BioComputing's Network-Graph Tool
Version 0.99

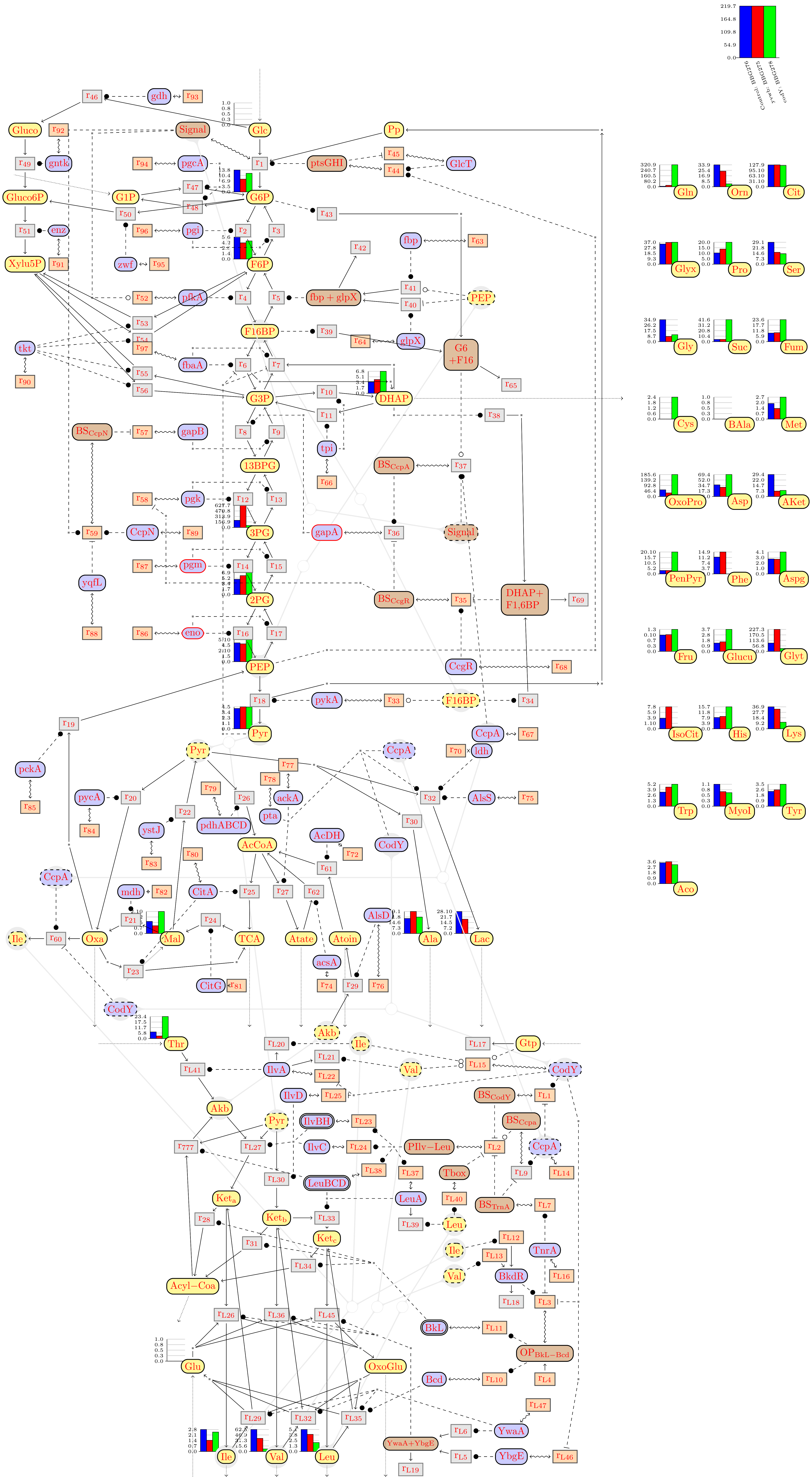
Joachim Niehren

Inria & BioComputing, Lille, France

1 Reaction Network Networks/b-subtilis.xml

Reaction Network. See file: Networks/b-subtilis.xml See Figure 1.

Analysis means-constituitive-6h



Control BH276
ywaA BH276
codY BH276
Gln
Orn
Cit
Glyx
Pro
Ser
Gly
Suc
Fum
Cys
BAla
Met
OxoPro
Asp
AKet
PenPyr
Phe
Aspg
Fru
Glucu
Glyt
IsoCit
His
Lys
Trp
MyoI
Tyr
Aco

Fig. 1. The Networks/b-subtilis.xml.

Name	Function
r_1	Phosphorylation of G
$r_{1'}$	degradation of Signal
r_2	Catalyse the conversion of G6P to F6P
r_3	Catalyse the conversion of F6P to G6P ?
r_4	Catalyse the conversion of F6P to F16BP
r_5	Catalyse the conversion of F16BP to F6P
r_6	Conversion of F16BP to G3P
r_7	Conversion of G3P to F16BP
r_8	Catalyse the conversion of G3P to 13BPG
r_9	Catalyse the conversion of 13BPG to G3P
r_{10}	Catalyse the conversion of G3P to DHAP
r_{11}	Catalyse the conversion of DHAP to G3P
r_{12}	Catalyse the conversion of 13BPG to 3PG
r_{13}	Catalyse the conversion of 3PG to 13BPG
r_{14}	Catalyse the conversion of 3PG to 2PG
r_{15}	Catalyse the conversion of 2PG to 3PG
r_{16}	Catalyse the conversion of 2PG to PEP
r_{17}	Catalyse the conversion of PEP to 2PG
r_{18}	Catalyse the conversion of PEP to Pyr
r_{33}	expression of pykA
$r_{33'}$	degradation of pykA
r_{34}	Express F16BP
r_{35}	Bind CcgR to gapA for inhibition
$r_{35'}$	degradation of BS_{CcgR}
r_{36}	Regulation of gapA activity, activation by CcpA and inhibition by CcgR
$r_{36'}$	degradation of gapA
r_{37}	Bind CcpA to gapA for activation
$r_{37'}$	degradation of BS_{CcpA}
r_{38}	Express DHAP
r_{39}	Expression of F16BP
r_{40}	Express glpX
r_{41}	Express fbp
r_{42}	degradation of fbp + glpX
r_{43}	Express G6P
r_{44}	Activation of GlcT activity
$r_{44'}$	degradation of ptsGHI
r_{45}	Inhibition of GlcT activity by pstGHI
$r_{45'}$	degradation of GlcT
r_{46}	Production of G throw Gluco
r_{47}	Catalyse the conversion of G1P to G6P
r_{48}	Catalyse the conversion of G6P to G1P
r_{49}	Production of Gluco throw Gluco6P
r_{50}	Production of G6P throw Gluco6P
r_{51}	Production of Xylu5P throw Gluco6P
r_{52}	expression of pfkA
$r_{52'}$	degradation of pfkA
r_{53}	Production of Xylu5P throw F6P
r_{54}	Production of Xylu5P throw F6P
r_{55}	Production of G3P throw Xylu5P
r_{56}	Production of Xylu5P throw G3P
r_{57}	Expression of gapB
$r_{57'}$	degradation of gapB
r_{58}	expression of pgk
$r_{58'}$	degradation of pgk
r_{59}	Bind CcpN to gapB for inhibition
$r_{59'}$	degradation of BS_{CcpN}
r_{63}	expression of fbp
$r_{63'}$	degradation of fbp
r_{64}	expression of glpX
$r_{64'}$	degradation of glpX
r_{65}	degradation of G6 +F16
r_{66}	degradation of tpi
$r_{66'}$	degradation of tpi
r_{67}	expression of CcpA
$r_{67'}$	degradation of CcpA
r_{68}	expression of CcgR
$r_{68'}$	degradation of CcgR
r_{69}	degradation of G6P + DH + F2
r_{86}	expression of eno
$r_{86'}$	degradation of eno
r_{87}	expression of pgm
$r_{87'}$	degradation of pgm
r_{88}	degradation of yqfL
$r_{88'}$	degradation of yqfL
r_{89}	expression of CcpN
$r_{89'}$	degradation of CcpN
r_{90}	degradation of tkt
$r_{90'}$	degradation of tkt
r_{91}	degradation of enz
$r_{91'}$	degradation of enz
r_{92}	degradation of gntk
$r_{92'}$	degradation of gntk
r_{93}	degradation of gdh
$r_{93'}$	degradation of gdh
r_{94}	expression of pgcA
$r_{94'}$	degradation of pgcA
r_{95}	degradation of zwf
$r_{95'}$	degradation of zwf
r_{96}	expression of pgi
$r_{96'}$	degradation of pgi

r_{97}	expression of fbaA
$r_{97'}$	degradation of fbaA
r_{20}	Production of Atoin throw Pyr
r_{21}	Production of Oxa throw Mal
r_{22}	Production of Pyr throw Mal
r_{23}	Production of TCA throw Oxa
r_{24}	Production of Mal throw TCA
r_{25}	Turn to TCA throw AcCoA
r_{26}	Production of AcCoA from Pyr
r_{27}	Production of Atate from AcCoA
r_{29}	Production of Atoin from Aceto
r_{30}	Production of Alanine from Pyr
r_{32}	Production of Lac from Pyr
r_{60}	Production of Ile from Oxa
r_{61}	Production of AcCoA from Atoin
r_{62}	Production of AcCoA from Atate
r_{70}	expression of ldh
$r_{70'}$	degradation of ldh
r_{72}	expression of AcDH
$r_{72'}$	degradation of AcDH
r_{74}	expression of acsA
$r_{74'}$	degradation of acsA
r_{75}	expression of AlsS
$r_{75'}$	degradation of AlsS
r_{76}	expression of eno
$r_{76'}$	degradation of AlsD
r_{77}	expression of ackA
$r_{77'}$	degradation of ackA
r_{78}	expression of pta
$r_{78'}$	degradation of pta
r_{79}	expression of pdhABCD
$r_{79'}$	degradation of pdhABCD
r_{80}	expression of CitA
$r_{80'}$	degradation of CitA
r_{81}	expression of CitG
$r_{81'}$	degradation of CitG
r_{82}	expression of mdh
$r_{82'}$	degradation of mdh
r_{83}	expression of ystJ
$r_{83'}$	degradation of ystJ
r_{84}	expression of pycA
$r_{84'}$	degradation of pycA
r_{85}	expression of pckA
$r_{85'}$	degradation of pckA
r_{19}	feedback reaction to PEP from Oxa
r_{L1}	bind CodY to PIlv$-$Leu for inhibition
	predition: single knockout, unsafe
	experiment: OK (we have this mutant)
$r_{L1'}$	degradation of BS_{CodY}
r_{L2}	activate PIlv$-$Leu promoter
	predition: no
	experiment: not done, because we need the expression of $Pilv - Leu$
	in order to activate the reaction r_{23}, r_{24}, r_{39}, r_{37}
$r_{L2'}$	degradation of PIlv$-$Leu
r_{L3}	bind BkdR to BkL Bcd promoter
	experiment: Ok
$r_{L3'}$	degradation of $OP_{BkL-Bcd}$
r_{L4}	constitutive expression of BkL Bcd operon
	experiment: Ok
r_{L5}	express YbgE
r_{L6}	express YwaA
r_{L7}	bind TnrA to PIlv$-$Leu promoter for inhibition
	predition: safe single knockout
	experiment: OK (we have this mutant)
$r_{L7'}$	degradation of BS_{TrnA}
r_{L9}	bind CcpA to PIlv$-$Leu promoter without BS_{TrnA} loop
$r_{L9'}$	degradation of BS_{Ccpa}
r_{L10}	expression of Bcd, activated by $OP_{BkL-Bcd}$
	experiment: OK (we have this mutant)
$r_{L10'}$	degradation of Bcd
r_{L11}	expression of BkL, activated by $OP_{BkL-Bcd}$
	experiment: OK (we have this mutant)
$r_{L11'}$	degradation of BkL
r_{L12}	activate BkdR by Ile
	experiment: Francois: I need to check what is the mechanism of this activation.
	If is via the Val-tRNA is not possible because the gene
	encoded for the valyl-tRNA synthetase is essential in B. subtilis
r_{L13}	activate BkdR by Val
	experiment: Francois: I need to check what is the mechanism of this activation
	if it is via the Ile-tRNA is not possible because the gene encoded
	for the isoleucyl-tRNA synthetase is essential in B. subtilis
r_{L14}	expression of CcpA
	predition: single-knockout, unsafe
	experiment: It seems to be possible but we do not see the interest since CcpA is
	an activator of $Pilv - Leu$ and a repressor of CodY
$r_{L14'}$	degradation of CcpA
r_{L15}	express and accelerate CodY (to be explained acceleration)
	OK (we have this mutant)
$r_{L15'}$	degradation of CodY
r_{L16}	expression of TnrA
	experiment: OK (we have this mutant)
$r_{L16'}$	degradation of TnrA
r_{L17}	Gtp degradation
r_{L18}	BkdR degradation
r_{L19}	YwaA+YbgE degradation
r_{L20}	disabeling of IlvA by Ile
r_{L21}	disabeling of IlvA by Val
r_{L22}	expression of IlvA inhibited by binding of CodY

	experiment: Ok but the IlvA expression is r_{21} ?
	(we have this mutant but the result were not good)
$r_{L22'}$	degradation of IlvA
r_{L23}	expression of IlvBH
	experiment: NO, because we need the expression of IlvBH in order to
	activate the reaction r_{30}, thereby producing Ket_b the precursor of Ket_c
$r_{L23'}$	degradation of IlvBH
r_{L24}	expression of IlvC
	experiment: NO, because we need the expression of IlvC in order to
	activate the reaction r_{30}, thereby producing KetB the precursor of Ket_c
$r_{L24'}$	degradation of IlvC
r_{L25}	expression of IlvD, inhibited by binding of CodY to promotor
	experiment: NO, because we need the expression of IlvD in order to activate
	the reaction r_{30}, thereby producing Ket_b the precursor of Ket_c
$r_{L25'}$	degradation of IlvD
r_{L26}	metabolic transformation of Keta to Ile activated by $_{YwaA+YbgE}$,
	after an amino addition taken from Glu, which becomes OxoGlu.
r_{L27}	metabolic transformation of Akb and Pyr into Keta
r_{777}	
r_{28}	prepare output of Keta activated by BkL
r_{L29}	degradation of Ile into Keta activated by YwaA and Bcd,
	with an amino transfer from OxoGlu which becomes Glu.
r_{L30}	metabolic transformation from Pyr to Ketb,
	activated by IlvD
r_{31}	prepare output of Ketb activated by BkL
r_{L32}	degradation of Val into Ketb activated by YwaA and Bcd
	with an amino transfer from OxoGlu which becomes Glu.
r_{L33}	metabolic transformation of Ketb into Ket_c,
	activated by LeuBCD and LeuA
r_{L34}	prepare output of Ket_c activated by BkL
r_{L35}	degradation of Leu into Ket_c ctivated by YwaA and Bcd
	with an amino transfer from OxoGlu which becomes Glu.
r_{L36}	metabolic transformation of Ketb to Val activated by $_{YwaA+YbgE}$,
	after an amino addition from Glu which becomes OxoGlu
r_{L37}	expression of LeuA
	experiment: NO, because we need the expression of leuA in order to activate
	the reaction r_{33}, thereby producing Ket_c the precursor of Leu
$r_{L37'}$	degradation of LeuA
r_{L38}	expression of LeuBCD
	experiment: NO, because we need the expression of leuBCD in order to activate
	the reaction r_{33}, thereby producing Ket_c the precursor of Leu
$r_{L38'}$	degradation of LeuBCD
r_{L39}	deactivation of LeuA by Leu
r_{L40}	Leucine attenuation
	experiment: OK (we have this mutant)
$r_{L40'}$	degradation of Tbox
r_{L41}	metabolic transformation of Thr into Akb using IlvA
r_{L45}	metabolic transformation of Ket_c to Leu activated by $_{YwaA+YbgE}$
	after an amino addition from Glu, which becomes OxoGlu
r_{L46}	expression of YbgE, inhibited by binding of CodY to promoter
	experiment: NO, because we need the expression of YbgE in order
	to activate the reaction r_5, which produce Leu
$r_{L46'}$	degradation of YbgE
r_{L47}	expression of YwaA
	experiment: Ok
$r_{L47'}$	degradation of YwaA

Fig. 3. Reactions of Networks/b-subtilis.xml

.

1.1 What Else

Comments to be treated A small FAQ

Question 1. Are r40 r41 candidates for KO ?

Question 2. Define Signal real name

Question 3. Do we add G1P outflow ? do we remove the inflow ? is pgcA an Accelerator ?

Question 4. Precision for CcpA from Tobish 1999?

Question 5. Repression of CodY by Val-Leu (r71)? (cf Carbon Catabolic Control of the Metabolic Network in B. Subtilis)

Question 6. Repression of production of Malate throw TCA by CcpA (r24)? (cf Positive regulation of B. Subtilis by CodY ...)

Question 7. Ilv actor meaning ?

A small FAQ

A small FAQ

Question 2. Why is reaction r_3 needed, given that r_4 produces $OP_{BkL-Bcd}$ anyway? Answer: since more $OP_{BkL-Bcd}$ is produced this way.

Question 3. Is Akb input from context needed, since Akb can also be produced from Thr (r_9)? Answer: yes since external pathways can produce it too.

Role	Short name	Chemical Species
Metabolites	Glc	D-Glucose
	G1P	Glucose-1-Phosphate
	G6P	Glucose-6-Phosphate
	F6P	Fructose-6-Phosphate
	F16BP	Fructose-1,6-Biphosphate
	G3P	Glyceraldehyde-3-Phosphate
	13BPG	1,3-Bisphosphoglycerate
	3PG	3-Phosphoglycerate
	2PG	2-Phosphoglycerate
	PEP	Phosphoenolpyruvate
	Pyr	Pyruvate
	DHAP	Dihydroxyacetonphosphate
	Pp	PyroPhosphate
	Gluco	Gluconate
	Gluco6P	Glucose-6-P
	Xylu5P	Xylulose-5-P
	TCA	Krebs cycle
	Atoin	Acetoin
	Atate	Acetate
	Ala	Alanine
	Lac	Lactate
	AcCoA	Acetyl CoA
	Oxa	Oxaloacetate
	Mal	D-Malate
	Ile	Isoleucine
	Leu	Leucine
	Val	Valine
	Akb	L-2-amino-acetoacetate
	Glu	L-Glutamate
	OxoGlu	Oxogluterate
	Gtp	Guanosine triphosphate
	$\mathrm{Ket_a}$	2-keto-3-methylvalerate
	$\mathrm{Acyl-Coa}$	Acyl Coenzime A
	$\mathrm{Ket_b}$	2-keto-isovalerate
	$\mathrm{Ket_c}$	2-keto-isocaproate
	Thr	Threonine deshydratase
	Gln	L-Glutamine
	Orn	L-Ornithine
	Cit	Citrate
	Glyx	Glyoxalat
	Pro	L-Proline
	Ser	L-Serine
	Gly	Glycine
	Suc	Succinate
	Fum	Fumarate
	Cys	L-Cysteine
	BAla	Beta-alanine
	Met	L-Methionine
	OxoPro	5-oxoproline
	Asp	Aspartate
	AKet	Alpha ketoglutaric acid
	PenPyr	Penylpyruvate
	Phe	L-Phenylalanine
	Aspg	L-Asparagine
	Fru	Fructose
	Glucu	Glucuronate
	Glyt	Glycerate
	IsoCit	Isocitrate
	His	L-Histidine
	Lys	L-Lysine
	Trp	L-Tryptophane
	MyoI	Myo-inositol
	Tyr	Tyrosine
	Aco	Trans-aconitic acid
Proteines	GlcT	Transcriptional antiterminator.
	pgi	Glu-6-Phosphate isomerase.
	pfkA	Phosphofructokinase.
	fbaA	Fructose-1,6-biphosphate aldolase
	gapB	Glyceraldehyde–phosphatedehydrogenase
	pgk	Phosphoglycerate kinase
	pgm	2,3-Biphosphoglycerate - Independent phosphoglycerate mutase
	eno	Enolase
	pykA	Pyruvate kinase
	tpi	Triose phosphate isomerase
	gapA	Glyceraldehyde-3-phosphate dehydrogenase
	CcgR	Transcritpional repressor
	CcpN	Transcriptional repressor
	yqfL	Positive regulator
	fbp	Fructose-1,6-biphosphatase class III
	glpX	Fructose-1,6-biphosphatase class II
	pgcA	α-phosphoglucomutase
	gdh	Glucose 1-deshydrogenase
	gntk	Gluconokinase
	enz	??
	tkt	Transketolase
	zwf	Glucose-6-phosphate 1-dehydrogenase
	CcpA	Transcriptional activator
	pdhABCD	Pyruvate dÃľshydrogenase
	ystJ	Enzyme malique
	CitA	Citrate synthase
	CitG	Fumarase
	mdh	Malate deshydrogenase
	pckA	Phosphoenolpyruvate carboxykinase
	pycA	Pyruvate carboxylase
	ackA	Acetate kinase
	pta	Phosphotransacetylase
	AcDH	Acetoin deshydrogenase
	acsA	Acetyl CoA synthetase
	AlsS	α-acetolactate synthetase
	AlsD	α-acetolactate-dehydrogenase
	ldh	Lactate dehydrogenase
	CodY	Transcriptional pleiotropic regulator
	Bcd	Branched chain amino-acid dehydrogenase
	BkL	2-oxoisovalerate dehydrogenase
	BkdR	Transcriptional activator of BkL
	IlvA	Threonine deshydratase
	IlvBH	Acetolactate synthase
	IlvC	Ketol-acid reductoisomerase
	IlvD	Dihydroxy-acid dehydratase
	LeuA	2-isopropylmalate synthase
	LeuBCD	3-isopropylmalate dehydratase
	TnrA	Nitrogen pleiotropic transcrptional regulator
	YbgE	Branched chain amino-acid aminotransferase
	YwaA	branched chain amino-acid aminotransferase
Actors	ptsGHI	Composed by ptsG, ptsH and ptsI
	fbp + glpX	Activity of fbp and glpX
	DHAP+ F1,6BP	Activity of G6P, DHAP, F6P and F16BP
	G6 +F16	Activity of G6P and FOneSixBP
	$\mathrm{BS_{CcpA}}$	Activity of CcpA binding to gapA
	$\mathrm{BS_{CcgR}}$	Activity of CcgR binding to gapA
	$\mathrm{BS_{CcpN}}$	Activity of CcpN binding to gapB
	Signal	Signal generated by the phosphorylation of G to G6P
	$\mathrm{PIlv-Leu}$	Activity of promoter of IlvBH IlvC LeuA LeuBCD operon
	$\mathrm{BS_{CodY}}$	Activity of CodY binding to promotor PIlvLeu
	$\mathrm{BS_{TrnA}}$	Activity of TnrA binding to promoter PIlvLeu
	$\mathrm{BS_{Ccpa}}$	Activity of CcpA binding to promotor PIlvLeu without $\mathrm{BS_{TrnA}}$ loop
	$\mathrm{OP_{BkL-Bcd}}$	Activity of promoter of BkL Bcd operon
	YwaA+YbgE	Activity of YbgE and YwaA
	Tbox	activity of tryptophan attenuation

Fig. 2. Molecules of Networks/b-subtilis.xml.