Table 1. ODEs used in the model based on mass balances.

ODE´s
$\frac{d}{dt}\, glc\_Ext = -v_{PTS\_Glc}$
$\frac{d}{dt} g6p = +v_{PTS\_Glc} - v_{PGI}$
$\frac{d}{dt} f6p = -v_{MPD} + v_{PGI} - v_{PFK} + v_{FBPase}$
$\frac{d}{dt} fbp = +v_{PFK} - v_{FBA} - v_{FBPase}$
$\frac{d}{dt} g3p = +2v_{FBA} - v_{GAPDH}$
$\frac{d}{dt} bpg = +v_{GAPDH} - v_{ENO}$
$\frac{d}{dt} pep = -v_{PTS\_Glc} + v_{ENO} - v_{PYK}$
$\frac{d}{dt} pyr = +v_{PTS\_Glc} - v_{PFL} - v_{PDC} + 2v_{PYK} - v_{LDH}$
$\frac{d}{dt}\, acetCoA = +v_{PFL} - v_{AE} - v_{ACK}$
$\frac{d}{dt}\, acetoin = +v_{PDC} - v_{BDH} - v_{Ace.\ Trsp.}$
$\frac{d}{dt}\, acetoin\_Ext = +v_{Ace.\ Trsp.}$
$\frac{d}{dt}\, 2{,}3butanediol = +v_{BD}$
$\frac{d}{dt}\, m1p = +v_{MPD} - v_{MP} + v_{PTS\_Mtl}$
$\frac{d}{dt}\, mannitol = +v_{MP} - v_{Mtl.\ Trsp}$
$\frac{d}{dt}\, mannitol\_Ext = -v_{PTS\_Mtl} + v_{Mtl.\ Trsp.}$
$\frac{d}{dt}\, lactate = +v_{LDH}$
$\frac{d}{dt}\, ethanol = +v_{AE}$
$\frac{d}{dt}\, acetate = +v_{ACK}$
$\frac{d}{dt} pi = +v_{ATPase} + 2v_{pi\, Trsp.} - v_{GAPDH} + v_{FBPase}$
$\frac{d}{dt}\, pi\_Ext = -v_{pi\ Trsp.}$
$\frac{d}{dt} atp = -v_{ATPase} + v_{ACK} - v_{Pi\, Trsp.} - v_{PFK} + v_{ENO} + v_{PYK}$
$\frac{d}{dt} nad = +2v_{AE} + v_{BDH} + v_{MPD} - v_{GAPDH} + v_{LDH}$
$\frac{d}{dt} CoA = +v_{ACK} - v_{PFL} + v_{AE}$
$\frac{d}{dt} formate = +v_{PFL}$

Electronic Supplementary Material (ESI) for Molecular BioSystems

Table 2. Initial and optimized kinetic model parameters.

Enzyme	Index	Parameter	Initial value	Source	Estimated value
PTS_Glc	1	$V_{max}^{PTS\_Glc}$	1	[-]	3.71 mmol/s
	2	K_a^{pi}	0.5	[-]	0.071 mM
	3	K_i^{fbp}	0.5	[-]	1.17 mM
	4	K_m^{g6p}	0.1	[1]	0.28 mM
	5	K_m^{glcExt}	0.015	[1]	0.049 mM
	6	K_m^{pep}	0.15	[1]	0.31 mM
	7	K_m^{pyr}	0.1	[1]	1.96 mM
ATPase	8	V_{max}^{ATPase}	1.25	[1]	3.29 mM/s
	9	K_m^{atp}	1.5	[1]	4.34 mM
	10	n^{ATPase}	3	[1]	[-]
pi Trsp.	11	$V_{max}^{pi.Trsp.}$	1	[-]	3.60 mmol/s
	12	K_i^{pi}	0.5	[-]	0.56 mM
	13	K_m^{adp}	0.5	[-]	0.19 mM
	14	K_m^{atp}	0.5	[-]	0.52 mM
	15	$K_m^{pi\_ext}$	0.5	[-]	0.75 mM
	16	K_m^{pi}	0.5	[-]	0.30 mM
PGI	17	K_{eq}^{PGI}	0.43	[3]	[-]
	18	V_{max}^{PGI}	651	[4]	21.68 mM/s
	19	K_m^{f6p}	0.147	[3]	3.14 mM
	20	K_m^{g6p}	0.28	[4]	0.20 mM
PFK	21	V_{max}^{PFK}	2.23	[1]	18.36 mM/s
	22	K_m^{adp}	0.49	[5]	10.74 mM
	23	K_m^{atp}	0.18	[1]	0.062 mM
	24	K_m^{f6p}	0.25	[1]	1.02 mM
	25	K_m^{fbp}	16.7	[5]	86.80 mM
FBA	26	K_{eq}^{PBA}	0.056	[1]	[-]
	27	V_{max}^{FBA}	9.9	[1]	56.13 mM/s
	28	K_m^{fbp}	0.17	[1]	0.30 mM
	29	K_m^{g3p}	2.8	[1]	10.11 mM
GAPDH	30	K_{eq}^{GAPDH}	0.0007	[1]	[-]
	31	V_{max}^{GAPDH}	37.58	[1]	30.01 mM/s
	32	K_m^{bpg}	0.05	[1]	0.048 mM
	33	K_m^{g3p}	0.25	[1]	0.18 mM
	34	K_m^{nadh}	0.067	[1]	0.64 mM
	35	K_m^{nad}	0.2	[1]	0.048 mM
	36	K_m^{pi}	2.35	[1]	6.75 mM
ENO	37	K_{eq}^{ENO}	27.55	[1]	[-]
	38	V_{max}^{ENO}	14.84	[1]	29.13 mM/s
	39	K_m^{adp}	0.2	[1]	0.41 mM
	40	K_m^{atp}	0.3	[1]	0.75 mM
	41	K_m^{bpg}	0.003	[1]	0.024 mM
	42	K_m^{pep}	0.53	[1]	1.39 mM

PYK	43	V_{max}^{PYK}	4.82	[1]	2.22 mM/s
	44	K_a^{fbp}	0.2	[1]	0.039 mM
	45	K_i^{pi}	0.5	[1]	3.70 mM
	46	K_m^{adp}	1	[1]	3.08 mM
	47	K_m^{atp}	10	[1]	29.60 mM
	48	K_m^{pep}	0.17	[1]	0.33 mM
	49	K_m^{pyr}	21	[1]	96.42 mM
	50	n^{PYK}	3	[1]	[-]
LDH	51	V_{max}^{LDH}	36.49	[1]	566.60 mmol/s
	52	K_a^{fbp}	0.002	[1]	0.018 mM
	53	K_i^{pi}	0.002	[1]	0.068 mM
	54	$K_m^{lactate}$	100	[6]	94.12 mM
	55	K_m^{nadh}	0.08	[6]	0.14 mM
	56	K_m^{nad}	2.4	[6]	3.08 mM
	57	K_m^{pyr}	1.5	[6]	0.01 mM
PFL	58	K_{eq}^{PFL}	650	[7]	[-]
	59	K_m^{CoA}	0.02	[8]	0.12 mM
	60	V_{max}^{PFL}	4.317	[6]	0.0023 mmol/s
	61	K_i^{g3p}	0.001	[9]	0.51 mM
	62	$K_m^{acetCoA}$	0.008	[6]	7.34 mM
	63	$K_m^{formate}$	24	[6]	54.27 mM
	64	K_m^{pyr}	1	[6]	5.78 mM
AE	65	V_{max}^{AE}	1.62	[6]	2.12 mmol/s
	66	K_i^{atp}	0.5	[-]	6.28 mM
	67	$K_m^{acetCoA}$	0.007	[6]	7.38 mM
	68	K_m^{CoA}	0.008	[6]	0.092 mM
	69	$K_m^{ethanol}$	1	[6]	2.28 mM
	70	K_m^{nadh}	0.025	[6]	0.43 mM
	71	K_m^{nad}	0.08	[6]	1.31 mM
ACK	72	V_{max}^{ACK}	8.93	[6]	3.84 mmol/s
	73	K_m^{adp}	0.5	[6]	1.17 mM
	74	K_m^{atp}	0.07	[6]	14.16 mM
	75	$K_m^{acetCoA}$	0.2	[6]	0.56 mM
	76	$K_m^{acetate}$	7	[6]	0.55 mM
	77	K_m^{CoA}	0.1	[6]	0.17 mM
PDC	78	K_{eq}^{PDC}	900000	[11]	[-]
	79	V_{max}^{PDC}	10	[6]	0.35 mM/s
	80	$K_m^{acetoin}$	0.5	[-]	0.050 mM
	81	K_m^{pyr}	5.2	[10]	0.26 mM

BDH	82	K_{eq}^{BDH}	1400	[6]	[-]
	83	V_{max}^{BDH}	1.75	[6]	2.29 mmol/s
	84	$K_{m}^{acetoin}$	0.06	[6]	5.62 mM
	85	$K_{m}^{butanediol}$	2.6	[6]	1.81 mM
	86	K_{m}^{nadh}	0.02	[6]	3.55 mM
	87	K_{m}^{nad}	0.16	[6]	1.30 mM
MPD	88	K_{eq}^{MPD}	200	[12]	[-]
	89	V_{max}^{MPD}	1	[2]	1.33 mM/s
	90	K_{i}^{f6p}	3.3	[2]	22.03 mM
	91	K_{m}^{f6p}	1.66	[2]	0.32 mM
	92	K_{m}^{m1p}	0.15	[2]	0.089 mM
	93	K_{m}^{nadh}	0.016	[2]	0.030 mM
	94	K_{m}^{nad}	0.06	[2]	0.37 mM
MP	95	V_{max}^{MP}	1	[-]	3.49 mM/s
	96	K_{m}^{m1p}	0.2	[13]	3.52 mM
	97	$K_{m}^{mannitol}$	0.5	[-]	0.24 mM
PTS_Mtl	98	V_{max}^{PTSMtl}	1	[-]	4.45 mmol/s
	99	K_{m}^{m1p}	0.5	[-]	0.36 mM
	100	$K_{m}^{mannitol\_Ext}$	0.5	[-]	0.013 mM
	101	K_{m}^{pep}	0.5	[-]	2.21 mM
	102	K_{m}^{pyr}	0.5	[-]	0.34 mM
Ace. Trsp.	103	$V_{max}^{Ace.Trsp.}$	1	[-]	1.60 mmol/s
	104	$K_{m}^{acetoin}$	0.5	[-]	1.89 mM
	105	$K_{m}^{acetoin\_Ext}$	0.5	[-]	7.05 mM
Mtl. Trsp.	106	$V_{max}^{Mtl.Trsp.}$	1	[-]	1.62 mmol/s
	107	$K_{m}^{mannitol\_Ext}$	0.5	[-]	0.94 mM
	108	$K_{m}^{mannitol}$	0.5	[-]	0.022 mM
FBPase	109	V_{max}^{FBPase}	1	[-]	0.097 mM/s
	110	K_{m}^{f6p}	0.5	[-]	1.91 mM
	111	K_{m}^{fbp}	0.5	[-]	0.41 mM
	112	K_{m}^{pi}	0.5	[-]	0.011 mM

Parameters with missing reference or not estimated represented by “[-]”. Here the initial V_{max} values units are given in mM/s and the initial K_m values in mM. All the abbreviations for the enzymes are explained in nomenclature.

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Table 3. Initial conditions of state variables (metabolites concentrations) for 40mM glucose pulse in the kinetic model.

Metabolite	Initial concentration (mM)	Source
glc_Ext	40	experimental
g6p	0	assumed
f6p	0	assumed
fbp	15.3	experimental
g3p	0	experimental
bpg	1.26	estimated
pep	2.48	estimated
pyr	0	experimental
lactate	0	experimental
acetoin	0	experimental
acetoin_Ext	0	experimental
2,3-butanediol	0	experimental
acetCoA	0	experimental
CoA	1	[1]
ethanol	0	experimental
formate	0	experimental
acetate	0	experimental
m1p	0	experimental
mannitol	0	experimental
mannitol_Ext	0	experimental
atp	4.89	estimated
adp	20.39	estimated
nad	4.67	experimental
nadh	$2.03 \cdot 10^{-6}$	estimated
pi	38.26	experimental
pi_Ext	50	experimental

All the abbreviations for the metabolites are explained in nomenclature.

Reference List

1. Hoefnagel MHN, van der Burgt A, Martens DE, Hugenholtz J, Snoep JL: **Time dependent responses of glycolytic intermediates in a detailed glycolytic model of *Lactococcus lactis* during glucose run-out experiments.** *Molecular Biology Reports* 2002, **29:** 157-161.

Table 4. Kinetic rate expressions used in the model.

Phosphotransferase System (PTS_Glc):

$$r_{PTS_{Glc}} = \left(\frac{[\mathrm{pi}]}{K_a^{pi} + [\mathrm{pi}]}\right)\left(\frac{K_i^{fbp}}{K_i^{fbp} + [\mathrm{fbp}]}\right)\frac{V_{max}^{PTS\_Glc}\left(\frac{[\mathrm{glc\_Ext}]}{K_m^{glc\_Ext}}\right)\left(\frac{[\mathrm{pep}]}{K_m^{pep}}\right)}{\left(1+\frac{[\mathrm{glc\_Ext}]}{K_m^{glc\_Ext}}\right)\left(1+\frac{[\mathrm{pep}]}{K_m^{pep}}\right)+\left(1+\frac{[\mathrm{g6p}]}{K_m^{g6p}}\right)\left(1+\frac{[\mathrm{pyr}]}{K_m^{pyr}}\right)-1}$$

Phosphoglucose isomerase (PGI):

$$r_{PGI} = \frac{V_{max}^{PGI}\frac{[\mathrm{g6p}]}{K_m^{g6p}} - \frac{V_{max}^{PGI}}{K_{eq}^{PGI}}\frac{[\mathrm{f6p}]}{K_m^{g6p}}}{1+\frac{[\mathrm{g6p}]}{K_m^{g6p}}+\frac{[\mathrm{f6p}]}{K_m^{f6p}}}$$

Phosphofructokinase (PFK):

$$r_{PFK} = \frac{V_{max}^{PFK}\left(\frac{[\mathrm{f6p}]}{K_m^{f6p}}\right)\left(\frac{[\mathrm{atp}]}{K_m^{atp}}\right)}{\left(1+\frac{[\mathrm{f6p}]}{K_m^{f6p}}\right)\left(1+\frac{[\mathrm{atp}]}{K_m^{atp}}\right)+\left(1+\frac{[\mathrm{fbp}]}{K_m^{fbp}}\right)\left(1+\frac{[\mathrm{adp}]}{K_m^{adp}}\right)-1}$$

Fructose-1,6-bisphosphate phosphatase (FBPase):

$$r_{FBPase} = \frac{V_{max}^{FBPase}\left(\frac{[\mathrm{fbp}]}{K_m^{fbp}}\right)}{\left(1+\frac{[\mathrm{fbp}]}{K_m^{fbp}}\right)+\left(1+\frac{[\mathrm{f6p}]}{K_m^{f6p}}\right)\left(1+\frac{[\mathrm{pi}]}{K_m^{pi}}\right)-1}$$

Fructose-1,6-bisphosphate aldolase (FBA):

$$r_{FBA} = \frac{V_{max}^{FBA}\frac{[\mathrm{fbp}]}{K_m^{fbp}} - \frac{V_{max}^{FBA}}{K_{eq}^{FBA}}\frac{[g3p]^2}{K_m^{fbp}}}{1+\frac{[\mathrm{fbp}]}{K_m^{fbp}}+\frac{[\mathrm{g3p}]}{K_m^{g3p}}+\left(\frac{[\mathrm{g3p}]}{K_m^{g3p}}\right)^2}$$

Glyceraldehyde-3-phosphate dehydrogenase (GAPDH):

$$r_{GAPDH} = \frac{V_{max}^{GAPDH}\frac{[\mathrm{g3p}]}{K_m^{g3p}}\frac{[\mathrm{nad}]}{K_m^{nad}}\frac{[\mathrm{pi}]}{K_m^{pi}} - \frac{V_{max}^{GAPDH}}{K_{eq}^{GAPDH}}\frac{[\mathrm{bpg}]}{K_m^{g3p}}\frac{[\mathrm{nadh}]}{K_m^{nad}}\frac{1}{K_m^{pi}}}{\left(1+\frac{[\mathrm{g3p}]}{K_m^{g3p}}\right)\left(1+\frac{[\mathrm{pi}]}{K_m^{pi}}\right)\left(1+\frac{[\mathrm{nad}]}{K_m^{nad}}\right)+\left(1+\frac{[\mathrm{bpg}]}{K_m^{bpg}}\right)\left(1+\frac{[\mathrm{nadh}]}{K_m^{nadh}}\right)-1}$$

Enolase (ENO):

$$r_{ENO} = \frac{V_{max}^{ENO}\frac{[\mathrm{bpg}]}{K_m^{g3p}}\frac{[\mathrm{adp}]}{K_m^{nad}} - \frac{V_{max}^{ENO}}{K_{eq}^{ENO}}\frac{[\mathrm{pep}]}{K_m^{bpg}}\frac{[\mathrm{atp}]}{K_m^{adp}}}{\left(1+\frac{[\mathrm{bpg}]}{K_m^{bpg}}\right)\left(1+\frac{[\mathrm{adp}]}{K_m^{adp}}\right)+\left(1+\frac{[\mathrm{pep}]}{K_m^{pep}}\right)\left(1+\frac{[\mathrm{atp}]}{K_m^{atp}}\right)-1}$$

Pyruvate kinase (PYK):

$$r_{PYK} = \left(\frac{[\mathrm{fbp}]}{K_a^{fbp} + [\mathrm{fbp}]}\right)\left(\frac{\left(K_i^{pi}\right)^{n^{PYK}}}{\left(K_i^{pi}\right)^{n^{PYK}} + ([\mathrm{pi}])^{n^{PYK}}}\right)\frac{V_{max}^{PYK}\left(\frac{[\mathrm{adp}]}{K_m^{adp}}\right)\left(\frac{[\mathrm{pep}]}{K_m^{pep}}\right)}{\left(1+\frac{[\mathrm{adp}]}{K_m^{adp}}\right)\left(1+\frac{[\mathrm{pep}]}{K_m^{pep}}\right)+\left(1+\frac{[\mathrm{atp}]}{K_m^{atp}}\right)\left(1+\frac{[\mathrm{pyr}]}{K_m^{pyr}}\right)-1}$$

L-lactate dehydrogenase (LDH):

$$r_{LDH} = \left(\frac{[\mathrm{fbp}]}{K_a^{fbp} + [\mathrm{fbp}]}\right)\left(\frac{K_i^{pi}}{K_i^{pi} + [\mathrm{pi}]}\right)\frac{V_{max}^{LDH}\left(\frac{[\mathrm{pyr}]}{K_m^{pyr}}\right)\left(\frac{[\mathrm{nadh}]}{K_m^{nadh}}\right)}{\left(1+\frac{[\mathrm{pyr}]}{K_m^{pyr}}\right)\left(1+\frac{[\mathrm{nadh}]}{K_m^{nadh}}\right)+\left(1+\frac{[\mathrm{lactate}]}{K_m^{lactate}}\right)\left(1+\frac{[\mathrm{nad}]}{K_m^{nad}}\right)}$$

Pyruvate dehydrogenase (PFL):

$$r_{PFL} = \left(\frac{K_i^{g3p}}{K_i^{g3p} + [\mathrm{g3p}]}\right)\frac{V_{max}^{PFL}\frac{[\mathrm{pyr}]}{K_m^{pyr}}\frac{[\mathrm{CoA}]}{K_m^{CoA}} - \frac{V_{max}^{PFL}}{K_{eq}^{PFL}}\frac{[\mathrm{acetCoA}]}{K_m^{pyr}}\frac{[\mathrm{formate}]}{K_m^{CoA}}}{\left(1+\frac{[\mathrm{pyr}]}{K_m^{pyr}}\right)\left(1+\frac{[\mathrm{CoA}]}{K_m^{CoA}}\right)+\left(1+\frac{[\mathrm{acetCoA}]}{K_m^{\mathrm{acetCoA}}}\right)\left(1+\frac{[\mathrm{formate}]}{K_m^{formate}}\right)-1}$$

Alcohol dehydrogenase (AE):

$$r_{AE} = \left(\frac{K_i^{atp}}{K_i^{atp} + [\mathrm{atp}]}\right)\frac{V_{max}^{AE}\left(\frac{[\mathrm{acetCoA}]}{K_m^{acetCoA}}\right)\left(\frac{[\mathrm{nadh}]}{K_m^{nadh}}\right)^2}{\left(1+\frac{[\mathrm{acetCoA}]}{K_m^{acetCoA}}\right)\left(1+\frac{[\mathrm{nadh}]}{K_m^{nadh}}+\left(\frac{[\mathrm{nadh}]}{K_m^{nadh}}\right)^2\right)+\left(1+\frac{[\mathrm{ethanol}]}{K_m^{ethanol}}\right)\left(1+\frac{[\mathrm{CoA}]}{K_m^{CoA}}\right)\left(1+\frac{[\mathrm{nad}]}{K_m^{nad}}+\left(\frac{[\mathrm{nad}]}{K_m^{nad}}\right)^2\right)-1}$$

Acetate kinase (ACK):

$$r_{ACK} = \frac{V_{max}^{ACK}\left(\frac{[\mathrm{acetCoA}]}{K_m^{acetCoA}}\right)\left(\frac{[\mathrm{adp}]}{K_m^{adp}}\right)}{\left(1+\frac{[\mathrm{acetCoA}]}{K_m^{acetCoA}}\right)\left(1+\frac{[\mathrm{adp}]}{K_m^{adp}}\right)+\left(1+\frac{[\mathrm{acetate}]}{K_m^{acetate}}\right)\left(1+\frac{[\mathrm{atp}]}{K_m^{atp}}\right)\left(1+\frac{[\mathrm{CoA}]}{K_m^{CoA}}\right)-1}$$

Pyruvate decarboxylase (PDC):

$$r_{PDC} = \frac{V_{max}^{PD}\left(\frac{[\mathrm{pyr}]}{K_m^{pyr}}\right)^2 - \frac{V_{max}^{PD}}{K_{eq}^{PD}}\frac{[\mathrm{acetoin}]}{K_m^{pyr}}}{\left(1+\frac{[\mathrm{pyr}]}{K_m^{pyr}}+\left(\frac{[\mathrm{pyr}]}{K_m^{pyr}}\right)^2\right)+\left(1+\frac{[\mathrm{acetoin}]}{K_m^{acetoin}}\right)-1}$$

2,3-Butanediol dehydrogenase (BDH):

$$r_{BDH} = \frac{V_{max}^{BD}\left(\frac{[\text{acetoin}]}{K_m^{acetoin}}\right)\left(\frac{[\text{nadh}]}{K_m^{nadh}}\right) - \frac{V_{max}^{BD}}{K_{eq}^{BD}}\frac{[2,3-\text{butanediol}]}{K_m^{acetoin}}\frac{[\text{nad}]}{K_m^{nadh}}}{\left(1+\frac{[\text{acetoin}]}{K_m^{acetoin}}\right)\left(1+\frac{[\text{nadh}]}{K_m^{nadh}}\right)+\left(1+\frac{[2,3-\text{butanediol}]}{K_m^{butanediol}}\right)\left(1+\frac{[\text{nad}]}{K_m^{nad}}\right)-1}$$

Acetoin transport (Ace. Trsp.):

$$r_{Ace.Trsp.} = \frac{V_{max}^{Ace.Trsp.}\left(\frac{[\text{acetoin}]}{K_m^{acetoin}}\right)}{\left(1+\frac{[\text{acetoin}]}{K_m^{acetoin}}\right)+\left(1+\frac{[\text{acetoin\_Ext}]}{K_m^{acetoin\_Ext}}\right)-1}$$

Mannitol-1-Phosphate dehydrogenase (MPD):

$$r_{MPD} = \left(\frac{K_i^{f6p}}{K_i^{f6p}+[\text{f6p}]}\right)\frac{V_{max}^{MPD}\frac{[\text{f6p}]}{K_m^{f6p}}\frac{[\text{nadh}]}{K_m^{nadh}} - \frac{V_{max}^{MPD}}{K_{eq}^{MPD}}\frac{[\text{m1p}]}{K_m^{f6p}}\frac{[\text{nad}]}{K_m^{nadh}}}{\left(1+\frac{[\text{f6p}]}{K_m^{f6p}}\right)\left(1+\frac{[\text{nadh}]}{K_m^{nadh}}\right)+\left(1+\frac{[\text{m1p}]}{K_m^{m1p}}\right)\left(1+\frac{[\text{nad}]}{K_m^{nad}}\right)-1}$$

Mannitol-1-Phosphatase (MP):

$$r_{MP} = \frac{V_{max}^{MP}\left(\frac{[\text{m1p}]}{K_m^{m1p}}\right)}{\left(1+\frac{[\text{m1p}]}{K_m^{m1p}}\right)+\left(1+\frac{[\text{mannitol}]}{K_m^{mannitol}}\right)-1}$$

Phosphotransferase System (PTS_Mtl):

$$r_{PTS\_Mtl} = \frac{V_{max}^{PTS\_Mtl}\left(\frac{[\text{mannitol\_Ext}]}{K_m^{mannitol\_Ext}}\right)\left(\frac{[\text{pep}]}{K_m^{pep}}\right)}{\left(1+\frac{[\text{mannitol\_Ext}]}{K_m^{mannitol\_Ext}}\right)\left(1+\frac{[\text{pep}]}{K_m^{pep}}\right)+\left(1+\frac{[\text{m1p}]}{K_m^{m1p}}\right)\left(1+\frac{[\text{pyr}]}{K_m^{pyr}}\right)-1}$$

Mannitol transport (Mtl. Trsp.):

$$r_{Mtl.Trsp.} = \frac{V_{max}^{Mtl.Trsp.}\left(\frac{[\text{mannitol}]}{K_m^{mannitol}}\right)}{\left(1+\frac{[\text{mannitol}]}{K_m^{mannitol}}\right)+\left(1+\frac{[\text{mannitol\_Ext}]}{K_m^{mannitol\_Ext}}\right)-1}$$

Phosphate transport (pi Trsp.):

$$r_{pi\ Trsp.} = \left(\frac{K_i^{pi}}{K_i^{pi}+[\text{pi}]}\right)\frac{V_{max}^{pi\ Trsp.}\left(\frac{[\text{atp}]}{K_m^{atp}}\right)\left(\frac{[\text{pi\_Ext}]}{K_m^{pi\_Ext}}\right)}{\left(1+\frac{[\text{atp}]}{K_m^{atp}}\right)\left(1+\frac{[\text{pi\_Ext}]}{K_m^{pi\_Ext}}\right)+\left(1+\frac{[\text{adp}]}{K_m^{adp}}\right)\left(1+\frac{[\text{pi}]}{K_m^{pi}}+\left(\frac{[\text{pi}]}{K_m^{pi}}\right)^2\right)-1}$$

ATP phosphatase (ATPase):

$$r_{ATPase} = V_{max}^{ATPase}\left(\frac{\left(\frac{[\mathrm{atp}]}{K_m^{atp}}\right)^{n^{ATPase}}}{\left(\frac{[\mathrm{atp}]}{K_m^{atp}}\right)^{n^{ATPase}} + 1}\right)$$

Electronic Supplementary Material (ESI) for Molecular BioSystems

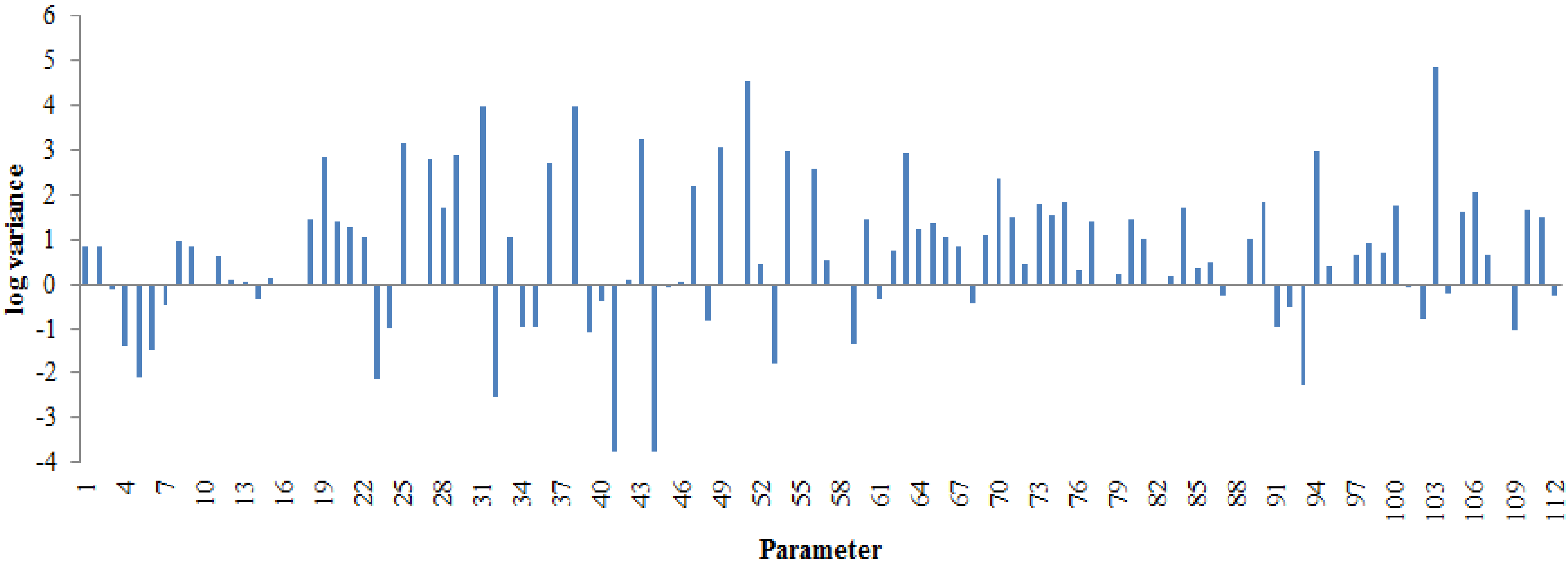

Figure 1. Variance analysis of the parameter set values of the kinetic model. For a better visualization the variance of every parameter are plotted with a logarithmic scale. The parameter indices correspond to the reaction numbers shown in Additional File 2.

Electronic Supplementary Material (ESI) for Molecular BioSystems

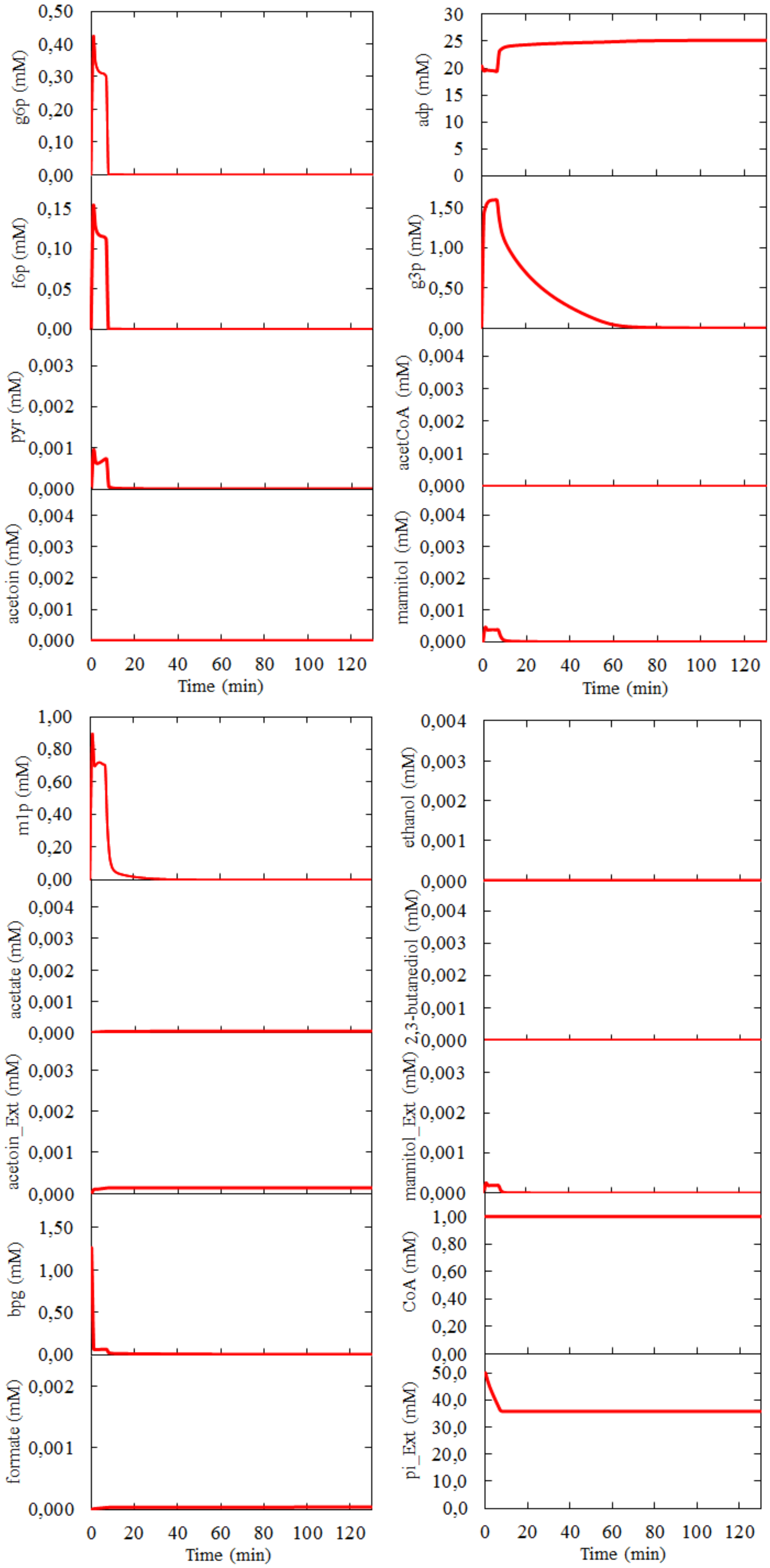

Figure 2. Simulation results for the initial metabolite concentrations and estimated kinetic parameter values listed in Additional File 3 and 2, respectively.

Figure 3. Correlation values of sensitivities between all pairs of fits from wilt-type strain for 2,3-butanediol (plots in lower triangle) and mannitol (plots in upper triangle).

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Figure 4. Correlation values of sensitivities between all pairs of fits from LDH mutant strain for 2,3-butanediol (plots in lower triangle) and mannitol (plots in upper triangle).

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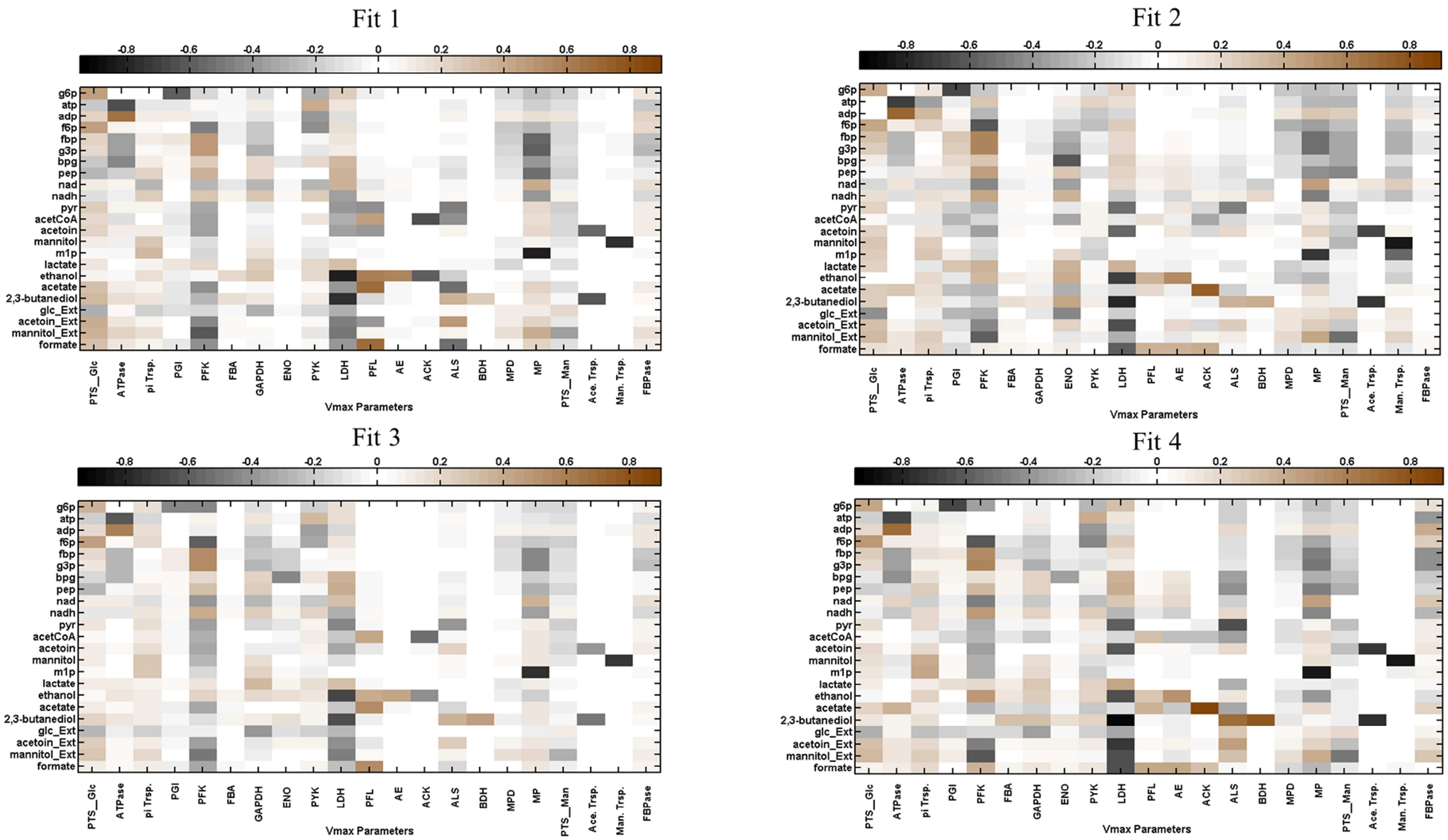
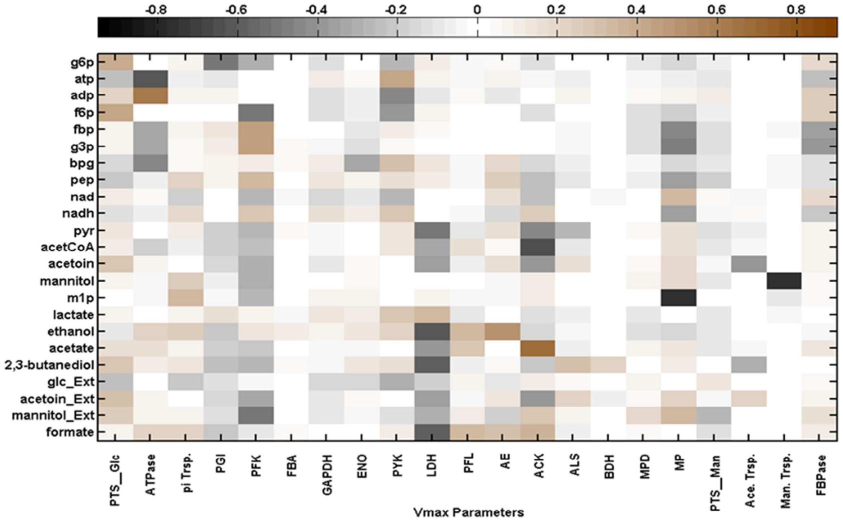
Figure 5. Correlation values of sensitivities between all pairs of fits from LDH/PTS^{Mtl} mutant strain for 2,3-butanediol (plots in lower triangle) and mannitol (plots in upper triangle).

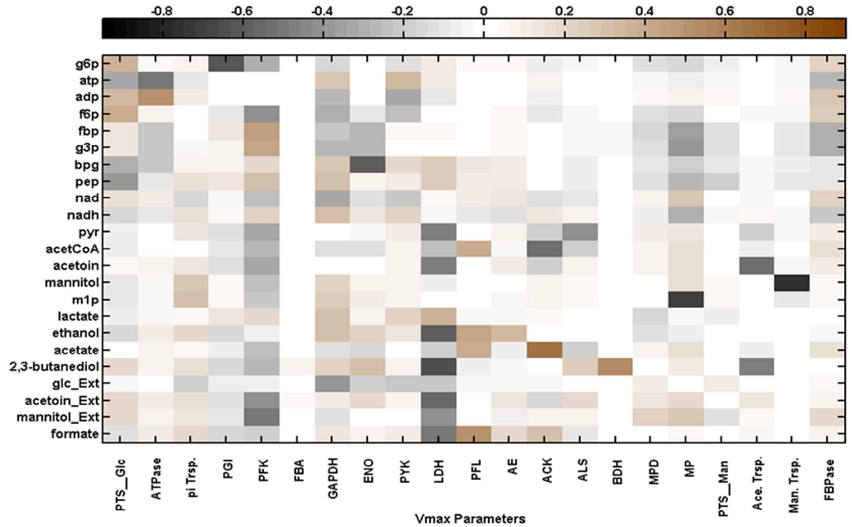

Fit 1
Fit 2
Fit 3
Fit 4
-0.8 -0.6 -0.4 -0.2 0 0.2 0.4 0.6 0.8
g6p
atp
adp
f6p
fbp
g3p
bpg
pep
nad
nadh
pyr
acetCoA
acetoin
mannitol
m1p
lactate
ethanol
acetate
2,3-butanediol
glc_Ext
acetoin_Ext
mannitol_Ext
formate
PTS__Glc
ATPase
pi Trsp.
PGI
PFK
FBA
GAPDH
ENO
PYK
LDH
PFL
AE
ACK
ALS
BDH
MPD
MP
PTS__Man
Ace. Trsp.
Man. Trsp.
FBPase
Vmax Parameters

Electronic Supplementary Material (ESI) for Molecular BioSystems

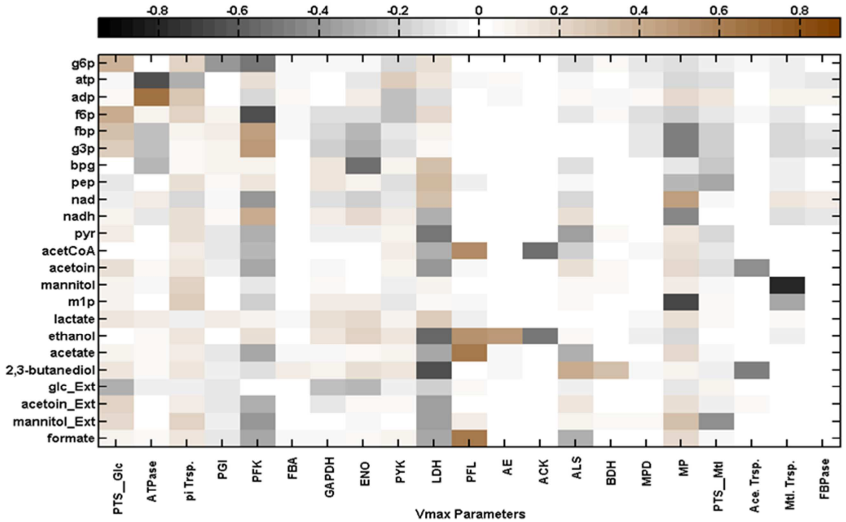
Fit 5



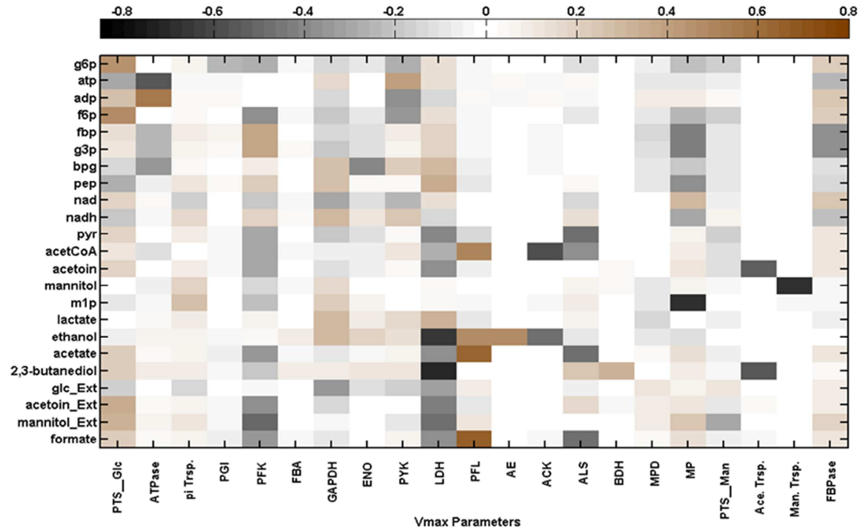
Fit 6



Fit 7



Fit 8



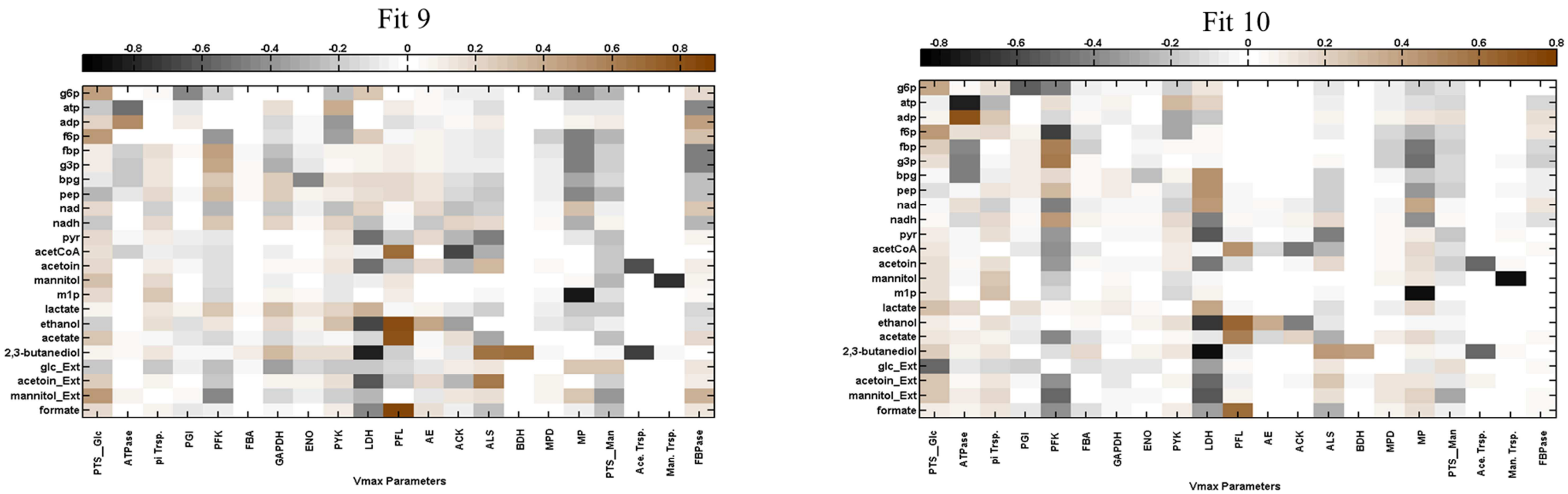


Figure 6. Heat maps showing the integrated response coefficients to variation in V_{max} parameters for all ten fits.