

# Reproducibility: an old friend, the laboratory notebook

Better reproducibility with documented code



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25 novembre 2022



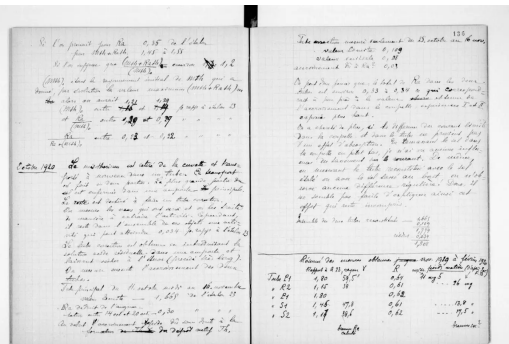
. This work is derived from the IFB and I2BC team members

- 1 The laboratory notebook
  - The aim
- 2 Notebook in bioinformatic
- 3 Practical training
  - Build your own documentation

# Paper version

Laboratory notebook allow to :

- Day-to-day recording each step in a process, experiments...



Source gallica.bnf.fr / Bibliothèque nationale de France, Département des Manuscrits, NAF 18422

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Laboratory notebook allow to :

- Day-to-day recording each step in a process, experiments...
- Report on the progress, and scientific experimentations from the idea to final conclusions

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- Keep track of knowledge in a lab
- Useful drafting a patent
- Proof of anteriority

# Paper version



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- Page numbered in each notebook

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At each research level :

- Researchers

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At each research level :

- Researchers
- Engineers

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- Researchers
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At each research level :

- Researchers
- Engineers
- Technicians
- Students...

End what's happen for bioinformatic ?

# Electronic version

Electronic Laboratory Notebooks (ELN)  
Modern LN since 2009 (C.U.R.I.E. Network)

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**eLabFTW**

# Electronic version

## Electronic Laboratory Notebooks (ELN) Modern LN since 2009 (C.U.R.I.E. Network)

eLabFTW EXPERIMENTS DATABASE TEAM SEARCH DOCUMENTATION

Experiments

Filter status Order by Sort 15 Create

Expand all - Select all

<p>Some microscopy experiment</p> <p>Next step: <b>analyze data</b></p> <p><input type="checkbox"/> <b>RUNNING</b> 2020.04.30   project SIMA </p> <p>video1</p>	<p>Another experiment</p> <p><input type="checkbox"/> <b>SUCCESS</b> 2020.04.30   project SIMA </p>	<p>Making fake experiments to do a screenshot</p> <p><input type="checkbox"/> <b>SUCCESS</b> 2020.04.30  elabweb elabftw.net </p>
<p>Looking at cells</p> <p><input type="checkbox"/> <b>SUCCESS</b> 2020.04.30 </p>	<p>A failed experiment</p> <p><input type="checkbox"/> <b>FAIL</b> 2020.04.30  sirna </p>	<p>无标题</p> <p><input type="checkbox"/> <b>SUCCESS</b> 2020.04.30 </p>
<p>Senza titolo</p> <p><input type="checkbox"/> <b>SUCCESS</b> 2020.04.27  </p>	<p>lock unlock</p> <p><input type="checkbox"/> <b>SUCCESS</b> 2020.04.22 </p>	<p>mathjax I</p> <p><input type="checkbox"/> <b>SUCCESS</b> 2020.04.21 </p>
<p>が無効になっています。</p> <p><input type="checkbox"/> <b>SUCCESS</b> 2020.04.20  </p>	<p>Processing of Sample #392A</p> <p><input type="checkbox"/> <b>SUCCESS</b> 2020.04.16   project X </p>	<p>analysis of sample #2343 from this company</p> <p><input type="checkbox"/> <b>NEED TO BE REDONE</b> 2020.04.16  project X </p>
<p>mathjax test <math>\frac{d}{dx} x\dot{x} = \dot{x}^2 + x\ddot{x}</math></p> <p><input type="checkbox"/> <b>SUCCESS</b> 2020.04.16 </p>	<p>Model test</p> <p><input type="checkbox"/> <b>RUNNING</b> 2020.04.07  nulla non sed </p> <p>omnis sit</p>	<p>Qui pariatur aut architecto fuga.</p> <p><input type="checkbox"/> <b>NEED TO BE REDONE</b> 2020.03.27   labore </p> <p>minus inventore qui ta'g</p>

NEXT PAGE

# Electronic version

## Electronic Laboratory Notebooks (ELN) Modern LN since 2009 (C.U.R.I.E. Network)



### Experiments

[Back to listing](#)

Tags

project SIMA

video1

Add a tag

Date

20200430

Status

Success

Title

Some microscopy experiment

Experiment

File Edit View Insert Format Tools Table

↶ ↷

Heading 2

B

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$x^2$

$x_2$

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Goal:

Show what an experiment looks like for [elabftw.net](http://elabftw.net).

Sample #	Concentration	Absorbance	Density	Something
1	20 $\mu$ M	0.239	3.4	102
2	30 $\mu$ M	0.193	4.1	1339

You can have colors too.

And use **bold**, *italics*, underline like you would do in a normal text processing application. Have some mathjax:  $\{x^y\}^z$  is  $\{x^y\}^z$ , and  $x^{\{y^z\}}$  is  $x^{\{y^z\}}$ .

This is a list:

- List item 1
- List item 2
- Now show an image in the text

# Electronic version

Electronic Laboratory Notebooks (ELN)  
Modern LN since 2009 (C.U.R.I.E. Network)

- dematerialised
- archivable
- sharable
- secure

# Electronic version

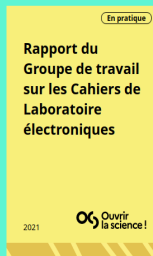
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But less and less adapted to recent evolutions of our work  
We need an electronic tool for individual traceability

# Electronic version

[Accueil](#) > [Bibliothèque de la science ouverte](#) > [Rapport du Groupe de travail sur les Cahiers de Laboratoire électroniques](#)



Le rapport du groupe de travail « Cahier de laboratoire électronique » (ELN) présente une vision partagée sur la définition, le cadrage, les usages et le périmètre fonctionnel de l'ELN, qui doit pouvoir s'intégrer dans les environnements informatiques et institutionnels existants. Il émet un ensemble de recommandations sur les critères de choix d'un outil et intègre une liste comparative d'outils existants.



# Electronic version

## Calendrier du projet



### Note de synthèse

- Caractéristiques techniques souhaitées
- Inventaire des solutions existantes sur le marché

J janvier 2021

### Mise en œuvre de la stratégie adoptée

- Mise en œuvre de la procédure d'achat (licences, etc.)
- Cahier des charges de la solution à développer

Mars-J uillet 2021

### Mise à disposition de ou des solutions sélectionnées

- Outils déployés sous licences CNRS
- Solution électronique développée en interne

J janvier 2022  
– J uin 2023



Cahier de laboratoire électronique 17.11.20 PR96



UNIVERSITÉ  
Clermont Auvergne

# Literate programming

What is literate programming ?

- 
1. Donald E. Knuth, Literate Programming, 1984  
. [https://en.wikipedia.org/wiki/Literate\\_programming#Workflow](https://en.wikipedia.org/wiki/Literate_programming#Workflow)

# Literate programming

What is literate programming ?

*"Let us change our traditional attitude to the construction of programs :  
Instead of imagining that our main task is to instruct a computer what to do, let us concentrate rather  
on explaining to humans what we want the computer to do."*<sup>1</sup>

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*"Literate programming is a programming paradigm introduced by Donald Knuth in which a computer  
program is given an explanation of its logic in a natural language, such as English, interspersed with  
snippets of macros and traditional source code, from which compilable source code can be generated."*

- 
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# Literate programming

What does it look like ?

# Literate programming



# This is an example title

I can add more infos about my code to explain to other users and aslo to remember what my code is doing

```
> - Cell with text to give informations
> - Cell with code to view what's happen
> - plot are also present in the output
> - You can export the raw file in jupyter format but also in pdf, word, tex...
```

## Subtitle for configuration import

```
[1]: import numpy as np
import matplotlib.pyplot as plt
%matplotlib inline
```

## Subtitle for my first plot

```
[2]: def gaussian(x, a, b, c):
      return a * np.exp(-b * (x-c)**2)

def noisy_gaussian():
    # gaussian array y in interval -5 <= x <= 5
    nx = 100
    x = np.linspace(-5.0, 5.0, nx)
    y = gaussian(x, a=2.0, b=0.5, c=1.5)
    noise = np.random.normal(0.0, 0.2, nx)
    y += noise
    return x, y

def fit(x, y, n):
    pfit = np.polyfit(x, y, n)
    yfit = np.polyval(pfit, x)
    return yfit

def plot(x, y, yfit):
    plt.plot(x, y, "r", label="Data")
```

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# Literate programming

What does it look like ?

Interactive programming interface allowing to combine both natural and computer languages

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What does it look like ?

Interactive programming interface allowing to combine both natural and computer languages

In one file

- Explanation
- Code
- Results
- Graphs and plots



# Literate programming

Why using literate programming frameworks ?

- Labbook

# Literate programming

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- Labbook
- Day-to-day analysis

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- Labbook
- Day-to-day analysis
- Make automatic reports

# Literate programming

Why using literate programming frameworks ?

- Labbook
- Day-to-day analysis
- Make automatic reports
- Write scientific article

# Literate programming

## example

Example of an article written using a notebook

---

. <https://www.frontiersin.org/articles/10.3389/fphys.2018.00787/full>

# Literate programming

## example

The screenshot shows the GitHub interface for the repository 'colomoto / colomoto-docker'. The repository is public and has 6 watchers, 6 forks, and 15 stars. The main content area displays a Jupyter Notebook file named 'Usecase - Mutations enabling tumour invasion.ipynb' under the path 'colomoto-docker / usecases'. The notebook was last updated by 'pauleve' on April 24, 2020. It has 1 contributor and 2513 lines of code (2513 sloc) with a size of 422 KB. The notebook content is visible, showing the title 'Prediction of Mutations to Control Pathways Enabling Tumour Cell Invasion with the CoLoMoTo Interactive Notebook (Tutorial)' and the authors: Nicolas Levy<sup>1,2</sup>, Aurélien Naldi<sup>3</sup>, Céline Hernandez<sup>3</sup>, Gautier Stoll<sup>4-6</sup>, Denis Thieffry<sup>3</sup>, Andrei Zinoviyev<sup>9-11</sup>, Laurence Calzone<sup>9-11</sup>, and Loïc Paulevé<sup>1,\*</sup>. The authors' affiliations are listed below the title.

**Prediction of Mutations to Control Pathways Enabling Tumour Cell Invasion with the CoLoMoTo Interactive Notebook (Tutorial)**

**Authors:** Nicolas Levy<sup>1,2</sup>, Aurélien Naldi<sup>3</sup>, Céline Hernandez<sup>3</sup>, Gautier Stoll<sup>4-6</sup>, Denis Thieffry<sup>3</sup>, Andrei Zinoviyev<sup>9-11</sup>, Laurence Calzone<sup>9-11</sup>, Loïc Paulevé<sup>1,\*</sup>

<sup>1</sup> LRI UMR 8623, Université Paris-Sud, CNRS, Université Paris-Saclay, Orsay, France; <sup>2</sup> École Normale Supérieure de Lyon, France; <sup>3</sup> Computational Systems Biology team, Institut de Biologie de l'École Normale Supérieure, CNRS UMR8197, INSERM U1024, École Normale Supérieure, PSL Université, Paris, France; <sup>4</sup> Université Paris Descartes/Paris V, Sorbonne Paris Cité, Paris, France; <sup>5</sup> Équipe 11 labellisée Ligue Nationale contre le Cancer, Centre de Recherche des Cordeliers, Paris, France; <sup>6</sup> Institut National de la Santé et de la Recherche Médicale, U1138; Paris, France; <sup>7</sup> Université Pierre et Marie

# Literate programming

## example

File Edit View Run Kernel Tabs Settings Help

Filter files by name

Name	Last Modified
test_quarto	7 hours ago
hello.ipynb	a minute ago

## Prediction of Mutations to Control Pathways Enabling Tumour Cell Invasion with the CoLoMoTo Interactive Notebook (Tutorial)

**Authors:** Nicolas Levy<sup>1,2</sup>, Aurélien Naldi<sup>3</sup>, Céline Hernandez<sup>3</sup>, Gautier Stoll<sup>4-8</sup>, Denis Thieffry<sup>3</sup>, Andrei Zinovyev<sup>9-11</sup>, Laurence Calzone<sup>9-11</sup>, Loïc Paulevé<sup>1,\*</sup>

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### Abstract

Boolean and multi-valued logical formalisms are increasingly used to model complex cellular networks. To ease the development and analysis of logical models, a series of software tools have been proposed, often with specific assets. However, combining these tools typically implies a series of cumbersome software installation and model conversion steps. In this respect, the *CoLoMoTo Interactive Notebook* provides a joint distribution of several logical modelling software tools, along with an interactive web Python interface easing the chaining of complementary analyses.

Our computational workflow combines (1) the importation of a GiNsim model and its display, (2) its format conversion using the Java library BioLQM, (3) the formal prediction of mutations using the OCaml software Pint, (4) the model checking using the C++ software NuSMV, (5) quantitative stochastic simulations using the C++ software MaBoSS, and (6) the visualisation of results using the Python library matplotlib. We rely on the CoLoMoTo Interactive Notebook to provide a thoroughly documented and executable notebook of our computational analysis.

To illustrate our approach, we use a recent Boolean model of the signalling network controlling tumour cell invasion and migration. Our model analysis culminates with the prediction of sets of mutations presumably involved in a metastatic phenotype. Beyond the specific application considered here, the resulting Jupyter notebook constitutes a tutorial for the use and combination of several logical modelling tools, which can be easily adapted to analyse other models. Furthermore, the notebook web interface and the companion Docker distribution of logical modelling tools greatly facilitate the production of accessible and reproducible model analysis workflows.

# Literate programming

## example

The screenshot shows the Frontiers website interface. At the top, there's a navigation bar with the Frontiers logo, 'About us', 'All journals', 'All articles', and a 'Submit your research' button. Below this is a secondary navigation bar for 'Frontiers in Physiology' with links to 'Sections', 'Articles', 'Research Topics', 'Editorial board', and 'About journal'. The main content area features a 'PROTOCOLS article' section with the journal name 'Front. Physiol.', date '06 July 2018', section 'Sec. Systems Biology Archive', and a DOI link. It also mentions the article is part of a research topic 'Logical Modeling of Cellular Processes: From Software Development to Network Dynamics' with a link to 'View all 23 Articles'. The article title is 'Prediction of Mutations to Control Pathways Enabling Tumor Cell Invasion with the CoLoMoTo Interactive Notebook (Tutorial)'. The authors listed are Nicolas Levy, Aurélien Naldi, Céline Hernandez, Gautier Stoll, Denis Thieffry, Andrei Zinovyev, Laurence Calzone, and Loïc Paulevé. At the bottom right, the 'Université Clermont Auvergne' logo is visible.

frontiers

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Frontiers in Physiology Sections ▾ Articles Research Topics Editorial board About journal ▾

**PROTOCOLS article**

Front. Physiol., 06 July 2018  
Sec. Systems Biology Archive  
<https://doi.org/10.3389/fphys.2018.00787>

This article is part of the Research Topic  
Logical Modeling of Cellular Processes: From Software Development to Network Dynamics  
[View all 23 Articles >](#)

## Prediction of Mutations to Control Pathways Enabling Tumor Cell Invasion with the CoLoMoTo Interactive Notebook (Tutorial)

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 Andrei Zinovyev<sup>9,10,11,12</sup>, Laurence Calzone<sup>9,10,11</sup> and Loïc Paulevé<sup>4\*</sup>

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Université Clermont Auvergne



# Markup

A markup language uses tags to define elements within a document.  
Three different types and usage :

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Three different types and usage :

- Presentational (used by traditional word-processing systems)
- Procedural, provides instructions to process the text (e.g. TeX, PostScript)
- Descriptive, to label documents parts (e.g. LaTeX, HTML, XML...)

# Markdown

Markdown is a Lightweight markup language  
Designed to be :



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- easy to write using any generic text editor (plain-text-formatting syntax)



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```
# Heading level 1
## Heading level 2
### Heading level 3

**Bold text**

*Italic*

~~strikethrough text~~

A [link](http://www.example.com)

Item list
- one point
  - a subpoint
- another point
- last point
```



# Markdown

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Used on Github to make the README.md

But how is this useful for literate programming ?

When you want to weave both code (to be interpreted) and formatting information, you precisely need a lightweight language for the formatting part.

## R notebooks vs Jupyter(Lab) notebook



VS



[www.educba.com](http://www.educba.com)

# R notebook

## 1 Sweave in 2002

*Leisch, Friedrich (2002). "Sweave, Part I : Mixing R and LaTeX : A short introduction to the Sweave file format and corresponding R functions"*

# R notebook

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*Leisch, Friedrich (2002). "Sweave, Part I : Mixing R and LaTeX : A short introduction to the Sweave file format and corresponding R functions"*

## 2 knitr in 2011

*"The knitr package was designed to be a transparent engine for dynamic report generation with R, solve some long-standing problems in Sweave, and combine features in other add-on packages into one package"*

# RMarkdown



2012 Rmarkdown was born !

---

. <https://rmarkdown.rstudio.com>

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# RMarkdown

2012 Rmarkdown was born !



*"When you run render, R Markdown feeds the .Rmd file to knitr, which executes all of the code chunks and creates a new markdown (.md) document which includes the code and its output. The markdown file generated by knitr is then processed by pandoc which is responsible for creating the finished format."*

# RMarkdown

```

1 ---
2 title: |
3   <center> Rapport d'analyse séquençage NGS </center>
4   <center> Détection de variants SARS-CoV-2 </center>
5 author: |
6   <center> Service de Virologie </center>
7   <center> Laboratoire de Biologie du CHU de Clermont-Ferrand </center>
8
9 date: "r format(Sys.time(), '%d %B %Y')""
10 output:
11   rmdformats::readthedown|
12 editor_options:
13   chunk_output_type: console
14 ---
15
16 # Configuration de l'analyse
17 ```{r config, engine.opts='-l',echo=F}
18 # chemin absolu vers les fichiers, scripts de l'application
19 lineage_analysis_dir <- "/home/pierre/Seafle/Seafle/lineage_analysis/"
20 #Sys.setenv(params = lineage_analysis_dir)
21 source(paste0(lineage_analysis_dir,"conf_R/initialize_lineage.txt"))
22 confR <- list.files(path = lineage_analysis_dir,pattern = conf_lineage,full.names = T,recursive = T)
23 # chargement du code R de configuration
24 source(confR)
25 # export for bash chunk the path of ANALYSE
26 Sys.setenv(ANALYSE = ANALYSE)
27 ```
28
29 ```
30 `r kable(config_files_input,col.names = "",caption = "Liste des fichiers de configurations")`

```

Configuration de l'analyse  
 Paramètres d'entrée de Covid-Seq depuis Basespace  
 Import des données de la séquence S  
 Création du jeu de données global  
 Liste des mutations de référence des clades  
 Analyse des patients et des contrôles  
 Analyse des mutations dans S  
 Rendu des résultats pour \*GLIMS\*  
 Rendu des résultats pour \*GISAID\*



# RMarkdown

## Rapport d'analyse séquençage NGS Détection de variants SARS- CoV-2

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clades

Analyse des patients et des contrôles

Analyse des mutations dans S

Rendu des résultats pour GLIMS

Rendu des résultats pour GISAIID



Service de Virologie  
Laboratoire de Biologie du CHU de  
Clermont-Ferrand

## Import des données de la séquence S

Nombre de séquences trouvées dans le fichier fasta depuis basespace : 93

Nombre de séquences trouvées dans le fichier fasta aligné via Nextclade : 93

## Création du jeu de données global

Le fichier de fusion des données contient 96 entrées

## Liste des mutations de référence des clades

Copy

CSV

Excel

PDF

Print

Show

10

entries

Search:

Tableau des mutations de références utilisées pour l'analyse des variants

scorpio_clade	lineage.ref	synonymous_mutation_ref
All	A	All
20A/EU2	B.1.160	C4543T,G5629T,C11497T,T26876C
20A/S:126A	B.1.620	C241T,C3037T,C15324T,T20049C,A23416T,T27795-,T27796-,A27797-,A28271T
20A/S:439K	B.1.258	C8047T
20A/S:98F	B.1.221	C28651T
20B/S:1122L	B.1.1.302	
20B/S:626S	B.1.1.277	
20B/S:732A	B.1.1.519	C203T,C222T,C241T,C3037T,C10954T,T19839C,C21306T,C29197T
20C/S:80Y	B.1.367	G4960T,C6070T,C7303T,C7564T,C10279T,C10525T,C10582T,C27804T

# Jupyter

- 1 2011 : IPython (interactive Python shell) with notebook functionalities

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. <https://jupyter.org/>

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  - A reference to the three core programming languages supported by Jupyter (Julia, Python and R)

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# Jupyter

What is it exactly ?

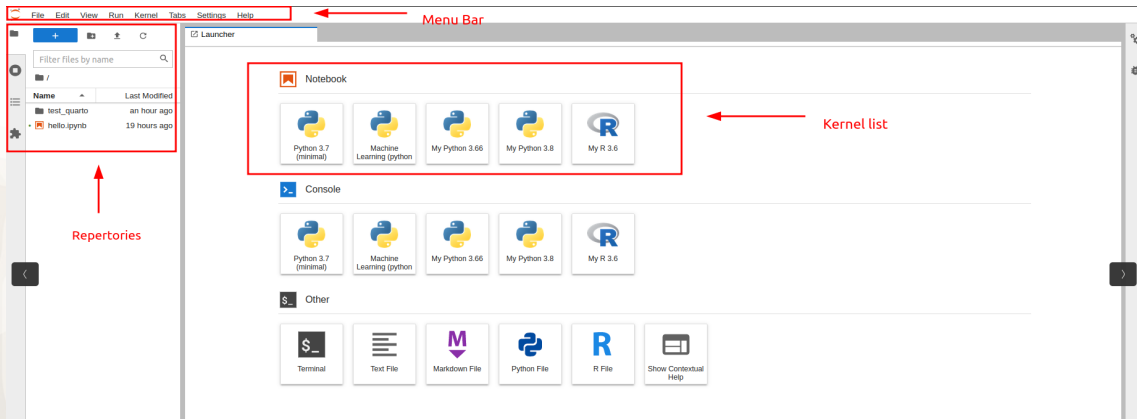
Web-based interactive computational environment

# Jupyter

What is it exactly ?

Web-based interactive computational environment

- Web-based : client/server

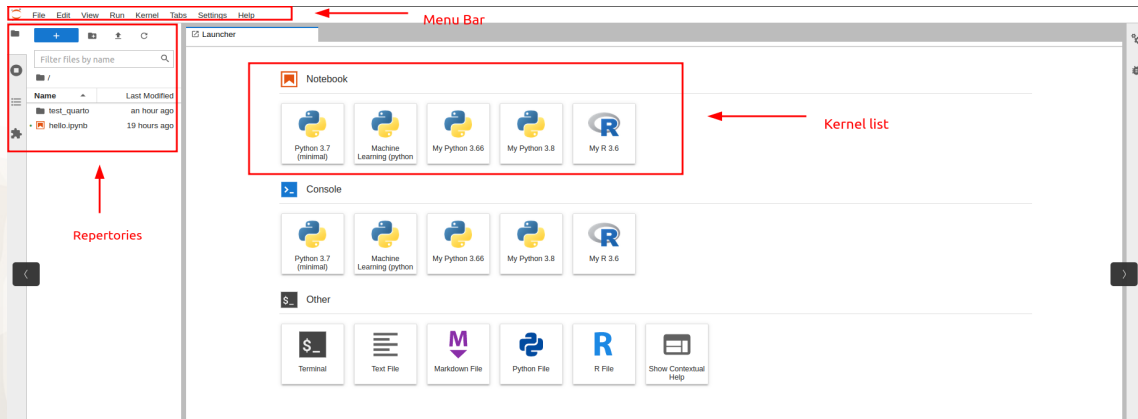


# Jupyter

What is it exactly ?

Web-based interactive computational environment

- Web-based : client/server
- Interactive : notebook system



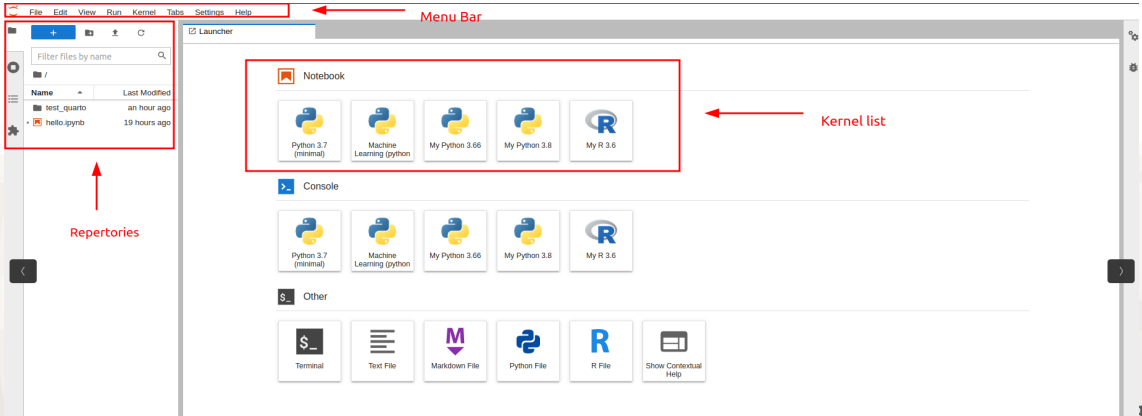


# Jupyter

What is it exactly ?

Web-based interactive computational environment

- Web-based : client/server
- Interactive : notebook system
- Computational environment : console, many kernels available...



# Jupyter

## What is it exactly ?

## Web-based interactive computational environment

The screenshot displays the Jupyter Notebook web interface. On the left is a file browser with a search bar and a table of files:

Name	Last Modified
test_quarto	an hour ago
hello.ipynb	19 hours ago

The main area shows a notebook cell with the following content:

In this graph, the vertices shown in white or orange denote components that are OFF (value 0) or ON (value 1) respectively.

**Assessing the probabilities to reach alternative attractors using MaBoSS**

MaBoSS [Stoll2017](https://doi.org/10.1093/bioinformatics/btx123) is a C++ software enabling the stochastic simulation of Boolean networks by translating them into continuous time Markov processes. Each node activation and inactivation is associated with an "up" and a "down" rate, which specify the propensity of the corresponding transitions. From a given state, the simulation integrates all the possible node updates and derives a probability and a duration for each transition. By default, all transitions are assigned the same rate. For a given set of initial conditions, MaBoSS produces time trajectories and estimates probabilities of model states over the whole simulation time. Steady state distributions can thus be approximated, provided that a sufficient number of sufficiently long simulations have been performed.

The aim of this section is to reproduce part of the results obtained by [Cohen2015](https://doi.org/10.1371/journal.pcbi.1004571) which show that a Notch (NICD) gain-of-function together with a p53 loss-of-function prevent reaching a stable apoptotic phenotype.

First, we convert the bioQM model to MaBoSS:

```
[ ]: wt_sim = biolqm.to_maboss(lqm)
```

The variable `wt_sim` is a Python object that gathers both the Boolean network rules and the settings for the simulations, including the transition rates.

### Simulation setup

The stochastic simulation of Boolean networks with MaBoSS requires the specification of several parameters.

#### Initial states

First, a distribution of initial states must be specified: each simulation then starts from a state sampled from this distribution. The distribution is determined by assigning a probability to start in state 0 or in state 1 to each node. By default, a node has a probability 1 to start in state 0.

The `maboss` Python library provides widgets to ease the assignment of this initial distribution. The following code enables the definition of a distribution of initial states with all nodes at 0, but `DNADamage` and `ECMicroenv` with equiprobable 0 and 1 values. After pressing "OK", the notebook cell will be replaced by the actual Python call resulting in equal probabilities for these two nodes to start in active or inactive states.

```
[ ]: maboss.wg_set_istate(wt_sim)

[ ]: #maboss.wg_set_istate(wt_sim)
maboss.set_nodes_istate(wt_sim, ["DNADamage", "ECMicroenv"],
                        [0.5, 0.5])
```

#### Output nodes

Using MaBoSS, we can focus on the output nodes and ignore the other nodes, which enable us to identify the corresponding phenotypes. This can be done using the following code:

## PRACTICE

- Jupyter training link
- Rmarkdown training link