Introduction to the Simulation of Recombinant Protein Expression: Python and Jupyter Notebook Basics & Biological Background Information

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The simulation (abbr. BioLabSim) is a typical biotechnological project whose experiments were imitated. The aim is to optimise the expression of a protein in a bacterium. To do this, simulated experiments must be carried out. First, the production strain will be characterised by temperature and biomass. Then, the correct promoter sequence must be designed and cloned. Finally, the production must be above a certain limit in order to be economically viable. This simulates some important data and decisions in biotechnology.

BioLabSim Jupyter Notebook

The program is based on a Python Jupyter Notebook in which Python program code and text/images are combined. The main page to work on, which should also be loaded automatically, is 1-Laboratory.ipynb. You just have to work through it from top to bottom and adjust the code cells in such a way that the simulations are successful.

The Notebooks are composed of a sequence of cells that can be either text or python code cells to be run. Code cells have a grey background and after execution the output is shown directly beneath. A blue stripe on the left edge of the screen marks the currently active cell. To activate a cell below or above, use the arrow down and up keys in Command mode.

Code cells can be edited and executed multiple times. Next to the code cells in the upper left corner the status of the cell is displayed in square brackets. If you have not executed a cell yet, the brackets are empty. If the computer is currently executing the code, an small star appears there. If the cell has been executed, a number corresponding to the execution order of the cells is shown.

More detailed information on how to use Jupyter Notebooks are given below in the Jupyter Notebook Cheat Sheet, which you will also find in the “Python and Jupyter Notebook basics” folder.

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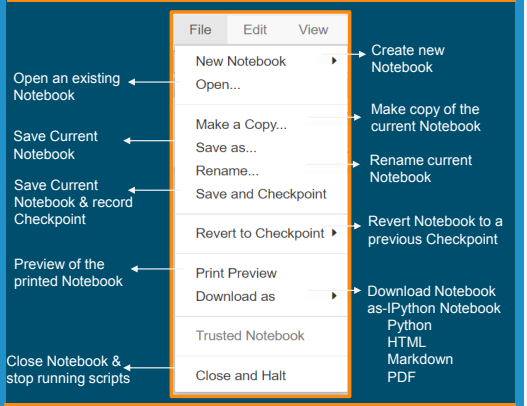
JUPYTER NOTEBOOK CHEAT SHEET

Learn PYTHON from experts at https://www.edureka.co

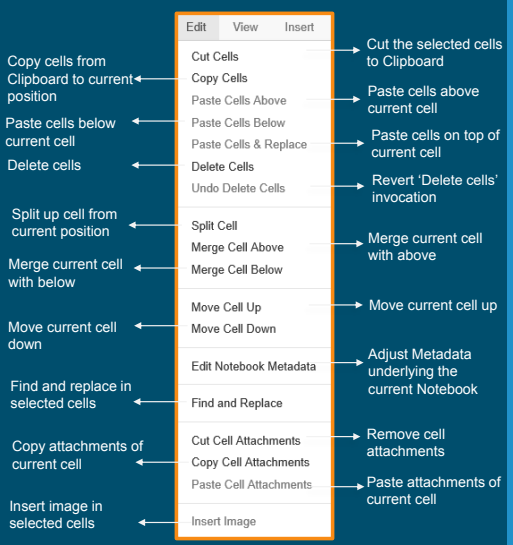
Jupyter Notebook

Jupyter Notebook is an open-source web application that allows you to create and share documents that contain live code, equations, visualizations and narrative text. It is used for data cleaning and transformation, numerical simulation, statistical modeling, data visualization, machine learning, and much more.

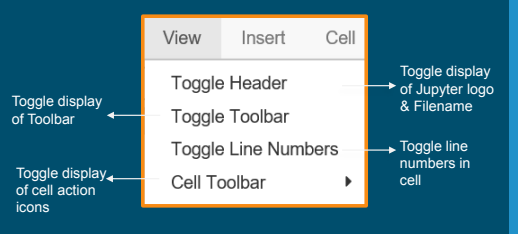
Saving/Loading Notebook



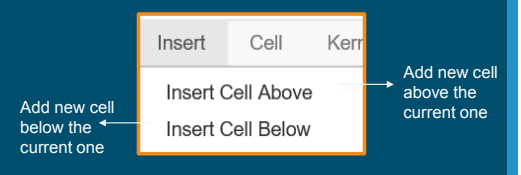
Edit Cells



View Cells



Insert Cells



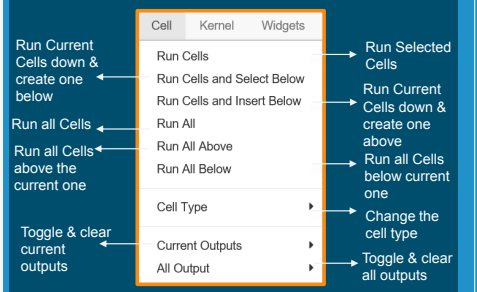
Keyboard Shortcuts

Command	Description
enter	enter edit mode
Command + a; Command + c; Command + v	select all; copy; paste
Command + z; Command + y	undo; redo
Command + s	save and checkpoint
Command + b; Command + a	insert cell below; insert cell above
Shift + Enter	run cell, select below
Shift + m	merge cells
Command +]; Command + [	indent; dedent
Ctrl + Enter	run cell
Option + Return	run cell, insert cell below
Escape	enter command mode
Escape + d + d	delete selected cell
Escape + y	change cell to code
Escape + m	change cell to markdown
Escape + r	change cell to raw
Escape + 1	change cell to Heading 1
Escape + n	change cell to heading n
Escape + b	create cell below
Escape + a	Insert cell above

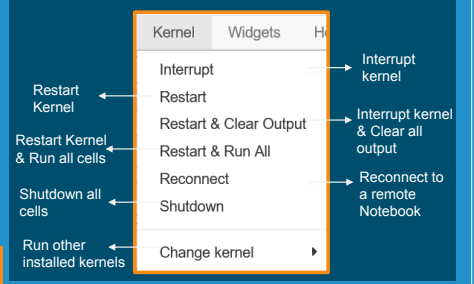
Magic Commands

Statement	Explanation	Example
%magic	Comprehensively lists and explains magic functions	%magic
%automagic	When active, enables you to call magic functions without the '%'	%automagic
%quickref	Launch IPython quick reference	%quickref
%pastebin	Pastebins lines from your current session.	%pastebin 3 18-20 ~1/1-5
%debug	Enters the interactive debugger	%debug
%hist	Print command input and output history	%hist
%pdb	Automatically enter python debugger after any exception	%pdb
%cpaste	Opens up a special prompt for manually pasting Python code for execution	%cpaste
%reset	Delete all variables and names defined in the current namespace	%reset
%run	Run a python script inside a notebook	%run script.py
%who, %who_ls, %whos	Display variables defined in the interactive namespace, with varying levels of verbosity	%who, %who_ls, %whos
%xdel	Delete a variable in the local namespace. Clear any references to that variable	%xdel variable
%time	Times a single statement	In [561]: %time method = [a for a in data if b.startswith('http')]

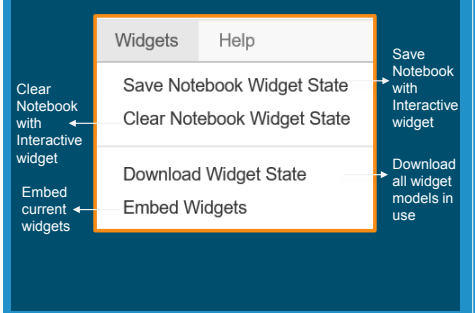
Execute Cells



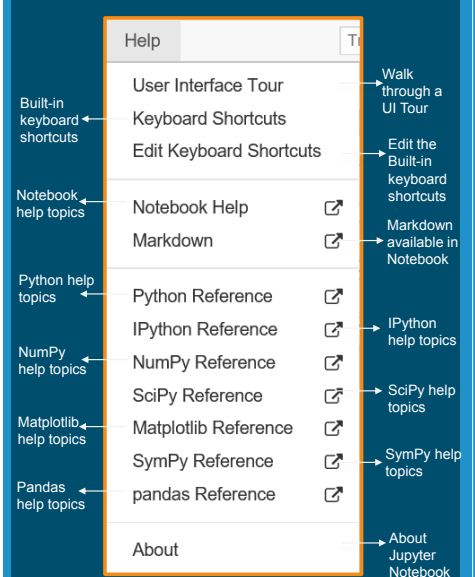
Kernel Cells



Widgets



Help



General Python Programming

To understand how the code cells need to be adapted, you first have to understand the basics of Python programming code. To do this, take a look at the following Python Basics Cheat Sheet, which you will also find in the “Python and Jupyter Notebook basics” folder.

Additionally you should know that comments to the code lines are introduced with a # and go to the end of the line.
In the code cells you will also find functions that need to be executed. It is important to know that the parameters required for the function are passed to the function in the form of a comma-separated list in round brackets directly after the function name. These parameters can be defined using variables before executing the function.

Python For Data Science *Cheat Sheet*

Python Basics

Learn More Python for Data Science Interactively at www.datacamp.com

Variables and Data Types

Variable Assignment

```
>>> x=5
>>> x
5
```

Calculations With Variables

```
>>> x+2
7
>>> x-2
3
>>> x*2
10
>>> x**2
25
>>> x%2
1
>>> x/float(2)
2.5
```

Sum of two variables
Subtraction of two variables
Multiplication of two variables
Exponentiation of a variable
Remainder of a variable
Division of a variable

Types and Type Conversion

```
str()    '5', '3.45', 'True'    Variables to strings
int()    5, 3, 1                Variables to integers
float()  5.0, 1.0               Variables to floats
bool()   True, True, True       Variables to booleans
```

Asking For Help

```
>>> help(str)
```

Lists

Also see NumPy Arrays

```
>>> a = 'is'
>>> b = 'nice'
>>> my_list = ['my', 'list', a, b]
>>> my_list2 = [[4,5,6,7], [3,4,5,6]]
```

Selecting List Elements

Index starts at 0

Subset

```
>>> my_list[1]
>>> my_list[-3]
```

Select item at index 1
Select 3rd last item

Slice

```
>>> my_list[1:3]
>>> my_list[1:]
>>> my_list[:3]
>>> my_list[:]
```

Select items at index 1 and 2
Select items after index 0
Select items before index 3
Copy my_list

Subset Lists of Lists

```
>>> my_list2[1][0]
>>> my_list2[1][:2]
```

my_list[list][itemOfList]

List Operations

```
>>> my_list + my_list
['my', 'list', 'is', 'nice', 'my', 'list', 'is', 'nice']
>>> my_list * 2
['my', 'list', 'is', 'nice', 'my', 'list', 'is', 'nice']
>>> my_list2 > 4
True
```

List Methods

```
>>> my_list.index(a)
>>> my_list.count(a)
>>> my_list.append('!')
>>> my_list.remove('!')
>>> del(my_list[0:1])
>>> my_list.reverse()
>>> my_list.extend('!')
>>> my_list.pop(-1)
>>> my_list.insert(0,'!')
>>> my_list.sort()
```

Get the index of an item
Count an item
Append an item at a time
Remove an item
Remove an item
Reverse the list
Append an item
Remove an item
Insert an item
Sort the list

Strings

```
>>> my_string = 'thisStringIsAwesome'
>>> my_string
'thisStringIsAwesome'
```

String Operations

```
>>> my_string * 2
'thisStringIsAwesomethisStringIsAwesome'
>>> my_string + 'Innit'
'thisStringIsAwesomeInnit'
>>> 'm' in my_string
True
```

String Operations

Index starts at 0

```
>>> my_string[3]
>>> my_string[4:9]
```

String Methods

```
>>> my_string.upper()
>>> my_string.lower()
>>> my_string.count('w')
>>> my_string.replace('e', 'i')
>>> my_string.strip()
```

String to uppercase
String to lowercase
Count String elements
Replace String elements
Strip whitespaces

Libraries

Import libraries

```
>>> import numpy
>>> import numpy as np
```

Selective import

```
>>> from math import pi
```

pandas — Data analysis
scikit-learn — Machine learning
NumPy — Scientific computing
matplotlib — 2D plotting

Install Python

ANACONDA — Leading open data science platform powered by Python
spyder — Free IDE that is included with Anaconda
jupyter — Create and share documents with live code, visualizations, text, ...

Numpy Arrays

Also see Lists

```
>>> my_list = [1, 2, 3, 4]
>>> my_array = np.array(my_list)
>>> my_2darray = np.array([[1,2,3],[4,5,6]])
```

Selecting Numpy Array Elements

Index starts at 0

Subset

```
>>> my_array[1]
2
```

Select item at index 1

Slice

```
>>> my_array[0:2]
array([1, 2])
```

Select items at index 0 and 1

Subset 2D Numpy arrays

```
>>> my_2darray[:,0]
array([1, 4])
```

my_2darray[rows, columns]

Numpy Array Operations

```
>>> my_array > 3
array([False, False, False,  True], dtype=bool)
>>> my_array * 2
array([2, 4, 6, 8])
>>> my_array + np.array([5, 6, 7, 8])
array([6, 8, 10, 12])
```

Numpy Array Functions

```
>>> my_array.shape
>>> np.append(other_array)
>>> np.insert(my_array, 1, 5)
>>> np.delete(my_array,[1])
>>> np.mean(my_array)
>>> np.median(my_array)
>>> my_array.corrcoef()
>>> np.std(my_array)
```

Get the dimensions of the array
Append items to an array
Insert items in an array
Delete items in an array
Mean of the array
Median of the array
Correlation coefficient
Standard deviation

BioLabSim – Biological Background Information

During the simulation you have to determine some parameters in different experiments, so that in the end the simulation is successful.

This includes the optimal growth temperature of your strain. It will be randomly initiated by the system based on the common temperature boundaries of mesophilic microorganisms. Identify this temperature range using the illustrated primer of the book “Biotechnology” from the year 2016 in the “Biological Background Information” folder.

Another task will be the design and cloning of the correct promoter sequence. A template will be given which serves as an aid for the creation of promoter sequences that meet the conditions for successfull promoter design. But you have to identify some hidden bases. Two important areas in the sequence to be identified are the recognition sequences that are responsible for gene expression. You can find out the optimal recognition sequences with the help of the paper “Bacterial sigma factors and anti-sigma factors” in the “Biological Background Information” folder. In order to perform a successful cloning, you have to design a suitable primer for each promoter. In addition, a melting temperature matching the primer sequence must be used. You can calculate the melting temperatures with the help of some formulas which you will find in the PDF-document called “Formulas for MW and TM calculation” in the “Biological Background Information” folder.