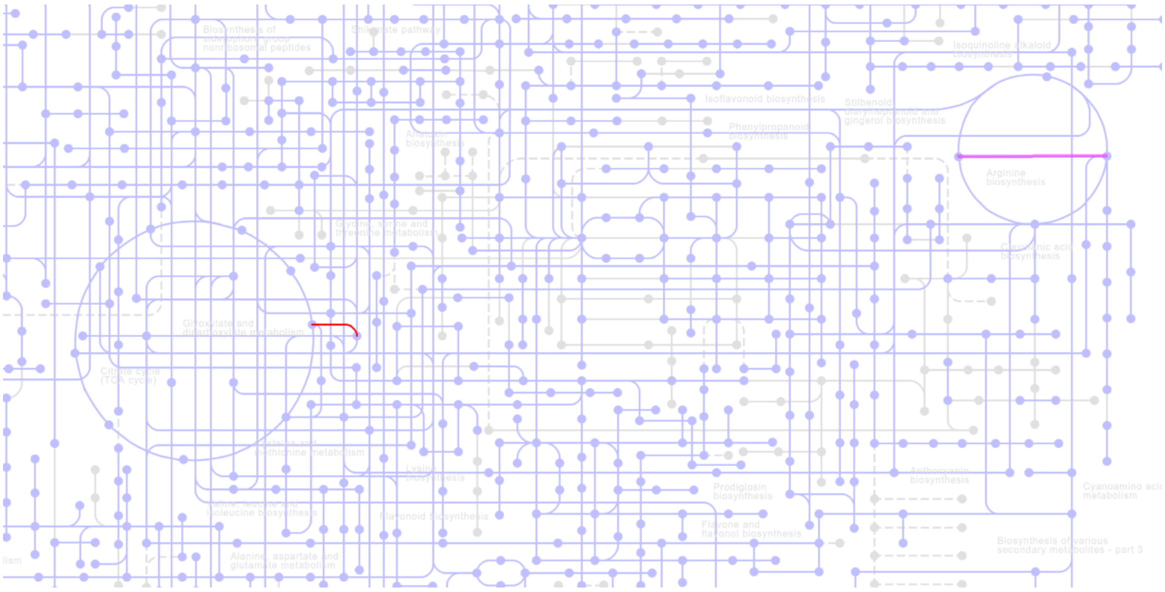
Assumptions:

KEGG metabolism of biomolecules in E coli.



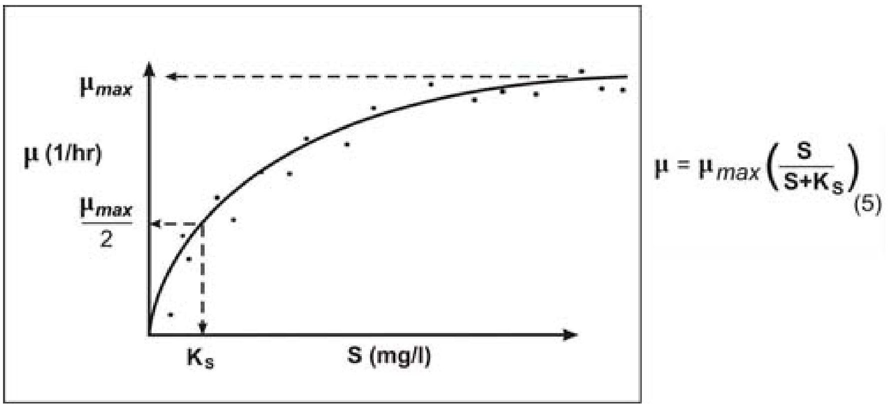
The two red lines represents pathways affected by iclR and ArcA.

Since the lines are separate in far distances, we can **assume that they affect 2 different substrates.**

Monod equation:

$$\mu = \frac{\mu_{max} C_s}{K_s + C_s}$$

This is an empirical equation to describe the **specific** growth rate of bacteria under **specific substrate.**



Permissions

Figure 4. Monod Equation fit to observed data.

Assume there are two growth-essential substrates that are linked to iclR and ArcA respectively.

Denote iclR substrate (**NOT iclR**) as s1.
Denote ArcA substrate (**NOT ArcA**) as s2.

$$\mu_{s1} = \frac{\mu_{max,s1} C_{s1}}{K_{s2} + C_{s1}}$$

$$\mu_{s2} = \frac{\mu_{max,s2} C_{s2}}{K_{s2} + C_{s2}}$$

$$\mu_{combined,\ s1s2} = \frac{\mu_{max,s1} C_{s1}}{K_{s2} + C_{s1}} * \frac{\mu_{max,s2} C_{s2}}{K_{s2} + C_{s2}}$$

The data collected:

Normal max growth rate: μ_n
iclR knockout growth rate: μ_i
ArcA knockout growth rate: μ_A

Find:

$\mu_{combined,\ s1s2}$

Solution:

$$\mu_{s1} = \frac{\mu_{max,s1} C_{s1}}{K_{s2} + C_{s1}}$$

Let the relative portion of concentration of substrate be u.
$C_{0,s1}$ is the normal growth concentration of the substrate.

$$\mu_{s1} = \frac{\mu_{max,s1} (u_{s1} C_{0,s1})}{K_{s2} + (u_{s1} C_{0,s1})}$$

$$\mu_{s1} = \frac{\mu_{max,s1} (u_{s1})}{(\frac{K_{s2}}{C_{0,s1}}) + (u_{s1})}$$

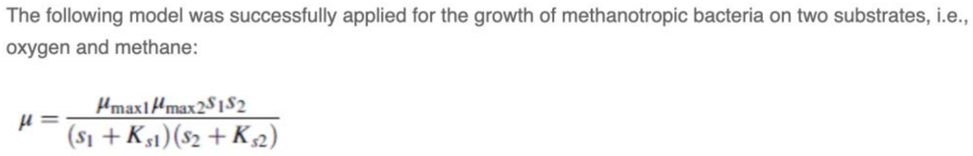
$$\mu_{s1} = \frac{\mu_{max,s1} (u_{s1})}{(K_1) + (u_{s1})}$$

Where $K_1 = \frac{K_{s2}}{C_{T,s1}}$, which is a constant.

Similarly,

$$\mu_{s2} = \frac{\mu_{max,s2}(u_{s2})}{(K_2) + (u_{s2})}$$

$$\mu_{combined,\ s1s2} = \frac{\mu_{max,s1}(u_{s1})}{(K_1) + (u_{s1})} * \frac{\mu_{max,s2}(u_{s2})}{(K_2) + (u_{s2})}$$



The following model was successfully applied for the growth of methanotropic bacteria on two substrates, i.e., oxygen and methane:

$$\mu = \frac{\mu_{\max 1}\mu_{\max 2}s_1 s_2}{(s_1 + K_{s1})(s_2 + K_{s2})}$$

Just like the above picture

Solve the equations:

$$\mu_n = \frac{\mu_{max,s1}(1)}{(K_1) + (1)}$$

$$\mu_i = \frac{\mu_{max,s1}(0.8)}{(K_1) + (0.8)}$$

Note: 0.8 is just an example. Find the metabolic flux paper and estimate the concentration decrease in terms of percentage/portion. (I think roughly is ok)

$$\mu_n = \frac{\mu_{max,s2}(1)}{(K_2) + (1)}$$

$$\mu_A = \frac{\mu_{max,s1}(0.8)}{(K_2) + (0.8)}$$

This should solve for $\mu_{max,s1}, \mu_{max,s2}, K_1, K_2$

Finally:

$$\mu_{combined,\ s1s2} = \frac{\mu_{max,s1}(0.8)}{(K_1) + (0.8)} * \frac{\mu_{max,s2}(0.8)}{(K_2) + (0.8)}$$

to mimic double gene knockout effect.

Extra (just a quick thought):

Try to predict/verify iclR_Rescue as well if have time.

Search for your promoter strength for iclR → Should have a curve to show maximum protein produced → substitute it as the maximum concentration predict/check iclR_Rescue using

$$\mu_{s1} = \frac{\mu_{max,s1}(u_{s1})}{(K_1) + (u_{s1})}$$

****Assume 1 iclR produce = 1 substrate produced**

References:
https://onlinelibrary.wiley.com/doi/epdf/10.1002/bit.260171104
Summary article:
https://ebrary.net/23958/environment/literature_review_growth_models
Monod graph:
https://www.cs.montana.edu/webworks/projects/stevesbook/contents/chapters/chapter002/section002/black/page001.html

ADD OIL!!!!!!!!