GINsim tutorial

Aurélien NALDI & Denis THIEFFRY

5th hands-on tutorial on *Logical Modelling*
Athens, September 9th, 2018

Follow instructions in the GINsim tutorial

frontiers

Frontiers in Physiology **9**: 646.

Logical modelling and analysis of cellular regulatory networks with GINsim 3.0

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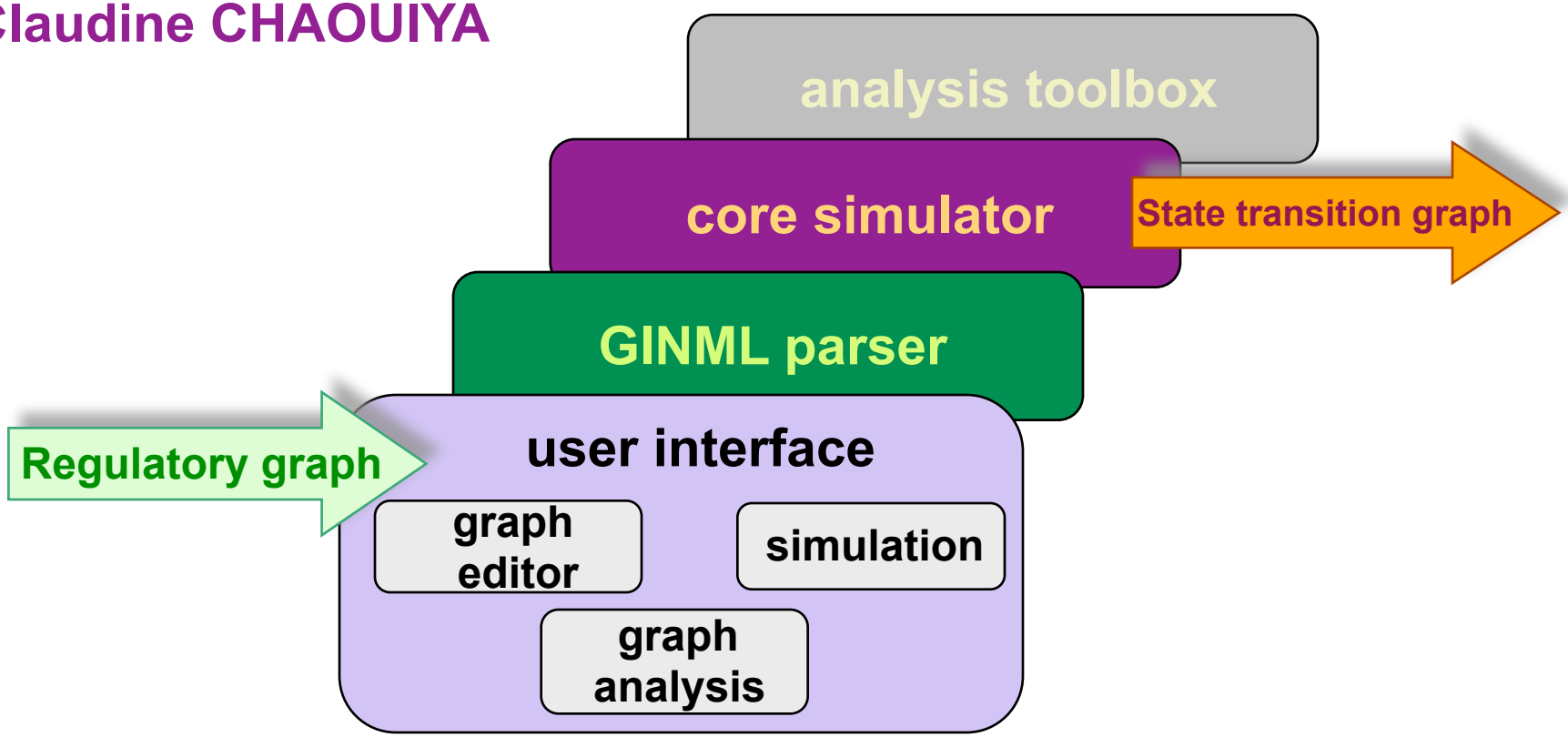
GINsim (Gene Interaction Networks simulation)

Aurélien NALDI
Pedro MONTEIRO
Claudine CHAOUIYA



Available at
http://ginsim.org

Naldi *et al.* (2018). *Frontiers in Physiology* **9**: 646.

Launching GINsim

- Open the tutorial file
- Make a folder to place all tutorial material
- Download **GINsim-3.0.0b** from **http://ginsim.org**
  (JAR file, including dependencies)
  from http://ginsim.org and put it in your [GINsim_Tuto] folder
- Double click on the jar file to **launch GINsim**
  Or on the command line: **java -jar path_to_GINsim**
  Add "**-Xmx4G**" before the path to increase Java memory for large models
- Follow the instructions from the **tutorial**
- Try to encode the model yourself and listen to the tricks!
  (it is a bit tricky the first time…)
- Save your model regularly

Loading GINsim 3.0 - http://ginsim.org

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Release Candidate

GINsim version: 3.0.0b
Release date: Mar 2018
File with dependencies included: GINsim-3.0.0b-with-deps.jar (13 Mb)
Change log: ChangeLog-3.0.0b.txt

Source tarball: GINsim-v3.0.0b.tgz (0.8 Mb)

Current Stable Release

GINsim version: 2.4 alpha
Release date: Mar 2010
File: GINsim-2.4.jar
Size: (1.44 Mb)
Change log: ChangeLog-2.4.txt

Old Stable Release

GINsim version: 2.3.1
Release date: Sep 2010
File: GINsim-2.3.1.jar
Size: (947 Kb)
Change log: ChangeLog-2.3.1.txt

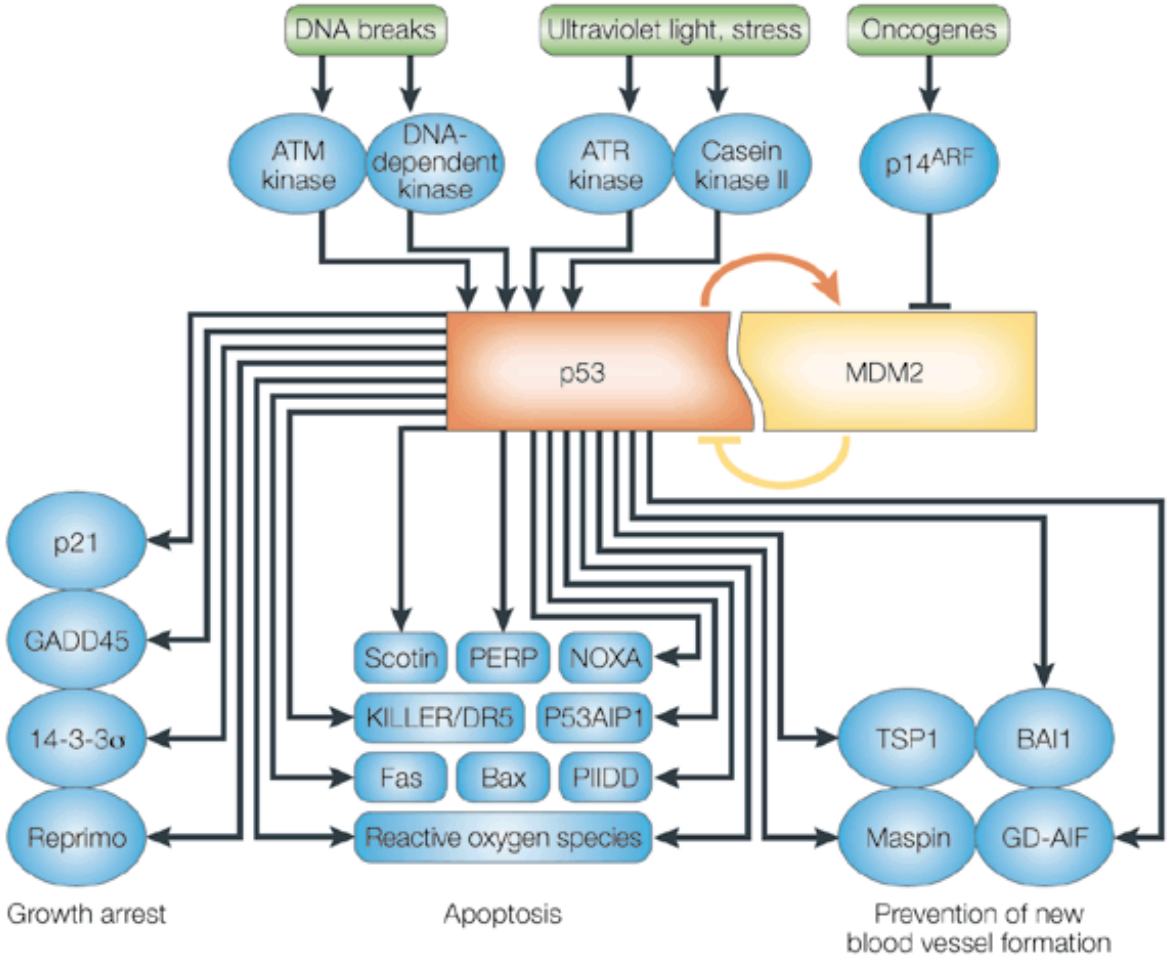
Nighly Build

You can grab the nightly build at http://ginsim.org/dev.

License:

Starting with version 2.9.3, GINsim is freely available under the terms of GPLv3 license (view full GNU GPL v3.0 license).
Older versions are freely available for academic use.

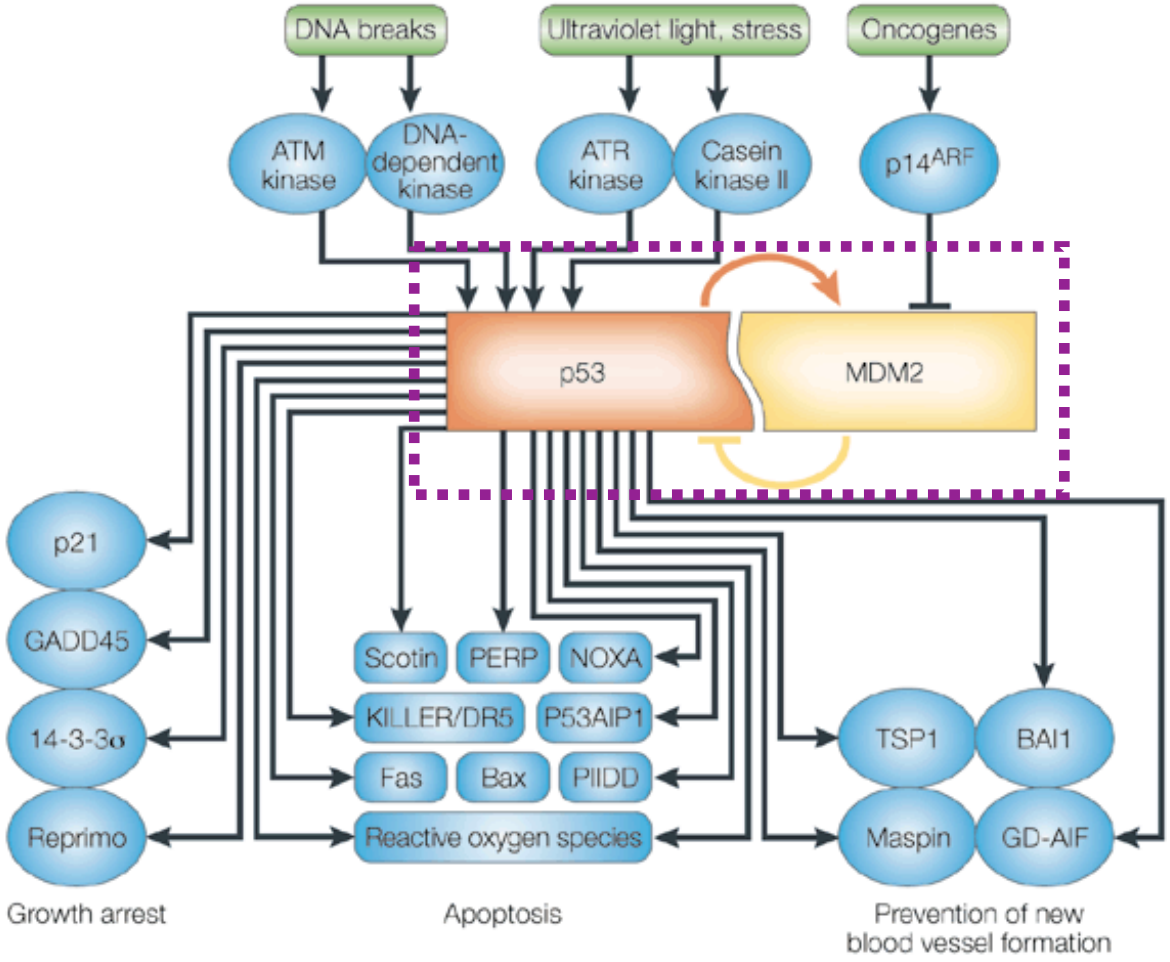
p53 regulation



Nature Reviews | Genetics

Hasty et al (2001)

p53 regulation



Nature Reviews | Genetics

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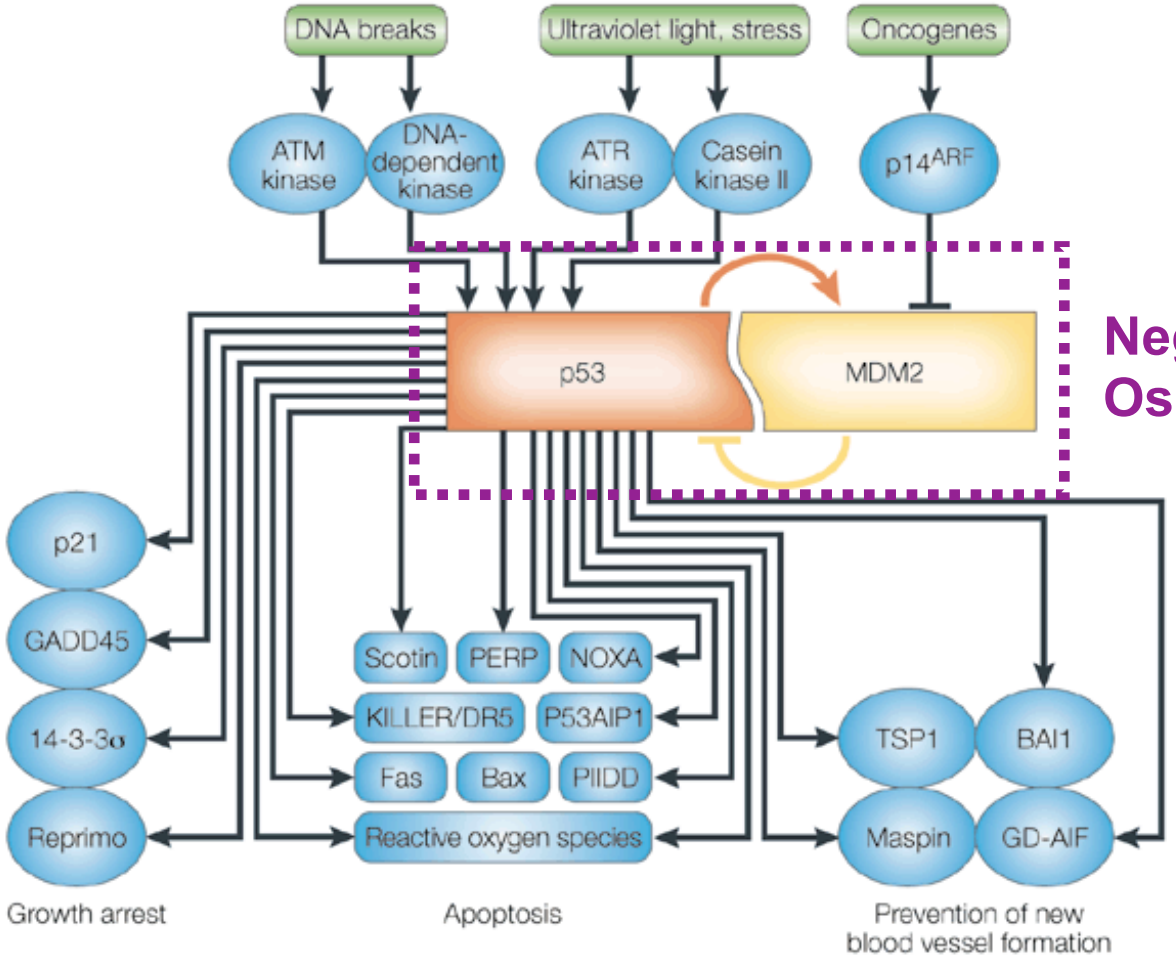
p53 regulation

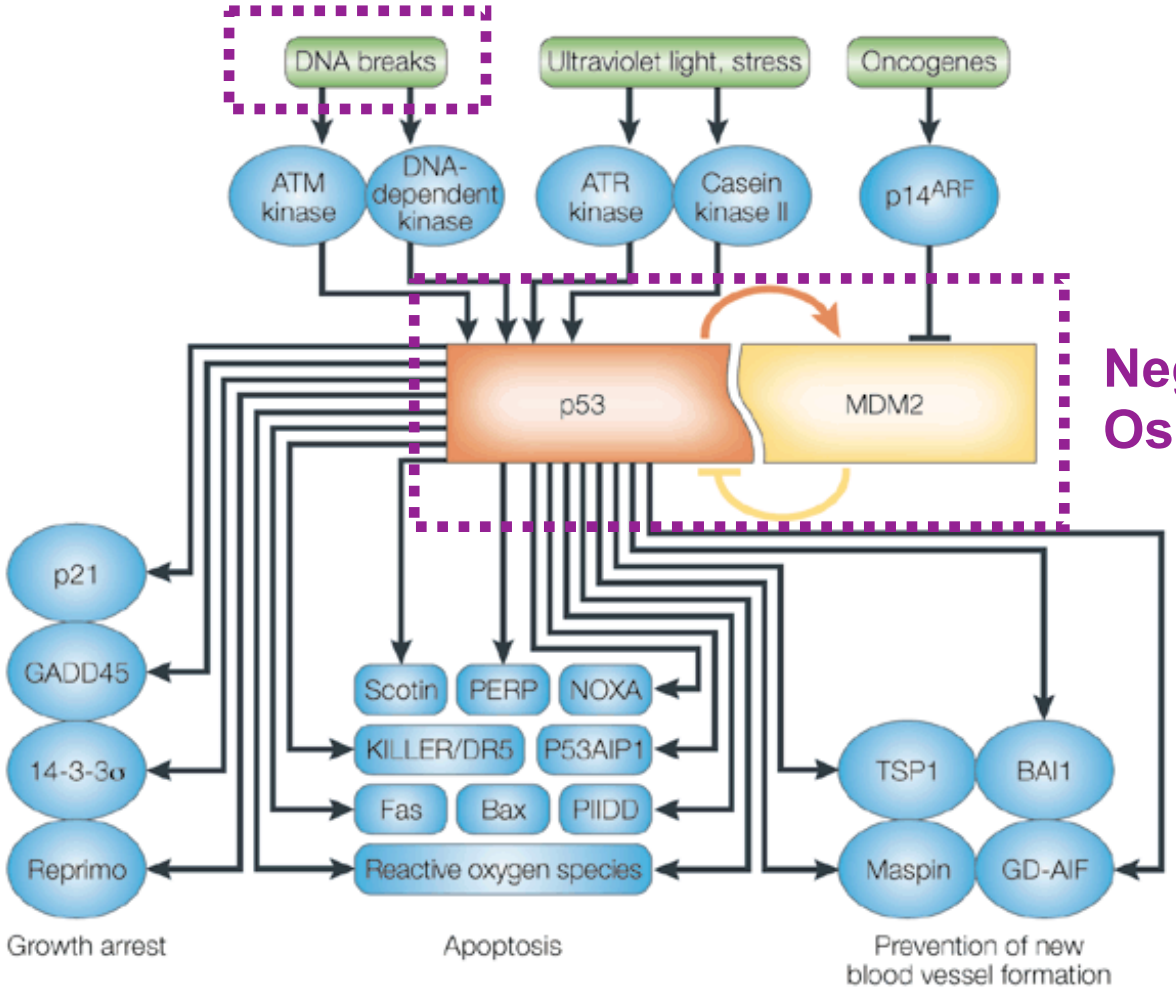


Negative loop
Oscillations

Nature Reviews | Genetics

Hasty et al (2001)

p53 regulation

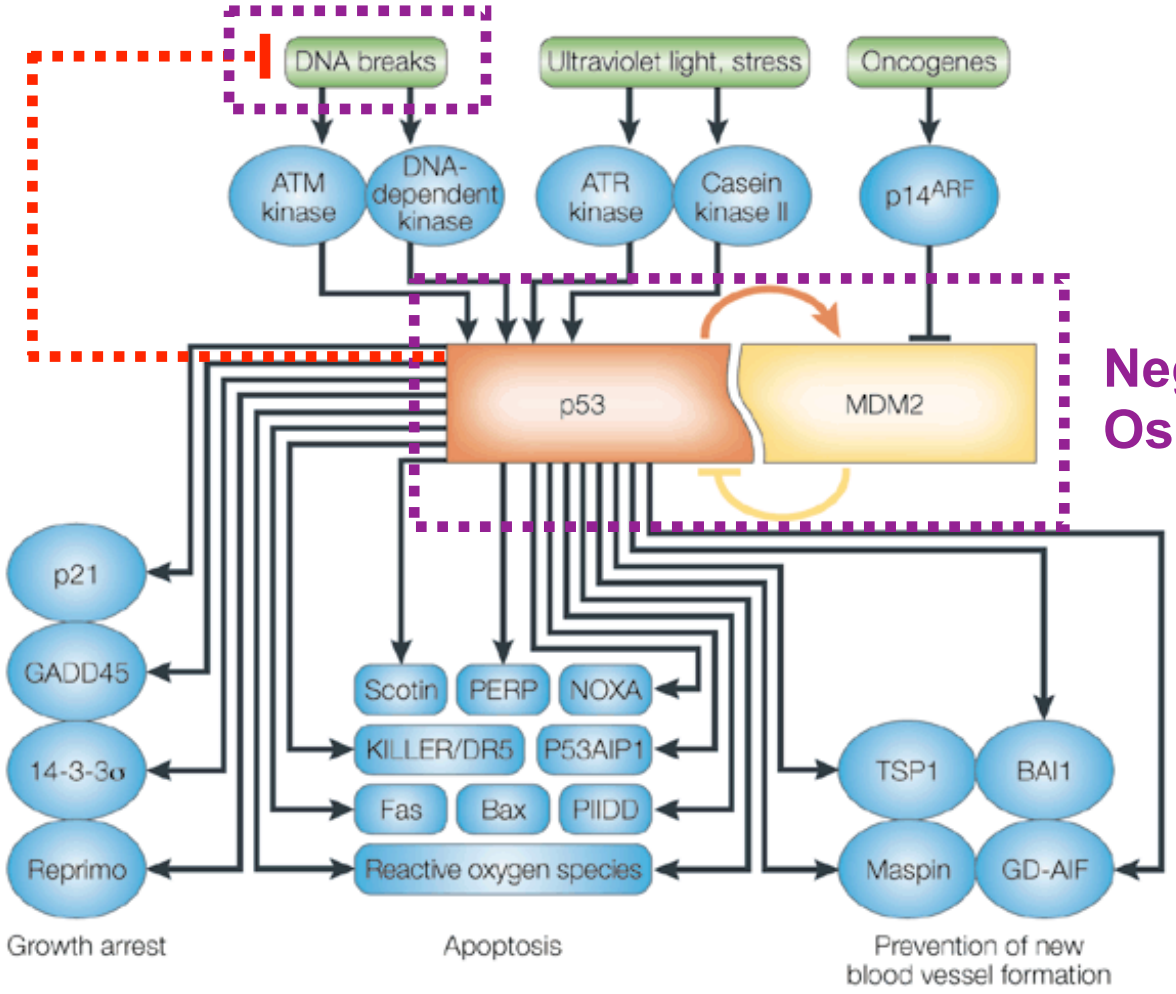


Negative loop
Oscillations

Nature Reviews | Genetics

Hasty et al (2001)

p53 regulation



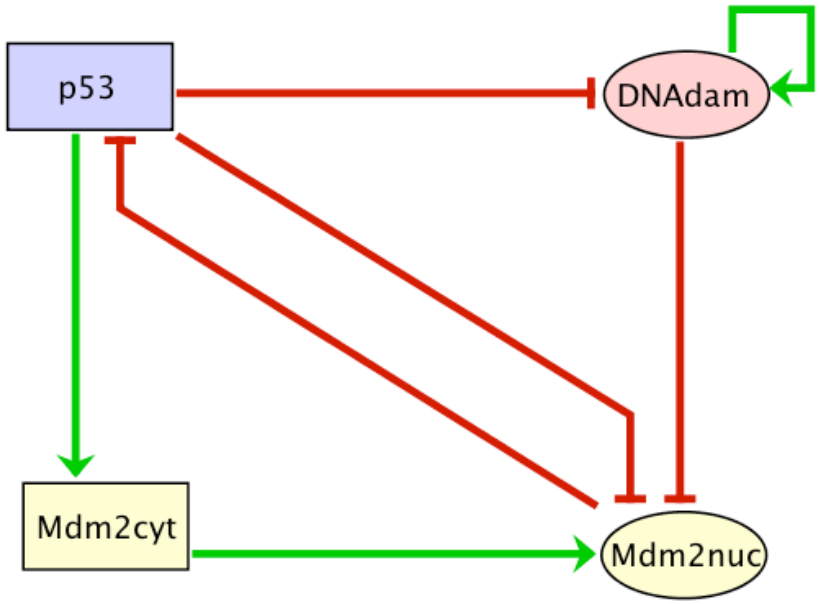
Negative loop
Oscillations

Nature Reviews | Genetics

Hasty et al (2001)

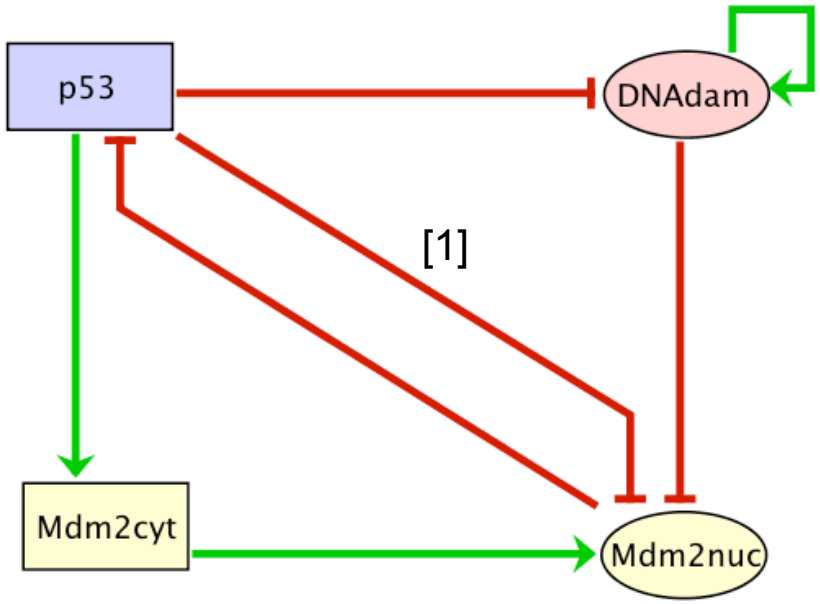
Logical modelling of the p53-Mdm2 network

Regulatory Graph



Logical modelling of the p53-Mdm2 network

Regulatory Graph



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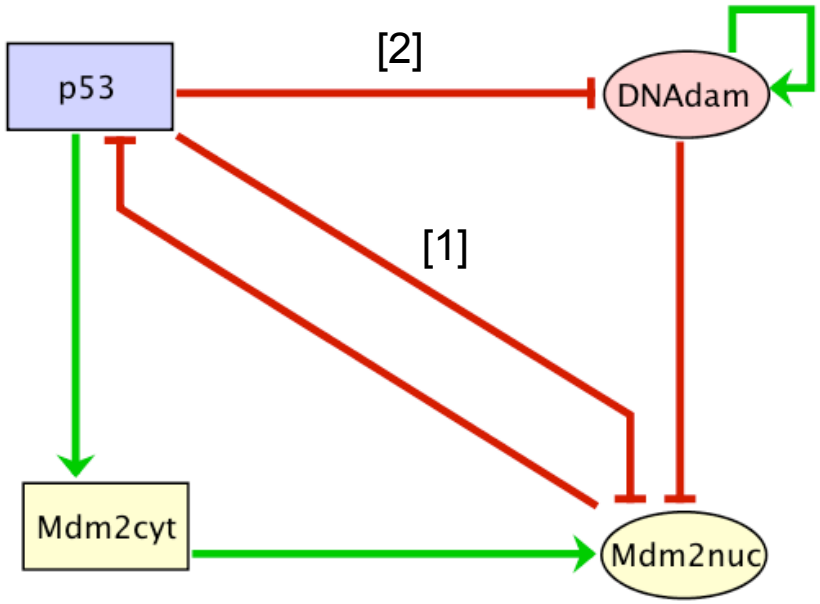
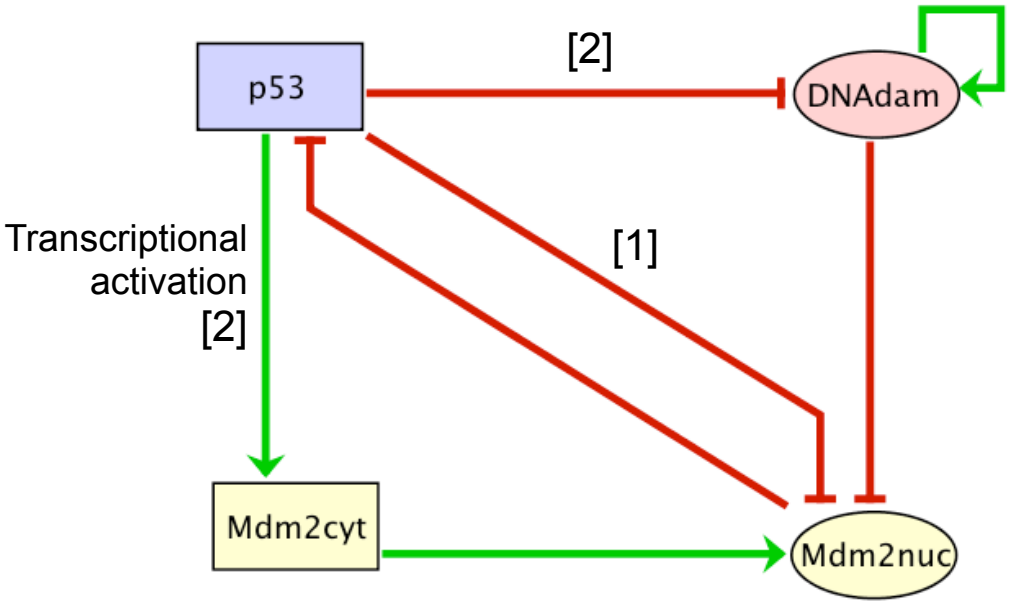


Logical modelling of the p53-Mdm2 network

Regulatory Graph



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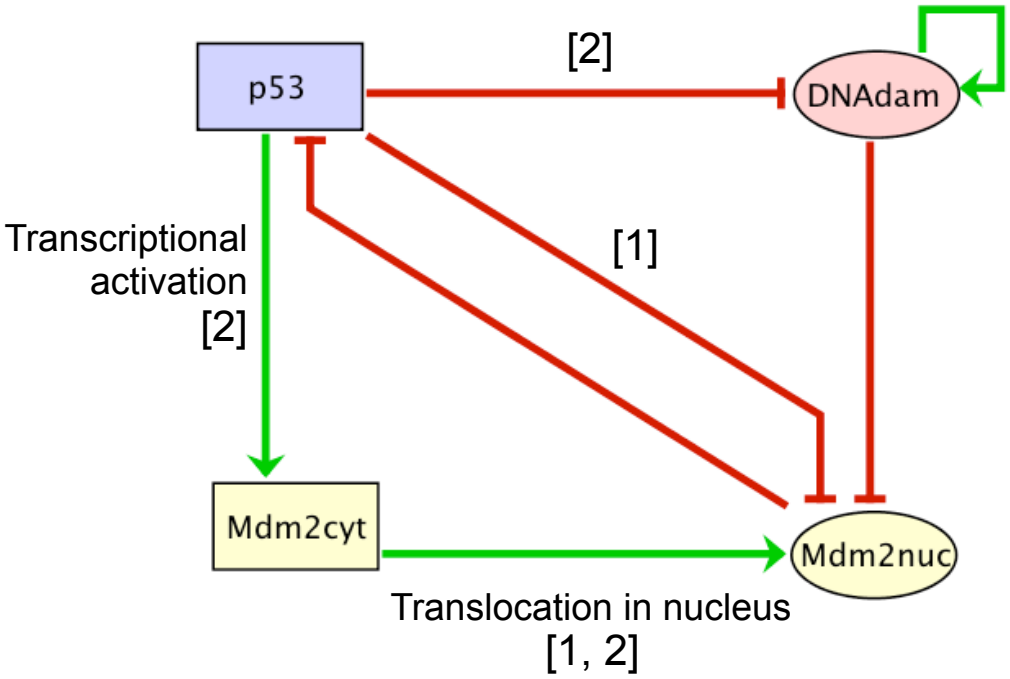
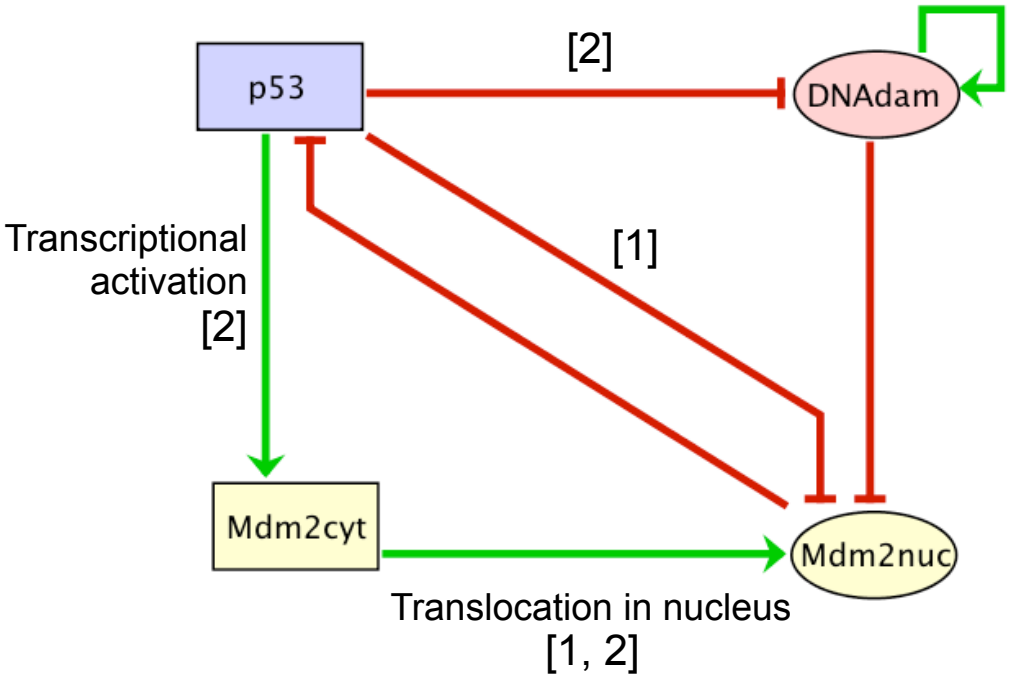


Logical modelling of the p53-Mdm2 network

Regulatory Graph

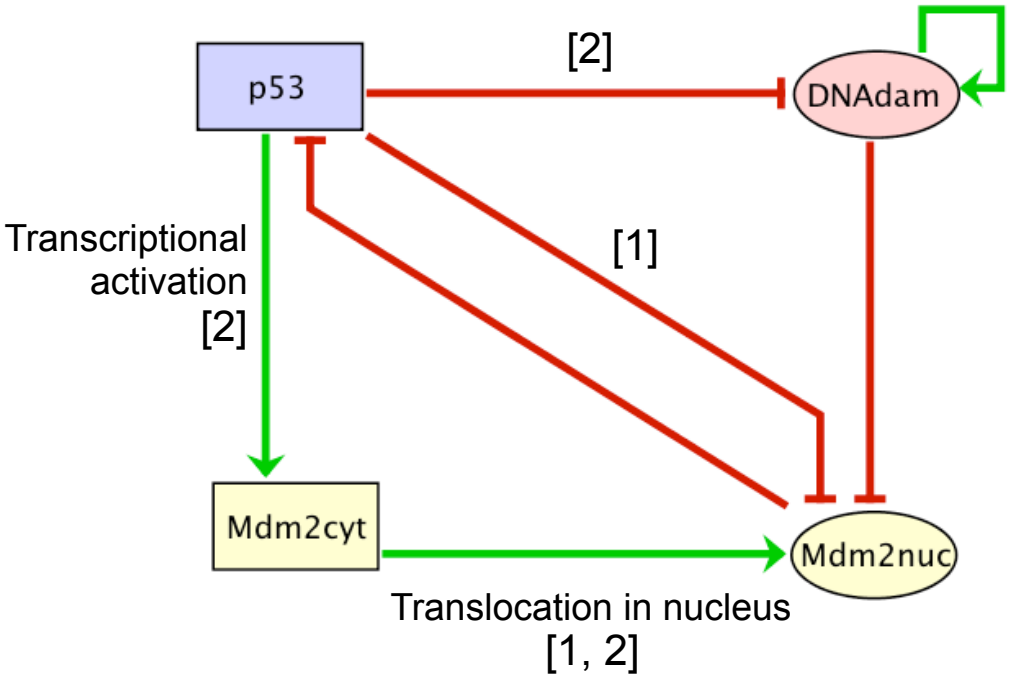


Logical rules

DNAdam => **1** IFF DNAdam **&** **!**p53:2

Logical modelling of the p53-Mdm2 network

Regulatory Graph



Logical rules

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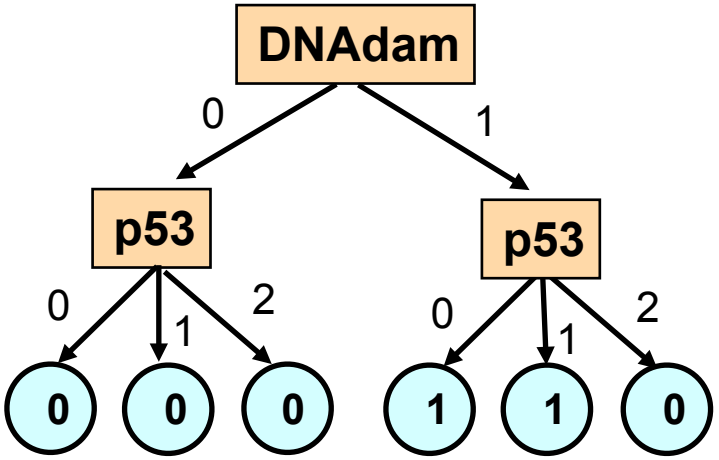
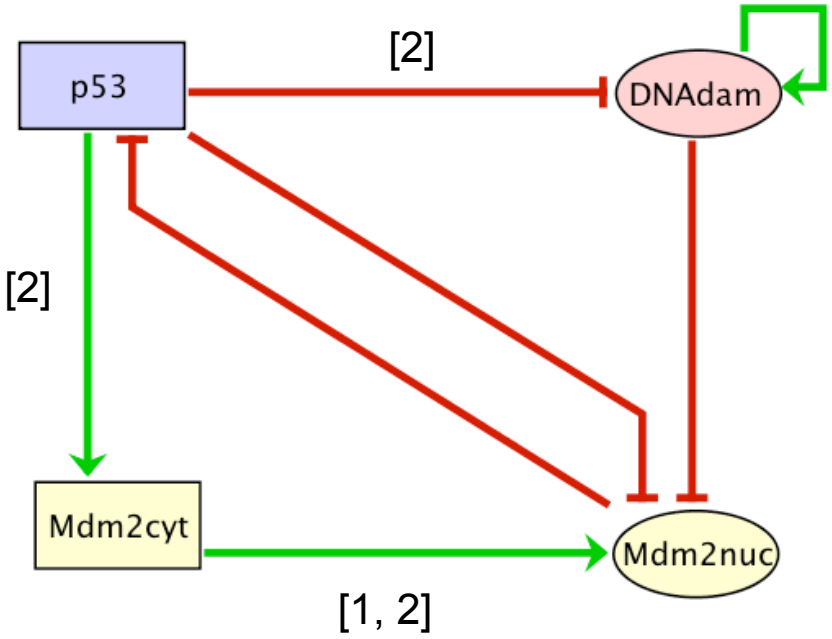


Decision tree

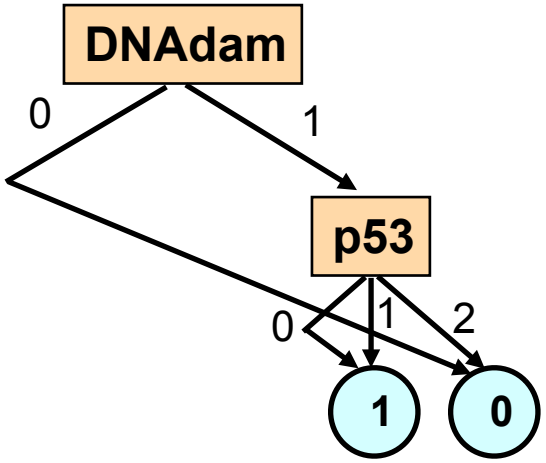
Logical modelling of the p53-Mdm2 network

Regulatory Graph



Logical rules

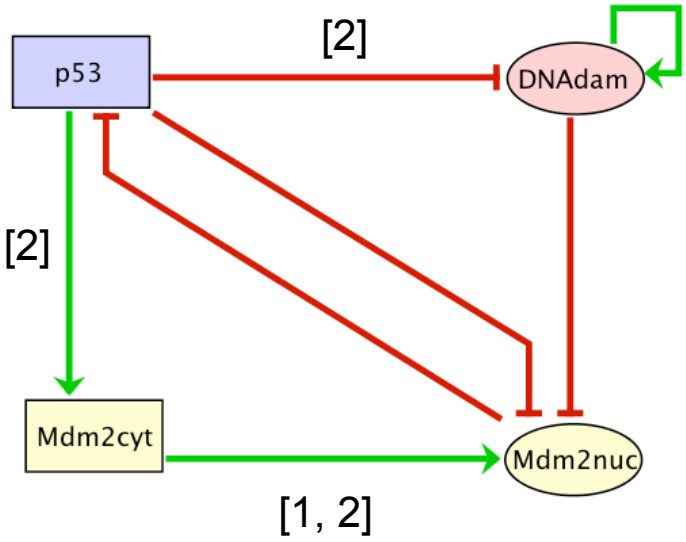
DNAdam => **1** IFF DNAdam **&** **!**p53:2



Decision diagram

Logical modelling of the p53-Mdm2 network

Regulatory Graph



Logical rules

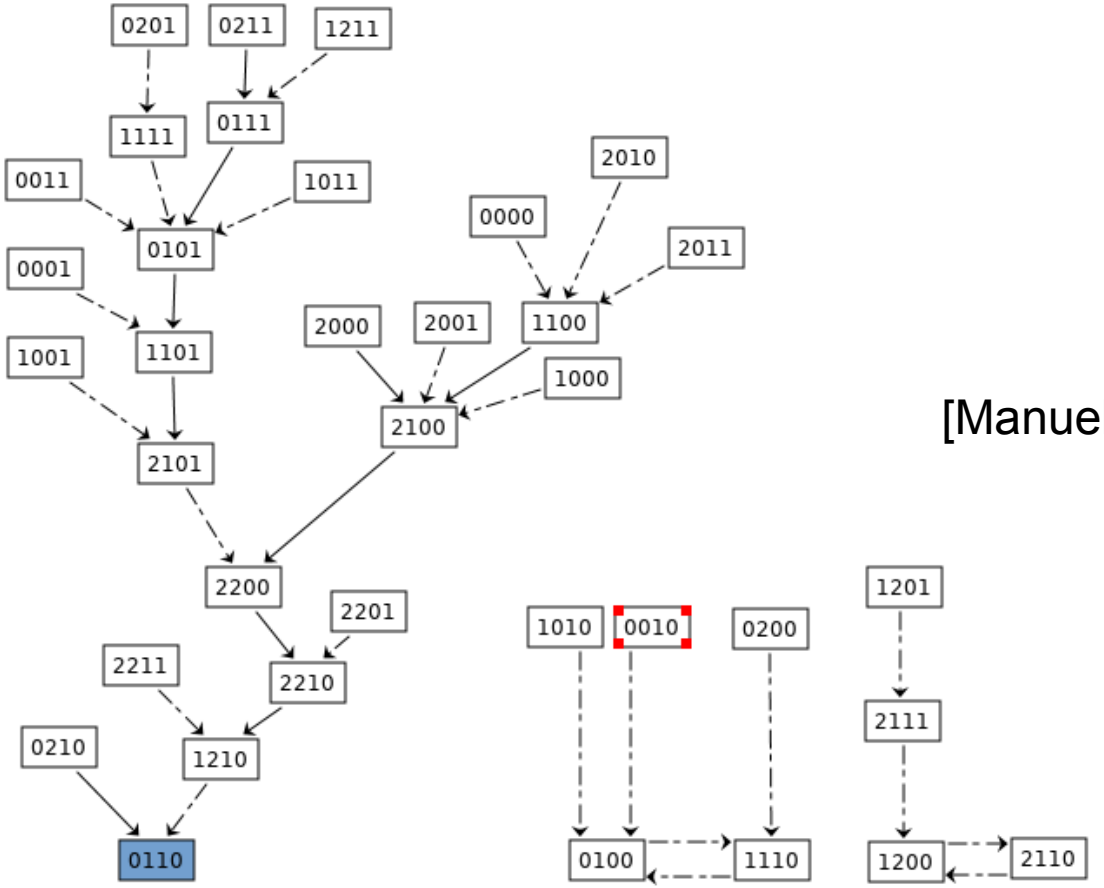
Components	Target levels	Boolean rules
p53	2	!Mdm2nuc
Mdm2cyt	2	p53:2
	1	!p53:2
Mdm2nuc	1	Mdm2cyt:2 | (Mdm2cyt:1 & !p53 & !DNAdam)
DNAdam	1	DNAdam & !p53:2

!, | and & stand for the Boolean operators NOT, OR and AND, respectively.

Default: other conditions leads each component => 0

Full synchronous simulation: STG

[p53,Mdm2cyt, Mdm2nuc, DNAdam]

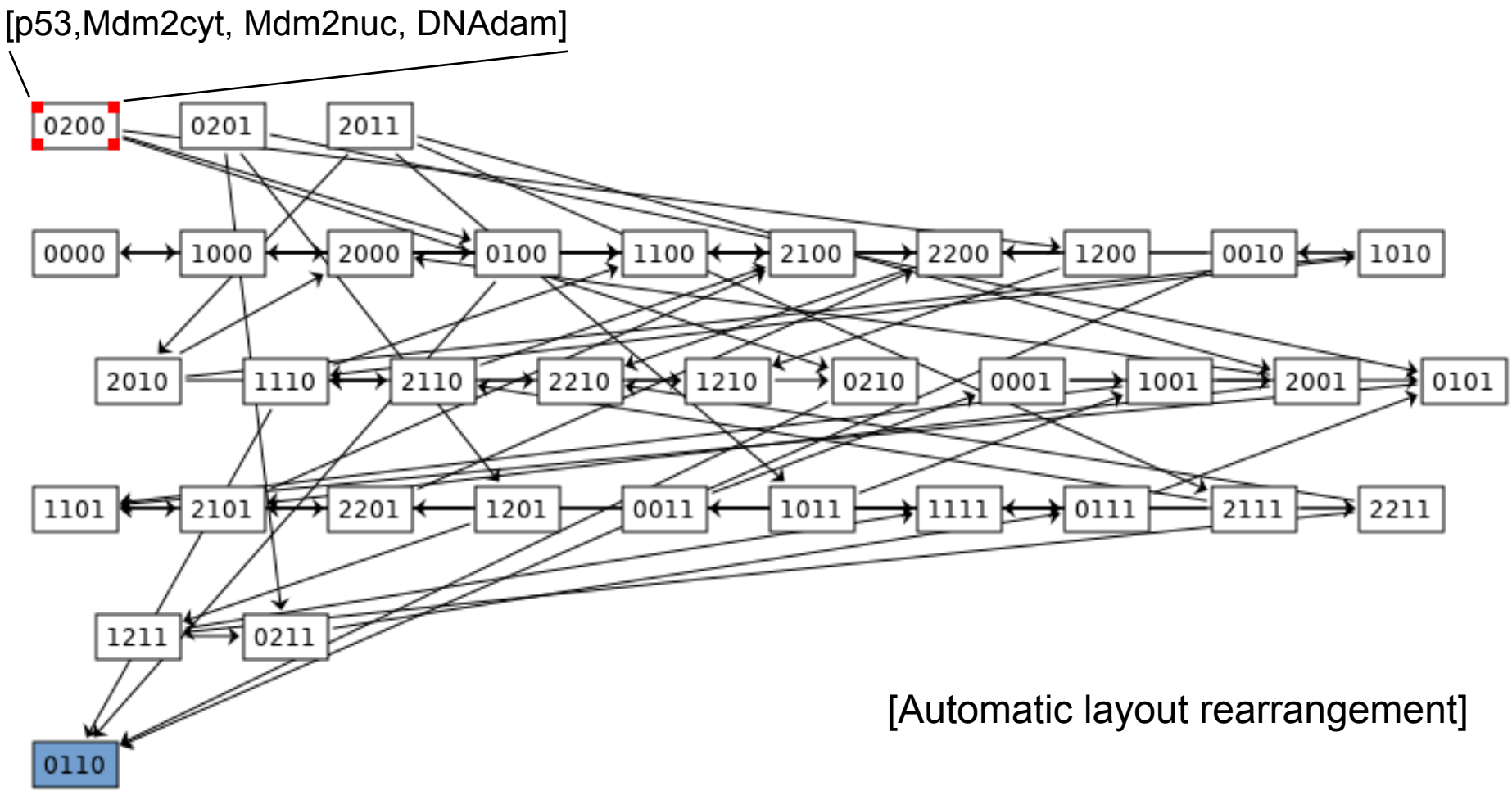


[Manuel layout rearrangement]

Stable (resting) state
with only Mdm2 (cyt/nuc) ON

Terminal cycles

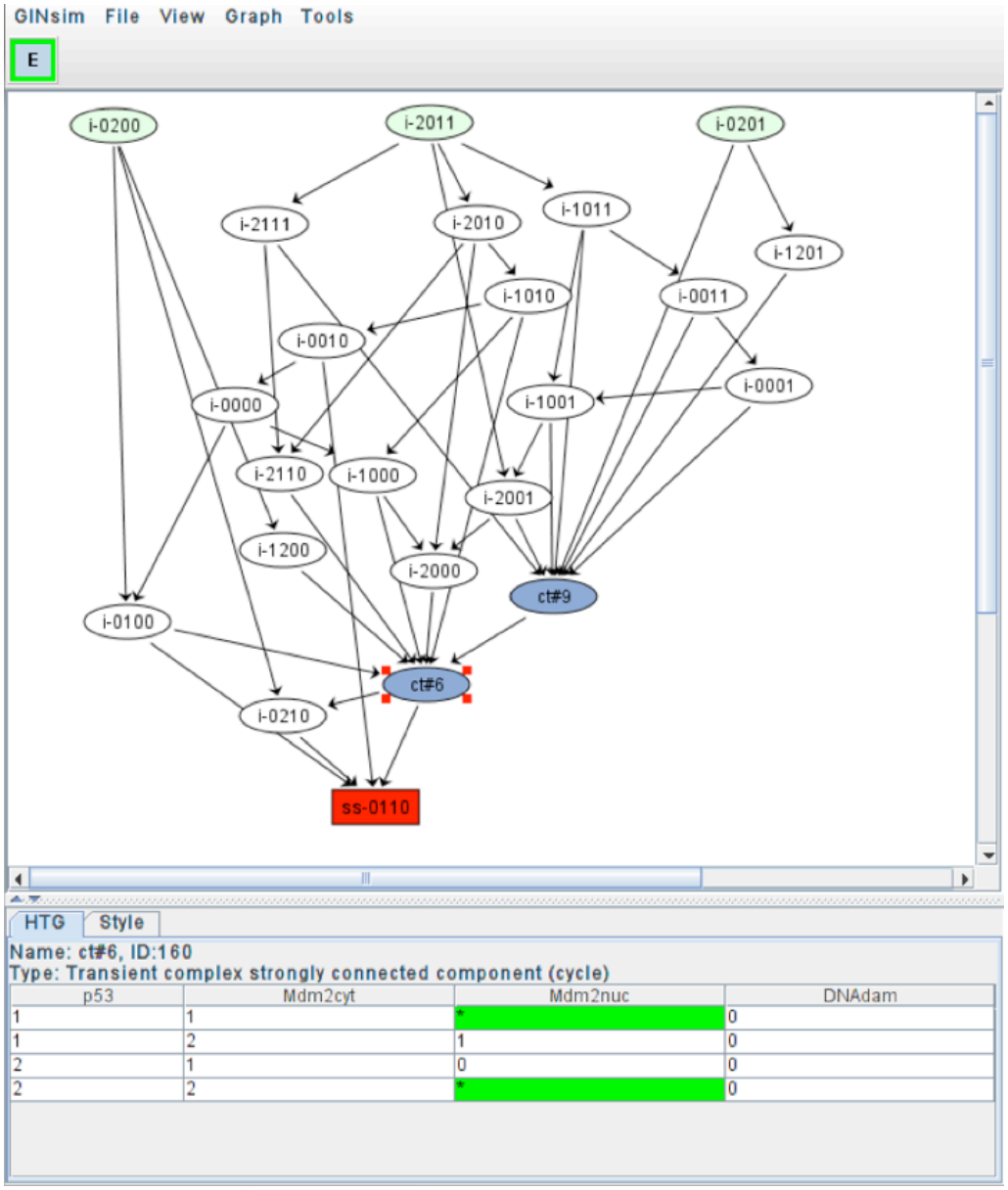
Full asynchronous simulation: state transition graph (STG)



[Automatic layout rearrangement]

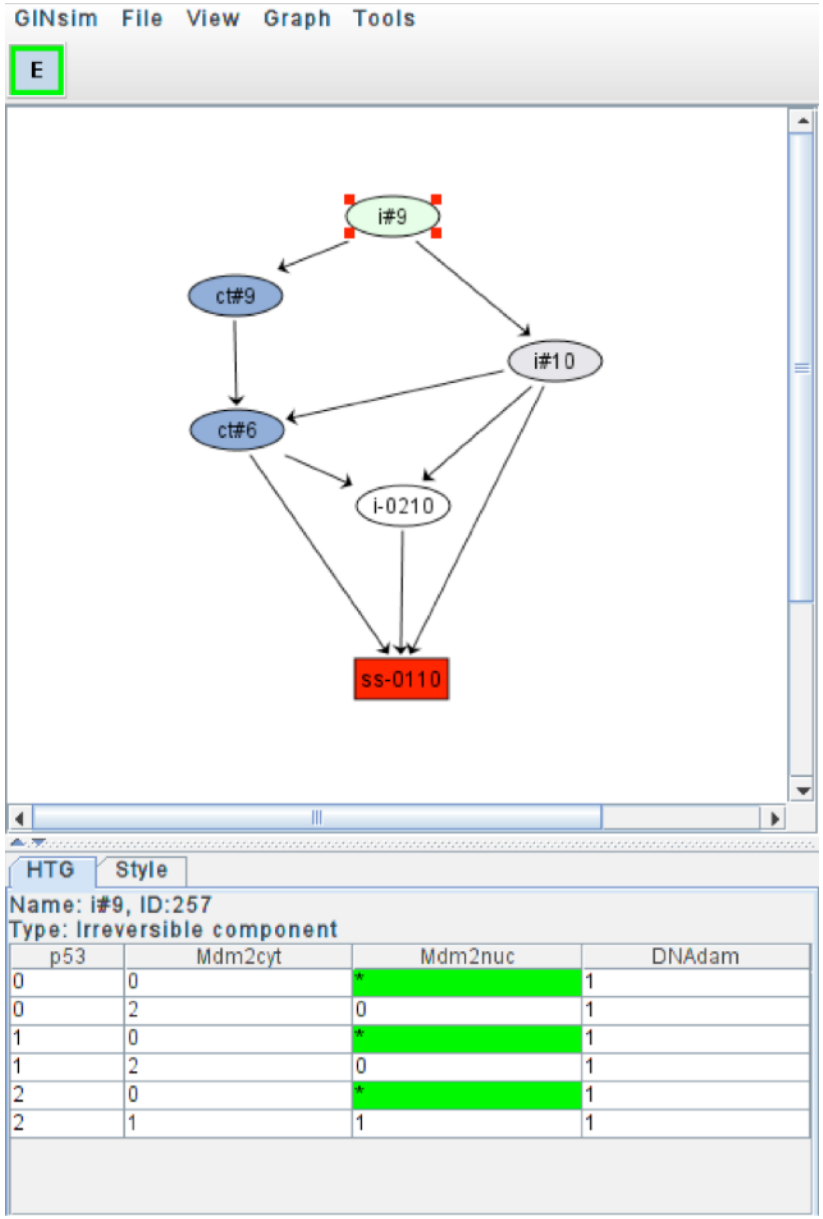
Stable (resting) state
with only Mdm2 (cyt/nuc) ON

Compression of asynchronous simulation: graph of strongly connected components (SCC)



[Manuel layout rearrangement]

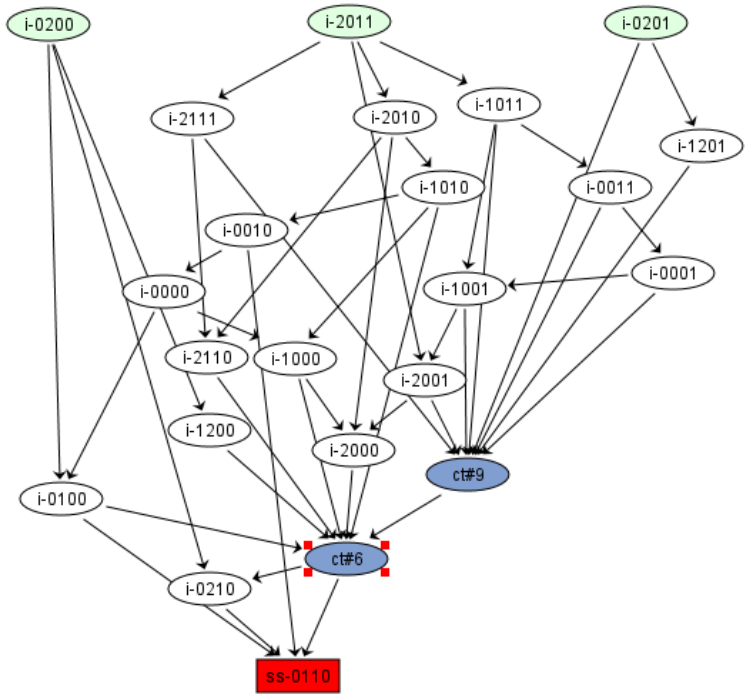
Compression of asynchronous simulation: Hierarchical transition graph (HTG)



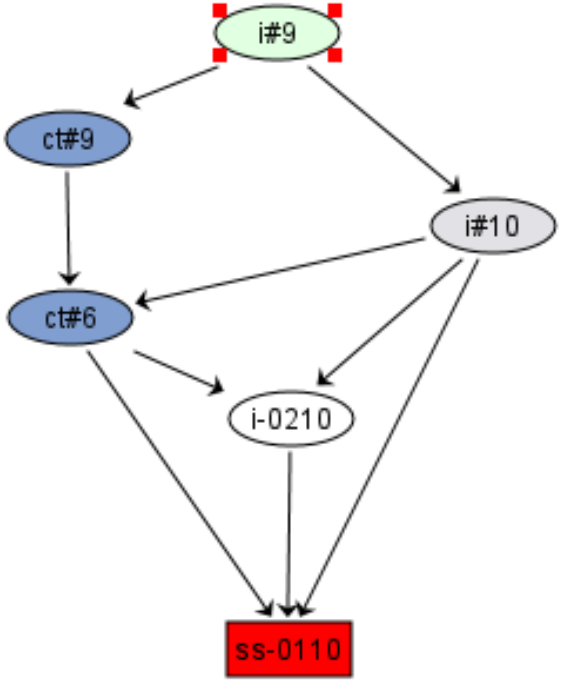
[Manuel layout rearrangement]

The HTG is generated with a modified version of Tarjan's algorithm (Bérenguier *et al.*, 2013).

Compression of asynchronous simulation: SCCG vs HTG



SCCG



HTG

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Boolean model of geroconversion	Mammal	Senescence
Budding yeast cell cycle (adapted from Irons, 2009)	Budding yeast, Yeast	Cell cycle
Budding yeast cell cycle (Fauré et al. 2009)	Budding yeast, Yeast	Cell cycle
Budding yeast cell cycle (Orlando et al. 2008)	Budding yeast, Yeast	Cell cycle
Budding yeast exit module	Budding yeast, Yeast	Cell cycle, Mitosis exit control
Cell fate decision network in the AGS gastric cancer cell line (Flobak et al 2015)	Mammal	Cancer
Control of Th1/Th2 cell differentiation	Mammal	Differentiation
Control of Th1/Th2/Th17/Treg cells differentiation	Mammal	Differentiation
Control of Th1/Th2/Th17/Treg/Tfh/Th9/Th22 cell differentiation	Blood cells, Mammal, T lymphocytes	Differentiation
Controlling the lysis-lysogeny decision in the phage lambda	Phage Lambda	Lysis-lysogeny decision
Core engine controlling the budding yeast cell cycle	Budding yeast, Yeast	Core engine, Cell cycle
Drosophila cell cycle	D. melanogaster	Cell cycle
Drosophila Dpp Signalling pathway	D. melanogaster	Development, Signalling, Wing Imaginal disk
Drosophila EGF Signalling pathway	D. melanogaster	Signalling

1 2 3 4 next › last »

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