

New in the Release 4.0

➤ CI Online Server

Cell Illustrator version 4.0 can be run directly from the website, without the need to install software on local computer. The new CI Online server offers several web services such as Project Manager and CSMLDB Search that can be accessed from the CI workspace.

CI Online is available at: <https://cionline.hgc.jp>

➤ CI Project Manager

CI Project Manager is a user interface to *CI Online Server*. CI Project Manager allows the user to create, store, organize and share CSML models (e.g. pathways) and other data on a remote server. Additionally you can access public and proprietary pathway libraries that are provided by the CI Online Server.

To access the remote pathway data and services, the user must be logged in to the CI Online Server.

➤ CSMLDB Search

The *CSMLDB Search Dialog Box* is an interface that allows for submitting queries to the remote CSMLDB database. The user can search in the CSMLDB database for molecules (entities) and reactions (processes) and import them into the canvas in CI workspace.

To access the remote CSMLDB database, the user must be logged in to the CI Online Server.

➤ Support for CSML 3.0 format

The native format of CI version 4.0 is the CSML 3.0, which enables for storing more biological properties. Please refer to www.csml.org website for more details.

➤ SECG - New Simulation Engine

SECG (Simulation Engine Code Generator) is a new simulation engine, which allows for faster simulation of large models. The new engine allows for running a batch of parameterized simulations - the same model can be simulated with varying values of selected parameter.

The SECG idea is to generate source code from the CSML model displayed in CI workspace. This source code can be used in an external program or framework.

➤ **CSO import/export**

The new input/output filter allows importing and exporting Cell System Ontology 3.0 models. CSO supports most of CSML features and allows for more flexible and extensible handling of biological data using Semantic Web OWL and RDF languages.

➤ **BioPAX import**

The new import filter enables the import of BioPAX level 2 ontology models. BioPAX ontology is popular biological pathway ontology language for biopathway exchange.

New in This Release 3.0

➤ **Import of SBML/CellML files**

New input filters allow importing models stored in the widely used CellML and SBML formats. The imported SBML/CellML models are converted to Cell Illustrator models and can be edited, analyzed, simulated or saved as any other Cell Illustrator model. This function converts SBML/CellML models, which use differential equations for representing relationships between entities, to CI models, which use the Petri Net formalism used in CI.

➤ **Library of SVG graphical elements**

The library of Biological Elements has been extended with SVG images representing biological entities, processes and cellular components. The library consists of: about 40 images for biological entities, more than 250 images for biological processes and about 70 images for cell components. Each image corresponds to one Gene Ontology (or Cell System Ontology) term. Each image can be edited in the SVG editor included in Cell Illustrator.

➤ **Enhancements in the Petri Net simulation engine**

New options for a better control of the simulation flow have been added. The weak firing and firing accuracy options available in the Simulation Settings facilitate the simulation of continuous models.

➤ **Improved Charts**

Charts dialog boxes have been enhanced for improved viewing, analysis and control of simulation results.

➤ **External References**

Since the version 3.0, Cell Illustrator offers an extensive support for external references to public databases, Gene or Cell Ontology terms, etc. These references can be defined in the new *Biological* tab of the *Element Setting* dialog box, as well as

in the redesigned *External References* dialog box. Also, *URL Templates* can be defined to access public databases. The URLs of the external references can be opened in the web browser.

➤ **Gene Network View**

The added *Gene Network Mode* enables the user to view and explore gene relationships networks. This mode offers a special visualization style and tools for the analysis of gene relationship networks, such as *Pathway Search*, *Sub-network Extraction* and *Network Merge*.

New in The Release 2.0

➤ **New kinetic styles for easier simulation of biological processes**

With the new kinetic styles of a process: *mass*, *stochastic mass* and *connector rate* you can build models more easily and define the kinetics of chemical reactions and biological processes. You just need to define reaction parameters such as *stoichiometry*, *rate*, *mass coefficients* and the process speed will be automatically calculated. Additionally, you can introduce random perturbations using the *stochastic mass* function, which allows for modeling reactions and processes of stochastic nature.

➤ **The Element Settings and Element Lists dialogs have been improved**

The Element Settings and Element Lists dialogs have been redesigned to simplify model building and analysis. For all process types, you can now view and set all process kinetic properties in one place; the Process Sheet.

➤ **New graph layout algorithms**

Using the Graph Layout dialog, you can “beautify” the layout of the model elements on the active canvas. This option can be especially useful when importing models from the BioPACS database or converting models from other formats.

➤ **Support for SVG files**

Scalable Vector Graphics (SVG) files can be added to the models as any other image files (PNG, JPEG). An editor of SVG files has been included into Cell Illustrator. All image files, in the PNG, JPEG and now also SVG format can be saved internally or externally in the Cell Illustrator models (CSML files).

➤ **The simulation can be executed at a remote Cell Illustrator Server.**

Large, time-consuming simulations can now be executed at a remote server, outside of the Cell Illustrator workspace. For this, Cell Illustrator Server, a new companion product of Cell Illustrator needs to be installed at the simulation server. One server can be accessed by multiple users of the Cell Illustrator desktop package, and the other way around: you can connect to more than one CI Server from your

desktop. After the simulation is submitted to a remote server you can continue to work with Cell Illustrator or other software without any loss of performance since the simulation does not take the CPU time of your workstation. The simulation results are returned by the server in the form of a CI log file, and can be viewed and analyzed in the CI Player application.

This solution is recommended for laboratories with a larger number of CI users.

➤ **Use Cell Illustrator as a front-end to your own simulation program.**

The advanced user of Cell Illustrator who would like it to run his own simulation program from CI Workspace can do so by replacing the default engine component at the Cell Illustrator Server with his program. The user-created engine must read an input model and write a log file in the Cell System Markup Language (CSML) which is the native format of Cell Illustrator files.

➤ **Integrate the command line Cell Illustrator simulation engine into your modeling environment.**

Cell Illustrator can be used to run simulations in the command line mode. This simulation engine works with Cell System Markup Language (CSML) input/output and can be called from user scripts or integrated with a custom GUI. Alternatively, you can utilize Cell Illustrator Server *web service* in your modeling environment.

➤ **The maximum memory for Cell Illustrator can be customized**

The new auxiliary program (*CIMemoryConfiguration*) allows you to customize the maximum memory for both Cell Illustrator applications: CI and CI Player.

New in The Release 1.6

➤ **The results of each simulation can be logged and saved into CI log files (CILs). The CIL files can be viewed and analyzed in the Cell Illustrator Player program.**

With Cell Illustrator Player, you can:

- deterministically replay a simulation run, even if the original simulation was of stochastic nature,
- display logged entity values and process states in the model view in the canvas,
- visualize entity value changes over time in a chart,
- quickly move forward and backward to a specific part of a simulation log,
- replay a simulation run in a step mode for debugging purposes,

- compare results of several simulation runs.
- **The new Simulation History dialog in Cell Illustrator allows you to view and manage all the simulation log files (CILs) for your model.**
- **The set of predefined elements in the Biological Elements dialog has been expanded.**

New in The Release 1.5

- **Enhanced implementation of hybrid Petri nets for bio-pathway modeling.**

The modeling features of Cell Illustrator have been refined in version 1.5; The parameters of discrete and continuous elements are unified now. Also, default parameter settings have been improved to make model creation easier for novice modelers.

- **Faster and more accurate simulation engine**

In Cell Illustrator 1.0, the minimum sampling interval was 0.001 Petri net time [pt]. In Cell Illustrator 1.5, the minimum sampling interval is 0.000001[pt]. Cell Illustrator 1.5 can realize 1000 times more accurate simulations and simulations which are 10 times faster.

- **Much improved GUI for model editing**

GUI interface offers many more editing options and it is easier to use.

- **Set of predefined Biological Elements**

You can create biological pathways faster and more intuitively by dragging appropriate elements from the new Biological Elements dialog and dropping them into a canvas window.

Hardware and Software Requirements

Cell Illustrator is available for Windows, Linux, Unix and Mac OS X platforms. In order to run Cell Illustrator correctly, Java version j2sdk 1.5.0 or higher needs to be installed. Java Runtime Environments (JRE) are available for download at: <http://java.com/> or <http://java.sun.com/downloads>.

The recommended hardware requirements are:

CPU: 2 GHz
RAM: 2 GB
Hard disk space: 1 GB

Licensing Information

To run Cell Illustrator, you need to register at a Cell Illustrator Online Server, e.g. at: <https://cionline.hgc.jp> or <https://cio.bioillustrator.com>

Since the version 3.0, CI offers new license types: *Pro*, *Draw* and *Classroom*. The main differences between the license types are in the simulation capabilities of CI and are briefly summarized in the table below.

| License Type | Description |
|--------------|--|
| CI Pro | Full version. Includes all simulation and editing/drawing. |
| CI Classroom | Limited version. Simulation of small models only (up to 30 entities). All editing/drawing capabilities |
| CI Draw | Limited version. No simulation capabilities. Full editing /drawing capabilities |

More detailed info about license types can be found at <http://www.cellillustrator.com/lineup>

Note: This manual describes all functions available in the CI (CI Pro license type). A given function described in this manual might be disabled or not available in the limited versions CI Draw and CI Classroom.

CI Memory Customization

When starting CI Online, you can set the maximum memory for Cell Illustrator in the *CI Authenticator* dialog box.

End User Documentation

The documentation for the Cell Illustrator version 3.0 includes the manuals listed below:

Cell Illustrator User Guide: Introduction to Cell Illustrator system

Cell Illustrator Reference Manual: Detailed description of Cell Illustrator functions

Cell Illustrator Player Reference Manual: Detailed description of Cell Illustrator Player functions

Cell Illustrator Server Installation Manual: Installation instructions for Cell Illustrator Server product (for IT System Administrators)

Cell Illustrator Gene Net Reference Manual: Detailed description of Cell Illustrator functions (Gene Network mode)

Cell Illustrator Gene Net User Guide: Introduction to the Gene Network mode of Cell Illustrator system