The Systems Biology Workbench (SBW) Version 1.0: Framework and Modules

Introduction
Progress in molecular biotechnology has fueled an explosion in the development of software tools. Regrettably, developers often end up recreating similar facilities in separate software packages.
In an effort to make it more attractive for developers to share rather than reimplement resources, we have implemented the Systems Biology Workbench (SBW), a free, open-source, application integration environment. Our goal has been to create a framework simple enough that software authors find it easier to provide an SBW interface than to reactivate functionality available in other tools. By doing so, we hope developers can concentrate on creating best-of-breed solutions in their areas of expertise.

What Does SBW Provide?
SBW provides libraries for enabling applications to learn about and communicate with each other. The applications may be running on separate computers.
SBW lets heterogeneous packages connect to each other using a remote procedure call mechanism based on a message-passing network protocol. The interfaces to SBW are encapsulated in client libraries for different languages.

Features of SBW Version 1.0
- Languages supported: C, C++, Delphi, Java, Perl, and Python.
- Windows (98, 2000, XP) and Linux supported, with MacOS X planned in the near future.
- Secure, distributed operation via SSH, featuring remote startup of brokers and applications.
- CORBA gateway for bidirectional communication between SBW-based apps and CORBA-based apps.
- Collection of basic applications provided with the SBW distribution, including:
  - A simple stochastic simulator based on the Gibson-Bruck variant of the Gillespie algorithm
  - An SBML-to-MATLAB ODE & Simulink translator
  - An SBML reader tool that allows a program to extract (via an API) components of an SBML model
  - A "clipboard" module that stores an SBML model description, and allows the easy transfer of models between separate modules
  - A "browser" module that allows querying SBW for registered modules and producing descriptions of each module's interface in Java or CORBA IDL
  - A simple plotting module for time-series data
  - A generic simulation control GUI interface
  - A collection of tutorial example modules in C, C++, Delphi and Java
- Extensive documentation—in addition to overview documents and published papers, every language library has its own programmer's manual and API reference.

SBW in Action: A Sample Session
Here is an example of using several SBW-enabled tools to create and simulate a two-compartment model of a hypothetical single-gene oscillatory circuit.

In this highly simplified model, there is a gene G which encodes its own repressor and is transcriptionally activated at a constant rate, $V_7$. Transcriptional activation of a gene G (which normally involves many enzymatic reactions) is summarized here as the production of active Rnap from source material, src, and degradation to acr. Transcribed mRN is then transported from the nucleus into the cytoplasm, where it is translated into the product P from constituent amino acids AA and where P is also subject to degradation.

Model Capture: Using a Visual Editor
Using the SBW-enabled JDesigner biochemical network editor, a user can create the model using a graphical interface.

Model Simulation: Exchanging Models via SBW
An application such as JDesigner can dynamically create a menu of tools with which it can interact, by querying SBW to find all installed SBW-enabled packages that provide services for processing biochemical models.

Here, picking the menu item "Simulation Service" invokes a generic simulation control GUI, which in turn invokes Jarnac, an ODE-based simulator for biochemical reaction networks.

Model Visualization and Analysis
Setting the run parameters for the simulation and selecting the output variables in the simulation control GUI allows the user to plot the values of quantities over time. The plot at the right shows how the concentrations of AA and P in the model oscillate over time.

A user can also perform other analyses on the model via SBW, e.g., by invoking the bifurcation analysis module.

Third-Party Modules Available For SBW
- Jarnac, a biochemical simulation package for Windows
- JDesigner, a visual biochemical network layout tool
- Passadena Twain, a simple interactive ODE solver
- A stochastic simulator based on Gillespie’s algorithm
- A bifurcation analysis module
- An optimization module
- An SBML validator for checking SBML model files
- An inspector that lists running modules & their services

Coming Attractions
More open-source developers are joining the SBW project, and together we are enhancing and extending SBW in many ways. Here is a preview of some coming attractions:
- Support for JDK 1.4
- Support for MacOS X
- MATLAB script interface
- New modules, including:
  - Graphical browser for the SBW environment
  - Rewritten SBML parser/writer for SBML Level 2
  - Improved generic GUI for simulators
  - Improved, full-featured plot module
  - New simulation engines

How to Get Started with SBW
The SBW version 1.0 package and extensive documentation are available from the project web site, http://www.sbw-sbml.org/.
SBW is distributed under the terms of the GNU LGPL.

Acknowledgments
The SBW project is funded by a generous grant from the Japan Science and Technology Corporation under the ERATO Kitano Symbiotic Systems Project.
We thank the following groups engaged in developing software tools for systems biology, for their feedback and guidance in developing SBW:
- BioSpice (Arkin et al.)
- Cellerator (Mjolsness et al.)
- DBsolve (Goryanin et al.)
- E-CELL (Tomita et al.)
- Gepasi (Mendes et al.)
- ProMoT/DIVA (Gillets et al.)
- StochSim (Bray et al.)
- Virtual Cell (Leew et al.)

We also thank the following individuals for their comments, suggestions and assistance: Tou-Mu Yi, Minso Moroshishi, Pieter van der Zee, Fred Livingston, Paul Shannon, Deanne Taylor, Andrew de Lea, Venkat Jagadish, Lukasz Salwinski, Mark Johnson, Richard Giuli, Greg Riddick, Michael Vanier.