



# BioSolar Cells

## Making Genome-scale Modeling Simpler

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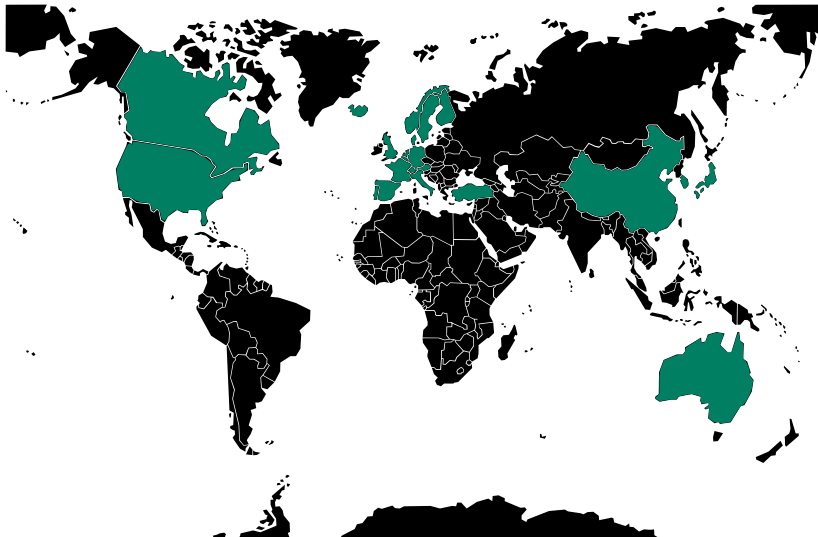
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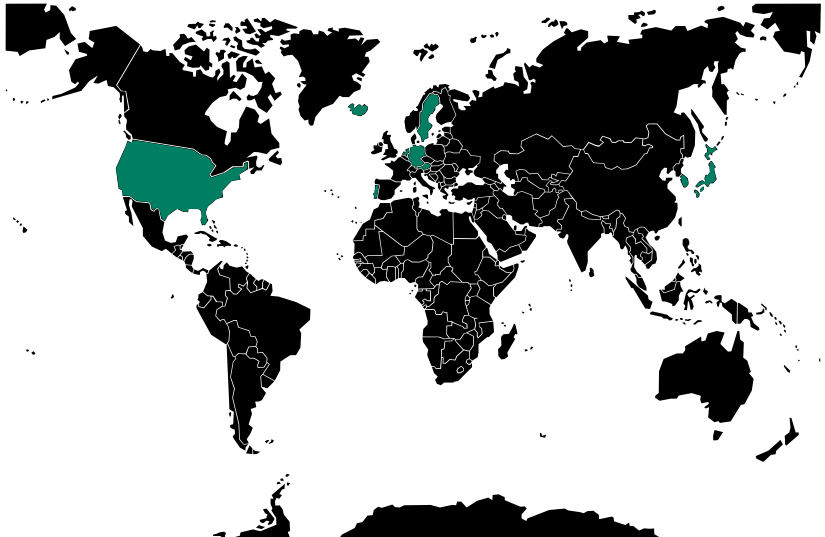
# What are they?

- Large models
- Links metabolic genes with metabolic reactions
- Only stoichiometry; no kinetics!
- Steady-state flux distributions
- No metabolite concentrations!

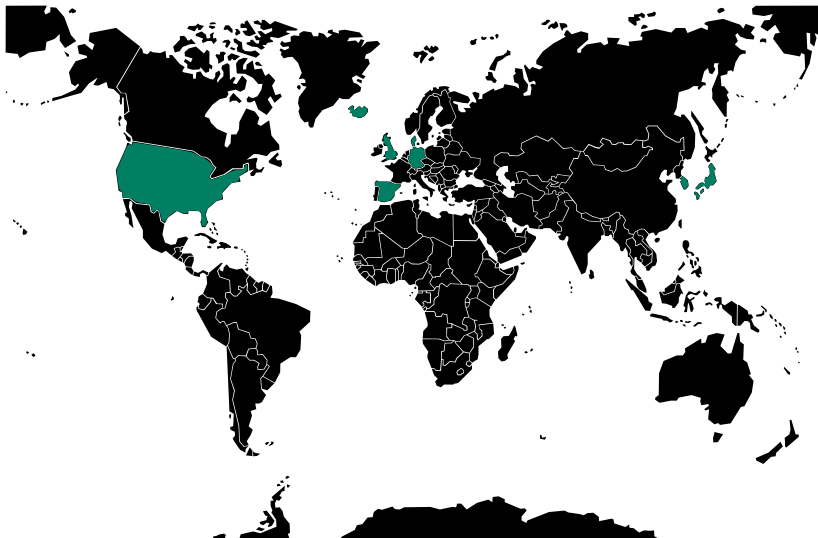
# Published Models



# Published tools

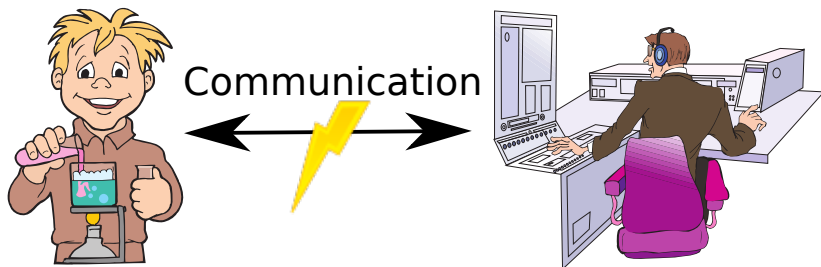


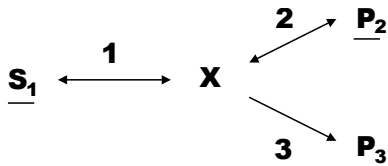
# Published Synechocystis models



**However  
But  
Nevertheless**

# Communication problem





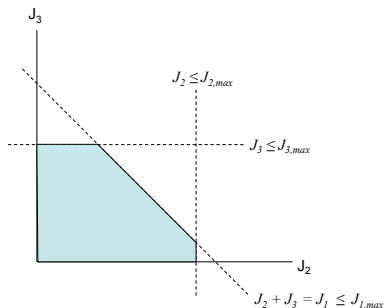
- $J \geq 0$
- $J_1 = J_2 + J_3$
- $J_1 \leq 10$ ,  $J_2 \leq 8$ , and  $J_3 \leq 6$
- $\max Z = 0.5J_2 + 0.5J_3$

We cannot determine  $[X]$ !



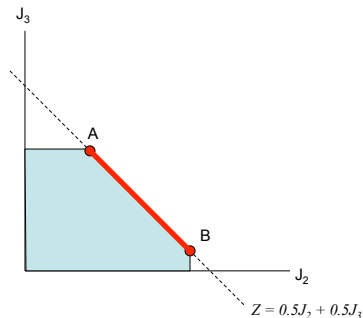
## Example: The solution space

- Capacity constraints bound solution space
- $Z = 0.5J_2 + 0.5J_3 = [0 - 5]$
- $J_1 = J_2 + J_3 = [0 - 10]$



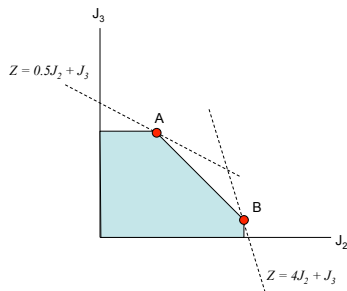
## Example: Optimal solution space

- $Z = 0.5J_2 + 0.5J_3 = 5$
- $J_1 = J_2 + J_3 = 10$
- Optimal solution is not unique!

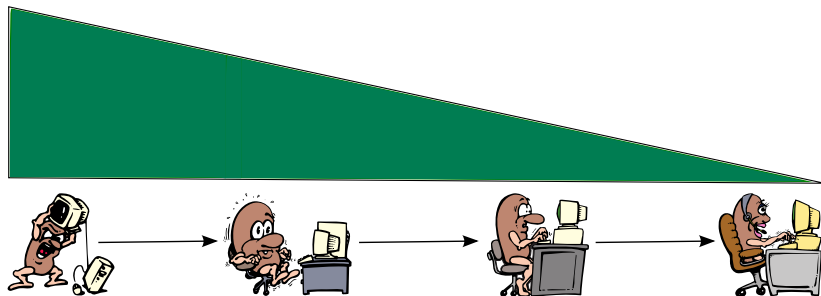


## Example: Optimal solution space with unequal weights

- **A:**  $Z = 0.5J_2 + J_3 = 8$
- **B:**  $Z = 4J_2 + J_3 = 34$
- $J_1 = J_2 + J_3 = 10$
- Optimal solution is unique



# The typical situation



# The common tool

```
cplx_constructLPfromFBA time: 0.1383
```

```
cplx_analyzeModel FBA --> LP time: 0.1400
```

```
Parallel mode: deterministic, using up to 2 threads for concurrent optimization.  
Tried aggregator 1 time.
```

```
LP Presolve eliminated 264 rows and 251 columns.
```

```
Aggregator did 335 substitutions.
```

```
Reduced LP has 218 rows, 320 columns, and 2227 nonzeros.
```

```
Initializing dual step norms . . .
```

```
Iteration log . . .
```

```
Iteration:    1    Dual objective      =      999999.000000
```

```
Iteration:   62    Dual objective      =     124837.892600
```

```
Iteration:  124    Dual objective      =           0.118388
```

```
Reinitializing dual norms . . .
```

```
Dual simplex solved model.
```

```
INFO: Model is optimal: 1
```

```
Solution status = 1 : optimal
```

```
Solution method = 2 : dual
```

```
Objective value = 0.0906484648094 ←
```

```
Status: Model is optimal
```

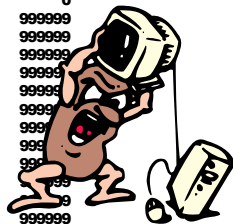
```
LPS_OPT
```

```
Model is optimal
```

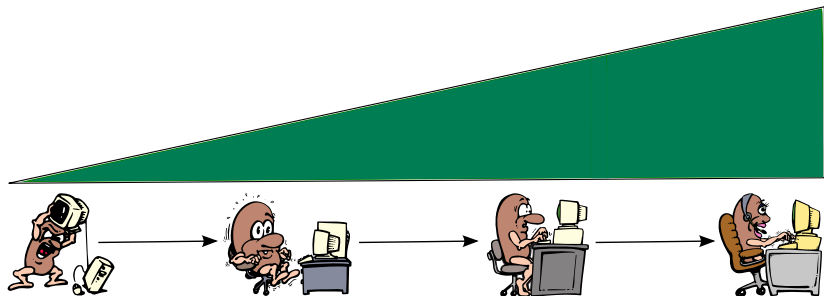


# The general FBA output

Number	Reaction	Flux value	LowerBound	UpperBound
1	R_ETOHtp	0	-999999	999999
2	R_MPBQ	2.4537E-005	-999999	999999
3	R_CTPS2	0	0	999999
4	R_CTPS1	0.013087102	0	999999
5	R_TMK	0	0	999999
6	R_UGLT	0	-999999	999999
7	R_PPTGS_Syn	0.002228983	0	999999
8	R_HPROb	0	-999999	0
9	R_HPROa	0	-999999	0
10	R_HEMEAS	1.9703E-005	0	999999
11	R_IPMD	0.046386488	0	999999
12	R_ADCS	0.000078867	0	999999
890	R_EX_glcglyc_e	0	0	999999
891	R_EAR80y	0.036720195	0	999999
892	R_MG2tex	0.002541428	-999999	999999
893	R_EX_mal_L_e	0	0	999999
894	R_G6PBDH	0	0	999999
895	R_SQD2_183_6_9_12	2.2305E-005	0	999999
896	R_3OAS141	0.001936926	0	999999
897	R_3OAS140	0.034783269	0	999999
898	R_ACLDC	0	-999999	999999
899	R_DXPRii	0.015816506	0	999999
900	R_GARFT	0	-999999	999999
901	R_G3PAT180	0.000108846	0	999999
902	R_CBFcu	13.66789315	0	999999
903	R_PRATPP	0.007567392	0	999999
904	R_PRAIS	0.028631283	0	999999
905	R_DM_cyanphy	0	0	999999
906	R_CPPPGO2	0	0	999999



# Goal

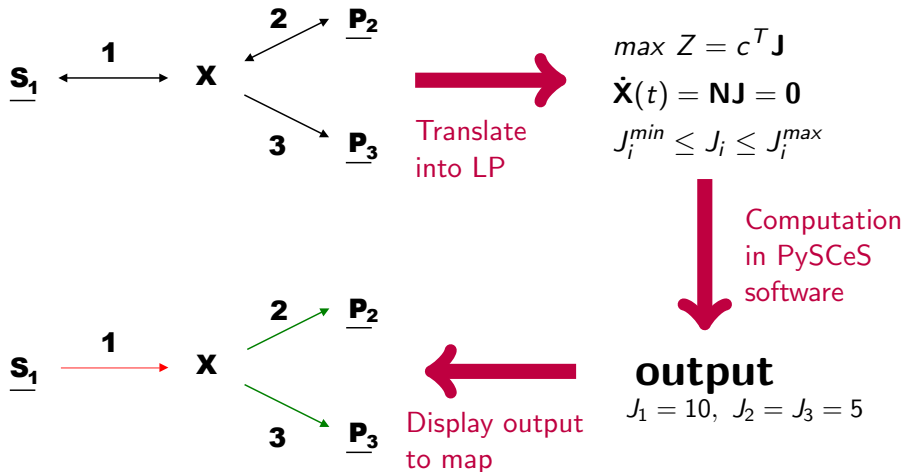


# But what if

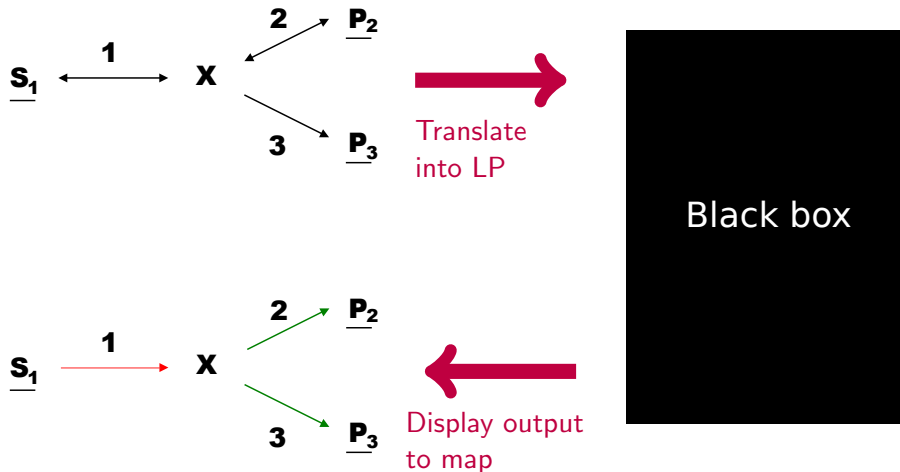




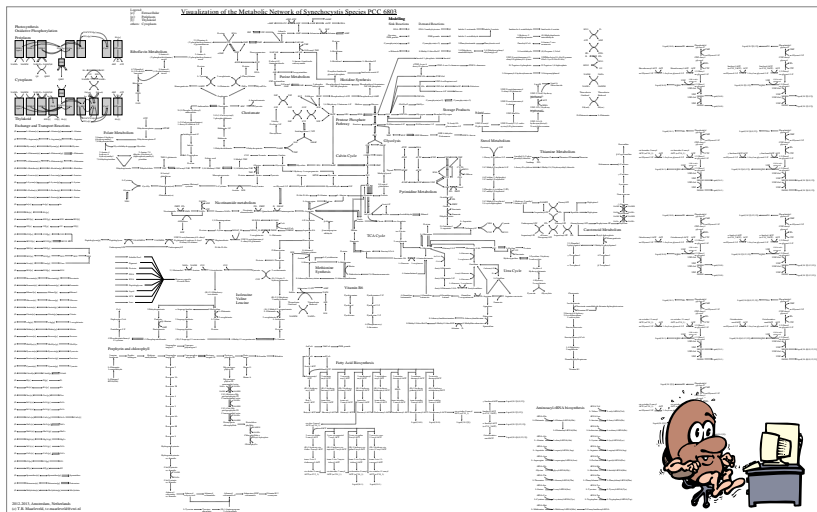
# Basic idea



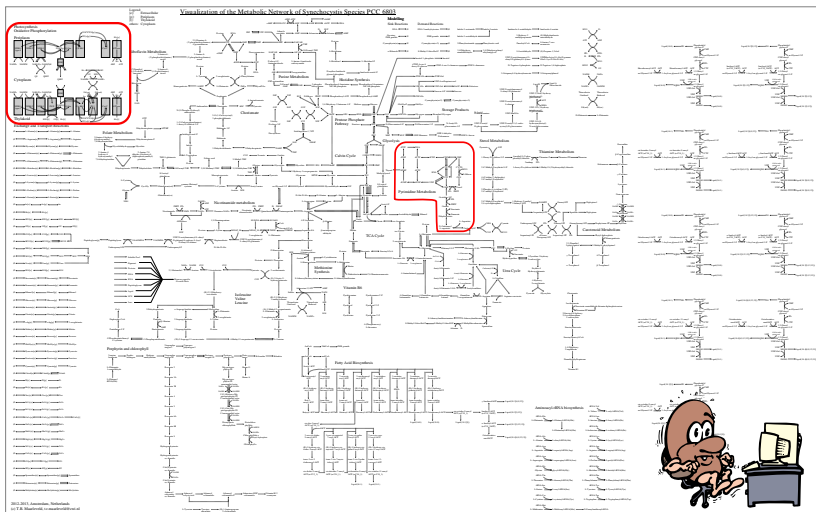
# Basic idea



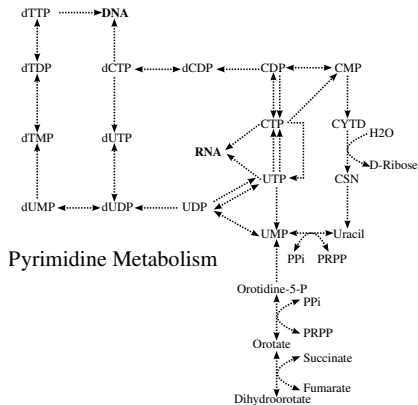
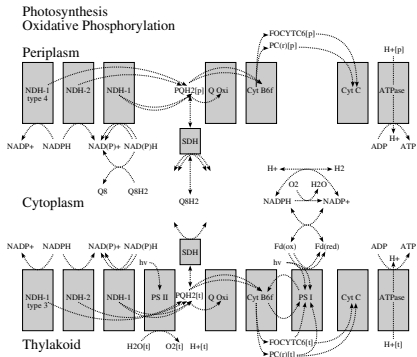
# Interactive map of Synechocystis metabolism



# Interactive map of Synechocystis metabolism

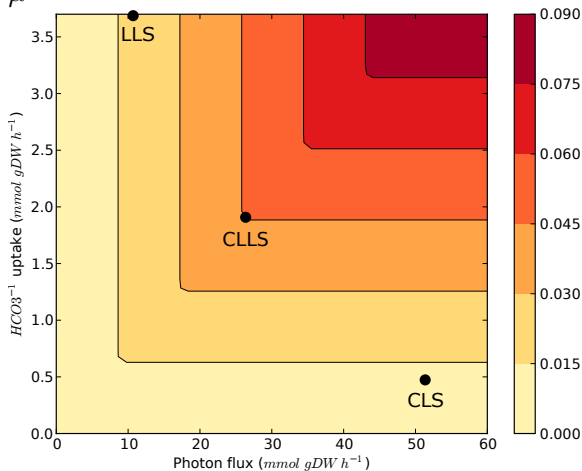


# After zooming in

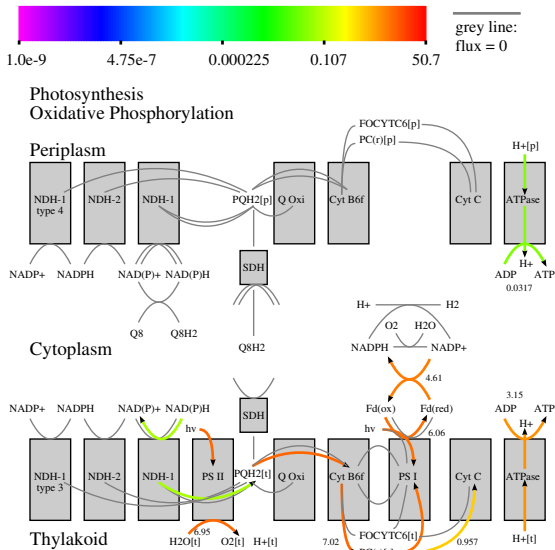


# Exploring different scenario's

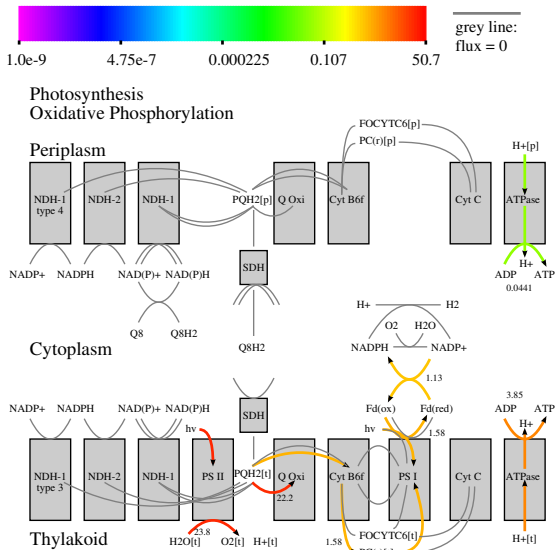
$$Z = \max \mu$$



# Carbon and Light Limiting State

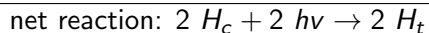
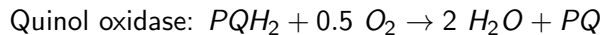
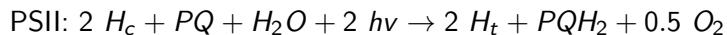


# Carbon Limiting State

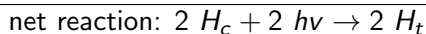
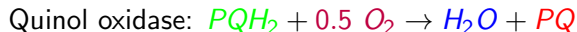
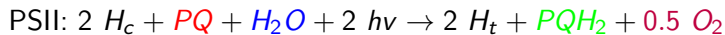




# Net effect

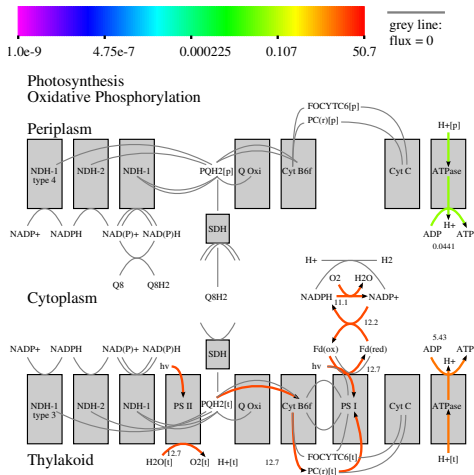


# Net effect



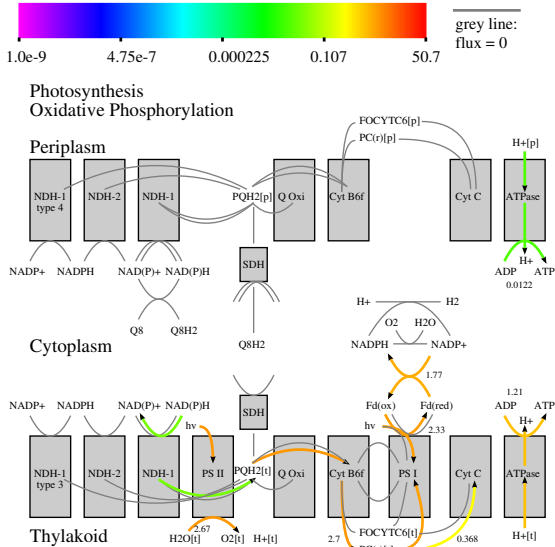
- net effect: ATP production!

# CLS Quinol Oxidase KO

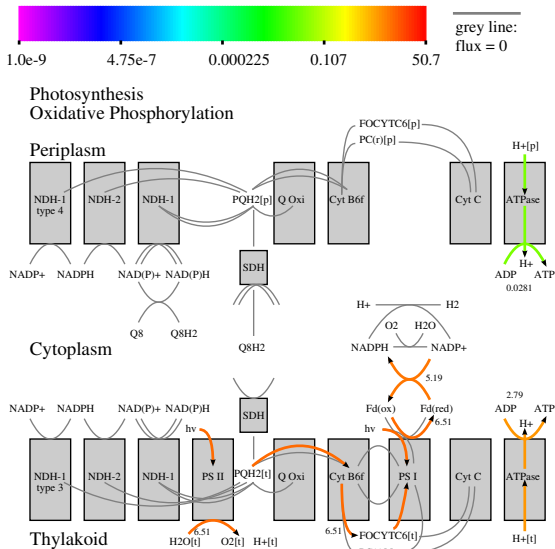


Note that: same value of the objective function!

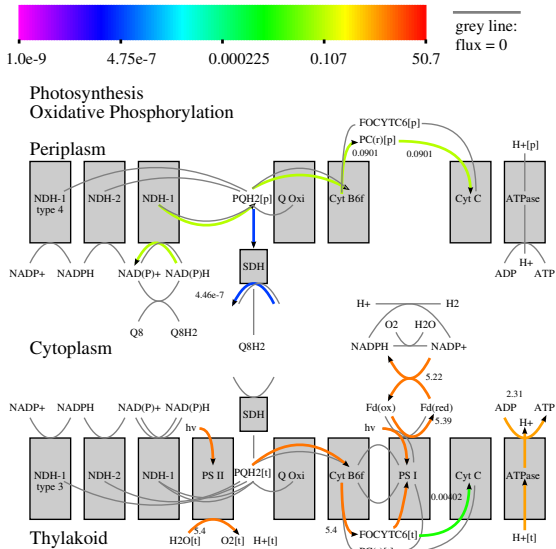
# Light limiting state



# Alternative Electron Pathway KO



# 2,3-Butanediol formation



# Overview of simulations

Situation	$J_{PSI}/J_{PSII}$	$J_{ATP}/J_{NADPH}$	$J_{RuBisCo,CO2}/J_{hv}$	$\mu$ ( $h^{-1}$ )
CLLS	0.87	1.6	0.085	0.045
CLS	0.066	7.3	0.011	0.012
LLS	1.0	1.6	0.085	0.017
KO AEF	1.0	1.3	0.075	0.040
Biofuel	1.0	1.3	0.13	0.0045

- Maximal values! (yield optimization)
- Experimental data helps constraining our model

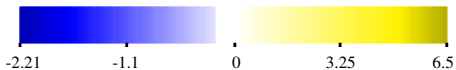
# How does this work??



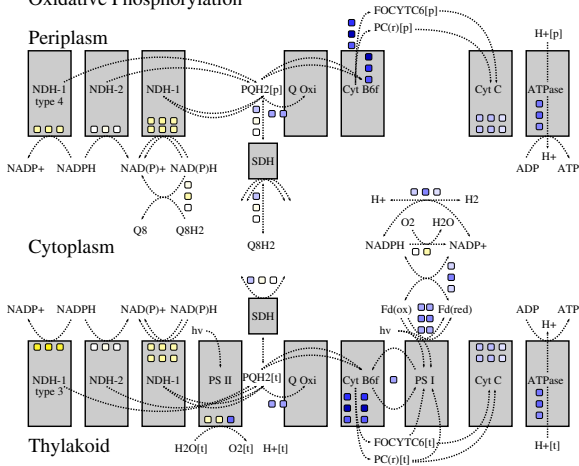


# Demonstration

# What else can we do?



Photosynthesis  
Oxidative Phosphorylation



# It's simpler!

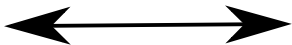
- Ready-to-use tool
- Data integration
- Modeling and visualization
- Repository



We need your help!



Communication



# Acknowledgments



- Joost Boele
- Brett Olivier
- Frank J. Bruggeman
- Bas Teusink

Simulations and visualization can be done on-line at  
<http://www.f-a-m-e.org/synechocystis>

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