Assignment 7

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1st March 2018

1 Growth coupling via knockouts

To create new mutants we knocked out genes to indirectly 'deactivate' reactions. We implemented the proposed algorithm in the handout. The proposed algorithm uses n nested loops to generate the set of possible combined knock outs from the set of the model's genes. This is basically the Cartesian product of the model's set of genes with it self in the n-th order. As it doesn't matter if gene A and gene B or gene B and gene A are knocked out we only consider combinations of n genes to reduce this set.

Table 1: Results of wild type e. coli

Metabolite	max flux	min flux
d-lactate	$-2.9 \cdot 10^{-15}$	0
acetate	0	0
ethanol	$-7.13 \cdot 10^{-15}$	0
succinate	$8.83 \cdot 10^{-15}$	0

Table 2: Results of mutants optimized for acetate production

candidate	genes	max growth	max flux	min flux
1	b3734 b1761 b3236	0.35	14.64	14.64
2	b3731 b1761 b3236	0.35	14.64	14.64

Table 3: Results for mutants optimized for d-lactate production

candidate	genes	max growth	max flux	min flux
1	b2287 b2283 b2987	0.21	$2.65 \cdot 10^{-12}$	0
2	b2287 b2283 b3493	0.21	$2.65 \cdot 10^{-12}$	0

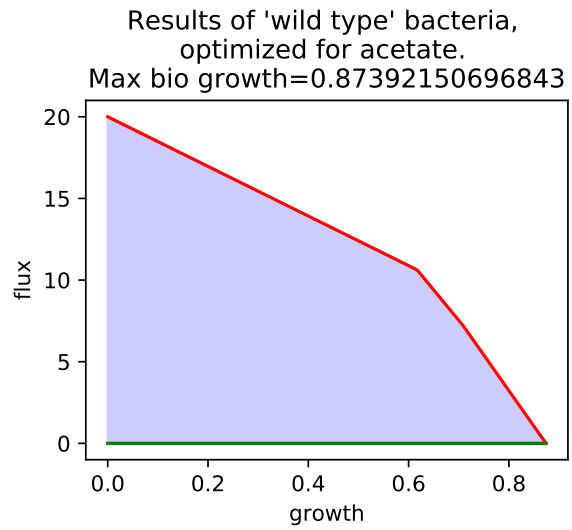
Table 4: Results for mutants optimized for succinate production

candidate	genes	max growth	max flux	min flux
1	b2029 b0114 b0724	0.47	6.43	6.43

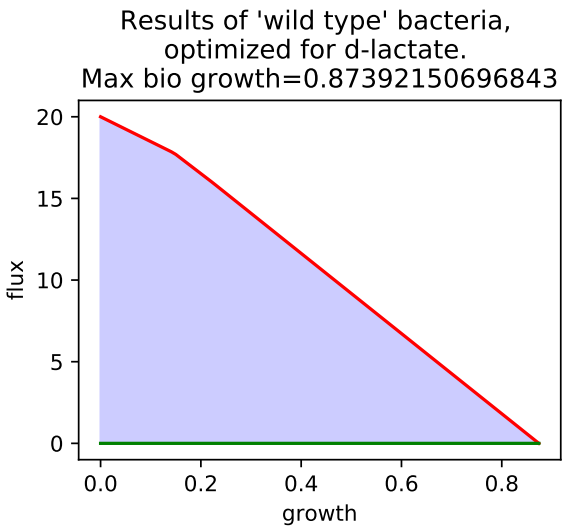
2	b0115 b0767 b0724		0.47	6.43	6.43

Table 5: Results for mutants optimized for ethanol production

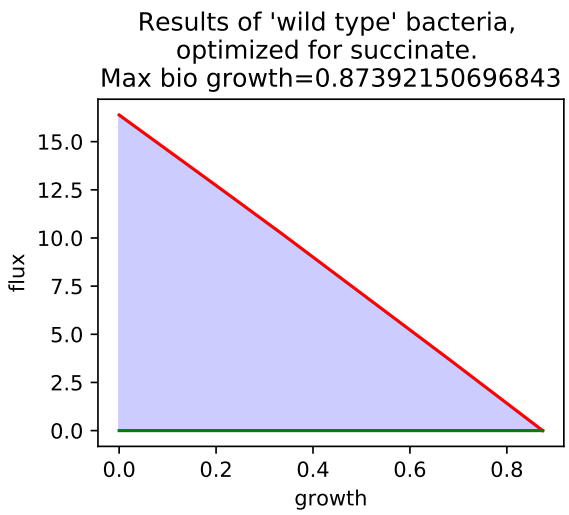
candidate	genes	max growth	max flux	min flux
1	b3736 b2282 b0767	0.2	14.67	14.09
2	b3736 b2276 b0767	0.2	14.67	14.09



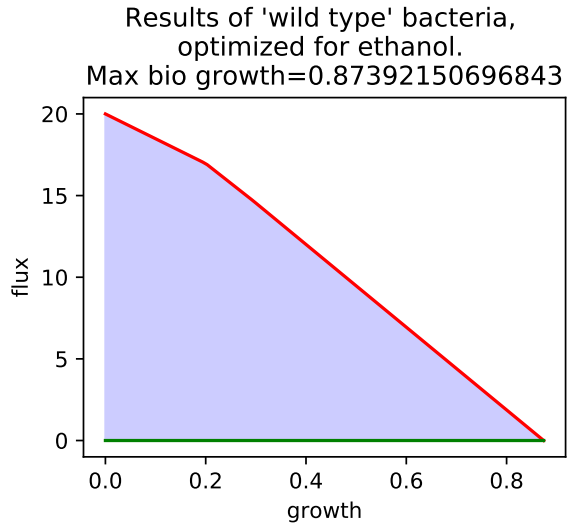
(a) Wild type e. coli, optimized for acetate



(b) Wild type e. coli, optimized for d-lactate

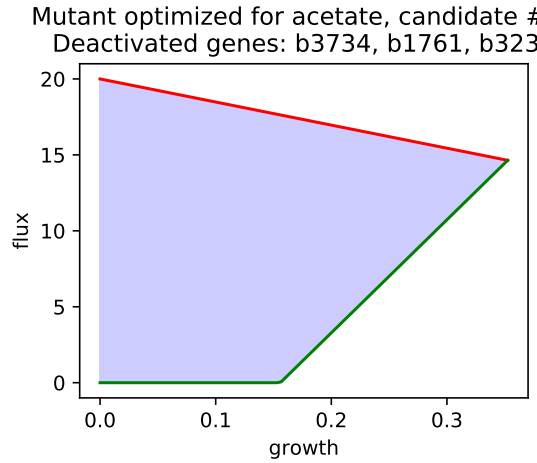


(c) Wild type e. coli, optimized for succinate

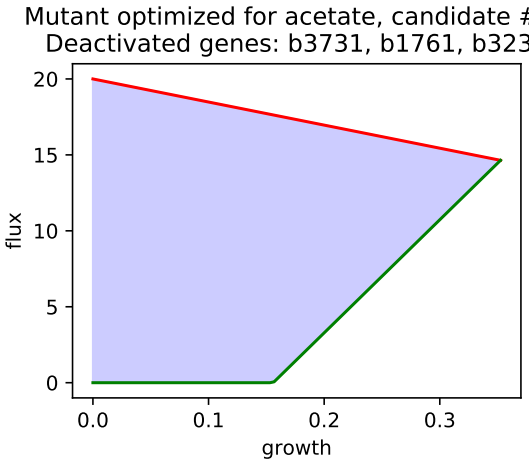


(d) Wild type e. coli, optimized for ethanol

Figure 1: Results of the wild type e. coli model

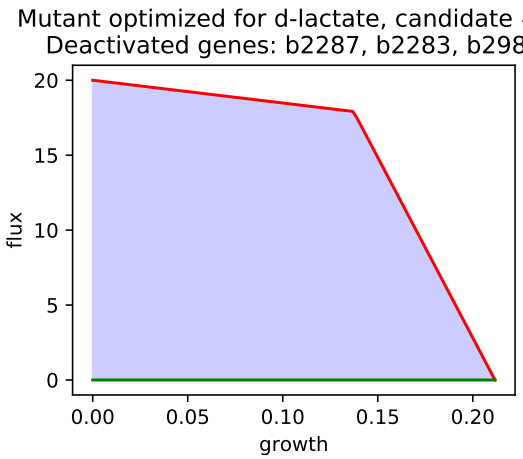


(a) 1st choice mutant for acetate production

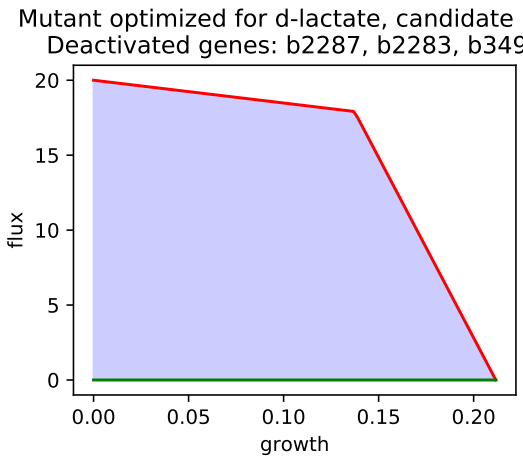


(b) 2nd choice mutant for acetate production

Figure 2: Mutants optimized for acetate production

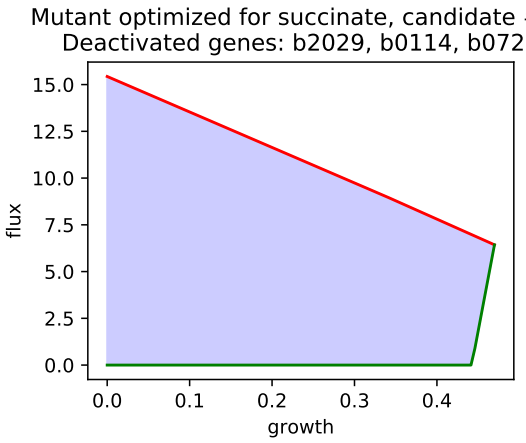


(a) 1st choice mutant for d-lactate production

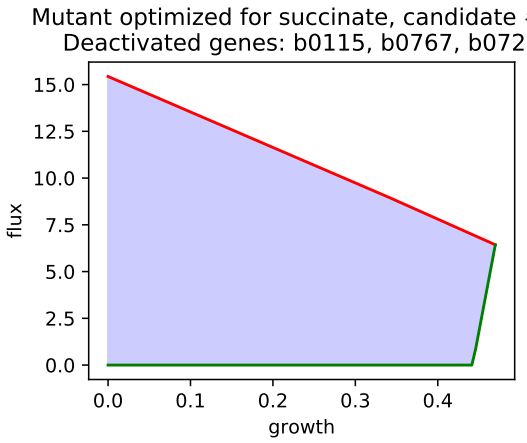


(b) 2nd choice mutant for d-lactate production

Figure 3: Mutants optimized for d-lactate production

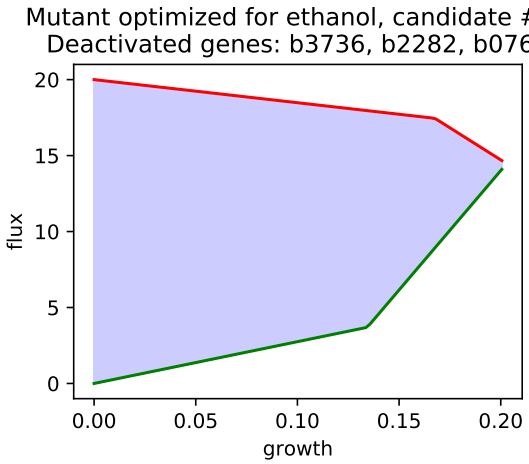


(a) 1st choice mutant for succinate production

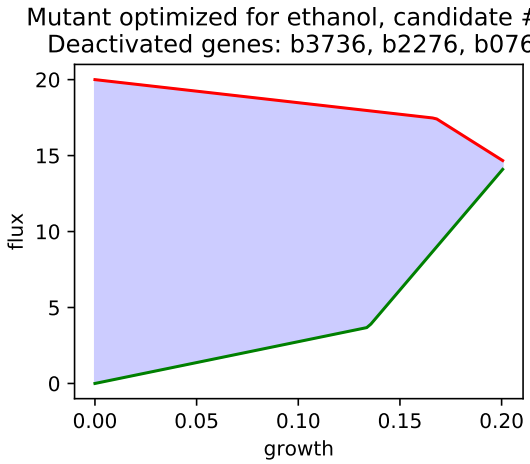


(b) 2nd choice mutant for succinate production

Figure 4: Mutants optimized for succinate production



(a) 1st choice mutant for ethanol production



(b) 2nd choice mutant for ethanol production

Figure 5: Mutants optimized for ethanol production

2 Production of a non-native compound

We consider the additional pathway in Figure 6 as suggested by [**BORODINA201557**]. We

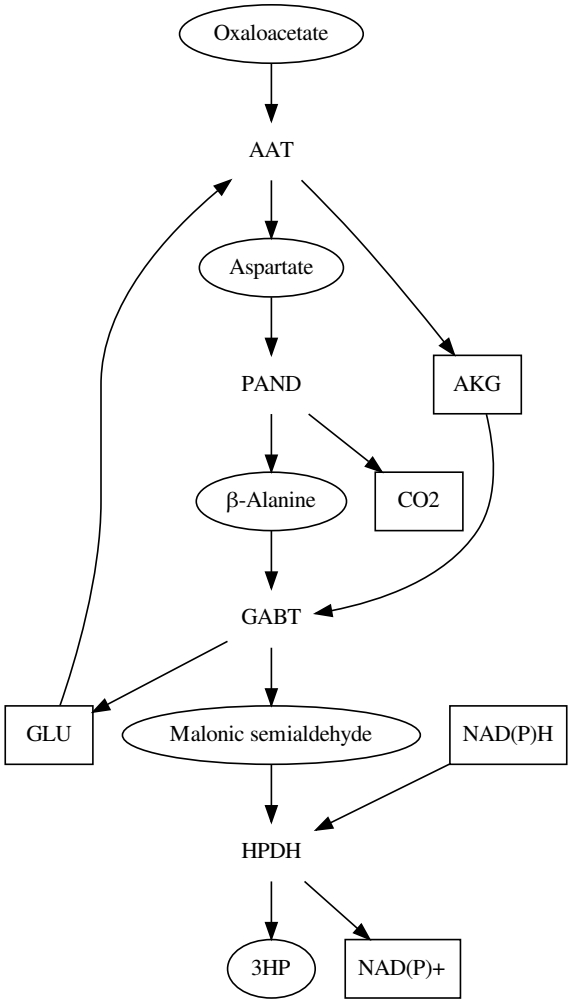


Figure 6: The pathway to be added

require the following additional metabolites:

- Aspartate, asp_c
- β-Alanine, ala_c
- Malonic Semaldehyde (3-Oxopropanoate), oxo_c
- 3HP, hpa_c
- L-Glutamate, glu_c

and the following additional reactions:

$$\text{oaa_c} + \text{glu_c} \rightarrow \text{asp_c} + \text{akg_c}$$
$$\text{asp_c} \rightarrow \text{ala_c} + \text{co2_c}$$
$$\text{ala_c} + \text{akg_c} \rightarrow \text{oxo_c} + \text{glu_c}$$
$$\text{oxo_c} + \text{nadph_c} \rightarrow \text{hpa_c} + \text{nadp_c}$$
$$\text{hpa_c} \rightarrow \text{hpa_e}$$

2.1 Results

i) Aerobic conditions yield ($\frac{\text{ex_hpa}}{\text{ex_glc}}$): 0.09823718127269748

ii) Anaerobic conditions yield ($\frac{\text{ex_hpa}}{\text{ex_glc}}$): 0.02415015570973515

The pathway is active, and produces HPA. Its phaseplane can be seen in Figure 7

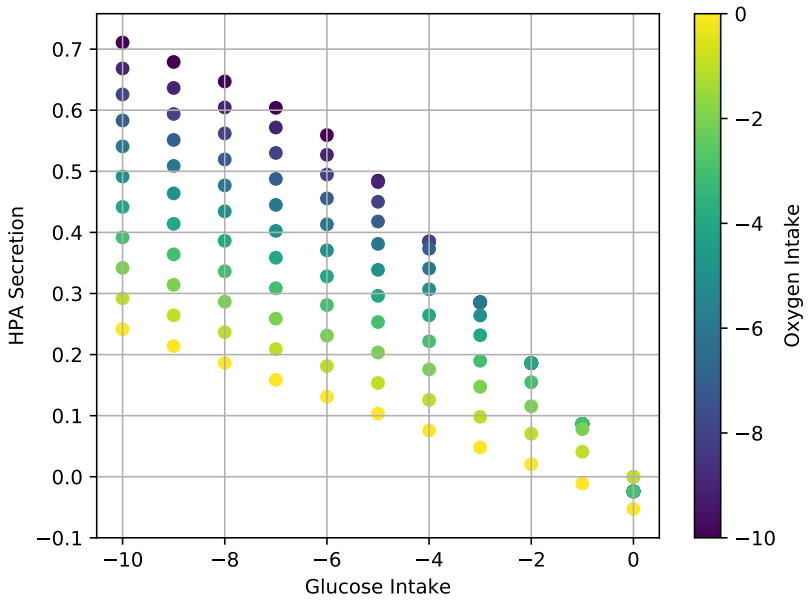
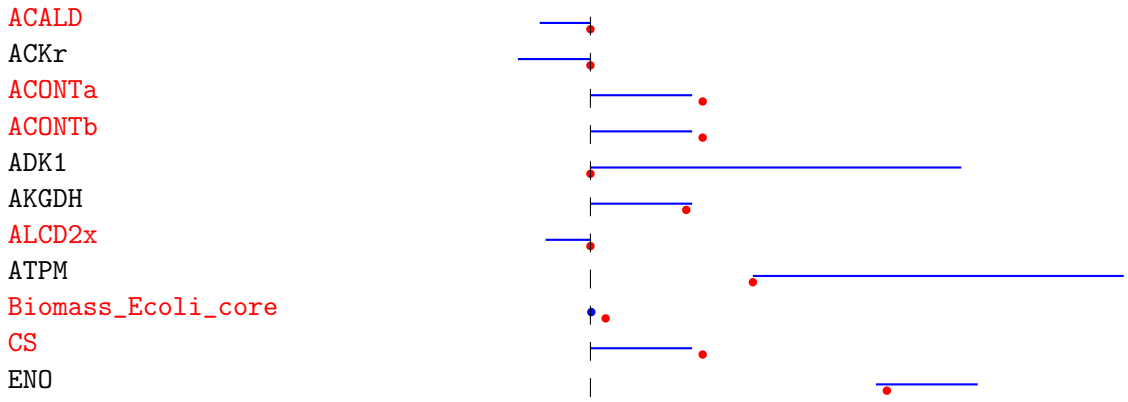


Figure 7: Phaseplane

3 Flux modulation

The flux modulation reveals the following ranges, with the non-overlapping ones coloured in red:



FBA
FBP
FRD7
FUM
G6PDH2r
GAPD
GLNS
GLUDy
GLUN
GLUSy
GND
ICDHyr
ICL
LDH_D
MALS
MDH
ME1
ME2
NADTRHD
PDH
PFK
PFL
PGI
PGK
PGL
PGM
PPC
PPCK
PPS
PTAr
PYK
RPE
RPI
SUCDi
SUCOAS
TALA
TKT1
TKT2
TPI