hard work involved in building such detailed kinetic models, it is rather surprising that so little attention is paid to presentation and conservation of existing kinetic models. Thus, no official repository of kinetic models currently exists and no standard method of presentation of kinetic models in scientific literature has been agreed upon. A number of initiatives have been started to collect kinetic models, such as the CellML (http://www.cellml.org) and SBML (http://www.sbml.org/) databases which have similar, but not identical, goals. Both projects use XML-based exchange formats. While CellML strives to describe the structure and underlying mathematics of cellular models in a very general way, SBML aims to be a generic platform for exchanging pathway and model reaction information between several existing applications. SBML compatibility is already integrated into several metabolic modelling packages, for example, SCAMP (Sauro, 1993), GEPASI (Mendes, 1997) and JARNAC (Sauro, 2000). However, neither of these databases is complete yet and the chances of finding 'the interesting model' that you have just read about in the literature are not necessarily good. Although a published model description should be sufficient for one to build the kinetic model, this could still be a daunting task since many model descriptions contain errors, are not complete or, due to a lack of a model description standard, are vague.

Aim of JWS Online
In December 2000, we started building our JWS Online Cellular System Modelling (Snoep & Olivier, 2002) site with the aim of providing: (1) a user-friendly, internet-based, application for running kinetic models of biological systems; (2) a repository of such models; (3) a facility to make the reviewing of papers containing kinetic models easier.

How does it work?
Currently, JWS Online has 22 models that can be interrogated via the internet using any browser that is capable of running JAVA™ applets (i.e. any modern web browsers that support the SUN Microsystems 1.2 plug-in) such as INTERNET EXPLORER 5 under Windows 98, 2000, XP, SAFARI under Mac OS X, and MOZILLA under Linux. The application software is implemented in the JAVA™ programming language using a client server model. This set-up makes it possible to run relatively large models on clients with a minimal hardware specification. The JWS client is a JAVA™ applet and runs in any web browser that supports JAVA 1.4 (JAVA2) and above. The client provides a graphical interface for the user, establishing communication links with the server and displaying the results of the calculation. Users have control over various model parameters (typically kinetic parameters, time and integration steps) and may select a steady-state calculation, time-course simulation, Metabolic Control Analysis or Structural Analysis of the model. The JWS server runs as a stand-alone JAVA™ program which uses J/LINK as an interface to facilitate all communication with MATHEMATICA by Wolfram Research (http://www.wolfram.com). All numerical calculations are performed using the server-side MATHEMATICA Kernel. The models are coded in J/LINK and dynamically linked into the server as modules allowing multiple, simultaneous modelling sessions.

Try it yourself
The easiest way to get to know the system is to direct your browser to either of the JWS Online Cellular Systems Modelling mirror sites (http://jjj.biochem.sun.ac.za or http://www.jjj.bio.vu.nl). Make sure you have the 1.2e plug-in installed, freely available for download from SUN Microsystems (http://java.sun.com/). After selecting 'database' on the home page, a selection of kinetic models is shown (Fig. 1), each of which can be selected by clicking on the model link. On doing so, an applet, functioning as a graphical interface, is downloaded (Fig. 2). The display is divided into two horizontal panels and one lower panel. The horizontal right-hand panel shows the pathway scheme of the system being modelled. If you place the cursor over any of the reaction steps (red dots) in this panel, the rate equation corresponding to that catalytic step is displayed in the bottom panel. The left-hand horizontal panel contains the applet. The applet has two tables where users can change any of the model’s parameter values or select...
**The Silicon Cell: detailed metabolic models**

- Detailed glycolytic model in *Lactococcus lactis* - [model](#)
- Glycolysis in *Trypanosoma brucei* - [model](#)
- A Computational Model for Glycogenolysis in Skeletal Muscle - [model](#)
- Pyruvate branches in *Lactococcus Lactis* - [model](#)
- Glycolysis in *Saccharomyces cerevisiae* - [model](#)
- Sucrose accumulation in sugarcane - [model](#)
- Bacterial phosphotransferase system - [model](#)
- Threonine synthesis pathway in E. coli - [model](#)
- Kinetics of Histone Gene Expression - [model](#)
- Glycolysis in *Saccharomyces cerevisiae*, 6 variables - [model](#)
- Full scale model of glycolysis in *Saccharomyces cerevisiae* - [model](#)
- Quantification of Short Term Signaling by the Epidermal GFR - [model](#)
- Red Blood Cell Model - [model](#)
- Mechanism of protection of peroxidase activity by oscillatory dynamics - [model](#)
- Dynamic model of *Escherichia coli* tryptohan operon - [model](#)

---

**Fig. 1.** Screen shot of the currently available silicon cell models in the JWS Online kinetic modelling database. More models are available in the Core models and Demonstration models section of the web site. Selecting the model-link results in downloading the model applet as shown for a core model in Fig. 2. Selecting the more-link leads to a web page with manuscript information and contact details of the authors. Selecting the sbml-link results in downloading the model description in SBML format.

---

**Fig. 2.** Screen shot of an example applet with two windows showing respectively a steady-state and time simulation result. The example model is listed in the Core models section of the JWS database and is a model by Wolf et al. (2000). The time simulation shows limit cycle oscillations and the steady-state calculation shows the metabolite concentrations and fluxes for the unstable steady-state.
which variables they would like plotted in a time simulation. A tabbed pane allows the user to select between three main option tabs: Sim, a time simulation; State, a steady-state analysis; or MCA, a Metabolic Control Analysis. On selection of any of these tabs, various sub-options, which are largely self-explanatory, are displayed. Most components have tooltips providing additional information if the cursor is placed over them. Upon pressing the ‘Evaluate Model’ button, the desired analysis is performed on the model by the JWS server and the results are sent back to the user and displayed in a separate window (Fig. 2).

Links to scientific journals
We are actively extending the contents of the database, adding new models coded from the literature and inviting modellers to submit model descriptions to us. We have largely automated the coding of models and the addition of new models to the database is relatively easy. In addition, we are collaborating with the systems biology workbench group at Caltech and have added a facility to download models in SBML format. Recently, to facilitate the reviewing of manuscripts that contain kinetic models, we have started to provide a service with the journal *Microbiology* and the *European Journal of Biochemistry*. When such a model is submitted to these journals, the authors are asked whether they would like the model to be made available on the JWS Online web site. If they agree, the model is made available only to the manuscript authors and reviewers on a secure site. Once the manuscript is accepted for publication, the model is moved to the public database. Precise guidelines for model submission are available in the online instructions for authors and at http://jjj.biochem.sun.ac.za/microbiology and http://jjj.biochem.sun.ac.za/ebj

Clearly, such collaborations will keep the model database up to date and ensure that models will not get lost and that they will have complete and correct descriptions. Although only a few manuscripts containing kinetic models are submitted to *Microbiology* each year, the journal has always had a liberal policy with respect to theoretical or modelling studies. We feel that the link to the JWS Online web site might stimulate more authors to submit their modelling manuscripts to the journal. An example of a *Microbiology* manuscript containing a model that was added to the database is the study on metabolic engineering of lactic acid bacteria published last year (Hoenfagel et al., 2002). All of the modelling experiments in the manuscript can be repeated on the web site, sensitivity for parameter values can be tested, time simulations and steady-state calculations can be verified. In addition, a complete control analysis using the matrix inversion method and a structural analysis can be made.

In addition to its role in research, JWS Online has been shown to be a very useful tool in educational programmes, be it in modelling curricula or metabolic regulation courses. For the hard-core modeller who wants to make considerable changes to the model, the download feature will be useful to run the model on SBML-compatible modelling software. We hope that JWS Online will provide a good and useful service to the broader scientific community. Any comments, either via e-mail or our online forums, are always welcome. If you have kinetic models that you would like added to the database, please send us an input file with the model description. Happy modelling!

**Jacky L. Snoep and Brett G. Olivier**

Triple-J group for Molecular Cell Physiology, Department of Biochemistry, University of Stellenbosch, Private Bag X1, Matieland 7602, Stellenbosch, South Africa

Correspondence: Jacky Snoep (jls@sun.ac.za)


DOI 10.1099/mic.0.C0124-0