

## Objective

The main objective of this project is to create a mathematical model for species *Pseudomonas aeruginosa* by using its known reactions and metabolites.

## Background

This project concerns the metabolism of a pathogen, i.e. *P. aeruginosa*, and its interactions with other organisms.

*P. aeruginosa* has an ability to maintain decades-long infections in the lungs of humans, due to the metabolic adaptability of its environment (Bartell et al., 2017).



This project serves in collaboration with UC San Diego hospitals regarding microbial interactions between *P. aeruginosa*, a pathogen found in the lungs of cystic fibrosis patients, and the bacterium *Bacillus subtilis*, which has been observed to kill *Pseudomonas* biofilms in hospitals. By creating models for these species, their microbial interactions can be predicted.

## References

- [Opencobra.github.io](https://opencobra.github.io). 2020. Home Page Available at: <https://opencobra.github.io/cobratoolbox/stable/>
- "Bartell, Jennifer A., et al. *Nature communications* 8.1 (2017): 1-13."
- [Bigg.ucsd.edu](http://bigg.ucsd.edu). *Bigg Models*. [online] Available at: <http://bigg.ucsd.edu/>
- [Static-content.springer.com](https://staticcontent.springer.com/esm/art%3A10.1038%2Fbnbt.1614/MediaObjects/41587_2010_BFnb1614_MOESM178_ESM.pdf). 2020. [online] Available at: [https://staticcontent.springer.com/esm/art%3A10.1038%2Fbnbt.1614/MediaObjects/41587\\_2010\\_BFnb1614\\_MOESM178\\_ESM.pdf](https://staticcontent.springer.com/esm/art%3A10.1038%2Fbnbt.1614/MediaObjects/41587_2010_BFnb1614_MOESM178_ESM.pdf)

## Methodology

Built a dictionary for *P. aeruginosa* using BiGG, a UCSD database containing information about "genome-scale metabolic network reconstructions."

BiGG Models

Curated and organized the dictionary to build a model for *P. aeruginosa* using COBRA Toolbox and MATLAB.

Perform simulations on the model through Fluid Balance Analysis (FBA), a process used to analyze constraint-based models.

FBA helps determine how an organism utilizes its metabolites and reactions that take place within it or in the extracellular matrix.

## Results

Created dictionaries for *P. aeruginosa* containing 1495 reactions and 1284 metabolites.

Abbreviation	Suggested Name	Reaction BiGG ID	Reaction BiGG name	Suggested Subsystems
rjB00270	succinate dehydrogenase	4M3QXHA	Succinate dehydrogenase	Citrate cycle (TCA cycle)
rxn06493	dihydrolypoamide dehydrogenase	4MTHACP	Dihydrolypoyl Dehydrogenase	Glyoxylate and dicarboxylate metabolism
rxn13808	assimilatory nitrite reductase	4MTRPE	Nitrate reductase	Nitrogen metabolism
rxn00623	sulfite reductase (NADPH2)	5MET3OH	Sulfite reductase	Sulfur metabolism

Table 1. Four reactions from the dictionary.

Abbreviation	Name	Suggested name
cpd02494[c]	(2,3-Dihydroxybenzoyl)adenylate	23dhba_c
cpd11475[c]	(2E)-Decenoyl-[acp]	dec2enACP_c
cpd11579[e]	ethanesulfonate	ethso3_e
cpd00109[c]	Cytochrome c3+	fcytC_c

Table 2. Four metabolites from the dictionary.

## Results

Performing simulations on our model via FBA produced valuable feedback regarding *P. aeruginosa* properties.

### Phenotypic Phase Plane Analysis

- Explains the interaction between two different reactions with varying parameters and the response variable, growth rate.

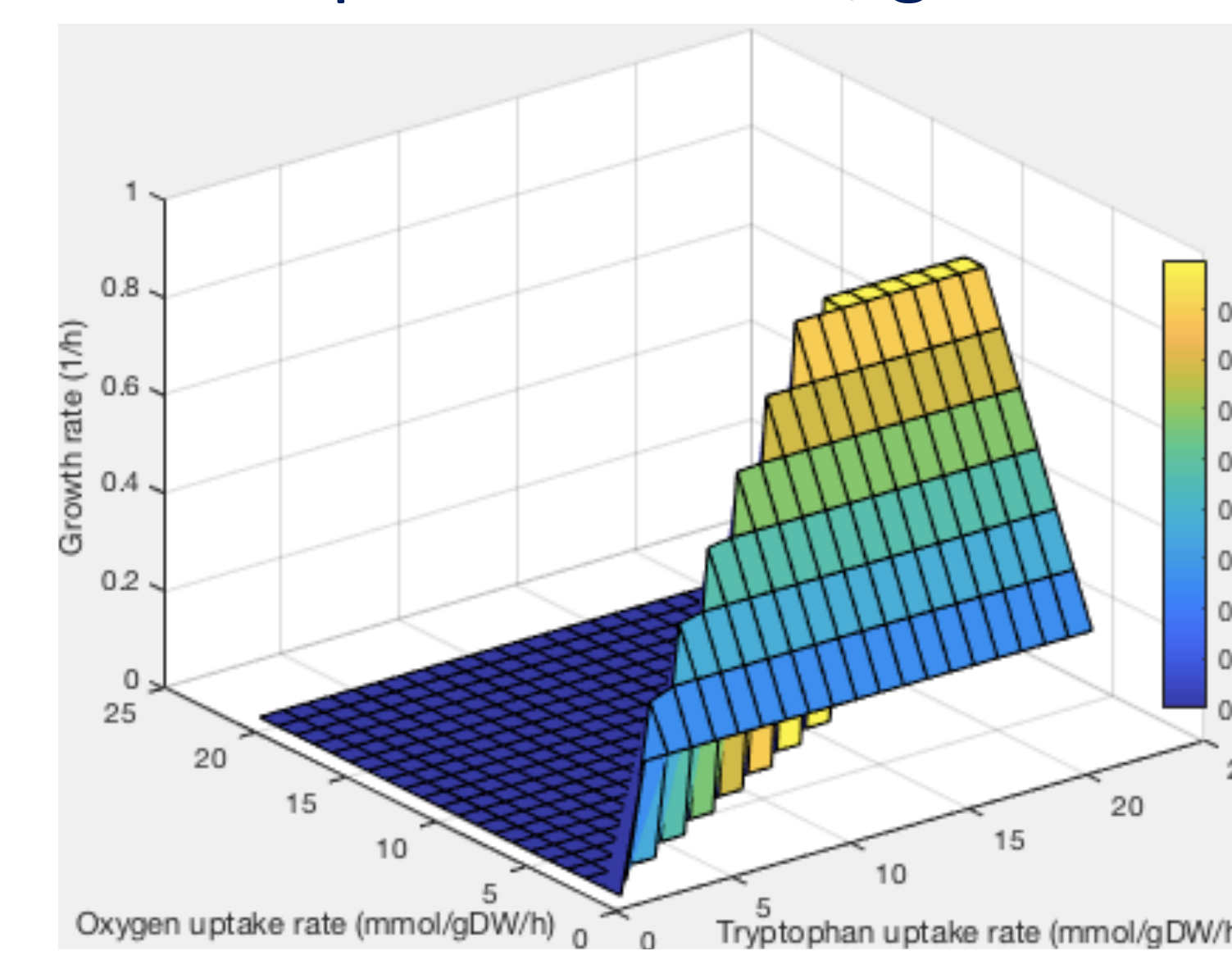


Figure 1. Oxygen and Tryptophan

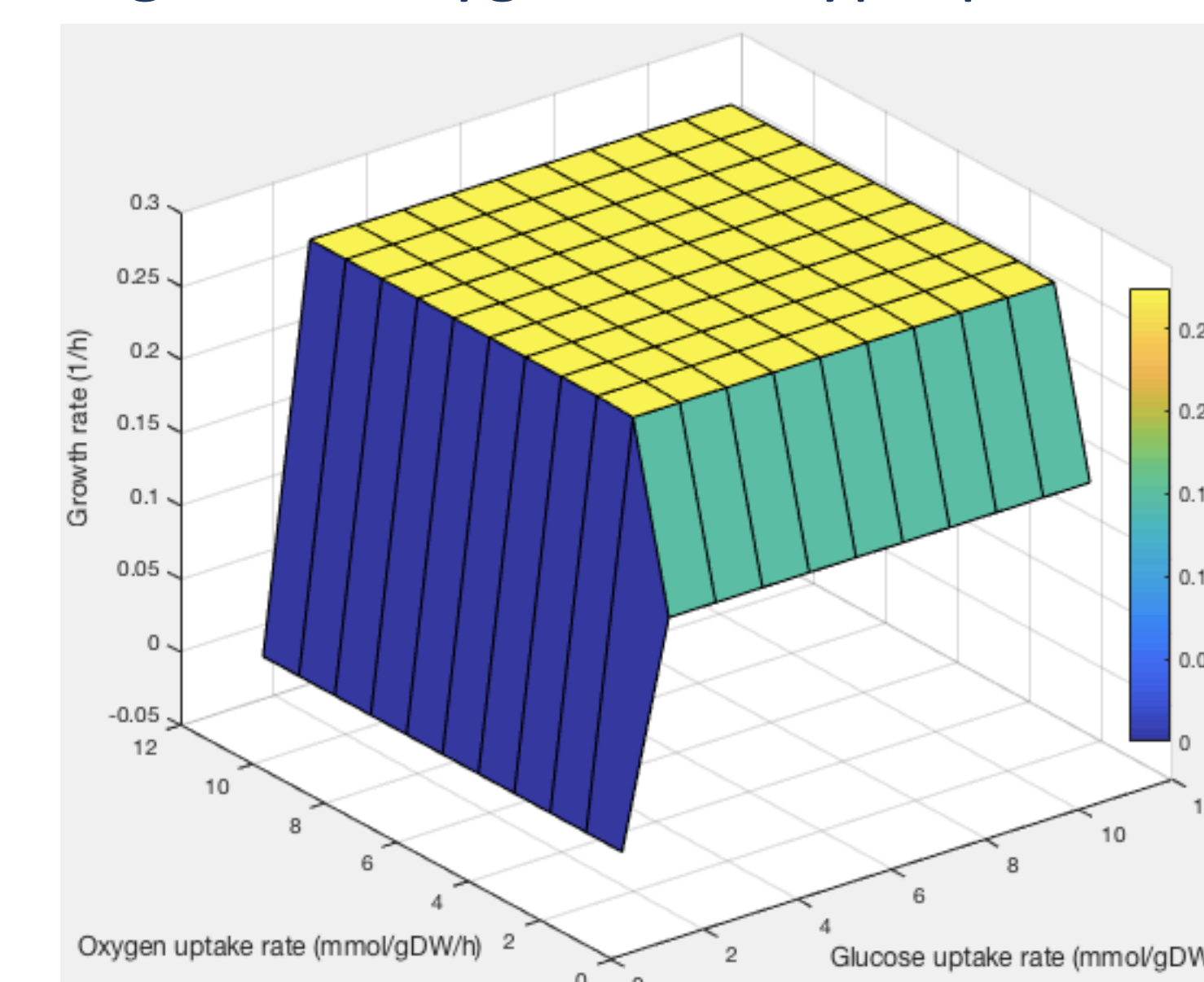


Figure 2. Oxygen and glucose

### Simulating Gene Knockouts

- By changing the reaction bounds and knocking out genes in pairs, its resulting relative growth rates can be plotted.

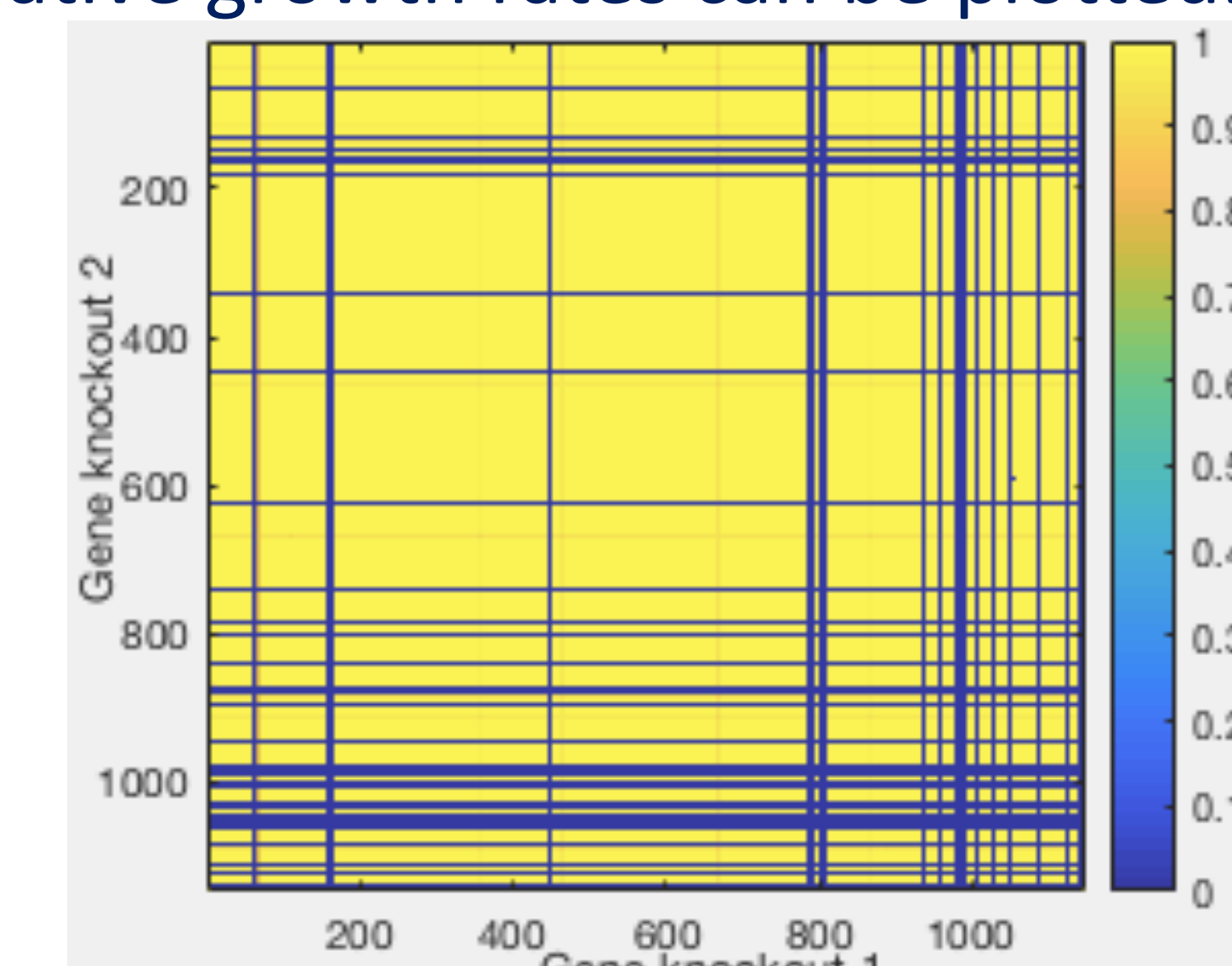


Figure 3. Gene knockouts for *P. aeruginosa*

## Results

### Model Properties

- Identifies the position of a certain pathway in a subsystem and sorts them.

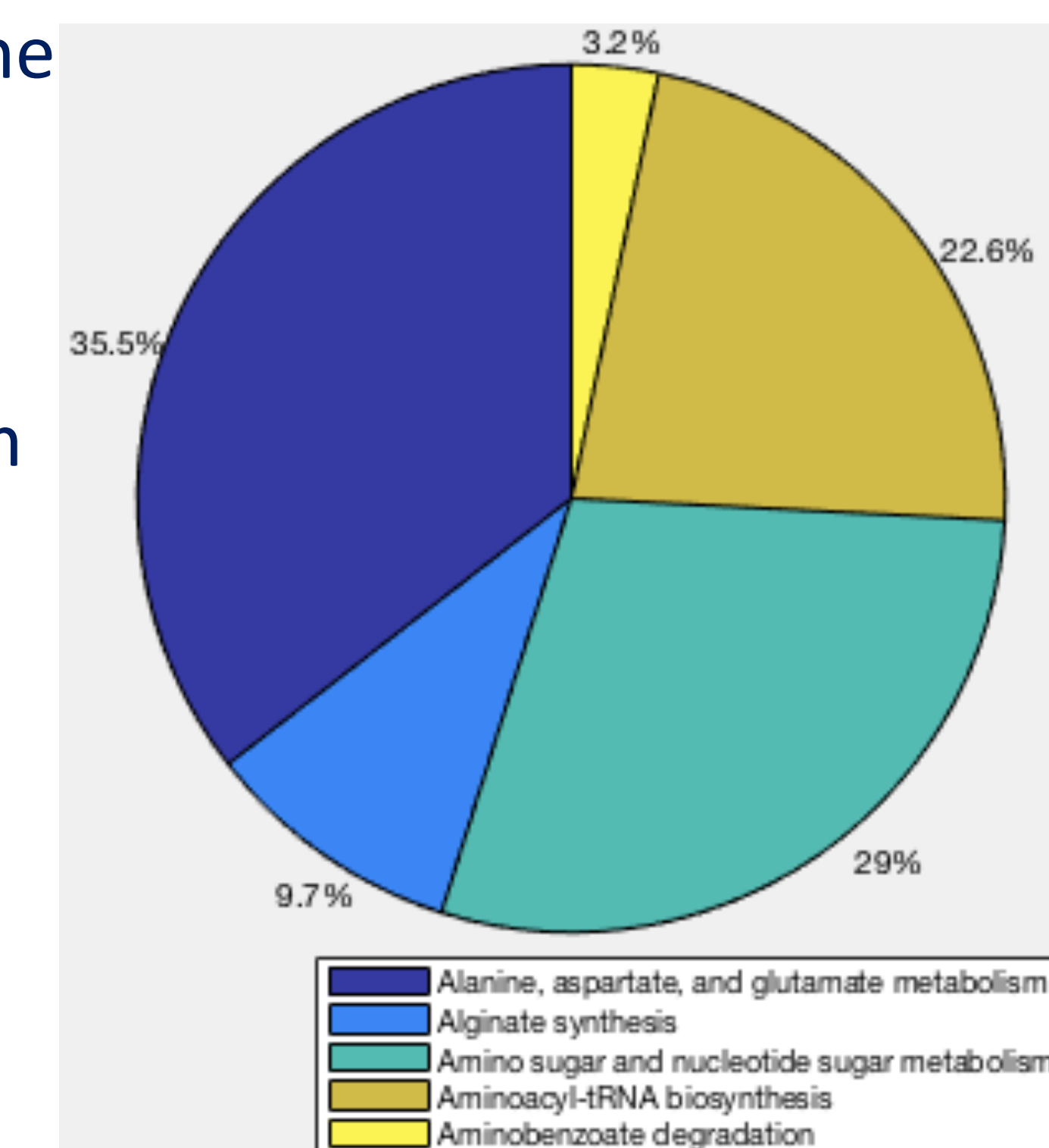


Figure 4. The first five sorted pathways.

### Topographical Features

- Shows the stoichiometry of the entire network (reaction by metabolites), where the nonzero entries are shown by dots.

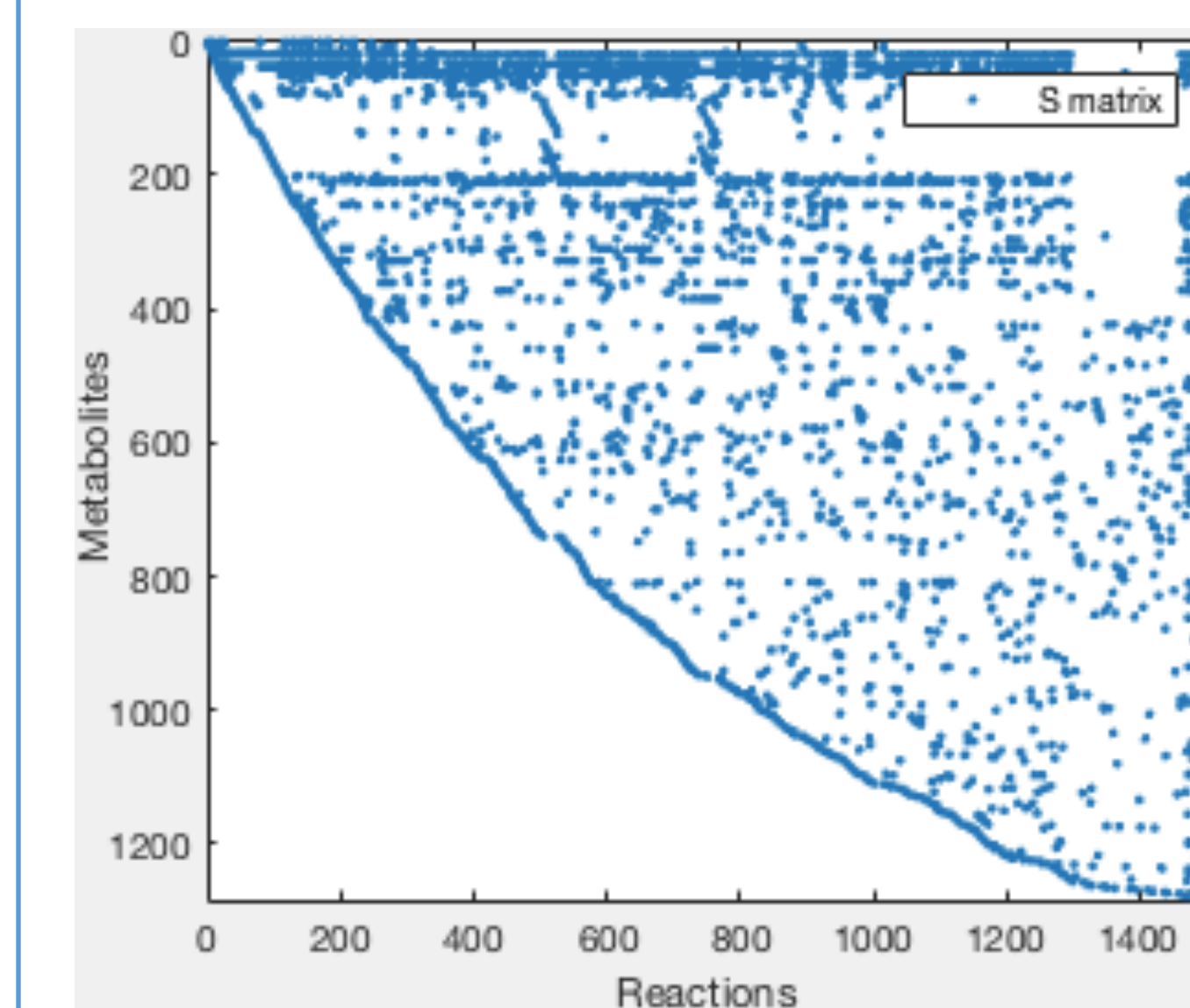


Figure 5. S matrix for *P. aeruginosa*

## Conclusions

*P. aeruginosa* PAO1 has been explored, its metabolism and reactions were used to determine its interaction with *B. subtilis*. The model *P. aeruginosa* PAO1 is now in BiGG nomenclature and ready to be part of a community model that includes *B. subtilis*. The reformatted model can accurately stimulate growth and robustness on various culture media compositions.

## Acknowledgements

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