

Table S1: Metabolic and carbon atom transition model used in this study

ID	Enzyme name	Reaction and carbon atom transition
tGln	Glutamine importer	Gln_ex[(1,2,3,4,5)] => Gln[(1,2,3,4,5)]
gs4	Glutaminase	Gln[(1,2,3,4,5)] => Glu[(1,2,3,4,5)]
tGlu	Glutamate transporter	Glu[(1,2,3,4,5)] = Glu_ex[(1,2,3,4,5)]
Gdh	Glutamate dehydrogenase	aKG_m[(1,2,3,4,5)] = Glu_m[(1,2,3,4,5)]
tGlc	Glucose importer	Glc_ex[(1,2,3,4,5,6)] => G6P[(1,2,3,4,5,6)]
fGlyco	Carbon storage (glycogen) degradation	Glyco_ex[(1,2,3,4,5,6)] => G6P[(1,2,3,4,5,6)]
Pgi	Phospho-glucose-isomerase	G6P[(1,2,3,4,5,6)] = F6P[(1,2,3,4,5,6)]
Pfk	Phosphofructokinase + fructose-1,6-bisphosphatase	F6P[(1,2,3,4,5,6)] = FBP[(1,2,3,4,5,6)]
fbpa	Fructose-bisphosphate aldolase	FBP[(1,2,3,4,5,6)] = DHAP[(3,2,1)] + GAP[(4,5,6)]
Tpi	Triphosphate isomerase	DHAP[(1,2,3)] = GAP[(1,2,3)]
gapdh	GAP dehydrogenase + biphosphoglycerate mutase	GAP[(1,2,3)] = 3PG[(1,2,3)]
Eno	Phosphoglycerate hydratase	3PG[(1,2,3)] = PEP[(1,2,3)]
pkm	Pyruvate kinase	PEP[(1,2,3)] => Pyr[(1,2,3)]
Ldh	Lactate dehydrogenase	Pyr[(1,2,3)] = Lac[(1,2,3)]
tLac	Lactate transporter	Lac[(1,2,3)] => Lac_ex[(1,2,3)]
G6Pdh	Glucose-6-phosphate dehydrogenase	G6P[(1,2,3,4,5,6)] => Ru5P [(2,3,4,5,6)] + CO2[(1)]
Rpi	Ribulose-5-phosphate isomerase	Ru5P[(1,2,3,4,5)] = R5P[(1,2,3,4,5)]
tkt1	Transketolase	R5P[(1,2,3,4,5)(6,7,8,9,10)] = S7P[(6,7,1,2,3,4,5)] + GAP[(8,9,10)]
Tald	Transaldolase	E4P[(1,2,3,4)] + R5P[(5,6,7,8,9)] = F6P[(5,6,1,2,3,4)] + GAP[(7,8,9)]
tkt2	Transketolase	S7P[(1,2,3,4,5,6,7)] + GAP[(8,9,10)] = E4P[(4,5,6,7)] + F6P[(1,2,3,8,9,10)]
tCO2	CO ₂ evolution	CO2[(1)] => CO2_ex[(1)]
MPC1	Pyruvate/H ⁺ symporter	Pyr[(1,2,3)] => Pyr_m[(1,2,3)]
CIC	Citrate/Malate antiporter	Cit_m[(1,2,3,4,5,6)] + Mal[(7,8,9,10)] => Cit[(1,2,3,4,5,6)] + Mal_m[(7,8,9,10)]
DIC	PO ₃ ⁴⁻ /Malate antiporter	Mal_m[(1,2,3,4)] = Mal[(1,2,3,4)]
GC1	Glutamate/H ⁺ symporter	Glu_m[(1,2,3,4,5)] = Glu[(1,2,3,4,5)]
OGC	Malate/aKG antiporter	Mal[(1,2,3,4)] + aKG_m[(5,6,7,8,9)] = Mal_m[(1,2,3,4)] + aKG[(5,6,7,8,9)]
AGC1	Aspartate/glutamate antiporter	Glu[(1,2,3,4,5)] + Asp_m[(6,7,8,9)] => Glu_m[(1,2,3,4,5)] + Asp[(6,7,8,9)]
mAla	Putative alanine transporter	Ala[(1,2,3)] = Ala_m[(1,2,3)]

mAsn	Putative asparagine transporter	$\text{Asn}[(1,2,3,4)] = \text{Asn_m}[(1,2,3,4)]$
Pdh	Pyruvate dehydrogenase	$\text{Pyr_m}[(1,2,3)] \Rightarrow \text{AcCoA_m}[(2,3)] + \text{CO2}[(1)]$
Cs	Citrate synthase	$\text{OAA_m}[(1,2,3,4)] + \text{AcCoA_m}[(5,6)] \Rightarrow \text{Cit_m}[(4,3,2,6,5,1)]$
Idh	Iso-citrate dehydrogenase	$\text{Cit_m}[(1,2,3,4,5,6)] = \text{aKG_m}[(1,2,3,4,5)] + \text{CO2}[(6)]$
Adh	aKG dehydrogenase + succinyl-CoA ligase + succinate dehydrogenase + fumarase	$\text{aKG_m}[(1,2,3,4,5)(6,7,8,9,10)] = \text{Mal_m}[(2,3,4,5)(10,9,8,7)] + \text{CO2}[(1)(6)]$
Mdh	Malate dehydrogenase	$\text{Mal_m}[(1,2,3,4)(5,6,7,8)] = \text{OAA_m}[(1,2,3,4)(8,7,6,5)]$
Pepck	Phosphoenolpyruvate carboxykinase	$\text{OAA}[(1,2,3,4)] = \text{PEP}[(1,2,3)] + \text{CO2}[(4)]$
me_c	Cytosolic malic enzyme	$\text{Mal}[(1,2,3,4)] = \text{Pyr}[(1,2,3)] + \text{CO2}[(4)]$
me_m	Mitochondrial malic enzyme	$\text{Mal_m}[(1,2,3,4)] = \text{Pyr_m}[(1,2,3)] + \text{CO2}[(4)]$
Pc	Pyruvate carboxylase	$\text{Pyr_m}[(1,2,3)] + \text{CO2}[(4)] = \text{OAA_m}[(1,2,3,4)]$
mdh_c	Cytosolic malate dehydrogenase	$\text{OAA}[(1,2,3,4)(5,6,7,8)] = \text{Mal}[(1,2,3,4)(8,7,6,5)]$
tSer	Serine importer	$\text{Ser_ex}[(1,2,3)] \Rightarrow \text{Ser}[(1,2,3)]$
phdgh	Phosphoglycerate dehydrogenase + phosphoserine phosphatase	$3\text{PG}[(1,2,3)] \Rightarrow \text{Ser}[(1,2,3)]$
sds	Serine dehydratase	$\text{Ser}[(1,2,3)] \Rightarrow \text{Pyr}[(1,2,3)]$
tAla	Alanine transporter	$\text{Ala}[(1,2,3)] = \text{Ala_ex}[(1,2,3)]$
alt_c	Cytosolic alanine aminotransferase	$\text{Pyr}[(1,2,3)] + \text{Glu}[(4,5,6,7,8)] = \text{Ala}[(1,2,3)] + \text{aKG}[(4,5,6,7,8)]$
alt_m	Mitochondrial alanine aminotransferase	$\text{Ala_m}[(1,2,3)] + \text{aKG_m}[(4,5,6,7,8)] = \text{Pyr_m}[(1,2,3)] + \text{Glu_m}[(4,5,6,7,8)]$
tAsp	Aspartate transporter	$\text{Asp_ex}[(1,2,3,4)] = \text{Asp}[(1,2,3,4)]$
tAsn	Asparagine importer	$\text{Asn_ex}[(1,2,3,4)] \Rightarrow \text{Asn}[(1,2,3,4)]$
ast_c	Cytosolic aspartate aminotransferase	$\text{Asp}[(1,2,3,4)] + \text{aKG}[(5,6,7,8,9)] = \text{OAA}[(1,2,3,4)] + \text{Glu}[(5,6,7,8,9)]$
ast_m	Mitochondrial aspartate aminotransferase	$\text{Asp_m}[(1,2,3,4)] + \text{aKG_m}[(5,6,7,8,9)] = \text{OAA_m}[(1,2,3,4)] + \text{Glu_m}[(5,6,7,8,9)]$
asns	Asparaginase	$\text{Asn_m}[(1,2,3,4)] = \text{Asp_m}[(1,2,3,4)]$
muG6P	Biomass formation from G6P	$\text{G6P}[(1,2,3,4,5,6)] \Rightarrow \text{G6P_X_ex}[(1,2,3,4,5,6)]$
muGAP	Biomass formation from GAP	$\text{GAP}[(1,2,3)] \Rightarrow \text{GAP_X_ex}[(1,2,3)]$
muRu5P	Biomass formation from Ru5P	$\text{R5P}[(1,2,3,4,5)] \Rightarrow \text{R5P_X_ex}[(1,2,3,4,5)]$
acl	Acetyl-CoA lyase	$\text{Cit}[(1,2,3,4,5,6)] \Rightarrow \text{OAA}[(6,3,2,1)] + \text{AcCoA}[(5,4)]$
muAcCoA	Biomass formation from AcCoA	$\text{AcCoA}[(1,2)] \Rightarrow \text{AcCoA_X_ex}[(1,2)]$
muSer	Biomass formation from	$\text{Ser}[(1,2,3)] \Rightarrow \text{Ser_X_ex}[(1,2,3)]$

	serine	
muAla	Biomass formation from alanine	Ala[(1,2,3)] => Ala_X_ex[(1,2,3)]
muAsp	Biomass formation from aspartate	Asp[(1,2,3,4)] => Asp_X_ex[(1,2,3,4)]
muAsn	Biomass formation from asparagine	Asn[(1,2,3,4)] => Asn_X_ex[(1,2,3,4)]
muGln	Biomass formation from glutamine	Gln[(1,2,3,4,5)] => Gln_X_ex[(1,2,3,4,5)]
muGlu	Biomass formation from glutamate	Glu[(1,2,3,4,5)] => Glu_X_ex[(1,2,3,4,5)]

Table S2: Specific uptake and release rates of extracellular metabolites and its Lower Boundary (LB) and Upper Boundary (UB)

Metabolites	Uptake/Secretion rate ($\mu\text{mol cell}^{-1} \text{h}^{-1}$) ¹	[LB UB] ²
D-glucose	-0.112	[-0.129 -0.095]
L-lactate	0.134	[0.106 0.163]
L-glutamine	-0.057	[-0.067 -0.047]
L-glutamate	0.023	[0.014 0.032]
L-asparagine	-0.017	[-0.017 -0.017]
L-aspartate	0.003	[0.002 0.004]
L-alanine	0.011	[0.009 0.013]
L-serine	-0.016	[-0.011 -0.021]
IgG ₁	0.443 ³	[0.354 0.532] ³

¹ value < 0 means uptake; value > 0 means secretion

²according to 95% confidence interval (linear regression)

³unit is in $\mu\text{g cell}^{-1} \text{h}^{-1}$