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| ABE 30100 |
| Microbial Consortium Modeling |
| Deliverable I |

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# Project Description

## Motivation

High-level organisms such as plants and animals synthesize complex compounds with properties beneficial to humans. As such, it is important for humans to harness the power and production of these compounds. Simpler organisms such as *Escherichia coli* and *Saccharomyces cerevisiae* have been engineered to become efficient producers of other beneficial products such as insulin and ethanol. As such, researchers have looked to use these same organisms to produce more complex molecules in an efficient and cost-effective manner.

## Concept in Literature

In their 2015 *Nature Biotechnology* paper, authors Zhou, Qiao, Edgar, and Stephanopoulos found that the most effective way to produce the anti-cancer drug paclitaxel is to ferment two organisms in consortium (Figure 1).

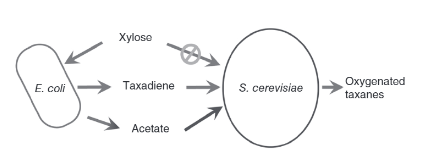


Figure 1: The mutualistic E. coli-S. cerevisiae consortium for production of paclitaxel (oxygenated taxanes) *(Zhou, Qiao, Edgar, & Stephanopoulos, 2015)*.

In this process, *E. coli* produce simple taxadiene molecules which the *S. cerevisiae* use as a scaffold around which to fold the final compound. The *E. coli* and *S. cerevisiae* also act as inhibitors upon each other such that one species does not out-compete the other. The *E. coli* consumes the carbon source xylose, which *S. cerevisiae* cannot digest, and produces acetate as a byproduct during the production of taxadiene. The acetate is toxic to the *E. coli* cells but can serve as a carbon source for the *S. cerevisiae* while it assembles the *E. coli*-produced taxadiene into paclitaxel. In addition, the authors found that the production of the final product was boosted by increasing the initial concentration of *S. cerevisiae* to prevent poisoning of the *E. coli* community with residual acetate, increasing expression of the oxygenation pathway in *S. cerevisiae* to increase production of the final product, and knocking out the oxidative phosphorylation pathway in *E. coli* which pulls Acetyl-CoA from the acetate pathway, thus drawing carbon away from the *S. cerevisiae*.

## Project Proposal

While the authors proved the concept in a lab setting, a mathematical model of the consortium was never produced. As such, I would like to model the behavior of the *S. cerevisiae-E. coli* fermentation to use xylose to produce paclitaxel as was described in the referenced paper. For simplicity, I will start by assuming that the fermentation is only composed of one *E. coli* cell and one *S. cerevisiae* cell and plan to increase the concentration of the cell types over time to reach the concentrations used in the paper.

# Model Description

## Quantitative Outputs

* Amount of paclitaxel as a function of time

## Input Parameters

* Initial concentration of xylose
* Initial concentration of *E. coli* cells
* Initial concentration of *S. cerevisiae* cells
* Initial temperature
* Initial pH

## Principles and Processes Modeled

* Conservation of mass
* Mass balances with chemical reactions
* Conservation of energy
* Fermentation
* Mass transfer
* Reaction rates
* Enzymatic reactions

# Appendix A: References

Zhou, K., Qiao, K., Edgar, S., & Stephanopoulos, G. (2015, April). Distributing a metabolic pathway among a microbial consortium enhances production of natural products. *Nature Biotechnology, 33*(4), 377-383.