into their use and adaptation to SBML.

Controlled vocabularies (as proposed by Sachs, see above) could also be used to define named kinetic laws (now their definition has been taken out of the core language definition).

Bounds on parameters and initial values: might it be possible to use rules to define upper and lower bounds? Context for bounds: e.g. flux-balance models. Should SBML be able to define distributions of values? Finney and Hucka will initiate (or rekindle) discussion on SBML-discuss mailing list.

Rindone volunteered to chair the *Constraints working group*, and to start a discussion on constraints on the mailing list.

Test/validation suites, compliance features, and controlled vocabularies fall naturally into a single category (namely *controlled vocabularies*).

17:15 **Andrew Finney, Mike Hucka** (SBML Editors)

Decision on next Forum meeting. Delegates agreed that meeting twice a year is costly, and probably not necessary. It was decided to consider decreasing the Forum meeting frequency to once per year, and organize 'hackathon'-style events 5 to 7 month after the Forum meeting. LeNovère volunteered to organize a hackathon at EBI (Hinxton, near Cambridge, UK) in April or May 2004. Finney and Hucka will arrange a web based survey to arrive at a definitive decision on this.

17:30 **Adjourned.**