Model Selection and Curation

Objective: Choose one or more metabolic models for organisms of interest. These could be single-species models that you will later combine into a community or existing multi-species models.

Tasks:

- Use COBRApy to load and inspect genome-scale metabolic models (GEMs) from databases like BiGG Models.

- Curate the models as necessary, ensuring that the GPR (gene-protein-reaction) associations are correct and complete.

- Validate the models by comparing predictions from Flux Balance Analysis (FBA) with experimental data.

2. Define Environmental Conditions

Objective: Set up the environmental parameters that will affect microbial growth and interactions in the simulation.

Tasks:

- Define the initial concentrations of substrates and other environmental factors.

- Use COBRApy to set up exchange reactions that will represent these environmental conditions.

3. Community Construction

Objective: If working with multiple species, construct a community model in COBRApy that combines individual species models.

Tasks:

- Combine models by merging them or defining interactions (e.g., metabolite cross-feeding) between them using COBRApy.

- Ensure that the community model respects the stoichiometry and mass-balance constraints for each species.

4. Dynamic Simulation with COMETS

Objective: Use COMETS to simulate how the community behaves over time under the defined conditions.

Tasks:

- Translate the curated models into a format usable by COMETS (if necessary).

- Set up spatial parameters in COMETS if modeling structured environments like biofilms.

- Run COMETS simulations over a range of time points to capture dynamics.

5. Data Analysis and Visualization

Objective: Analyze the simulation data to understand the metabolic interactions and dynamics of the community.

Tasks:

- Use Python scripts to parse and analyze output data from COMETS simulations.

- Visualize changes in metabolite concentrations, biomass, and flux distributions over time.

- Compare simulation results against experimental data for validation.

6. Sensitivity Analysis

\*\*Objective\*\*: Assess the robustness of the model predictions to parameter changes.

\*\*Tasks\*\*:

- Perform sensitivity analysis to understand the impact of various parameters on the model output.

- Use COBRApy to tweak model parameters (e.g., reaction bounds, objective coefficients) and observe the effects on simulation outcomes in COMETS.

### 7. Report Findings

\*\*Objective\*\*: Communicate the results of the simulation and their biological implications.

\*\*Tasks\*\*:

- Prepare a detailed report or presentation that covers the methods, results, and conclusions.

- Discuss the biological significance of the simulation results and how they contribute to the understanding of the microbial community.

### Example Project Idea:

\*\*Microbial Interactions in the Human Gut Microbiome\*\*: A project could involve simulating the interactions between various bacterial species in the human gut. The project would start with curating individual metabolic models for representative gut bacteria, simulating their interactions and nutrient competition within the gut environment using COMETS, and then analyzing how dietary changes (e.g., high fiber vs. high fat) could impact community composition and metabolic output (e.g., short-chain fatty acid production).

By completing such a project, you would demonstrate skills in model curation, simulation, and analysis, as well as an understanding of how these simulations can provide insights into complex biological systems.