Flux balance analysis of synechocystis

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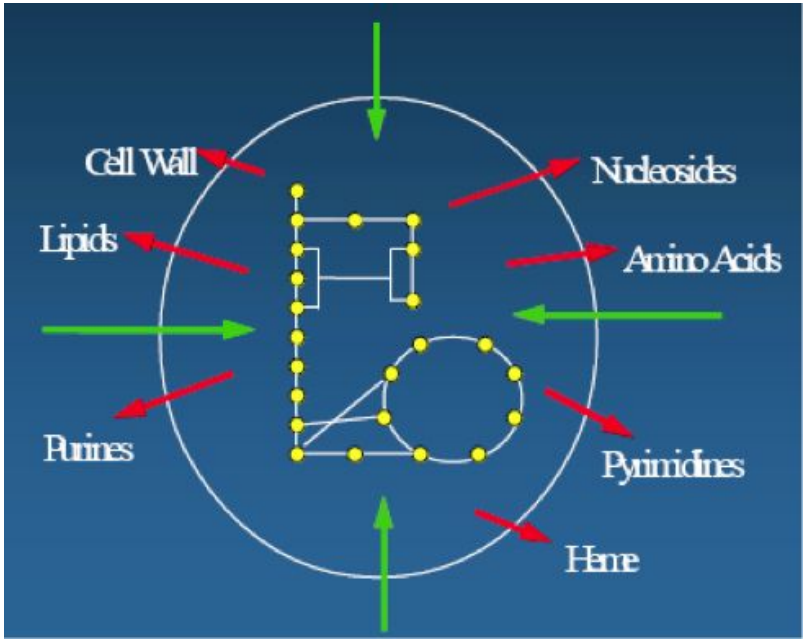
Outline

Summer 2015 research work by Ashley D’Souza

- FBA (flux balance analysis)
- Synechocystis
- FAME (mathematical modeling tool)
- Adding biofuel pathway to metabolic map
- Maximize biomass/growth rate
- Maximize biofuel
- Biomass & biofuel relationship

What is flux balance analysis?

- Flux = rate of a reaction
- Mathematical method of simulating metabolic networks
  - steady-state assumption
  - flow of metabolites
  - optimization of different modes
- Linear inequalities describe balanced metabolite flow
- Linear programming computes optimal organism behavior



Synechocystis

- Cyanobacteria that is a biofuel candidate with:
  - Genetic alterations to introduce a biofuel-producing pathway
  - Suitable environmental conditions

FAME

- Used FBA tool at http://f-a-m-e.org
- Loaded synechocystis model
- Added biofuel metabolic pathway to model
- Altered conditions to maximize (using flux-balance analysis) biomass growth or biofuel flux, with environment constraints
  - light-limiting
  - carbon-limiting

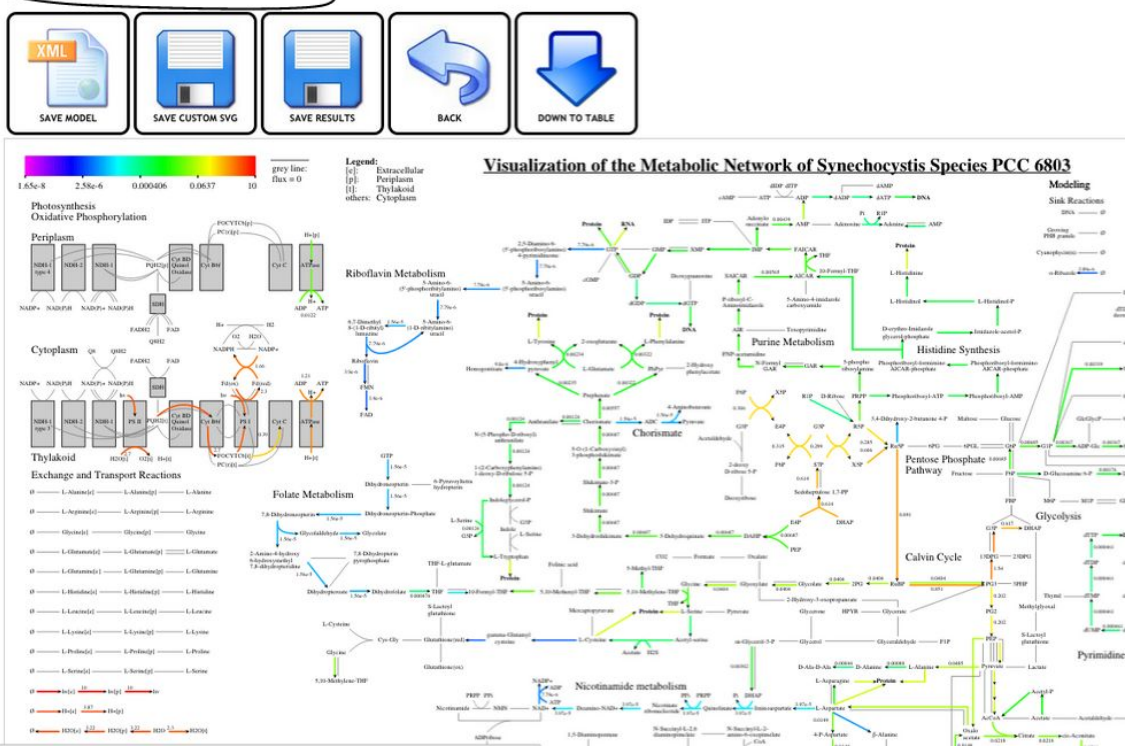
FAME synechocystis model

About the behavior of this *Synechocystis* model
By default, this model will grow autotrophically, but you can select alternate growth conditions by applying the constraints changes below. These sets of constraints allow you to reproduce the figure panels in the manuscript that describes the map of *Synechocystis* metabolism.

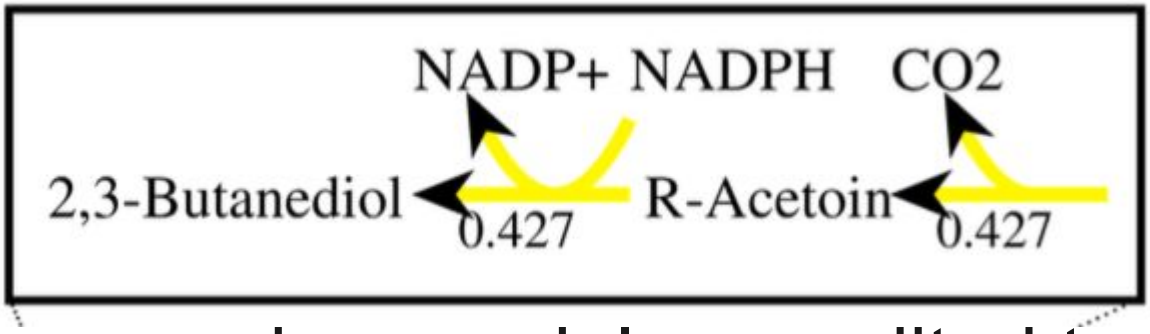
Select a figure to reproduce . . .

- ✓ Figure 2A – Autotrophic growth
- Figure 2B – Growth on glycogen
- Figure 2C – Growth on glycogen w/ proline degradation
- Figure 3B/S2A – Carbon & Light Limiting State (autotrophic)
- Figure 3C – Light Limiting State (autotrophic)
- Figure 3D – Carbon Limiting State (autotrophic)
- Figure 5B/S2B – Carbon & Light Limiting State (biofuel production)
- Figure 5C – Light Limiting State (biofuel production)
- Figure 5D – Carbon Limiting State (biofuel production)
- Figure S1A – Carbon Limiting State (autotrophic, quinol KD)
- Figure S1B – Carbon & Light Limiting State (autotrophic, AEF KD)
- Color bar – Execute these commands for a consistent color bar
- Custom instructions (enter your own)

Objective R_BiomassAuto : 0.0174435453726

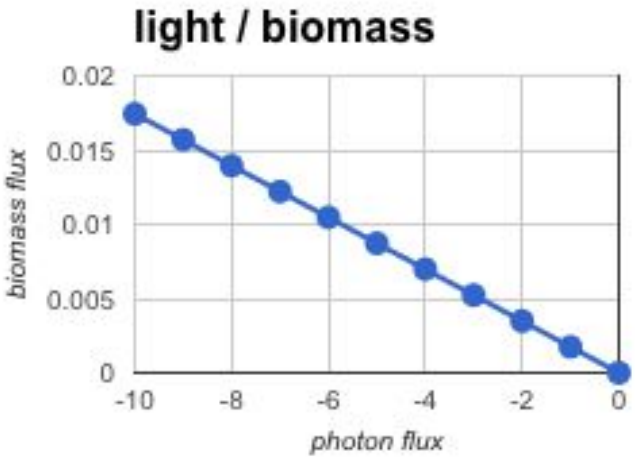


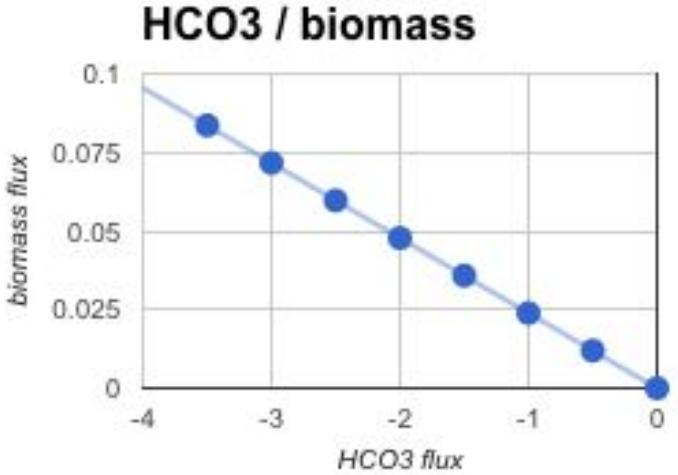
Adding Biofuel Pathway



- The organism model was edited to add this biofuel pathway
  - This would correspond to specific gene edits in the DNA of synechocystis

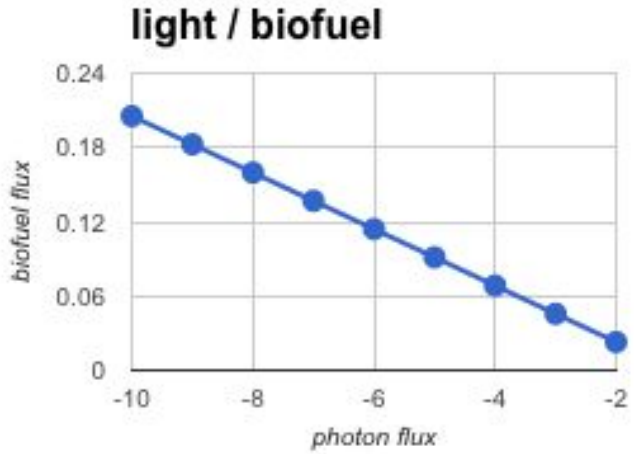
Optimize biomass growth

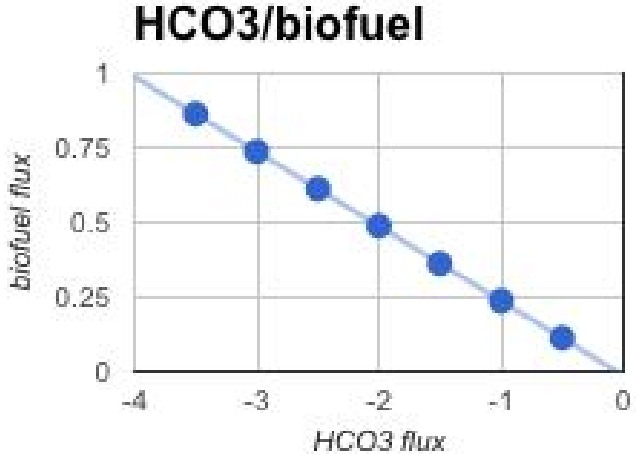




All other factors constant

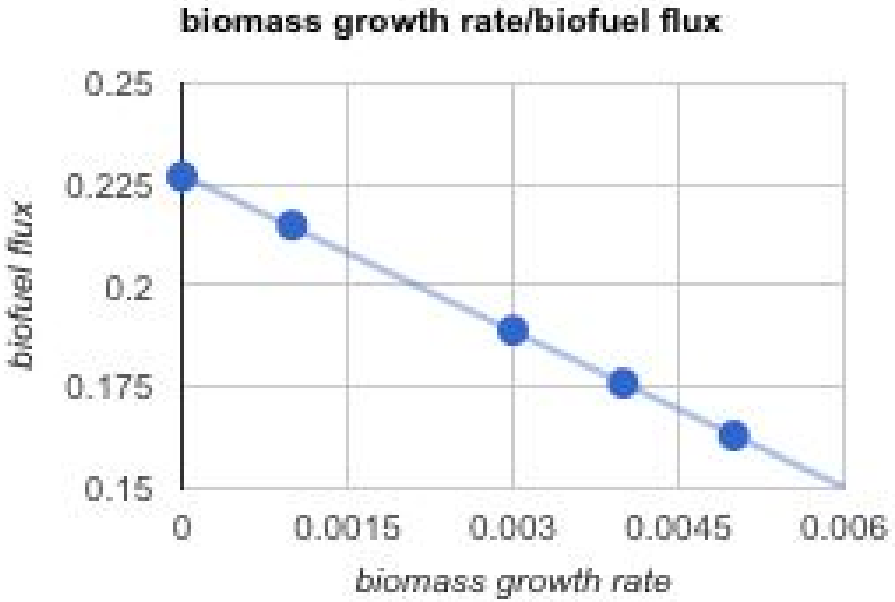
Optimize biofuel- new pathway





biomass growth rate set at constant 10% of max

Biomass & biofuel relationship



Conclusion

Organism goal	**Observations**
Maximize growth	As light level and/or carbon level decreases, growth decreases
Maximize biofuel production with fixed growth rate (10% of max)	As light level and/or carbon level decreases, production decreases
Maximize biofuel production with varying growth rates	As growth rate increases, biofuel production decreases
The analyses suggest that with a genetic modification to enable this biofuel pathway and suitable environmental conditions, synechocystis could be a realistic biofuel-producing candidate	
The analyses also showed the different network activations for different objective functions e.g. maximize growth vs. maximize biofuel production vs. ...	