## Introduction

- Curcumin is the major bioactive natural product in turmeric (*Curcuma longa*), which is commonly used as a food additive (flavor and colorant) and traditional medicine for thousands of years.
- Antioxidant[1], anti-cancer[2], anti-allergic[3], anti-inflammatory[4], and anti-Alzheimer’s[5] effects
- Current production relies on extraction of producing plants: requires large quantities of farmland and organic solvents[6]
- Microbial production represents a great alternative: saves time and materials.
- Microorganisms can be engineered to produce curcumin by incorporating curcumin biosynthetic enzymes.
- Testing various parameters in lab experiments is time-consuming and labor-intensive.
- This work aims to establish a computer model to simulate the production of curcumin in *Escherichia coli*.

## Results

- An average of 100 simulations resulted in 486.565 µM curcumin yield.
- C3H may be the limiting enzyme due to rate of p-coumaroyl-CoA production
- Overexpression modeling analysis was done to test C3H hypothesis

### Enzyme Kinetics Data

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Substrate</th>
<th>$K_m$ (µM)</th>
<th>$k_{cat}$ (1/s)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAL</td>
<td>L-tyrosine</td>
<td>1492.2</td>
<td>155</td>
<td>[7]</td>
</tr>
<tr>
<td>4CL</td>
<td>p-coumaric acid</td>
<td>25.1</td>
<td>16.329</td>
<td>[8]</td>
</tr>
<tr>
<td>4CL</td>
<td>caffeic acid</td>
<td>11</td>
<td>4.408533</td>
<td>[9]</td>
</tr>
<tr>
<td>4CL</td>
<td>ferulic acid</td>
<td>56.7</td>
<td>7.475801</td>
<td>[8]</td>
</tr>
<tr>
<td>C3H</td>
<td>p-coumaric acid</td>
<td>143.03</td>
<td>0.0347</td>
<td>[10]</td>
</tr>
<tr>
<td>C3H</td>
<td>p-coumaroyl-CoA</td>
<td>143.03</td>
<td>0.0347</td>
<td>[10]</td>
</tr>
<tr>
<td>COMT</td>
<td>caffeic acid</td>
<td>59.5</td>
<td>0.0347</td>
<td>[11]</td>
</tr>
<tr>
<td>DCS</td>
<td>feruloyl-CoA</td>
<td>46</td>
<td>0.02 (n=1.8)</td>
<td>[13]</td>
</tr>
<tr>
<td>CURS</td>
<td>feruloyl-CoA</td>
<td>18</td>
<td>0.018333</td>
<td>[13]</td>
</tr>
</tbody>
</table>

### Michaelis-Menten Equation

$$rate = \frac{K_m \cdot [E] \cdot [S]}{K_m + [S]}$$

### Hill Equation

$$rate = \frac{K_m \cdot [E] \cdot [S]^n}{K_m + [S]^n}$$

### Code snippet

```plaintext
module partial_pathway

[] fcoa > 0 -> v1: (facoa’ = facoa + 1) & (fcoa’ = fcoa – 1);
[] fcoa > 0 & facoa > 0 -> v2:(cur’ = cur + 1) & (facoa’ = facoa – 1);
endmodule
```

## Conclusions and Future Work

- More work is to be done to increase curcumin yield.
- Perform over- and under-expression experiments for optimization.
- Using the information from our representative model, we will validate the model in the lab.

### References