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KEN3170_Assignment_Metabolic_Mod...
Document

This is an assignment for one of my courses, the deadline is today at midnight.
I had other assignments to work on which made me very late for this one and i don't have time to go through all the lectures and labs to learn everything.

I need you to tell me all the information there is to know and in depth about part 4 of this assignment, which is the one I will do myself.

before that, I want you to explain briefly about the first 3 parts, so i don't get lost in the part 4 explanations.

your answer should be 1/3rd about the first 3 parts, and 2/3 about the 4th part.
it should include :
what this assignment is about (goal)
the expected output of my and my teammate parts
general explanation, and in depth explanation for part 4a, 4b, and 4c

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Parta

🧠 OVERVIEW: What this assignment is about

The goal of this assignment is to **integrate gene expression data into the E. coli core metabolic model** using **COBRApy** (a Python package for constraint-based modeling) and explore how enzyme activity constraints affect **flux predictions** and **metabolic behavior**.

You will:

- **Visualize metabolic constraints** based on gene expression data.
- **Modify model constraints** to reflect those values.
- **Analyze reaction behavior** under these constraints.
- **Perform FBA** (Flux Balance Analysis) and **FVA** (Flux Variability Analysis).
- In **Part 4**, focus on **biomass production**, identifying bottlenecks, and interpreting inactive pathways.

🧩 PARTS 1–3: Summary (1/3 of the explanation)

🔹 Part 1: Visualize Maximal Reaction Activity on ESCHER Map

You load the `e_coli_core_expression.csv` data into the **non-interactive ESCHER map** and analyze it visually.

- **1a:** Check whether reaction fluxes along a linear pathway still appear equal. In theory, expression data

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does **not enforce mass balance**, so values can differ unlike FBA-predicted fluxes.

- **1b:** Identify reactions without expression data. Reasons may include:
  - Reactions not associated with any known enzyme (e.g., spontaneous reactions).
  - Transport/exchange reactions without enzyme involvement.

🔹 Part 2: Apply Constraints in COBRApy Based on Maximal Activity

You're integrating expression data into the COBRA model by modifying reaction flux bounds:

- **Reversible reactions**: bounds = `[-value, +value]`.
- **Irreversible reactions**: bounds = `[0, value]`.
- **Missing data**: leave as-is.
- **Special reactions**:
  - `EX_glc__D_e` (glucose exchange): **remove flux bound cap**.
  - `ATPM` (maintenance energy): **keep lower bound** unchanged.

Expected output: a printed table showing each reaction's new lower and upper bounds.

🔹 Part 3: Perform Flux Variability Analysis (FVA)

Using `flux_variability_analysis()`, determine **mir d max possible fluxes** for each reaction, given the constraints.

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constraints.

- **3a:** Print the min and max for each reaction.
- **3b:** Find reactions with expression constraints where **maximal flux** is not fully used.
  - Reason: **network structure**, bottlenecks, or alternative pathways.
- **3c:** Count reactions with **positive minimal flux** (must-carry flux).
  - Reason: reactions critical to biomass or energy maintenance (e.g., ATPM).

🔬 PART 4: In-Depth Explanation (2/3 of the explanation)

🧪 GOAL OF PART 4

Use the updated metabolic model (with expression constraints) to:

- **Optimize biomass production** (simulate growth).
- **Identify limiting reactions** (bottlenecks).
- **Explain inactive pathways** (even when capacity exists).

🔹 4a. Carry out an FBA optimization of biomass

✅ **What to do:**

Run the FBA using:

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Run the FBA using:

```python
solution = model.optimize()
print(solution.objective_value)
```

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This will **maximize the flux through the biomass reaction**, considering your new enzyme activity constraints.

📌 **Expected Output:**
A **single number** representing the **maximum biomass production rate** (growth rate in 1/h or similar units).

🧠 **Interpretation:**
Compare this value to the original unconstrained model (from the practical). You'll likely see a **lower biomass rate** due to the **gene expression constraints limiting some reactions**.

🔹 4b. Identify bottlenecks (reactions at their upper bound)

✅ **What to do:**
After solving for `solution`, loop through all reactions and find those where:

```python
```

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These are reactions that are fully "used" — they are at their **maximal capacity**.

Example code:

```python
for rxn in model.reactions:
    flux = solution.fluxes[rxn.id]
    if abs(flux - rxn.upper_bound) < 1e-6:
        print(f"Bottleneck: {rxn.id} at max flux {flux}")
```

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📌 **Expected Output:**
A list of **reaction IDs** that are **rate-limiting steps** in biomass production.

🧠 **Interpretation:**
These reactions are **constraining the overall metabolic throughput**. If their maximal activity were increased, biomass might improve. These are great candidates for **genetic engineering** in metabolic engineering contexts.

🔹 4c. Pick a constrained but unused reaction and explain it

✅ **What to do:**
Loop over all reactions and find **any with:**

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- A **non-zero upper bound** (from the gene expression data),
- But a **flux of exactly zero** in the FBA solution.

Example code:

```python
for rxn in model.reactions:
    flux = solution.fluxes[rxn.id]
    if flux == 0 and rxn.upper_bound > 0:
        print(f"Unused reaction with capacity: {rxn.id}")
```

Then, **pick one** and use the **ESCHER online map** to inspect the reaction's location in the network:

- Is it part of a pathway with missing inputs/outputs?
- Is it a dead-end?
- Is it part of an **alternative pathway** that's not needed under current conditions?

📌 **Expected Output:**

- One **reaction ID** (with max activity but zero flux).
- An explanation based on **network topology**.

🧠 **Interpretation:**
Some reactions are **inactive** not because they are disabled, but because **the metabolic network chooses more efficient or shorter routes**. This shows how network structure determines which reactions are used.

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✅ What You Submit

You are responsible for **Part 4**, so your final submission should include:

- **4a:** Biomass production rate value.
- **4b:** List of bottleneck reactions (with explanation).
- **4c:** One constrained but unused reaction with **network-based explanation**.

Keep your code outputs clean and include **brief written explanations** for each sub-question.

Let me know if you want me to help you **write the code** for Part 4 or test some outputs — I can walk you through it line by line.

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