1 Tutorial: Running Monoids in Jupyter Notebook with Python 3.0 and SageMath for End-Product Inhibition Cases

Author: Marco Polo Castillo-Villalba.

Step 1: Install a Jupyter Notebook Platform

Follow the steps below based on your operating system (Windows/macOS/Linux):

- 1. Visit:https://www.anaconda.com/products/distribution
- 2. Download the appropriate installer:
- Windows: .exe
- macOS: .pkg
- Linux: .sh
- 3. Run the installer and follow the setup instructions (default settings are recommended).
- 4. After installation:
- Open Anaconda Navigator and click "Launch" under Jupyter Notebook, OR
- Open a terminal (or Anaconda Prompt) and run: jupyter notebook. On Ubuntu: jupyter-notebook.

Step 2: Follow the Screenshots to Run Monoids for End-Product Inhibition Cases

Note: The script supports monoid generation for cones of dimension n = 1 up to n = 9. Use the correct filenames for each case. For example: Cone3n_1.txt, Cone3n_2.txt, ..., Cone9n_10.txt.

Note: To concatenate all the individual output files into one, use the following command format in Linux:

```
cat *_TF_DNA31.sage >> OUT31_TF_DNAsage.txt
```

Replace 31 with the corresponding number for your case. For n=4, you would run:

```
cat *_TF_DNA41.sage >> OUT41_TF_DNAsage.txt
cat *_TF_DNA42.sage >> OUT42_TF_DNAsage.txt
cat *_TF_DNA43.sage >> OUT43_TF_DNAsage.txt
cat *_TF_DNA44.sage >> OUT44_TF_DNAsage.txt
cat *_TF_DNA45.sage >> OUT45_TF_DNAsage.txt
```

Case for the length of the pathway n=7. Allosteric system for end-product inhibition (lysine-aspartate).

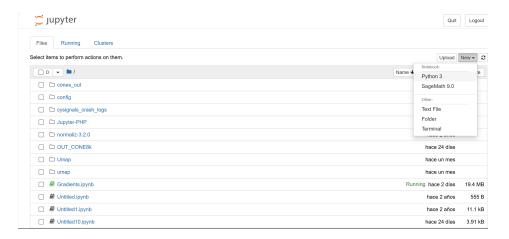


Figure 1: Open a new notebook using Python 3.

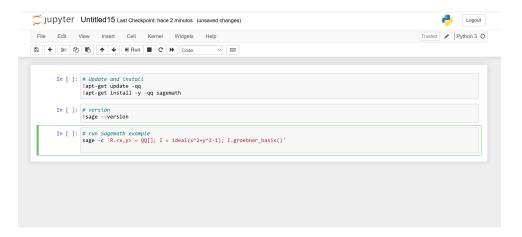


Figure 2: Install the platform needed to run algorithms in computational algebraic geometry. For computing monoid generators, copy and paste the code shown in this figure into your notebook.

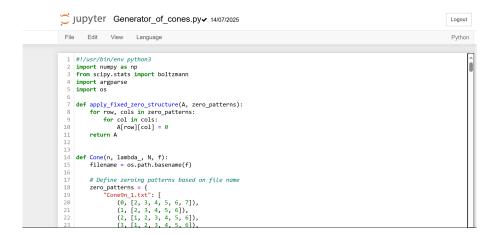


Figure 3: Open the script file <code>Generator_of_cones.py</code>, which is available in the GitHub repository. Copy and paste it into a new Python notebook. You can wirte the Linux line: python3 <code>Generator_of_cones.py</code> -n 500 -f <code>Cone3n_1.txt</code>

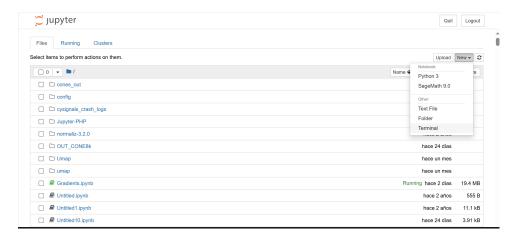


Figure 4: Once SageMath version 9.0 is installed, open a new notebook in SageMath.

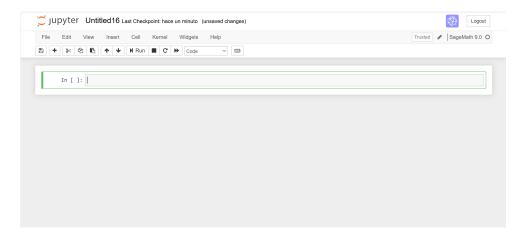


Figure 5: A new SageMath notebook will open. Leave it open; you'll run a script in this notebook shortly.

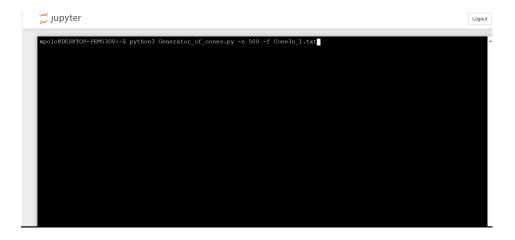


Figure 6: Open a new terminal in Jupyter. Type the command shown in the figure. File names must follow the naming convention: $Cone3n_1.txt$, $Cone3n_2.txt$, ..., $Cone7n_8.txt$, depending on the length n of the pathways. The -n 500 option generates 500 random matrices using the Boltzmann distribution.

```
[0. 0. 0. 0.]

Matrix 498:

[[0. 0. 0. 0.]

[0. 0. 0. 0.]

[0. 0. 0. 0.]

[0. 0. 0. 0.]

[0. 0. 0. 0.]

[0. 0. 0. 0.]

[0. 0. 0. 0.]

[0. 0. 0. 0.]

[0. 0. 0. 0.]

[0. 0. 0. 0.]

[0. 0. 0. 0.]

[0. 0. 0. 0.]

[0. 0. 0. 0.]

[0. 0. 0. 0.]

[0. 0. 0. 0.]

[0. 0. 0. 0.]

[0. 0. 0. 0.]

[0. 0. 0. 0.]

[0. 0. 0. 0.]
```

Figure 7: After generating 500 random matrices, save them in a single file using the command shown. The output file in this case is OUT31_TF_DNAsage.txt.

💢 jupyter	Quit	Logout
□ □ 0011_ICS	nace 2 anos	0.8
□ □ OUT2_TF_DNA.txt	hace 2 años	422 kB
□ □ OUT2_TF_DNA.txt:Zone.ldentifier	hace 2 años	242 B
□ □ OUT2_TF_DNAsage.txt	hace 17 días	28.4 kB
OUT31_TF_DNAsage.txt	hace unos segundos	36.9 kB
□ □ OUT41_TF_DNAsage.txt	hace 10 días	42.9 kB
□ □ OUT42_TF_DNAsage.txt	hace 10 días	35.4 kB
□ □ OUT44_TF_DNAsage.txt	hace 9 días	35.4 kB
□ □ OUT61_TF_DNAsage.txt	hace 13 días	54.9 kB
□ □ OUT62_TF_DNAsage.txt	hace 10 días	44.4 kB
□ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □	hace 14 días	10 1 kR

Figure 8: You can verify the saved output file in the Jupyter file tree as shown.

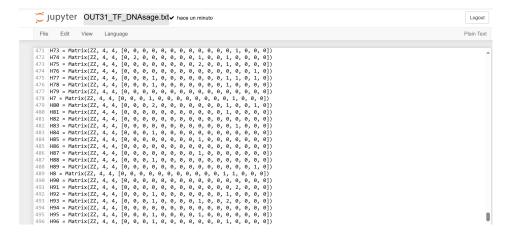


Figure 9: The content of the output file should appear as shown. These files are formatted for execution in SageMath.

```
| Logout | File | Edit | View | Insert | Cell | Kernel | Widgets | Help | Trusted | SageMath 9.0 | Code | SageMath 9.0 | SageM
```

Figure 10: Return to the SageMath notebook left open in Figure 5. Copy and paste the script from the file Sagemathscrpt.txt (available in the GitHub repository). Make sure to set the filename at the beginning of the script (e.g., OUT31_TF_DNAsage.txt).

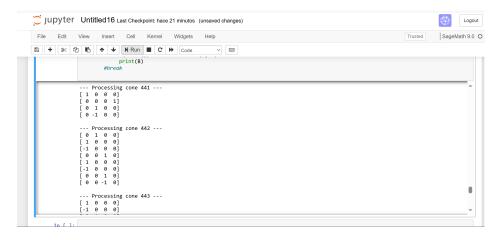


Figure 11: After pasting the script into the notebook, run it. The output will be 500 matrix representations of monoids for the selected pathway length n.



Figure 12: You only write in new terminal on you Jupyter-Notebook the line in linux: python3 Generator_of_cones.py -n 500 -f Cone $7n_1$ 1.txt



Figure 13: After write the following liux line to get your files in an only file: cat *_TF_DNA71.sage >> OUT71_TF_DNAsage.txt



Figure 14: You can visualize this file in your environment path on Jupyter platform.

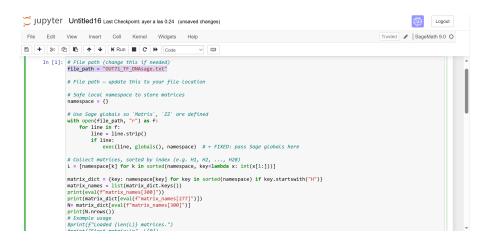


Figure 15: Now, to execute the script for monoid on Sagemath platform. Write correctly the name of you out file, in this case: OUT71_TF_DNAsage.txt



Figure 16: Run the script and the processing of the first matrices will be visualized on your screen.

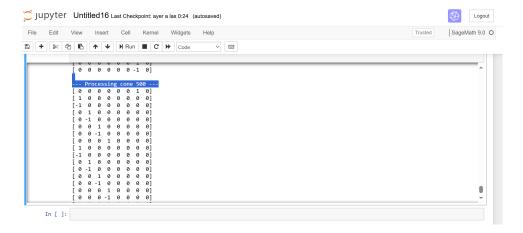


Figure 17: Finally, if you script run correctly, it will be visualized the last matrix, in this for n = 500. You can change this number of simulations. Only consider the RAM on you device.

2 Technical considerations about this pipeline.

Important considerations of this pipeline: You can run the complete pipeline for genotype arithmetic via the Jupyter Notebooks provided in the following [GitHub repository link]. Here, there is a tutorial to run examples to a different pathway length with n = 3, 4, 5, 6, 7, 8, 9. An important remark is that the families of orthogonal cones used in the simulations have row lattice-vectors that are mutually orthogonal. You can always transform a face of any of these cones through a linear transformation. Therefore, from the 500 simulated matrices, you can select a subset of lattice-vectors that form an identity matrix. This identity matrix can then be permuted freely, since matrix permutations are also linear transformations. These facts are supported by two key theorems used in our methodology: Birkhoff's Theorem and the theorem related to magic squares (i.e., matrices whose rows and columns all sum to the same value). These theorems state that every doubly stochastic matrix can be expressed as a convex combination of permutation matrices; see [1], [2]. Based on these results, we justify the matrices presented in our application example in Table 1. Using these principles, the permuted identity matrices shown in Table 1 can be derived.

Note: The 5 step of the pipline is calculated by hand in the last row in Table 1. The constraints are calculated according to the formula given in (2).

```
Permutation of rows \sim

\begin{vmatrix}
0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0
\end{vmatrix}

0 \quad 0 \quad 1 \quad 0 \quad 0 \quad 0 \quad 0 \quad 0
0 \ 0 \ 0 \ 1
  1 \quad 0 \quad 0 \quad 0 \quad 0 \quad 0
0 0
                                              0 0 0
                                                                    0
            0
               0
      0
                  0
                     1
                                                                1
      0
         0
            0
0 0 1 0 0 0 0 0
0 0 0
                                              0 0 0
0
  0 \quad 0
        0
            0
                  0
                     1
                                                                    0
   1 \ 0 \ 0 \ 0 \ 0 \ 0
Permutation of rows, \tilde{\phantom{a}}
\begin{bmatrix}
0 & 0 & 1 & 0 & 0 \\
0 & 0 & 0 & 1 & 0 \\
0 & 0 & 0 & 0 & 1
\end{bmatrix}
                     0
                      0
                      0
                                              0 0 0
                      1
                                              1 0 0
0 \quad 0
0 0 0 0 0 0 0
                     1
                                              0 0 0 0
                                              0 0 0
0 0 0 0
```

By linear transformation such as permutation in rows and transpositions of columns and rwos. It produces the first matrix in the fourth column (Table 1). Finally, we sum the permuted matrices, therefore, the total Gene Matrix interaction is:

$$M(Total) = \begin{pmatrix} 3 & 1 & 1 & 1 & 0 & 0 & 1 & 1* \\ 1 & 4 & 3 & 0 & 0 & 0 & 0 & 0* \\ 0 & 3 & 4 & 0 & 1 & 0 & 0 & 0 \\ 2 & 0 & 0 & 5 & 0 & 1 & 0 & 0* \\ 0 & 0 & 0 & 1 & 6 & 1 & 0 & 0 \\ 1 & 0 & 0 & 0 & 1 & 6 & 0 & 0* \\ 1 & 0 & 0 & 0 & 0 & 0 & 7 & 0* \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 & 7* \end{pmatrix}$$

Multiply the lattice vector (1,0,0,0,0,0,-g,1), only by the marked rows in asterisk. The Genotype Arithmetic for case n=7 and in agreement formula (3), is given by:

$$3-g+1 \ge 0,$$

$$1 > 0,$$

 $2 > 0,$
 $1 > 0,$
 $1 - 7g \ge 0,$
 $7 > 0.$

We summarize all these inequalities. $16 - 8g \ge 0$, implies. $\mathbf{g} = 2.0$.

2.1 Example for length of the pathway, case n=3.

You only need to write in new terminal on Jupyter, the following instruction, Fig 18.

Once chosen, the cones 26 and 27. You can see that the yellow rows conform to the identity matrix with size 4x4. As is shown below:

$$\begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \text{ Permuting rows, 1 with 2} \begin{pmatrix} 0 & 1 & 0 & 0 \\ 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix}$$

$$\begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \text{ Permuting rows, 1-2 and 2-3} \begin{pmatrix} 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix}$$

$$\begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \text{ Permuting rows, 1-2, 2-3, 3-4} \begin{pmatrix} 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \\ 1 & 0 & 0 & 0 \end{pmatrix}$$

$$\begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \text{ Permuting rows, 1 with 2} \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix}$$

The total sum of these matrices is given by the total gene matrix interaction:

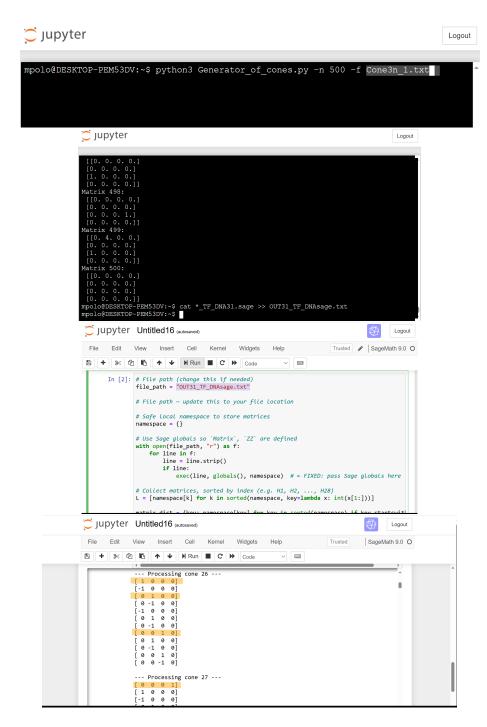


Figure 18: Generation of random orthogonal case for file name: Cone3n_1.txt. Generation of output file with name: OUT31_TF_DNAsage.txt. We write the file name, OUT31_TF_DNAsage.txt in the top of script: Sagemathscript.txt and Run this script. Finally it will be visible 500 generated random matrices. We chose the cones 26 and 27.

$$M(Total) = \begin{pmatrix} 2 & 2 & 0 & 0* \\ 1 & 0 & 3 & 0 \\ 1 & 1 & 1 & 1* \\ 1 & 0 & 0 & 3* \end{pmatrix}$$

We multiply the informative lattice vector (1,0,-g,1) row by row, only by the rows in asterisk, and hence.

The Genotype Arithmetic is given by:

$$(2,2,0,0) * (1,0,-g,1) = 2 \ge 0,$$

 $(1,1,1,1) * (1,0,-g,1) = 1 - g + 1 \ge 0,$
 $(1,0,0,3) * (1,0,-g,1) = 1 + 3 \ge 0,$

Add all the inequalities. It yields: $8 - g \ge 0$, $\mathbf{g} \le \mathbf{8}$. Therefore, we take $\mathbf{g} = \mathbf{8}$.

References

- [1] Cox D, Little J, O'Shea D. Ideals, varieties, and algorithms: an introduction to computational geometry and commutative algebra. 2nd ed. Springer; 2004.
- [2] Brualdi RA. Combinatorial matrix classes. Cambridge University Press; 2010. Available from: https://doi.org/10.1017/CBO9780511721182.
- [3] Kluyver, T., Ragan-Kelley, B., Fernando P'erez, Granger, B., Bussonnier, M., Frederic, J., ... Willing, C. (2016). Jupyter Notebooks a publishing format for reproducible computational workflows. In F. Loizides B. Schmidt (Eds.), Positioning and Power in Academic Publishing: Players, Agents and Agendas (pp. 87–90).
- [4] William Stein and David Joyner. SAGE: System for Algebra and Geometry Experimentation. ACM SIGSAM Bulletin, volume 39, number 2, pages 61–64, 2005.