

MP GeneticSynth

Quick Start Guide

A quick guide for downloading and launching MP GeneticSynth
with references to all other resources (docs, models, exps)

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MP GeneticSynth website
<http://mplab.sci.univr.it/plugins/mpgs/index.html>

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1. Download and launch
MP GeneticSynth

Main steps

MP GeneticSynth is a MetaPlab plug-in and it is available from version 1.3 of MetaPlab.

The **quickest way** to start using MP GeneticSynth is by following these **7 steps** (see also <http://mplab.sci.univr.it/plugins/mpgs/index.html>):

1. **Download MetaPlab-1.3**
2. **Unzip MetaPlab**
3. **Run MetaPlab**
4. **Load a model**
5. **Browse the model**
6. **Run MP GeneticSynth plugin**
7. **Use MP GeneticSynth**

Details of each step are reported in the next few slides.

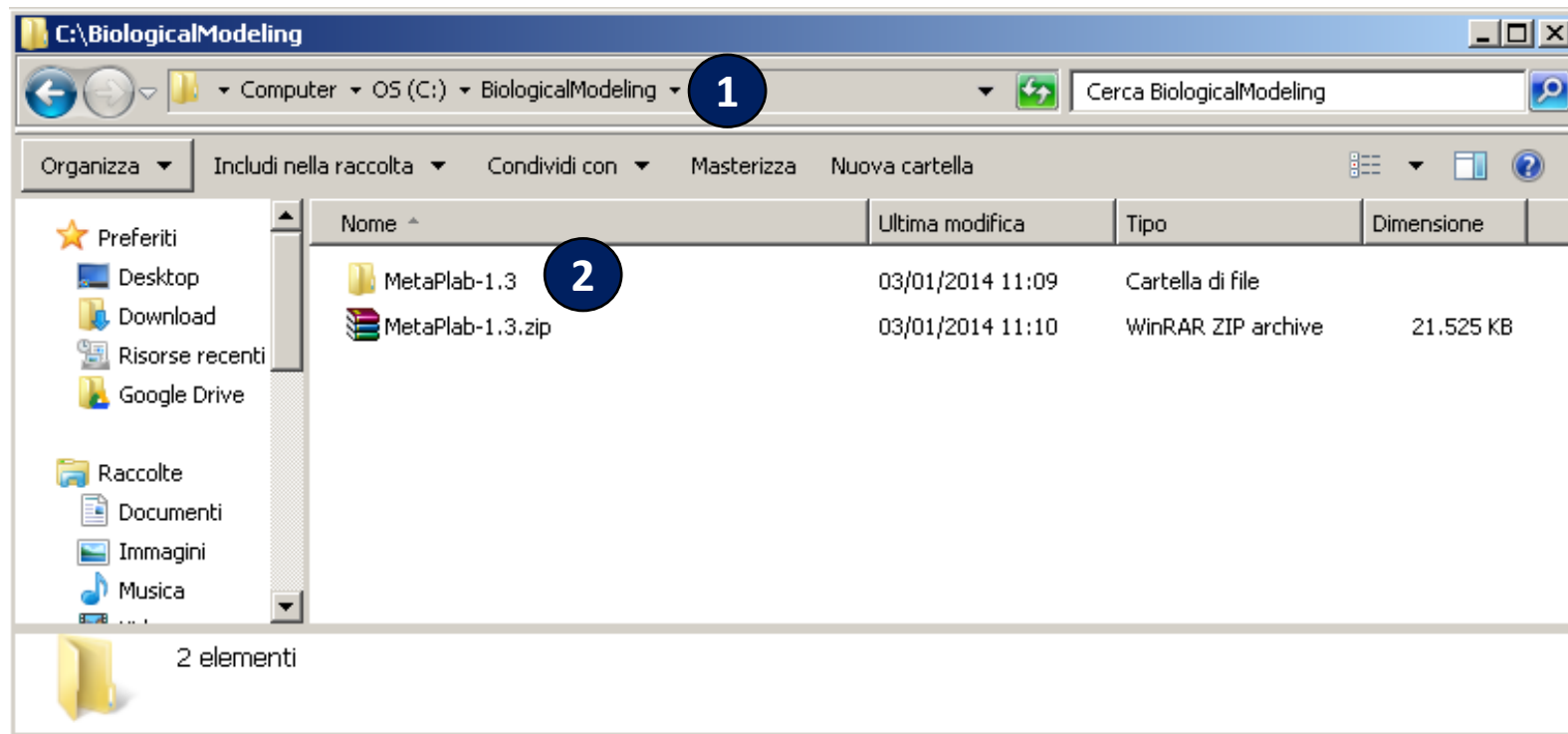
1. Download MetaPlab1.3

The screenshot shows a web browser window displaying the MetaPlab website's download page. The address bar shows the URL `http://mplab.sci.univr.it/downloads/Downloads.php`. The page content includes a sidebar with navigation links (MP Systems, Publications, Links, Team, News) and a main section for "MetaPlab release 1.3". This section features a "Download Here" link (20.83 MB), a "How to get start with MetaPlab" section, a "Download Source Code" link, and a "Previous releases" section with links for releases 1.2, 1.1, and 1.0. A file save dialog box titled "Apertura di MetaPlab-1.3.zip" is overlaid on the page, showing the file type as "Compressed (zipped) Folder (21,0 MB)" and the source as "http://mplab.sci.univr.it". The dialog offers options to "Aprirlo con WinRAR.ZIP (predefinita)" or "Salva file", with "Salva file" selected. A graph showing three overlapping curves is visible in the background of the dialog box.

1. Open your web browser and go to the Download section of the MetaPlab's website
2. Click on the link "Download Here" for MetaPlab release 1.3
3. Click on button "OK" to save the MetaPlab-1.3.zip file in your computer (here we saved the file in the directory C:\BiologicalModeling)



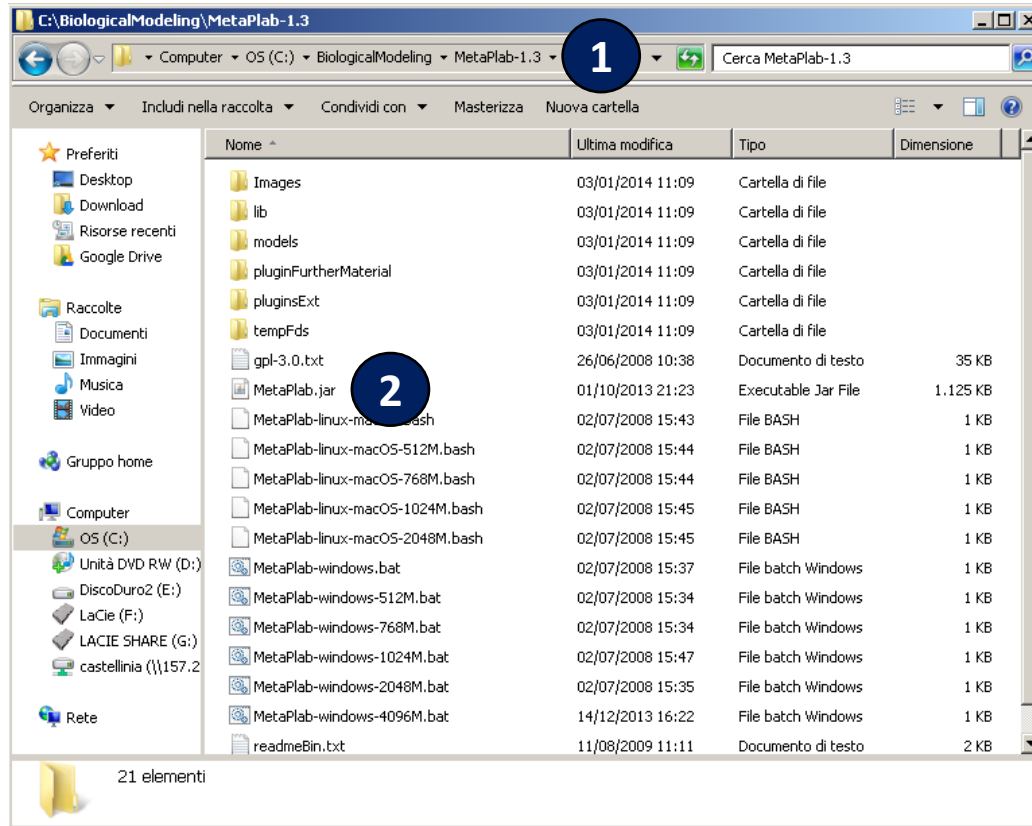
2. Unzip MetaPlab



1. Open the directory where you have saved the file MetaPlab-1.3.zip
2. Unzip the file. The directory MetaPlab-1.3 appears



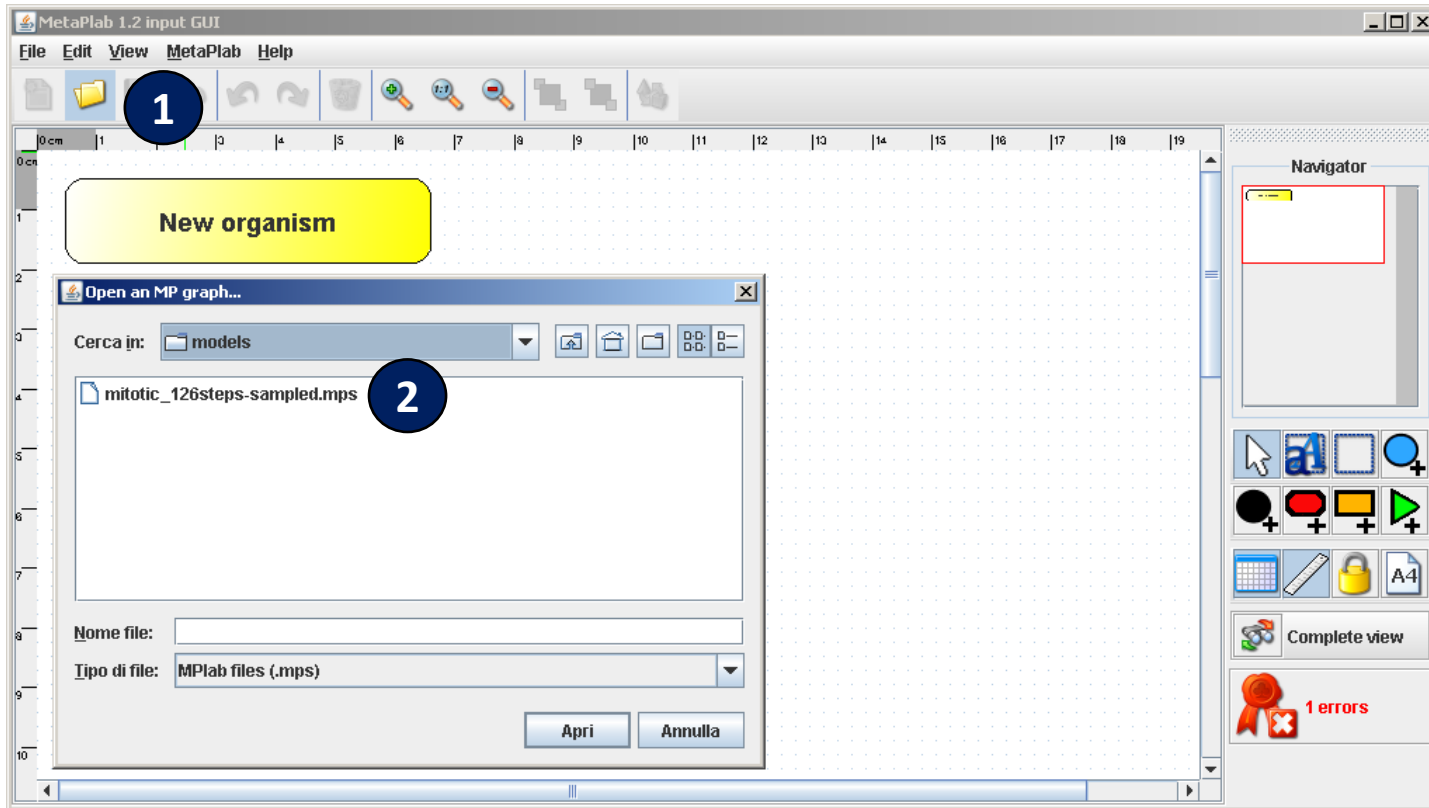
3. Run MetaPlab



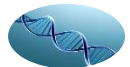
1. Open the directory MetaPlab-1.3
2. Click on file MetaPlab.jar to run MetaPlab. The main graphical interface appears



4. Load a model



1. Click on the "folder" button
2. Select the folder "pluginFurtherMaterial\GeneticSynth\models" in the MetaPlab-1.3 installation folder. Then select the file mitotic_126steps-sampled.mps. The mitotic model appears



5. Browse the model (1/2)

The screenshot displays the MetaPlab 1.2 input GUI. On the left, a yellow box titled "Mitotic oscillator" contains a description and a table of model constants. The main area shows a network diagram of "Cyclin synthetization and degradation" with nodes F1, F2, C, R1, R2, IOGate, and V1. A blue circle labeled "1" highlights node C. Below the diagram is the "Cyclin properties dialog" with fields for Identifier (C), Name (Cyclin), Quantity (0.01), and Molar weight (1.0). A blue circle labeled "2" highlights the "Edit time series" button. To the right, the "C time series" window shows a table of values and a chart. A blue circle labeled "3" highlights the chart area.

Mitotic oscillator
Description: Model of the mitotic oscillator found in early amphibian embryos.

Model constants		
ID (name)	Value	M. unit
K1 (none)	0.005	none
K2 (none)	0.005	none
K3 (none)	0.005	none
K4 (none)	0.005	none

Cyclin properties dialog

Identifier: C
Name: Cyclin
Quantity: 0.01
Molar weight: 1.0

No errors found while checking user inputs

Background color: [Blue box]
Default color: [Blue box]
Horizon: Center
Vertic: []

Submit Edit time series

C time series

Step	Value
0	0,01
1	0,04
2	0,069
3	0,098
4	0,127
5	0,155
6	0,183
7	0,211
8	0,238
9	0,265
10	0,291
11	0,318
12	0,344
13	0,369
14	0,395
15	0,42

Chart
C time series

Values: 0,00 to 0,60
Simulation steps: 0 to 130

Visualize chart lines [checked]
Visualize chart points [unchecked]

Refresh

1. Once the model is open, double click on one substance (blue nodes). Here we select **cycline (C)**
2. Click on button "**Edit time series**" to visualize the time series observed for this substance
3. On the left the time series values, on the right the related chart.

5. Browse the model (2/2)

The screenshot shows the MetaPlab 1.2 software interface. On the left, a yellow box titled "Mitotic oscillator" contains a description and a table of model constants. The main workspace displays a network diagram titled "Cyclin synthetization and degradation" with nodes F1, F2, R1, R2, C, V4, and IOGate. An "F1 properties dialog" box is open, showing fields for Identifier, Evolution, Time Series, and Add. information. The dialog also includes a background color selector (orange), alignment options, and buttons for Submit, Edit time series, and Cancel. A red error message is displayed: "ERROR: the evolution formula and the time series are void".

Mitotic oscillator

Description: Model of the mitotic oscillator found in early amphibian embryos.

ID (name)	Value	M. unit
K1 (none)	0.005	none
K2 (none)	0.005	none
K3 (none)	0.005	none
K4 (none)	0.005	none
KKa (none)	0.02	μM
Kc (none)	0.5	μM
Kd (none)	0.01	min^{-1}
V2 (none)	1.5	min^{-1}
V4 (none)	0.5	min^{-1}
Vk1 (none)	3.0	min^{-1}
Vk3 (none)	1.0	min^{-1}
Vd (none)	0.25	$\mu\text{M}/\text{min}$
Vi (none)	0.025	$\mu\text{M}/\text{min}$

F1 properties dialog

Identifier: F1

Evolution:

Time Series: none

Add. information: none

ERROR: the evolution formula and the time series are void

Background color:

Horizontal alignment: Center

Vertical alignment: Center

Submit Edit time series Cancel

1. Close the substance detail windows and double click on one flux regulation function (orange nodes). Here we select function **F1** that regulates reaction R1.
2. The "**Evolution**" field is empty. We have to automatically generate flux regulation functions from observed time series.

6. Run MP GeneticSynth

The screenshot shows the MetaPlab 1.2 input GUI. The main window displays a metabolic network diagram with nodes F1, F2, F4, F7, and R7, and edges labeled 'Cyclin synthetization and degradation', 'cdc2 kinase activation', and 'Cyclin activation and deactivation'. An IOGate node is also present. A yellow box highlights a table with the following data:

Vd (none)	0.25	$\mu\text{M}/\text{min}$
Vi (none)	0.025	$\mu\text{M}/\text{min}$

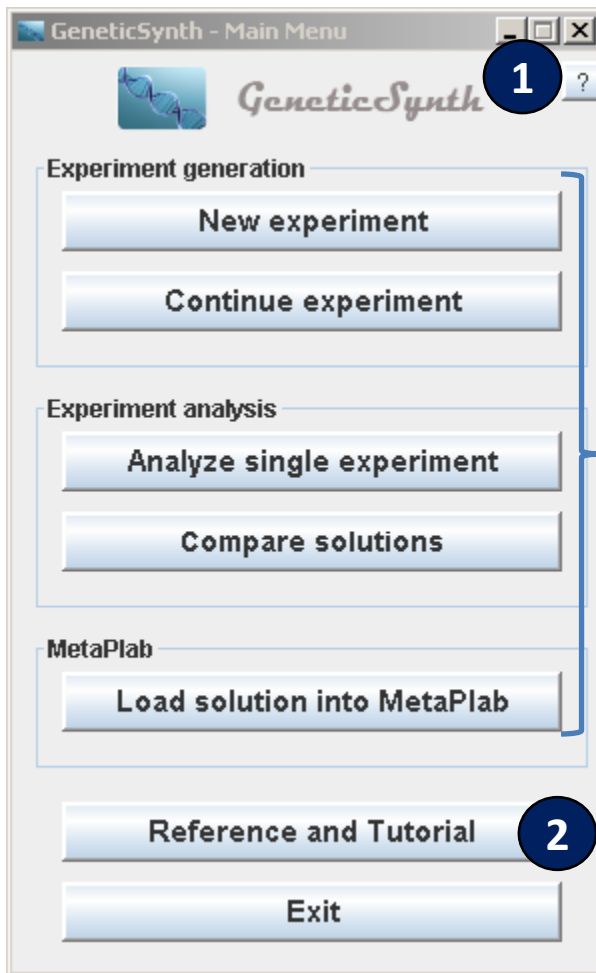
The 'MetaPlab 1.2 plugin manager' window is open, showing the 'Local MP plugins' list with 'GeneticSynth plugin' selected. The 'Run' button is highlighted. The 'GeneticSynth' main menu is also open, showing options for 'Experiment generation', 'Experiment analysis', and 'MetaPlab'.

Numbered callouts indicate the steps: 1. Click on the plugin manager button; 2. Select the MP GeneticSynth plugin; 3. Click on the "Run" button; 4. The MP GeneticSynth Main Menu opens.

1. Click on the plugin manager button
2. Select the **MP GeneticSynth** plugin
3. Click on the "Run" button
4. The MP GeneticSynth Main Menu opens



7. Use GeneticSynth



1. Move the mouse over the “?” button to visualize the help of this window (this button is present in every window of the MP GeneticSynth plugin).
2. Click on the “**Reference and Tutorial**” button to visualize references to the main published papers about the MP GeneticSynth plugin and tutorials describing the main features of the plugin.
3. Click on one of the following buttons to start working with MP GeneticSynth:
 - “**New experiment**” to generate new regulation functions
 - “**Continue experiment**” to continue a previous experiment
 - “**Analyze single experiment**” to analyze regulation functions generated in an experiment
 - “**Compare solutions**” to compare regulation functions from several experiments
 - “**Load solution into MetaPlab**” to load regulation functions into the MetaPlab model and continue the analysis or simulation of the model

4. Refer to the next slides to continue

2. Documentation: List and references

Documentation: list and references (1/2)

This list gathers together and briefly explains the content of all documentation resources available in the directory

[MetaPlab-1.3/pluginFurtherMaterial/MPGeneticSynth/docs](#)

and **online** at

<http://mplab.sci.univr.it/plugins/mpgs/index.html>

1. **QuickStartGuide.pdf** (suggested as first step): quick start guide for installing and running MP GeneticSynth with references to all other resources (docs, models, exps).
2. **MitoticCaseStudyVideo.mp4** (suggested as second step): a video version of the step-by-step tutorial that explains how to use MP GeneticSynth to generate and analyze regulation functions for the case study of the mitotic oscillator in early amphibian embryos.
3. **MitoticCaseStudyTutorial.pdf** (suggested as third step): a step-by-step tutorial that explains how to use MP GeneticSynth to generate and analyze regulation functions for the case study of the mitotic oscillator in early amphibian embryos.
4. **MainGuide.pdf** (suggested as main reference): main guide of MP GeneticSynth. It explains all functionalities and graphical interface elements (buttons, charts, etc.). Moreover, it reports installation procedures and references to other documentation documents.
5. **Javadoc** (suggested for developers): API documentation of MP GeneticSynth code. All packages, classes and methods are explained.

Documentation: list and references (2/2)

Analytical and optimization methodologies used by MP GeneticSynth are formally explained in the following scientific papers:

- Castellini,A., Zucchelli,M., Busato,M., Manca, V. (2013) *From time series to biological network regulations: an evolutionary approach*, Molecular BioSystems, 9(2), 225-233.
- A. Castellini, V. Manca, and M. Zucchelli. *Towards an evolutionary procedure for reverse-engineering biological networks*. In C. A. Coello Coello et al, editor, Artificial Immune Systems - 11th International Conference, ICARIS 2012, Lecture Notes in Computer Science 7597, pages 271-285. Springer, 2012.
- Castellini,A., Manca,V., Zucchelli,M., Busato,M. (2012) *A genetic approach for synthesizing metabolic models from time series (poster)*. In Proceedings of GECCO '12, Philadelphia, USA.



3. Test Models: List and references

Test Models: list and references

This list gathers together and briefly explains model files available in directory [MetaPlab1.3/pluginFurtherMaterial/MPGeneticSynth/models](#)

and **online** at

<http://mplab.sci.univr.it/plugins/mpgs/index.html>

Please, refer to the next section, i.e., Experiment list, to analyze experiemnt results related to these models

1. **Mitotic**: mitotic oscillator in early amphibian embryos proposed in 1991 Goldbeter. This is a minimal model based on ordinary differential equations (refer to the tutorial [MitoticCaseStudyTutorial.pdf](#) for more information).
2. **Noisy Mitotic**: mitotic oscillator with the addiction of noise.
3. **Predator-prey**: Lodka-Volterra model for predator-prey system.
4. **Chaotic logistic map**: synthetic model of the logistic map with parameter $r=3.9$; a chaotic dynamics from which MP GeneticSynth manages to infer regulation mechanisms.
5. **Vega**: a synthetic model having a complex oscillatory dynamics from which MP GeneticSynth manages to infer regulation mechanisms.



4. Test Experiments: List and references

Test Experiments: list and references

This list gathers together and briefly explains experiment files available in the **local** directory

MetaPlab1.3/pluginFurtherMaterial/MPGeneticSynth/models

or **online** at

<http://mplab.sci.univr.it/plugins/mpgs/index.html>

Please, refer to section 4 of the tutorial *MitoticCaseStudyTutorial.pdf* to learn how to analyze these experiments with *MP GeneticSynth*.

1. **Mitotic** (local and online): mitotic oscillator in early amphibian embryos, One experiment is reported in the local directory, other experiments online.
2. **Noisy Mitotic** (online): mitotic oscillator with the addition of noise.
3. **Predator-prey** (online): Lotka-Volterra model for predator-prey system.
4. **Chaotic logistic map** (online): synthetic model of the chaotic logistic map; a very complex dynamics from which *GeneticSynth* manages to infer regulation mechanisms.
5. **Vega** (online): synthetic model having a complex oscillatory dynamics from which *GeneticSynth* manages to infer regulation mechanisms