# BioComputing's Network-Graph Tool
# Version 0.99

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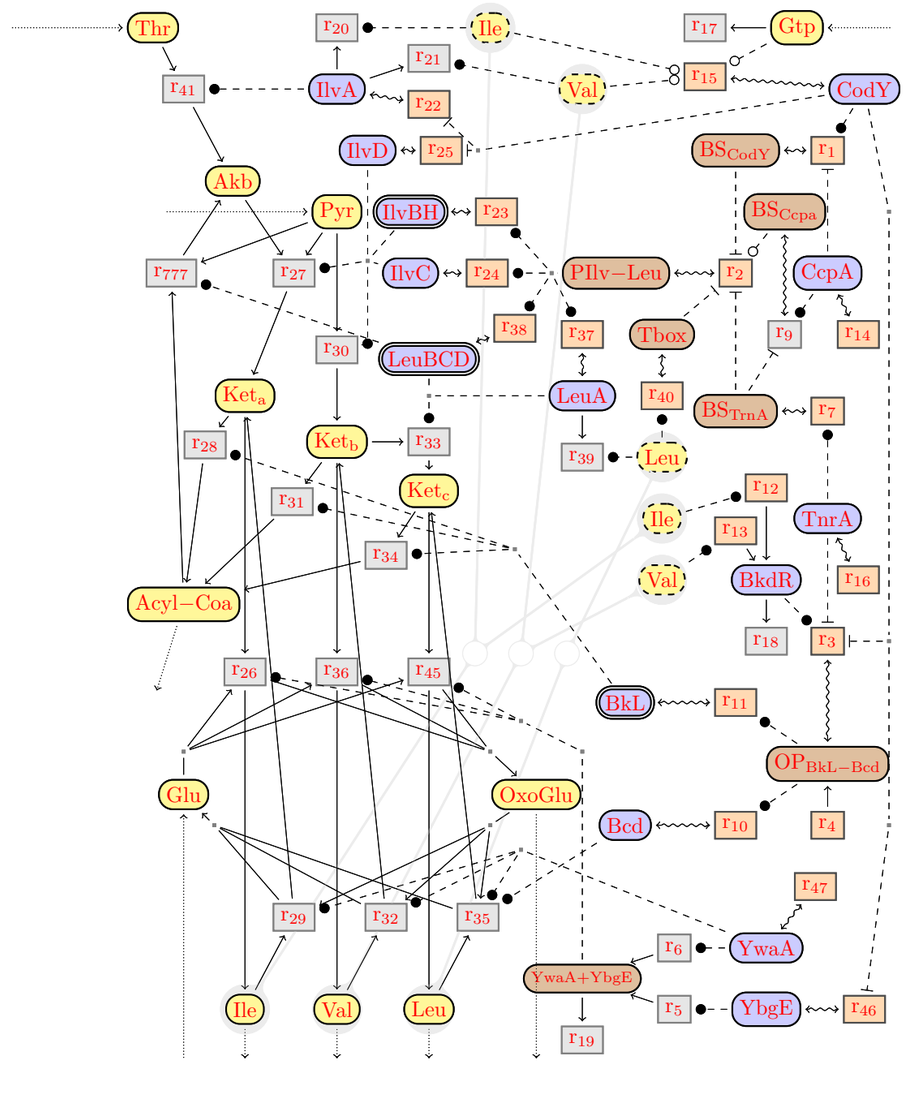
## 1 Reaction Network Networks/leucine.xml

*Reaction Network.* See file: `Networks/leucine.xml` See Figure 1.

*Analysis* `test`




S1. Solution

**Fig. 1.** The Networks/leucine.xml.

| Name | Function |
|---|---|
| $r_1$ | bind CodY to PIlv−Leu for inhibition<br>predition: single knockout, unsafe<br>experiment: OK (we have this mutant) |
| $r_{1'}$ | degradation of $BS_{CodY}$ |
| $r_2$ | activate PIlv−Leu promoter<br>predition: no<br>experiment: not done, because we need the expression of Pilv − Leu<br>in order to activate the reaction $r_{23}$, $r_{24}$, $r_{39}$, $r_{37}$ |
| $r_{2'}$ | degradation of PIlv−Leu |
| $r_3$ | bind BkdR to BkL Bcd promoter<br>experiment: Ok |
| $r_{3'}$ | degradation of $OP_{BkL-Bcd}$ |
| $r_4$ | constitutive expression of BkL Bcd operon<br>experiment: Ok |
| $r_5$ | express YbgE |
| $r_6$ | express YwaA |
| $r_7$ | bind TnrA to PIlv−Leu promoter for inhibition<br>predition: safe single knockout<br>experiment: OK (we have this mutant) |
| $r_{7'}$ | degradation of $BS_{TrnA}$ |
| $r_9$ | bind CcpA to PIlv−Leu promoter without $BS_{TrnA}$ loop |
| $r_{9'}$ | degradation of $BS_{Ccpa}$ |
| $r_{10}$ | expression of Bcd, activated by $OP_{BkL-Bcd}$<br>experiment: OK (we have this mutant) |
| $r_{10'}$ | degradation of Bcd |
| $r_{11}$ | expression of BkL, activated by $OP_{BkL-Bcd}$<br>experiment: OK (we have this mutant) |
| $r_{11'}$ | degradation of BkL |
| $r_{12}$ | activate BkdR by Ile<br>experiment: Francois: I need to check what is the mechanism of this activation.<br>If is via the Val-tRNA is not possible because the gene<br>encoded for the valyl-tRNA synthetase is essential in B. subtilis |

| | |
|---|---|
| $r_{13}$ | activate BkdR by Val<br>experiment: Francois: I need to check what is the mechanism of this activation<br>if it is via the Ile-tRNA is not possible because the gene encoded<br>for the isoleucyl-tRNA synthetase is essential in B. subtilis |
| $r_{14}$ | expression of CcpA<br>predition: single-knockout, unsafe<br>experiment: It seems to be possible but we do not see the interest since CcpA is<br>an activator of Pilv − Leu and a repressor of CodY |
| $r_{14'}$ | degradation of CcpA |
| $r_{15}$ | express and accelerate CodY (to be explained acceleration)<br>OK (we have this mutant) |
| $r_{15'}$ | degradation of CodY |
| $r_{16}$ | expression of TnrA<br>experiment: OK (we have this mutant) |
| $r_{16'}$ | degradation of TnrA |
| $r_{17}$ | Gtp degradation |
| $r_{18}$ | BkdR degradation |
| $r_{19}$ | $_{\text{YwaA+YbgE}}$ degradation |
| $r_{20}$ | disabeling of IlvA by Ile |
| $r_{21}$ | disabeling of IlvA by Val |
| $r_{22}$ | expression of IlvA inhibited by binding of CodY<br>experiment: Ok but the IlvA expression is $r_{21}$ ?<br>(we have this mutant but the result were not good) |
| $r_{22'}$ | degradation of IlvA |
| $r_{23}$ | expression of IlvBH<br>experiment: NO, because we need the expression of IlvBH in order to<br>activate the reaction $r_{30}$, thereby producing $Ket_b$ the precursor of $Ket_c$ |
| $r_{23'}$ | degradation of IlvBH |
| $r_{24}$ | expression of IlvC<br>experiment: NO, because we need the expression of IlvC in order to<br>activate the reaction $r_{30}$, thereby producing KetB the precursor of $Ket_c$ |
| $r_{24'}$ | degradation of IlvC |
| $r_{25}$ | expression of IlvD, inhibited by binding of CodY to promotor<br>experiment: NO, because we need the expression of IlvD in order to activate<br>the reaction $r_{30}$, thereby producing $Ket_b$ the precursor of $Ket_c$ |
| $r_{25'}$ | degradation of IlvD |
| $r_{26}$ | metabolic transformation of Keta to Ile activated by $_{\text{YwaA+YbgE}}$,<br>after an amino addition taken from Glu, which becomes OxoGlu. |
| $r_{27}$ | metabolic transformation of Akb and Pyr into Keta |
| $r_{777}$ | |
| $r_{28}$ | prepare output of Keta activated by BkL |
| $r_{29}$ | degradation of Ile into Keta activated by YwaA and Bcd,<br>with an amino transfer from OxoGlu which becomes Glu. |
| $r_{30}$ | metabolic transformation from Pyr to Ketb,<br>activated by IlvD |
| $r_{31}$ | prepare output of Ketb activated by BkL |
| $r_{32}$ | degradation of Val into Ketb activated by YwaA and Bcd<br>with an amino transfer from OxoGlu which becomes Glu. |
| $r_{33}$ | metabolic transformation of Ketb into $Ket_c$,<br>activated by LeuBCD and LeuA |
| $r_{34}$ | prepare output of $Ket_c$ activated by BkL |
| $r_{35}$ | degradation of Leu into $Ket_c$ ctivated by YwaA and Bcd<br>with an amino transfer from OxoGlu which becomes Glu. |
| $r_{36}$ | metabolic transformation of Ketb to Val activated by $_{\text{YwaA+YbgE}}$,<br>after an amino addition from Glu which becomes OxoGlu |
| $r_{37}$ | expression of LeuA<br>experiment: NO, because we need the expression of leuA in order to activate<br>the reaction $r_{33}$, thereby producing $Ket_c$ the precursor of Leu |
| $r_{37'}$ | degradation of LeuA |
| $r_{38}$ | expression of LeuBCD<br>experiment: NO, because we need the expression of leuBCD in order to activate<br>the reaction $r_{33}$, thereby producing $Ket_c$ the precursor of Leu |
| $r_{38'}$ | degradation of LeuBCD |
| $r_{39}$ | deactivation of LeuA by Leu |
| $r_{40}$ | Leucine attenuation<br>experiment: OK (we have this mutant) |
| $r_{40'}$ | degradation of Tbox |
| $r_{41}$ | metabolic transformation of Thr into Akb using IlvA |
| $r_{45}$ | metabolic transformation of $Ket_c$ to Leu activated by $_{\text{YwaA+YbgE}}$<br>after an amino addition from Glu, which becomes OxoGlu |
| $r_{46}$ | expression of YbgE, inhibited by binding of CodY to promoter<br>experiment: NO, because we need the expression of YbgE in order<br>to activate the reaction $r_5$, which produce Leu |
| $r_{46'}$ | degradation of YbgE |
| $r_{47}$ | expression of YwaA<br>experiment: Ok |
| $r_{47'}$ | degradation of YwaA |

**Fig. 3.** Reactions of Networks/leucine.xml

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### 1.1 What Else

***Comments to be treated*** 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 | Ile | Isoleucine |
| | Leu | Leucine |
| | Val | Valine |
| | Akb | L-2-amino-acetoacetate |
| | Glu | L-Glutamate |
| | OxoGlu | Oxogluterate |
| | Gtp | Guanosine triphosphate |
| | $\text{Ket}_{\text{a}}$ | 2-keto-3-methylvalerate |
| | $\text{Acyl}-\text{Coa}$ | Acyl Coenzime A |
| | $\text{Ket}_{\text{b}}$ | 2-keto-isovalerate |
| | $\text{Ket}_{\text{c}}$ | 2-keto-isocaproate |
| | Pyr | Pyruvate |
| | Thr | Threonine deshydratase |
| Proteines | Bcd | Branched chain amino-acid dehydrogenase |
| | BkL | 2-oxoisovalerate dehydrogenase |
| | BkdR | Transcriptional activator of BkL |
| | CcpA | Carbon catabolite control protein A |
| | CodY | Transcriptional pleiotropic regulator |
| | 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 | $\text{PIlv}-\text{Leu}$ | Activity of promoter of IlvBH IlvC LeuA LeuBCD operon |
| | $\text{BS}_{\text{CodY}}$ | Activity of CodY binding to promotor PIlvLeu |
| | $\text{BS}_{\text{TrnA}}$ | Activity of TnrA binding to promoter PIlvLeu |
| | $\text{BS}_{\text{Ccpa}}$ | Activity of CcpA binding to promotor PIlvLeu without $\text{BS}_{\text{TrnA}}$ loop |
| | $\text{OP}_{\text{BkL}-\text{Bcd}}$ | Activity of promoter of BkL Bcd operon |
| | $_{\text{YwaA}+\text{YbgE}}$ | Activity of YbgE and YwaA |
| | Tbox | activity of tryptophan attenuation |

**Fig. 2.** Molecules of Networks/leucine.xml.