**Generic Model**

**Recon3D Model was modified prior to reconstruction of cell-type/tissue specific reconstruction:**

- To use in cancer models:

- Gene ‘8041’ (present in model as 8041.1) was removed from the model, as it was discontinued in the entrez database. The reaction that it corresponds to was not removed, but the gene was removed from the GPR.

- *biomass\_maintenance* and *biomass\_maintenance\_noTrTr* were removed, as *biomass\_reaction* is the most indicated

- Artificial sinks and drug modules were removed

- Resulting blocked reactions and the respective genes and metabolites that end up with no reaction associated due to this removal were removed

- To use in T-cell models:

- Gene ‘8041’ (present in model as 8041.1) was removed from the model, as it was discontinued in the entrez database. The reaction that it corresponds to was not removed, but the gene was removed from the GPR.

- A biomass reaction from the macrophage model iAB-AMØ-1410 was added (named *biomass\_mac*) and *biomass\_maintenance\_noTrTr* was removed. Thus three different biomasses will be available to test: *biomass\_reaction*, *biomass\_maintenance* and *biomass\_mac*.

- Artificial sinks and drug modules were removed

- Resulting blocked reactions and the respective genes and metabolites that end up with no reaction associated due to this removal were removed

- With this, we have 3 generic Recon3D models, the original one (*Recon3D*), the one to use in cancer reconstruction models (*Recon3D\_forCancer*) and the one to use in T-cell reconstruction models (*Recon3D\_forTcells*, used in T-cell models)

- Each model was then tested for the ability to perform tasks that all cells should be able to perform (tasks from *Richelle A. et al (2019*).

- The capacity to carry flux through the biomasses reactions was also tested, using the Plasmax, HPLM and RPMI media.

**Units:** mmol gDW-1 h-1 -> mmol of metabolite per gram of dry weight of cell per hour

**Biomasses**

**To generate the T-Cells models:**

Compare models reconstructed with different biomasses:

- *biomass\_reaction* from Recon3D model;

|  |  |  |  |
| --- | --- | --- | --- |
| **Reactants** | **Metabolite ID** | **Metabolite Name** | **Stoichiometry** |
|  | ala\_L[c] | L-Alanine [cytoplasm] | 0.505626 |
| arg\_L[c] | L-Arginine[cytoplasm] | 0.35926 |
| asn\_L[c] | L-Asparagine[cytoplasm] | 0.279425 |
| asp\_L[c] | L-Aspartic acid[cytoplasm] | 0.352607 |
| atp[c] | Adenosine triphosphate[cytoplasm] | 20.704451 |
| chsterol[c] | Cholesterol[cytoplasm] | 0.020401 |
| clpn\_hs[c] | Cardiolipin[cytoplasm] | 0.011658 |
| ctp[c] | Cytidine triphosphate[cytoplasm] | 0.039036 |
| cys\_L[c] | L-Cysteine[cytoplasm] | 0.046571 |
| datp[n] | Deoxyadenosine triphosphate[cytoplasm] | 0.013183 |
| dctp[n] | dCTP[cytoplasm] | 0.009442 |
| dgtp[n] | dGTP[cytoplasm] | 0.009898 |
| dttp[n] | Thymidine 5'-triphosphate[cytoplasm] | 0.013091 |
| g6p[c] | Glucose 6-phosphate[cytoplasm] | 0.275194 |
| gln\_L[c] | L-Glutamine[cytoplasm] | 0.325996 |
| glu\_L[c] | L-Glutamic acid[cytoplasm] | 0.385872 |
| gly[c] | Glycine[cytoplasm] | 0.538891 |
| gtp[c] | Guanosine triphosphate[cytoplasm] | 0.036117 |
| h2o[c] | Water[cytoplasm] | 20.650823 |
| his\_L[c] | L-Histidine[cytoplasm] | 0.126406 |
| ile\_L[c] | L-Isoleucine[cytoplasm] | 0.286078 |
| leu\_L[c] | L-Leucine[cytoplasm] | 0.545544 |
| lys\_L[c] | L-Lysine[cytoplasm] | 0.592114 |
| met\_L[c] | L-Methionine[cytoplasm] | 0.153018 |
| pail\_hs[c] | 1-Phosphatidyl-1D-Myo-Inositol[cytoplasm] | 0.023315 |
| pchol\_hs[c] | Phosphatidylcholine[cytoplasm] | 0.154463 |
| pe\_hs[c] | Phosphatidylethanolamine[cytoplasm] | 0.055374 |
| pglyc\_hs[c] | Phosphatidylglycerol[cytoplasm] | 0.002914 |
| phe\_L[c] | L-Phenylalanine[cytoplasm] | 0.259466 |
| pro\_L[c] | L-Proline[cytoplasm] | 0.412484 |
| ps\_hs[c] | Phosphatidylserine[cytoplasm] | 0.005829 |
| ser\_L[c] | L-Serine[cytoplasm] | 0.392525 |
| sphmyln\_hs[c] | Sphingomyelin[cytoplasm] | 0.017486 |
| thr\_L[c] | L-Threonine[cytoplasm] | 0.31269 |
| trp\_L[c] | L-Tryptophan[cytoplasm] | 0.013306 |
| tyr\_L[c] | L-Tyrosine[cytoplasm] | 0.159671 |
| utp[c] | Uridine triphosphate[cytoplasm] | 0.053446 |
| val\_L[c] | L-Valine[cytoplasm] | 0.352607 |
| **Products** | **Metabolite ID** | **Metabolite Name** | **Stoichiometry** |
|  | adp[c] | ADP[cytoplasm] | 20.650823 |
| h[c] | Hydrogen Ion[cytoplasm] | 20.650823 |
| pi[c] | Phosphate[cytoplasm] | 20.650823 |
| **Lower Bound** | 0 | | |
| **Upper Bound** | 1000 | | |

- *R\_biomass\_mac* from iAB-AMØ-1410 model (a macrophage model, built from Recon1 model), also added to the generic model Recon3D (with id *biomass\_mac*)

|  |  |  |  |
| --- | --- | --- | --- |
| **Reactants** | **Metabolite ID** | **Metabolite Name** | **Stoichiometry** |
|  | ala\_L[c] | L-Alanine [cytoplasm] | 0.396559456 |
| alpa\_hs[c] | Lysophosphatidic Acid [cytoplasm] | 0.011499127 |
| amp[c] | Adenosine monophosphate [cytoplasm] | 0.048664064 |
| arg\_L[c] | L-Arginine[cytoplasm] | 0.325724532 |
| asn\_L[c] | L-Asparagine[cytoplasm] | 0.215407845 |
| asp\_L[c] | L-Aspartic acid[cytoplasm] | 0.282759085 |
| atp[c] | Adenosine triphosphate[cytoplasm] | 25.17352552 |
| chsterol[c] | Cholesterol[cytoplasm] | 0.020930954 |
| cmp[c] | Cytidine monophosphate[cytoplasm] | 0.042373167 |
| cys\_L[c] | L-Cysteine[cytoplasm] | 0.127154496 |
| dag\_hs[c] | Diglyceride[cytoplasm] – 1,2.diacylglycerol-LD-TAG pool | 0.0036682 |
| damp[c] | Deoxyadenosine monophosphate[cytoplasm] | 0.021495345 |
| dcmp[c] | dCMP[cytoplasm] | 0.014937443 |
| dgmp[c] | 2'-Deoxyguanosine 5'-monophosphate[cytoplasm] | 0.014937443 |
| dtmp[c] | 5-Thymidylic acid[cytoplasm] | 0.021495345 |
| gln\_L[c] | L-Glutamine[cytoplasm] | 0.280436629 |
| glu\_L[c] | L-Glutamic acid[cytoplasm] | 0.424428935 |
| gly[c] | Glycine[cytoplasm] | 0.366948135 |
| glygn2[c] | Glycogen, Structure 2 (Glycogenin-1,6-{7[1,4-Glc], 4[1,4-Glc]}) [cytoplasm] | 0.528027894 |
| gmp[c] | Guanosine monophosphate[cytoplasm] | 0.043710887 |
| h2o[c] | Water[cytoplasm] | 25.17352552 |
| hdca[c] | Palmitic acid[cytoplasm] | 0.004850777 |
| hdcea[c] | Palmitoleic acid[cytoplasm] | 0.001222285 |
| his\_L[c] | L-Histidine[cytoplasm] | 0.153862747 |
| ile\_L[c] | L-Isoleucine[cytoplasm] | 0.25953452 |
| leu\_L[c] | L-Leucine[cytoplasm] | 0.580614138 |
| lys\_L[c] | L-Lysine[cytoplasm] | 0.351852168 |
| met\_L[c] | L-Methionine[cytoplasm] | 0.126573882 |
| ocdca[c] | Stearic acid[cytoplasm] | 0.004736708 |
| ocdcea[c] | Oleic acid[cytoplasm] | 0.003853116 |
| pail\_hs[c] | 1-Phosphatidyl-1D-Myo-Inositol[cytoplasm] PI pool | 0.003741686 |
| pchol\_hs[c] | Phosphatidylcholine[cytoplasm] PC-LD pool | 0.031527146 |
| pe\_hs[c] | Phosphatidylethanolamine[cytoplasm] – PE-LD pool | 0.021107135 |
| pglyc\_hs[c] | Phosphatidylglycerol[cytoplasm] – PG-CL pool | 0.008918017 |
| phe\_L[c] | L-Phenylalanine[cytoplasm] | 0.214246617 |
| pro\_L[c] | L-Proline[cytoplasm] | 0.346626641 |
| ps\_hs[c] | Phosphatidylserine[cytoplasm] – PS-LD pool | 0.001024655 |
| ser\_L[c] | L-Serine[cytoplasm] | 0.476684207 |
| sphmyln\_hs[c] | Sphingomyelin[cytoplasm] – SM pool | 0.007049706 |
| tag\_hs[c] | Triglyceride[cytoplasm] TAG-VLDL pool | 0.002742439 |
| thr\_L[c] | L-Threonine[cytoplasm] | 0.303661194 |
| trp\_L[c] | L-Tryptophan[cytoplasm] | 0.069673697 |
| ttdca[c] | Myristic acid[cytoplasm] | 0.00136164 |
| tyr\_L[c] | L-Tyrosine[cytoplasm] | 0.156185203 |
| ump[c] | Uridine 5'-monophosphate[cytoplasm] | 0.04602478 |
| val\_L[c] | L-Valine[cytoplasm] | 0.347207255 |
| **Products** | **Metabolite ID** | **Metabolite Name** | **Stoichiometry** |
|  | adp[c] | ADP[cytoplasm] | 25.17352552 |
| h[c] | Hydrogen Ion[cytoplasm] | 25.17352552 |
| pi[c] | Phosphate[cytoplasm] | 25.17352552 |
| **Lower Bound** | 0 | | |
| **Upper Bound** | 1000 | | |

**To generate the cancer models:**

- *biomass\_reaction* from Recon3D model

|  |  |  |  |
| --- | --- | --- | --- |
| **Reactants** | **Metabolite ID** | **Metabolite Name** | **Stoichiometry** |
|  | ala\_L[c] | L-Alanine [cytoplasm] | 0.505626 |
| arg\_L[c] | L-Arginine[cytoplasm] | 0.35926 |
| asn\_L[c] | L-Asparagine[cytoplasm] | 0.279425 |
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| atp[c] | Adenosine triphosphate[cytoplasm] | 20.704451 |
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| datp[c] | Deoxyadenosine triphosphate[cytoplasm] | 0.013183 |
| dctp[c] | dCTP[cytoplasm] | 0.009442 |
| dgtp[c] | dGTP[cytoplasm] | 0.009898 |
| dttp[c] | Thymidine 5'-triphosphate[cytoplasm] | 0.013091 |
| g6p[c] | Glucose 6-phosphate[cytoplasm] | 0.275194 |
| gln\_L[c] | L-Glutamine[cytoplasm] | 0.325996 |
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| gly[c] | Glycine[cytoplasm] | 0.538891 |
| gtp[c] | Guanosine triphosphate[cytoplasm] | 0.036117 |
| h2o[c] | Water[cytoplasm] | 20.650823 |
| his\_L[c] | L-Histidine[cytoplasm] | 0.126406 |
| ile\_L[c] | L-Isoleucine[cytoplasm] | 0.286078 |
| leu\_L[c] | L-Leucine[cytoplasm] | 0.545544 |
| lys\_L[c] | L-Lysine[cytoplasm] | 0.592114 |
| met\_L[c] | L-Methionine[cytoplasm] | 0.153018 |
| pail\_hs[c] | 1-Phosphatidyl-1D-Myo-Inositol[cytoplasm] | 0.023315 |
| pchol\_hs[c] | Phosphatidylcholine[cytoplasm] | 0.154463 |
| pe\_hs[c] | Phosphatidylethanolamine[cytoplasm] | 0.055374 |
| pglyc\_hs[c] | Phosphatidylglycerol[cytoplasm] | 0.002914 |
| phe\_L[c] | L-Phenylalanine[cytoplasm] | 0.259466 |
| pro\_L[c] | L-Proline[cytoplasm] | 0.412484 |
| ps\_hs[c] | Phosphatidylserine[cytoplasm] | 0.005829 |
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| trp\_L[c] | L-Tryptophan[cytoplasm] | 0.013306 |
| tyr\_L[c] | L-Tyrosine[cytoplasm] | 0.159671 |
| utp[c] | Uridine triphosphate[cytoplasm] | 0.053446 |
| val\_L[c] | L-Valine[cytoplasm] | 0.352607 |
| **Products** | **Metabolite ID** | **Metabolite Name** | **Stoichiometry** |
|  | adp[c] | ADP[cytoplasm] | 20.650823 |
| h[c] | Hydrogen Ion[cytoplasm] | 20.650823 |
| pi[c] | Phosphate[cytoplasm] | 20.650823 |
| **Lower Bound** | 0 | | |
| **Upper Bound** | 1000 | | |

**References**

Richelle A, Chiang AWT, Kuo CC, Lewis NE (2019) *Increasing consensus of context-specific metabolic models by integrating data-inferred cell functions.* PLOS Computational Biology 15(4): e1006867. <https://doi.org/10.1371/journal.pcbi.1006867>