# QUANTIFYING INTERSPECIES METABOLIC EXCHANGES IN MICROBIAL COMMUNITIES WITH DYNAMIC FLUX BALANCE ANALYSIS

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## BACKGROUND/OBJECTIVES

Via interspecies metabolic exchanges, microbial communities are able to convert chemical nutrients into complex chemical compounds, which can be used for production of biofuels and biomaterials.

**Motivation:**

Perform *in silicio* studies of microbial consortia to evaluate their potential use in producing biofuels and biomaterials, eliminating pollutants, treating wastewater, or other biotechnology applications.

**Objective:**

Formulate a mathematical model to simulate the behavior of a microbial system and predict flowrates of metabolites.

## INTRODUCTION

This is a simulation of a well-characterized, natural, hot spring microbial mat community in Yellowstone National Park [1]. It contains a sulfate-reducing bacteria (SRB) and two photoheterotrophic bacteria, filamentous anoxygenic bacteria (FAP) and Synechococcus spp. (SYN). This mat is a good case study for microbial communities because the guilds exhibit different behaviors between day & night, and the community contains all of the prototypical metabolite exchange interactions described in [2].

## INTERACTION TYPES

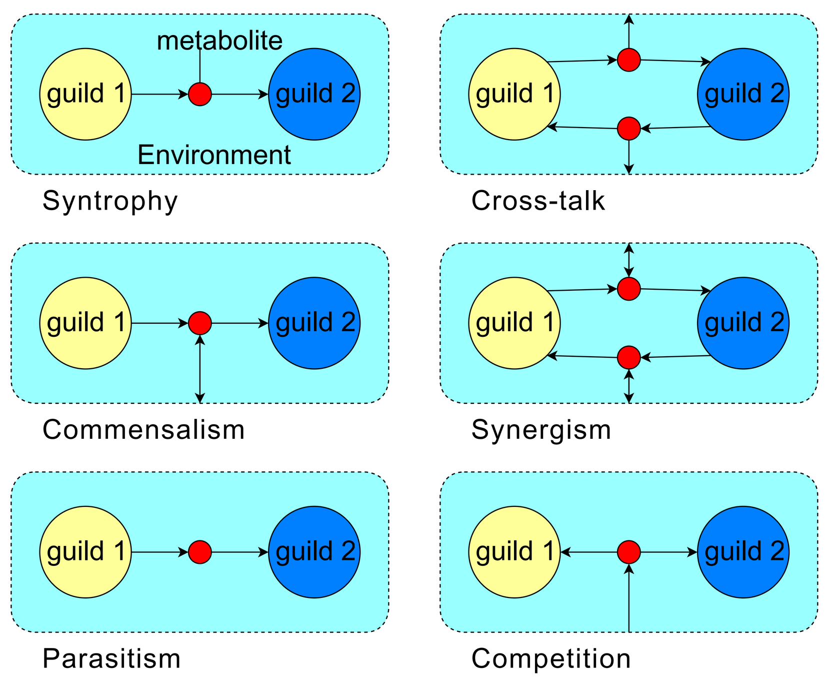



**Figure 1:** Yellow & blue circles: 2 different guilds. Red circles: metabolite. Aquamarine: environment. *Interaction diagrams adapted from [2]*

## FLUX BALANCE ANALYSIS (FBA)

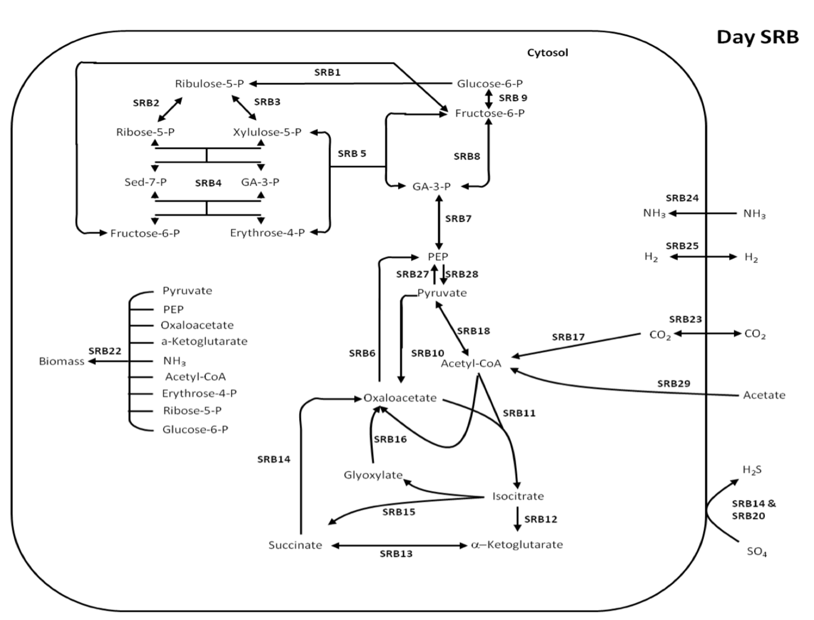



**Figure 8:** Daytime metabolic model of SRB

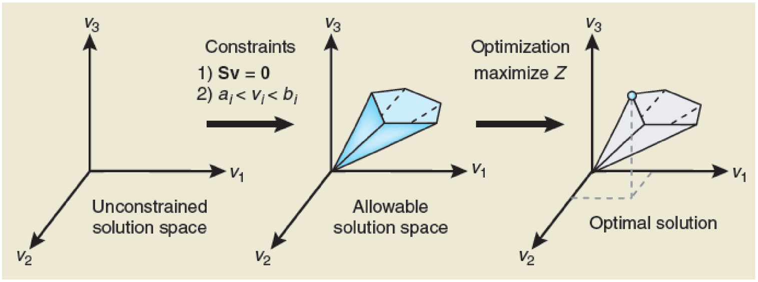
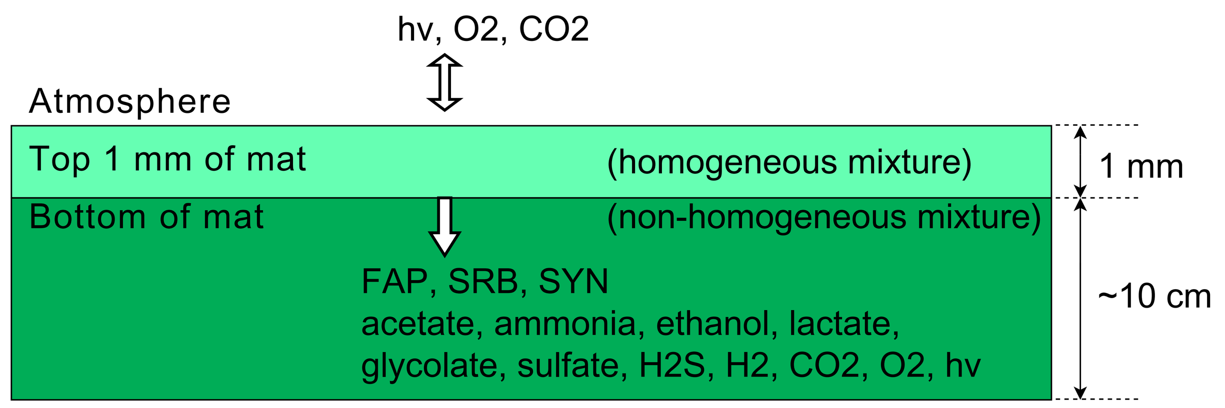



**Figure 9:** FBA solution space

FBA writes a flux balance for each metabolite in the metabolism and assumes quasi-steady state. This creates an undetermined linear program, which FBA solves by assuming that the microorganism will try to maximize its growth rate.

## MODEL DEVELOPMENT




**Model Assumptions**

1. Cost coefficients for biomass flux are normalized
2. Concentration of metabolites exchanged by more than one organism are at steady state
3. Residence time of community is 59 weeks
4. Mass fraction of carbon in each guild is 1/2

**Three mass balances** *Metabolites (i) entering mat from atmosphere*

$$\frac{dc_i}{dt} = n_{in,j} + \sum_k (-f_{i,k})C_k - \frac{c_i}{\tau} \quad (1)$$

*Metabolites (j) consumed/produced in mat*

$$\frac{dc_j}{dt} = \sum_k (-f_{j,k})C_k - \frac{c_j}{\tau} \quad (2)$$

*Biomass (k)*

$$\frac{dC_k}{dt} = \left(\frac{f_k C_{mole}\mu}{x_k}\right) C_k - \frac{C_k}{\tau} \quad (3)$$

**Definitions**

$c_i$ - concentration of metabolite i
$C_k$ - concentration of guild k
$n_{in,j}$ - system inlet molar flowrate of metabolite j
$f_{i,k}$ - flux of metabolite *i* exchanged in guild *k*
$\tau$ - residence time
$C_{mole}$ - moles of carbon per mole of biomass
$\mu$ - molecular weight of carbon
$x_k$ - mass fraction of carbon in guild k

## FUTURE WORK

Apply methodology to consortia in bioprocesses such as fermentation or production of biofuels. Consider the accumulation of metabolite within guild for use at different time in the diel cycle.

## SUMMARY

Community behavior highlights:

- SYN outcompeted the other guilds because it can choose not to share essential metabolites.
- Uptake of ammonia and acetate by FAP is limited by light available.
- SRB reaches a constant growth rate with FAP because FAP is interacting syntrophically with SRB via hydrogen exchange.

Advantages of modeling approach:

1. Mass of each guild is considered when performing FBA.
2. Normalizing the maximum biomass fluxes forces independent guilds to share with dependent guilds.

Modeling challenges faced:

1. Absence of experimentally determined flux values for the individual guilds.
2. Determining reasonable assumptions about the community.

## RESULTS

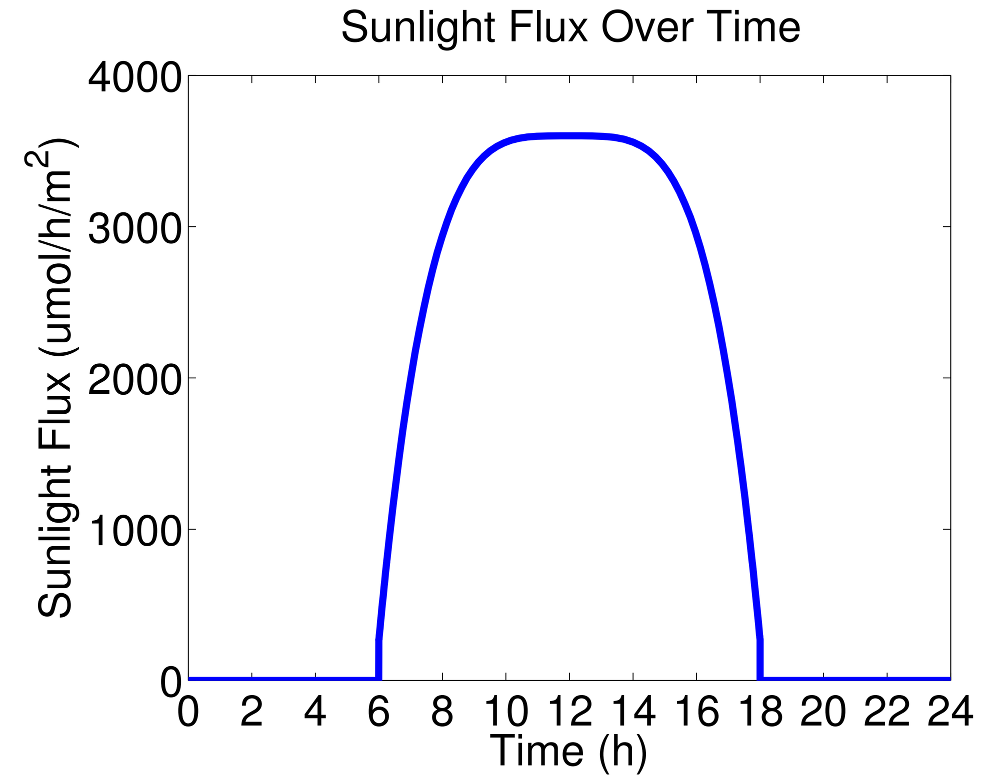



**Figure 2:** Maximum light available was chosen to be: 1 $\frac{\mu mol}{sm^2}$

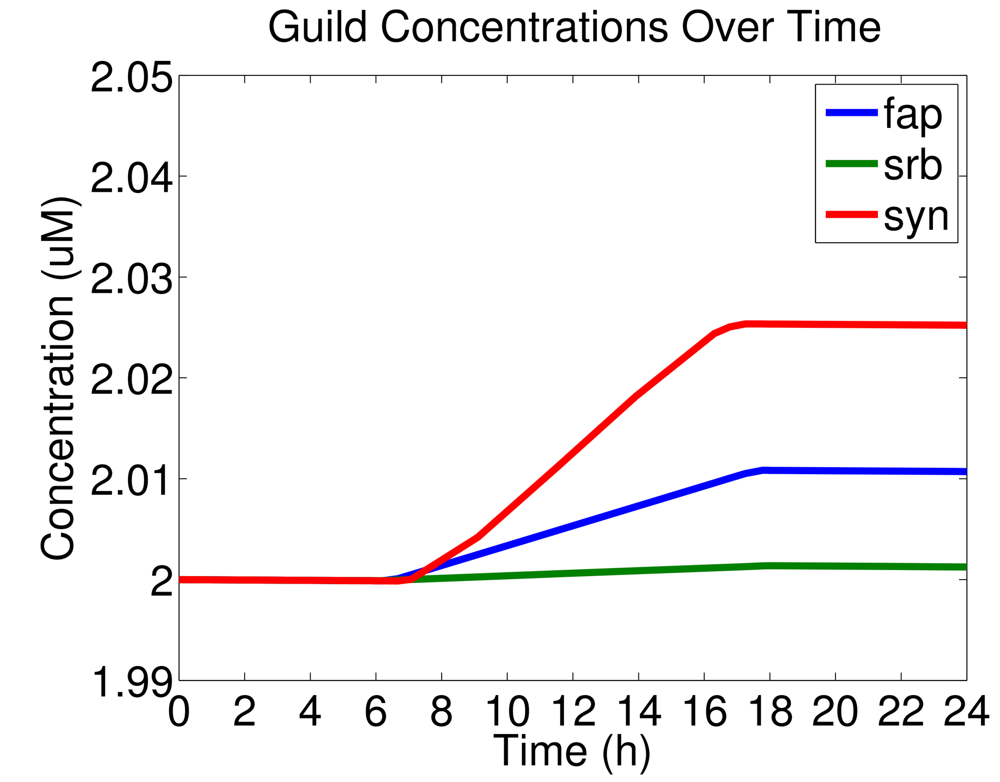



**Figure 4:** Photosynthetic SYN outcompetes photosynthetic FAP during day

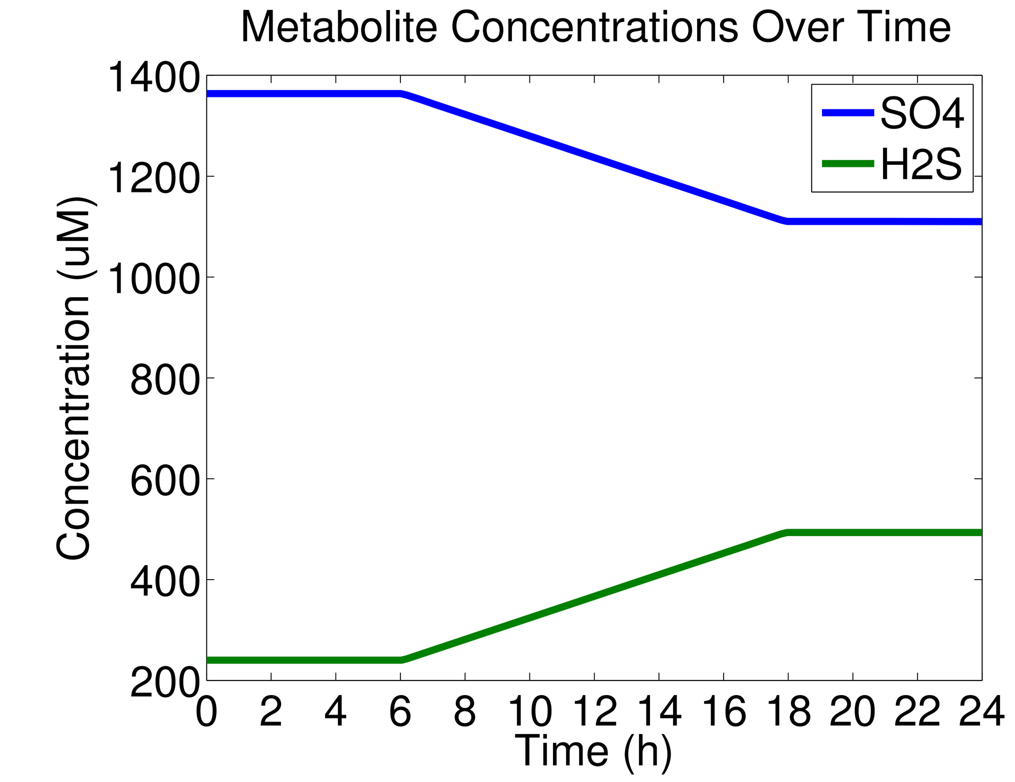



**Figure 6:** Sulfur reduction with minimal SRB growth during day time

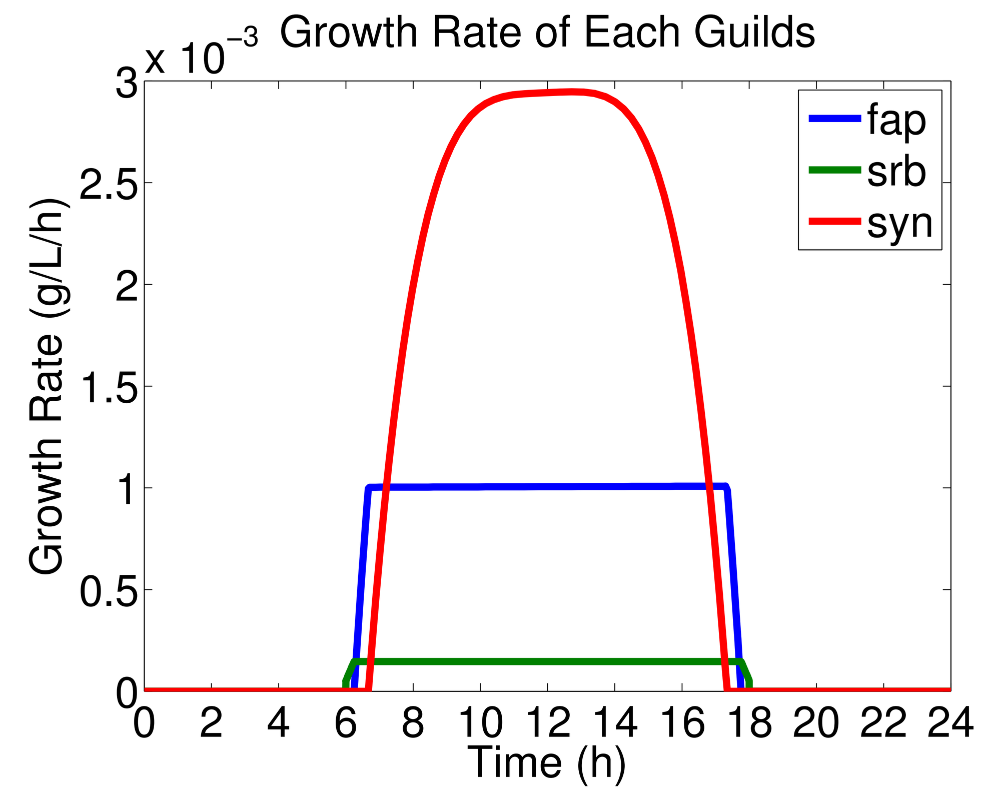



**Figure 3:** FAP reaches maximum growth rate once critical light intensity is reached

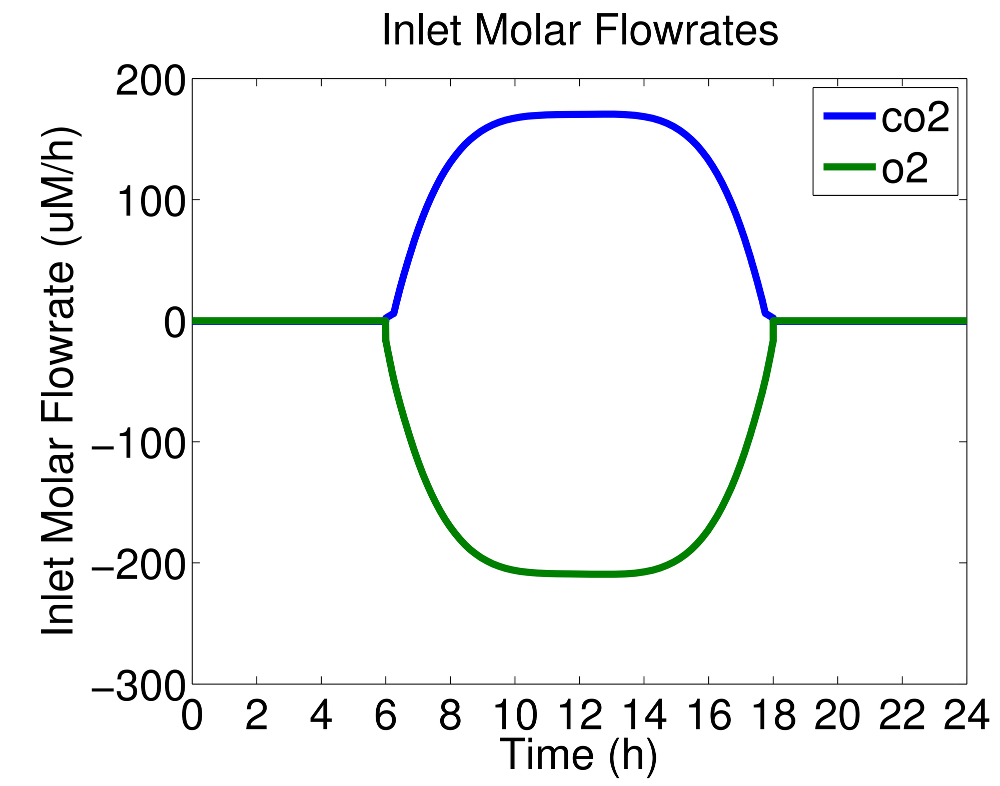



**Figure 5:** CO2 uptake and O2 release by photosynthetic community

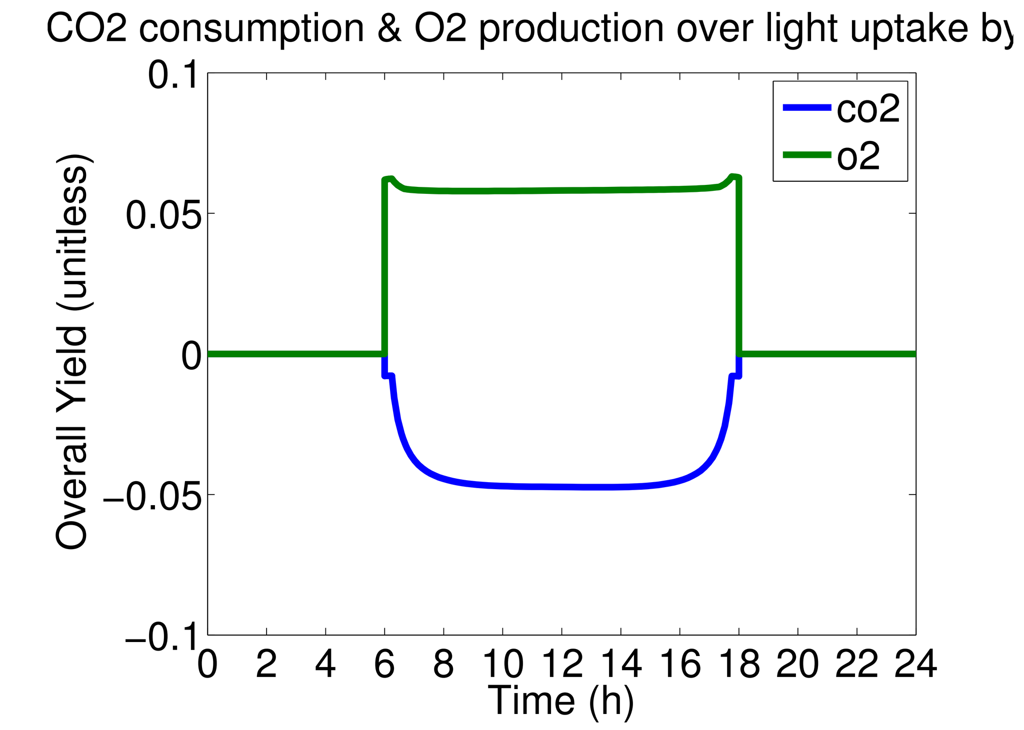



**Figure 7:** Excess light is absorbed when O2 production reaches ss

## REFERENCES

1. Taffs, R. *et al.* BMC Systems Biology, 2009, 3:114.
2. Zomorrodi AR, Maranas CD PLoS Comput Biol 8(2): e1002363. doi:10.1371/journal.pcbi.1002363

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