

Sigmoid: A Scalable System for Pathway Bioinformatics and Systems Biology

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Abstract:

Motivation: Progress in systems biology critically depends on developing scalable informatics tools to model and visualize complex biological systems, and flexibly store information about these systems and their models. Scalability of these tools is critical to address the multi-scale and size complexity of biological systems.

Here we describe *Sigmoid*, a generative, scalable software infrastructure for pathway bioinformatics and systems biology. Sigmoid consists of a three-tier architecture of distributed modules. (See Figure 1.)

Tier one: The back end currently consists two modules: the Sigmoid model database and the model simulation module. The Sigmoid pathway modeling database (PostgreSQL) schema along with the Sigmoid Java API is autogenerated from UML diagrams by using Axgen and Velocity templates. Model simulation is handled by Cellerator/kMech, a model generation package using the Mathematica computer algebra system, which provides a library of re-usable reaction models that can be expressed in a simple, higher level language. Future additions to this tier include parameter analysis and data mining technologies.

Tier two: The middleware, a layer of web services designed to facilitate communications between back end and the front end is written in Java and, harnesses the Apache SOAP/AXIS technologies as a framework. Communication to the Mathematica/Cellerator solver is handled via the Mathematica/Java interface Jlink, and the interface to the Sigmoid database utilizes the object relational bridge API, OJB.

Tier three: The front end consists of the Sigmoid Model Explorer (SME) graphical user interface. (See Figure 2.) SME allows the user to graphically visualize, design, and edit pathway models along with their associated parameters, initial conditions and properties. Model storage to the database is available to designated model curators at this time. Model simulation is accomplished by SME passing them through the middleware to the Mathematica/Cellerator solver. Model simulation results can then be visualized and compared within SME. Sigmoid database models can be browsed, searched and passed to SME via Java Web Start at www.sigmoid.org.

There are several features of the Sigmoid architecture that, in aggregate, position it uniquely within realm of the currently available systems biology software systems. Sigmoid uses the web services framework to create a truly distributed system. This flexible framework offers powerful modularity that, in conjunction with the generative nature of the Sigmoid coding cycle, offers a significantly reduced development time for integration of new components. Also, the OJB object relational bridge, offers the

advantages of oriented programming in conjunction with relational databasing. Sigmoid capitalizes on the robust mathematical software tools and problem solving environment that Mathematica offers, along with the Cellerator/kMech packages designed to facilitate biological modeling via automated equation generation. The synthesis of these features yields a flexible scalable architecture that not only allows for manageable adoption of new system components, but may open the ability to play within yet larger bioinformatics frameworks.

Availability: All sigmoid modeling software components and supplementary information are available through: <http://www.igb.uci.edu/servers/sb.html>.

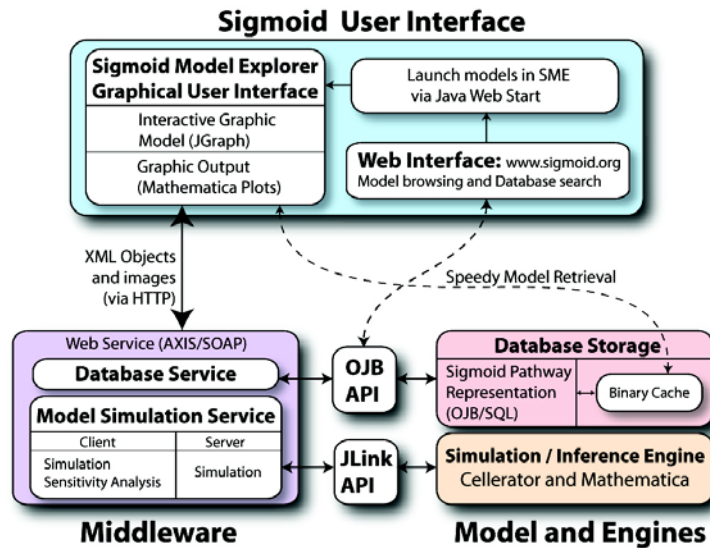


Figure 1: The Sigmoid Architecture

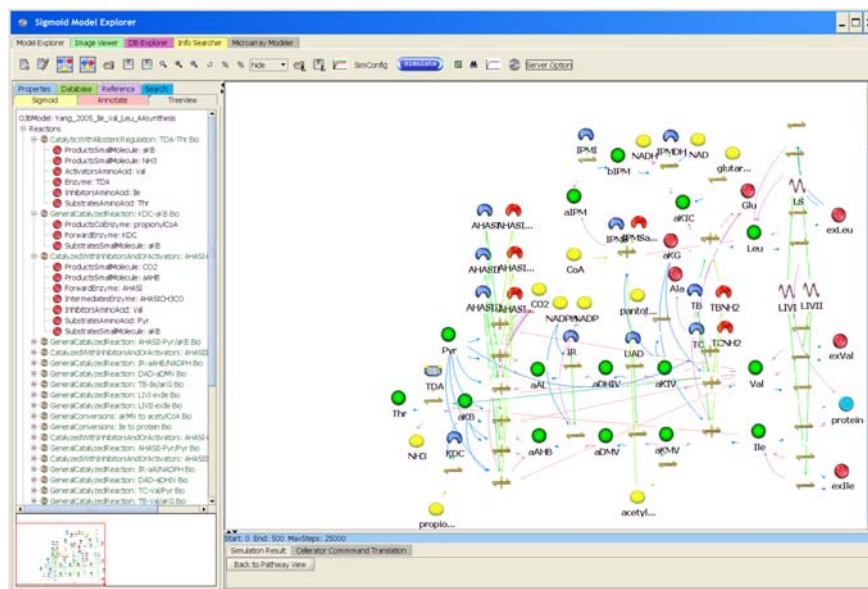


Figure 2: The Sigmoid Model Explorer illustrating the (Yang) Ile/Val/Leu amino acid biosynthesis model.