

BioComputing's Network-Graph Tool

Version 0.99

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1 Reaction Network `Networks/b-subtilis.xml`

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

Analysis `diff-means-constitutive-10h-6h`

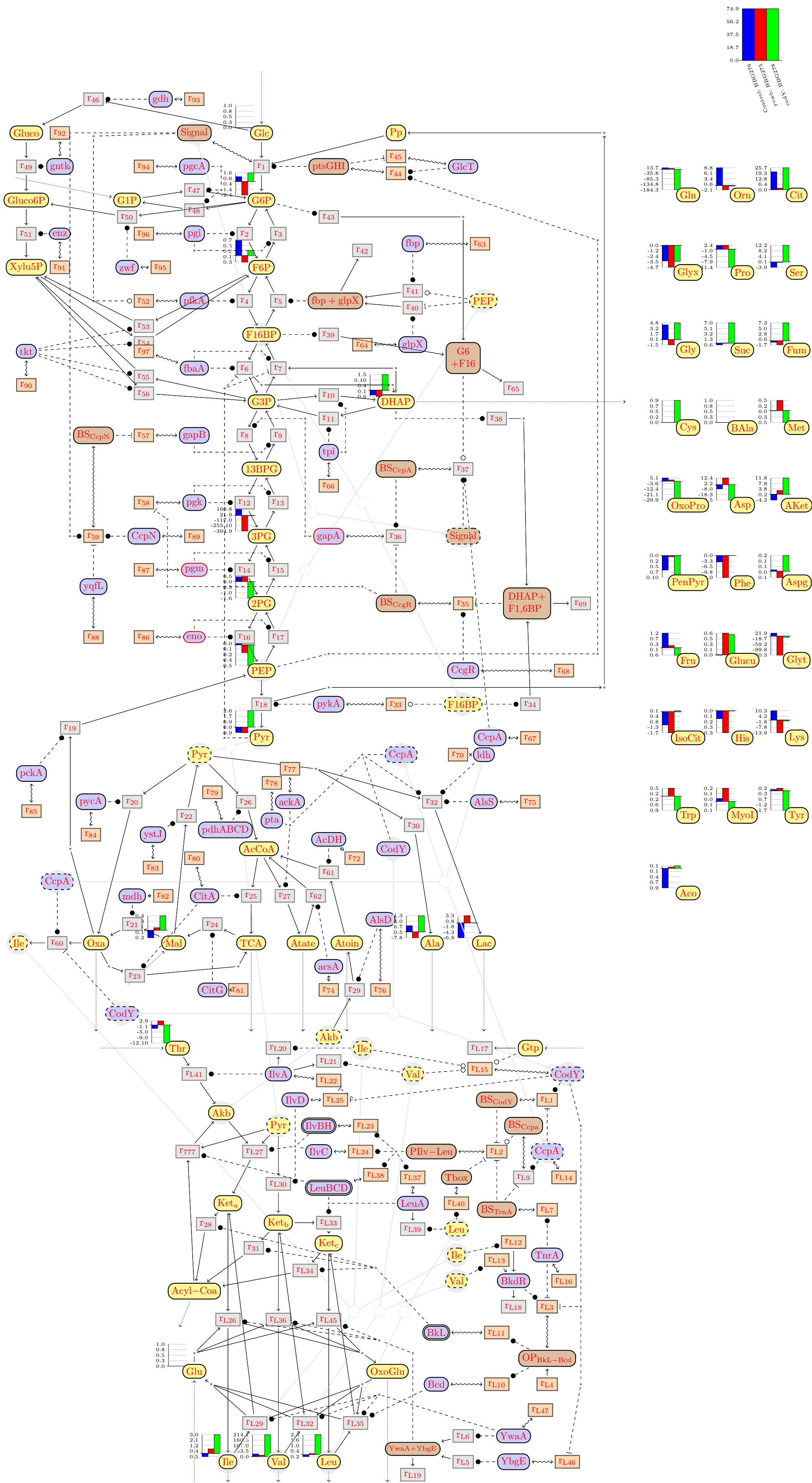


Fig. 1. The Networks/b-subtilis.xml.

| 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 |

| | |
|------|--|
| r97 | expression of fbaA |
| r97' | degradation of fbaA |
| r20 | Production of Atoin throw Pyr |
| r21 | Production of Oxa throw Mal |
| r22 | Production of Pyr throw Mal |
| r23 | Production of TCA throw Oxa |
| r24 | Production of Mal throw TCA |
| r25 | Turn to TCA throw AcCoA |
| r26 | Production of AcCoA from Pyr |
| r27 | Production of Atate from AcCoA |
| r29 | Production of Atoin from Aceto |
| r30 | Production of Alanine from Pyr |
| r32 | Production of Lac from Pyr |
| r60 | Production of Ile from Oxa |
| r61 | Production of AcCoA from Atoin |
| r62 | Production of AcCoA from Atate |
| r70 | expression of ldh |
| r70' | degradation of ldh |
| r72 | expression of AcDH |
| r72' | degradation of AcDH |
| r74 | expression of acsA |
| r74' | degradation of acsA |
| r75 | expression of AlsS |
| r75' | degradation of AlsS |
| r76 | expression of eno |
| r76' | degradation of AlsD |
| r77 | expression of ackA |
| r77' | degradation of ackA |
| r78 | expression of pta |
| r78' | degradation of pta |
| r79 | expression of pdhABCD |
| r79' | degradation of pdhABCD |
| r80 | expression of CitA |
| r80' | degradation of CitA |
| r81 | expression of CitG |
| r81' | degradation of CitG |
| r82 | expression of mdh |
| r82' | degradation of mdh |
| r83 | expression of ystJ |
| r83' | degradation of ystJ |
| r84 | expression of pycA |
| r84' | degradation of pycA |
| r85 | expression of pckA |
| r85' | degradation of pckA |
| r19 | feedback reaction to PEP from Oxa |
| rL1 | bind CodY to Pilv–Leu for inhibition |
| rL1' | predition: single knockout, unsafe |
| rL2 | experiment: OK (we have this mutant) |
| rL2' | degradation of BS _{CodY} |
| rL3 | activate Pilv–Leu promoter |
| rL3' | predition: no |
| rL4 | experiment: not done, because we need the expression of Pilv – Leu |
| rL4' | in order to activate the reaction r23, r24, r39, r37 |
| rL5 | degradation of Pilv–Leu |
| rL6 | bind BkdR to BkL Bcd promoter |
| rL7 | experiment: Ok |
| rL7' | degradation of OP _{BkL–Bcd} |
| rL8 | constitutive expression of BkL Bcd operon |
| rL9 | experiment: Ok |
| rL10 | express YbgE |
| rL11 | express YwaA |
| rL12 | bind TnrA to Pilv–Leu promoter for inhibition |
| rL13 | predition: safe single knockout |
| rL14 | experiment: OK (we have this mutant) |
| rL15 | degradation of BS _{TnrA} |
| rL16 | bind CcpA to Pilv–Leu promoter without BS _{TnrA} loop |
| rL17 | degradation of BS _{CcpA} |
| rL18 | expression of Bcd, activated by OP _{BkL–Bcd} |
| rL19 | experiment: OK (we have this mutant) |
| rL20 | degradation of Bcd |
| rL21 | expression of BkL, activated by OP _{BkL–Bcd} |
| rL22 | experiment: OK (we have this mutant) |
| rL23 | degradation of BkL |
| rL24 | activate BkdR by Ile |
| rL25 | experiment: Francois: I need to check what is the mechanism of this activation. |
| rL26 | If is via the Val-tRNA is not possible because the gene |
| rL27 | encoded for the valyl-tRNA synthetase is essential in B. subtilis |
| rL28 | activate BkdR by Val |
| rL29 | experiment: Francois: I need to check what is the mechanism of this activation |
| rL30 | if it is via the Ile-tRNA is not possible because the gene encoded |
| rL31 | for the isoleucyl-tRNA synthetase is essential in B. subtilis |
| rL32 | expression of CcpA |
| rL33 | predition: single-knockout, unsafe |
| rL34 | experiment: It seems to be possible but we do not see the interest since CcpA is |
| rL35 | an activator of Pilv – Leu and a repressor of CodY |
| rL36 | degradation of CcpA |
| rL37 | express and accelerate CodY (to be explained acceleration) |
| rL38 | OK (we have this mutant) |
| rL39 | degradation of CodY |
| rL40 | expression of TnrA |
| rL41 | experiment: OK (we have this mutant) |
| rL42 | degradation of TnrA |
| rL43 | Gtp degradation |
| rL44 | BkdR degradation |
| rL45 | YwaA+YbgE degradation |
| rL46 | disabeling of IlvA by Ile |
| rL47 | disabeling of IlvA by Val |
| rL48 | expression of IlvA inhibited by binding of CodY |

| | |
|--------------|--|
| | experiment: Ok but the IlvA expression is r21 ? (we have this mutant but the result were not good) |
| rL22' | degradation of IlvA |
| rL23 | expression of IlvBH |
| | experiment: NO, because we need the expression of IlvBH in order to activate the reaction r30 , thereby producing Ket_b , the precursor of Ket_c |
| rL23' | degradation of IlvBH |
| rL24 | expression of IlvC |
| | experiment: NO, because we need the expression of IlvC in order to activate the reaction r30 , thereby producing KetB the precursor of Ket_c |
| rL24' | degradation of IlvC |
| rL25 | 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 r30 , thereby producing Ket_b , the precursor of Ket_c |
| rL25' | degradation of IlvD |
| rL26 | metabolic transformation of Keta to Ile activated by YwaA+YbgE , after an amino addition taken from Glu , which becomes OxoGlu . |
| rL27 | metabolic transformation of Akb and Pyr into Keta |
| r777 | |
| r28 | prepare output of Keta activated by BkL |
| rL29 | degradation of Ile into Keta activated by YwaA and Bcd , with an amino transfer from OxoGlu which becomes Glu . |
| rL30 | metabolic transformation from Pyr to Ketb , activated by IlvD |
| r31 | prepare output of Ketb activated by BkL |
| rL32 | degradation of Val into Ketb activated by YwaA and Bcd with an amino transfer from OxoGlu which becomes Glu . |
| rL33 | metabolic transformation of Ketb into Ket_c , activated by LeuBCD and LeuA |
| rL34 | prepare output of Ket_c activated by BkL |
| rL35 | degradation of Leu into Ket_c ctivated by YwaA and Bcd with an amino transfer from OxoGlu which becomes Glu . |
| rL36 | metabolic transformation of Ketb to Val activated by YwaA+YbgE , after an amino addition from Glu which becomes OxoGlu |
| rL37 | expression of LeuA |
| | experiment: NO, because we need the expression of leuA in order to activate the reaction r33 , thereby producing Ket_c the precursor of Leu |
| rL37' | degradation of LeuA |
| rL38 | expression of LeuBCD |
| | experiment: NO, because we need the expression of leuBCD in order to activate the reaction r33 , thereby producing Ket_c the precursor of Leu |
| rL38' | degradation of LeuBCD |
| rL39 | deactivation of LeuA by Leu |
| rL40 | Leucine attenuation |
| | experiment: OK (we have this mutant) |
| rL40' | degradation of Tbox |
| rL41 | metabolic transformation of Thr into Akb using IlvA |
| rL45 | metabolic transformation of Ket_c to Leu activated by YwaA+YbgE after an amino addition from Glu , which becomes OxoGlu |
| rL46 | 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 r5 , which produce Leu |
| rL46' | degradation of YbgE |
| rL47 | expression of YwaA |
| | experiment: Ok |
| rL47' | 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 **r3** needed, given that **r4** 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** (**r9**)? 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 |
| | Ket _a | 2-keto-3-methylvalerate |
| | Acyl-Coa | Acyl Coenzyme A |
| | Ket _b | 2-keto-isovalerate |
| | 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-aconicic 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 | Transcriptional 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 dĀfshydrogenase |
| | 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 |
| | BS _{CcpA} | Activity of CcpA binding to gapA |
| | BS _{CcgR} | Activity of CcgR binding to gapA |
| | BS _{CcpN} | Activity of CcpN binding to gapB |
| | Signal | Signal generated by the phosphorylation of G to G6P |
| | Pilv-Leu | Activity of promoter of IlvBH IlvC LeuA LeuBCD operon |
| | BS _{CodY} | Activity of CodY binding to promoter PilvLeu |
| | BS _{TnrA} | Activity of TnrA binding to promoter PilvLeu |
| | BS _{CcpA} | Activity of CcpA binding to promoter PilvLeu without BS _{TnrA} loop |
| | 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.