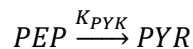
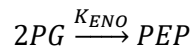
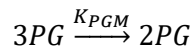
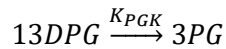
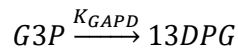
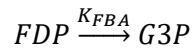
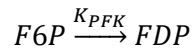
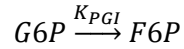
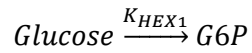


## Homework 1: Numerical Analysis of Core Glycolysis Network

Consider the core glycolysis pathway of human metabolism, consisting of the following representative enzymatic reactions:



The mass balance equation for each metabolite can be described as follows:

$$\frac{dX}{dt} = S \cdot K \cdot X,$$

where:

- $X$  is the vector of metabolite concentrations.
- $S$  is the stoichiometric matrix derived from the reaction scheme.
- $K$  is the kinetic matrix representing enzyme-catalyzed reaction rates.

When the system reaches steady state, the metabolite concentrations remain constant, leading to  $dX/dt = 0$ . Therefore, the steady-state concentrations are determined by solving the linear system  $S \cdot K \cdot X = 0$ .

Note1: We assume that each reaction follows linear kinetics (i.e.,  $v_i = k_i \cdot [X]$ ), which is why the kinetic matrix  $K$  is diagonal and constant. Consequently, the system  $dX/dt = S \cdot K \cdot X$  is linear in the metabolite concentrations.

Note2: Because  $S \cdot K \cdot X = 0$  is underdetermined in its raw form, it will not yield a unique solution without additional constraints on the metabolite concentrations.

## Questions

1. Construct and display the stoichiometric matrix by following this methodology:

- Each reaction corresponds to a column of the matrix.
- Each metabolite corresponds to a row of the matrix.
- For metabolites acting as reactants, add -1 in the corresponding cell.
- For metabolites acting as products, add +1 in the corresponding cell.
- If the metabolite does not participate in the reaction, the corresponding cell value is 0.

Since there are 10 metabolites and 9 reactions, your matrix should be 10x9.

In the stoichiometric matrix S, row 1 corresponds to Glucose, row 2 to G6P, row 3 to F6P, ..., row 10 to PYR. Keep this row labeling consistent with any further usage (e.g., in matrix A).

**!!! However, after you construct the S matrix, for your matrix to respect the mass balances, you must remove the rows regarding the boundary metabolites Glucose and PYR (1<sup>st</sup> and last row). After this modification, your new S matrix is of 8x9 size.**

2. Construct and display the kinetic matrix K, given the following reaction rates (mM/s):

$K_{HEX1}$	$K_{PGI}$	$K_{PFK}$	$K_{FBA}$	$K_{GAPD}$	$K_{PGK}$	$K_{PGM}$	$K_{ENO}$	$K_{PYK}$
0.3	0.4	0.3	0.1	0.8	0.7	0.6	0.6	0.5

The K matrix is an **9x9 diagonal matrix** with the corresponding kinetic parameters from the table above.

3. Initially, formulate the linear algebraic system  $Ax = b$  as follows:

- Matrix A is the product  $S \cdot K$  (size 8x9).
- Vector b is initially a zero vector (size 8x1).
- Vector x is the metabolite concentrations as follows:

$$x = \begin{bmatrix} \text{Glucose} \\ \text{G6P} \\ \text{F6P} \\ \text{FDP} \\ \text{G3P} \\ \text{13DPG} \\ \text{3PG} \\ \text{2PG} \\ \text{PEP} \end{bmatrix}$$

Since the linear system is underdetermined, we must include an additional constraint to obtain a unique solution. The constraint is the information that the concentration of glucose entering the pathway is 2 mM. To include the constraint:

- **We must add an extra row in matrix A corresponding to glucose.** This new row has a value of 1 in the position of A matrix that is multiplied with the glucose concentration, while the rest of the positions are zeros. At the end of this step the new size of A matrix is **9x9**. (!!! Be careful to add the value 1 in the correct position)
- **We must add an extra row in matrix b to reflect the glucose concentration of 2 mM.** At the end of this step the new size of b vector is **9x1**. (!!! The added row of b vector should be in the same position as the added row in A matrix, for the constraint to be applied correctly)
- **Vector x remains the same.**

4. Write one function for solving linear systems using the direct method of Gauss elimination and another function for solving linear systems using the iterative method of Gauss-Seidel. Your code should return the vector  $x$ , that corresponds to the concentration of each metabolite at the steady-state.

5. Solve the Linear System of Equations  $Ax = b$  using once the direct method of Gauss elimination and once the iterative method of Gauss-Seidel. Discuss your results. Was it feasible to solve the system using a direct method? Did the iterative method that you used converge, and if yes was the solution realistic? What were the initial guesses and tolerances that you used? How different are the solutions that you acquired using the 2 different methods? Finally, solve the Linear System using the Python built-in function (no need to write your own code for this method) of the Generalized Minimal Residual Method (GMRES) How did your results and the solution time were affected?

### **Final remarks**

- You should write and execute your code in Python.
- Your solution to Homework 1 should be summarized in a single PDF or Word file, where you should report the methodology that you followed. Discuss your results and draw conclusions based on the concentration values that you observe.
- You should also provide a folder with all created Python files and all data files that your code needs to run by itself in case we need to run your code.
- Homework 1 should be delivered by Tuesday, 8th of April 2025, 23:59 through the Moodle page.
- One submission per person is expected.

Solutions are corrected and graded. The grades will be posted on the Moodle page.