

# BENG 123 Final Project

## Instructions

For this project, you are required to work **individually or in pairs** to achieve three main goals:

### Part 1: Reconstruction of the Red Blood Cell (RBC) metabolic model

Assemble a “core” metabolic model representing RBC metabolism. The provided pathway models and the hemoglobin module must be integrated into a single steady-state model.

Files for the following models have been provided:

1. Glycolysis
2. Pentose Phosphate Pathway
3. AMP Salvage Network
4. Hemoglobin

A notebook called **Assembling\_RBC\_Model\_Template.ipynb** has also been provided for this part. See the rubric below for specifics on what to display in the notebook for full points

### Part 2: Reconstruction of Enzyme Module(s)

Construct an enzyme module and integrate the enzyme module into the RBC model from Part 1. Notebooks providing the information necessary to construct the enzyme modules are available for download from Piazza.

The possible enzyme modules can be chosen from the following table:

Dehydrogenases	Kinases
Glyceraldehyde-3-phosphate dehydrogenase (GAPD)	Adenylate kinase (ADK1)
Glucose-6-phosphate dehydrogenase (G6PDH)	Phosphofructokinase (PFK)
Phosphogluconate dehydrogenase (GND)	Phosphoglycerate kinase (PGK)
L-lactate dehydrogenase (LDH_L)	Pyruvate kinase (PYK)

Note: Hexokinase (HEX1) and Glucose-6-Phosphate Isomerase (PGI) cannot be used for main enzyme, but CAN be used for extra credit.

A notebook called **Integrating\_Enzymes\_Template.ipynb** has also been provided for this part. See the rubric below for specifics on what to display in the notebook for full points.

### Part 3: Simulation Case Studies and Analysis

Perform three simulation case studies that explore the systems level regulatory effects of the enzymes. Be sure to include a driving reason behind the case study, physiologically relevant perturbations, examination of dynamic responses, and comparisons to the baseline steady state model.

A notebook called **Simulation\_Case\_Study\_Template.ipynb** has also been provided for this part. See the rubric below for specifics on what to display in the notebook for full points

## Writing the Final Report

Write up a report on your findings from the simulation case study. The final report should be a neatly compiled PDF document using 12 pt. font and single spacing. **There is a 9 figure maximum** (3 case studies with at most 3 figures per case study), so only include your most important figures in the final report. Keep figures to a reasonable size. You may include additional supportive figures in an appendix, but they will not be graded. There is no page limit, but be concise! Overwriting can get points docked, especially if incorrect information is added into the report. See the rubric below for specifics on what to include in the report to get full points.

## Project Submission Guidelines

**Read this section carefully to avoid mistakes break code and/or lose points in the submission.**

All submissions are to be .zip files with the name: **STUDENT1\_STUDENT2\_PROJECT**. This file is to be turned in through Canvas by only one of the two students. **The project deadline is 3/18/22 by 11:59 pm.**

**NO PROJECT WILL BE ACCEPTED AFTER 3/18/22 11:59 PM.**

Within the zipped folder, submissions are expected to include the following:

1. The final report saved as a single PDF file with the required sections outlined in the rubric. The report should be saved in the **final\_report** folder.
2. All figures generated that are included in the report should be saved in the **final\_report/figures** folder as .PNG or .PDF files.
3. All model files that are used in the project, included in the **models** directory.
4. All iPython notebooks utilized in the project. The following notebooks are expected:
  - a. One notebook for Part 1: Reconstruction of the RBC metabolic model. This notebook contains the code for assembling the RBC model **without** enzyme modules.
  - b. One notebook for Part 2: Reconstruction of Enzyme Module(s). This notebook contains the code for **integrating** enzyme modules into the RBC model.
  - c. All enzyme module construction. Every enzyme module should be built in a separate notebook. They should be named based on the enzyme module reconstructed in that notebook (e.g., Hexokinase built in the HEX1.ipynb notebook).
  - d. All notebooks utilized in performing case studies and generating the figures for the report.

**Any changes to these submission guidelines will be announced on Piazza and in class.**

## Extra Credit Opportunity

1. We will be giving up to a total of +3% points of extra credit to your final grade for exceptional project reports.

2. Extra credit will be determined based on quality and not quantity. There is a 9 figure maximum, but a project could receive all 3% of extra credit with fewer than 9.
3. Criteria for extra credit include:
  - a. A clear understanding of the RBC metabolic network.
  - b. A clear understanding of how your chosen enzyme module(s) behave within/affect the system.
  - c. Thoughtful selection of the case studies to elucidate network-level behaviors with strong citations to validate reasoning.
4. Any other additional enzymes (more than the one required) can add +1% per enzyme so long as the enzymes are correctly built, added to the system, and are utilized/analyzed in the simulation case studies in addition to the primary chosen enzyme. Up to **3** additional enzymes can be built for a total of **3%** extra credit points are possible.
5. **Up to 3% extra credit for a well-written, concise, and high quality report with high quality case studies. Extra enzymes can help with this, but are not required with thoughtful selection of case studies and graphical visualizations**
6. **Extra credit is determined at the discretion of instructor.**

## GRADING BREAKDOWN

The project comprises 30% of your total grade. The weighted point breakdown is as follows:

Construction of the RBC and Enzyme Modules:	10% of total grade
Final Report	20% of total grade
Extra Credit	+3% applied to final grade

Note: You may comment your code as you wish. However, coding comments **will not** affect the grading of the project.

## **MODULE - 50 TOTAL POINTS** *(prior to weighting)*

### **Part 1: Formation of RBC Model (10 points)**

1. Import the glycolysis, pentose phosphate pathway, AMP metabolism, and hemoglobin models from the provided files.
2. Form the RBC network correctly by integrating the glycolysis, pentose phosphate pathway, AMP metabolism, and hemoglobin modules. Display the correct model overview.
3. Define the steady state. Display the correct steady state flux map, PERCs values, and the equilibrium constants in an organized DataFrame.
4. Graphically verify that the model is in steady state.

### **Part 2: Enzyme Module Construction (20 points)**

5. Small metabolites are defined correctly.
6. Enzyme mechanisms are defined correctly
7. Steady state enzyme concentrations are symbolically determined correctly.
8. Numerical values for equilibrium constants are defined correctly and printed.
9. Numerical values for small metabolites are defined correctly and printed.
10. Extract and display the enzyme total equation in terms of rate constants.
11. Numerical values for rate constants are determined correctly with an optimization error less than  $1e-6$ , and displayed.
12. Steady state concentrations for module forms are calculated correctly and displayed.
13. Reconstructed enzyme module passes a quality control and assurance check.
14. Module is integrated into the RBC model to form the base model and a steady state can be obtained.

### **Part 3: Simulation Case Studies (12 points)**

15. Case study is correctly introduced.
16. Modified model is correctly set up to explore in the case study.
17. Graphical verification that the modified model can reach a steady state AND/OR perturbation is performed correctly, depending on case study.
18. Generated plots have labels and proper axis limits.

### **Notebook organization and clarity (8 points)**

19. Notebooks are organized and legible.
20. Submission is organized correctly.

## FINAL REPORT - 100 TOTAL POINTS *(prior to weighting)*

Section	Additional details	Points
Abstract	<ol style="list-style-type: none"> <li>1. What did you do?</li> <li>2. Why did you do it?</li> <li>3. How did you do it?</li> <li>4. Why does it matter?</li> </ol>	10
Introduction	<ol style="list-style-type: none"> <li>5. General description of red blood cell (RBC) model (8 pts) <ol style="list-style-type: none"> <li>a. Why are RBCs important?</li> <li>b. Brief description of subsystems.</li> <li>c. What are the methods used to analyze the RBC?</li> </ol> </li> <li>6. Description of enzymes modeled. (8 pts) <ol style="list-style-type: none"> <li>d. Key function(s) of modeled enzyme(s).</li> <li>e. Structure and regulatory mechanisms of enzyme.</li> </ol> </li> <li>7. Introduce the case studies performed. (9 pts) <ol style="list-style-type: none"> <li>f. What are the case studies?</li> <li>g. What is the driving reason behind each case study?</li> </ol> </li> </ol>	25
Methods	<ol style="list-style-type: none"> <li>8. A paragraph describe tools and algorithms used in this project. (2.5 pts)</li> <li>9. A paragraph describing the implementation of the case study and justification behind the process. (2.5 pts) <ol style="list-style-type: none"> <li>a. What did you adjust, were any assumptions made, and why is it a valid approach?</li> </ol> </li> </ol>	5
Results	<ol style="list-style-type: none"> <li>10. For each case study, characterize the dynamic responses observed with respect to the perturbation/phenomena being explored. <ol style="list-style-type: none"> <li>a. Compare/contrast the response to the baseline model.</li> <li>b. All figures need standalone captions, labels, and relevant explanations (~2-4 sentences).</li> </ol> </li> <li>11. Graphical visualization of results <ol style="list-style-type: none"> <li>a. Only show results with meaning, meaningless and/or redundant figures will lose points. A few meaningful, interesting, and well-thought out figures would be better.</li> <li>b. Be mindful of axes scales and artificial results that could be generated.</li> </ol> </li> <li>12. Just report results (e.g., numerical values, observed dynamic trends, etc.) in this section. <ol style="list-style-type: none"> <li>a. Analysis should be done in the discussion.</li> </ol> </li> <li>13. Point distribution depends on number of case studies, generated figures, and explanations.</li> </ol>	25
Discussion	<ol style="list-style-type: none"> <li>14. Explain the significance of the results (15 pts) <ol style="list-style-type: none"> <li>a. Use the baseline model as a reference.</li> </ol> </li> <li>15. Discuss the implications of the results in terms of human physiology. (10 pts)</li> <li>16. Discuss the implication of your results in a global, societal, economic, and/or environmental context. (5 pts)</li> </ol>	30
Works Cited	<ol style="list-style-type: none"> <li>17. A minimum of 10 citations utilized. <ol style="list-style-type: none"> <li>a. Citations must be used in the text to count.</li> <li>b. Any journal citation style, must be consistent.</li> </ol> </li> </ol>	5