

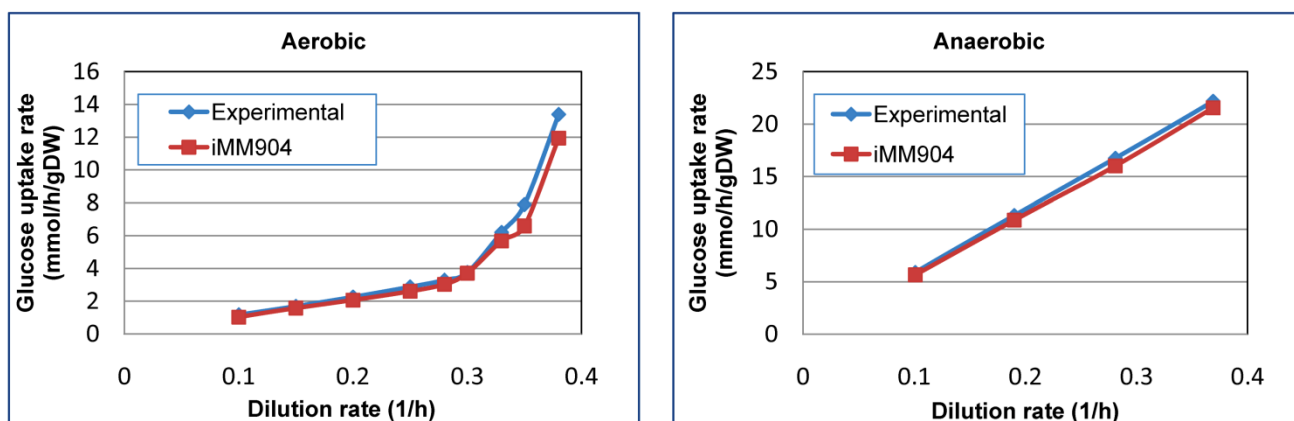
## Additional File S3.

### Supplemental Figures

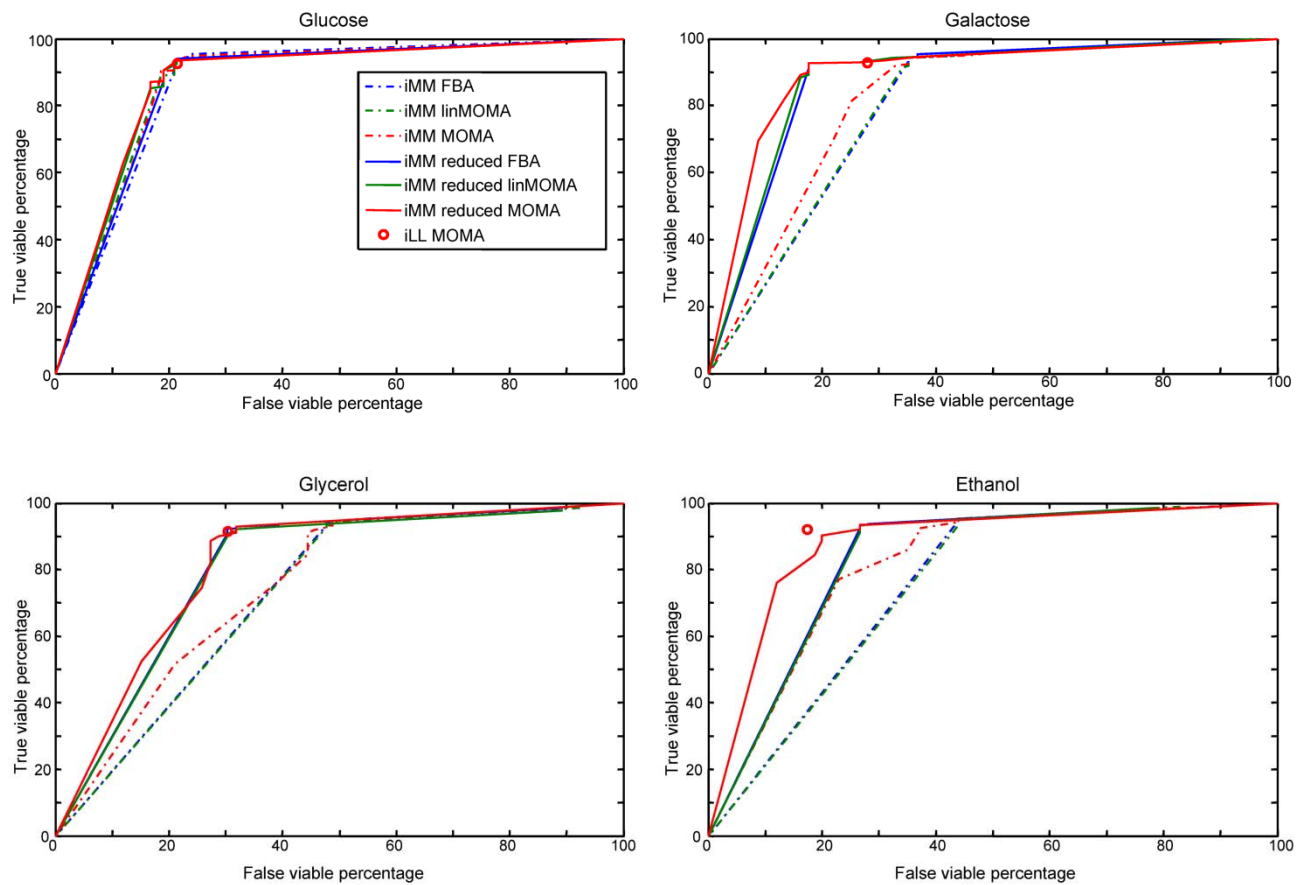
**Figure S1.**

**Aerobic and anaerobic glucose uptake rates at different dilution rates.**

Measured experimental and *iMM904* values were plotted and shown to be comparably similar under both conditions.



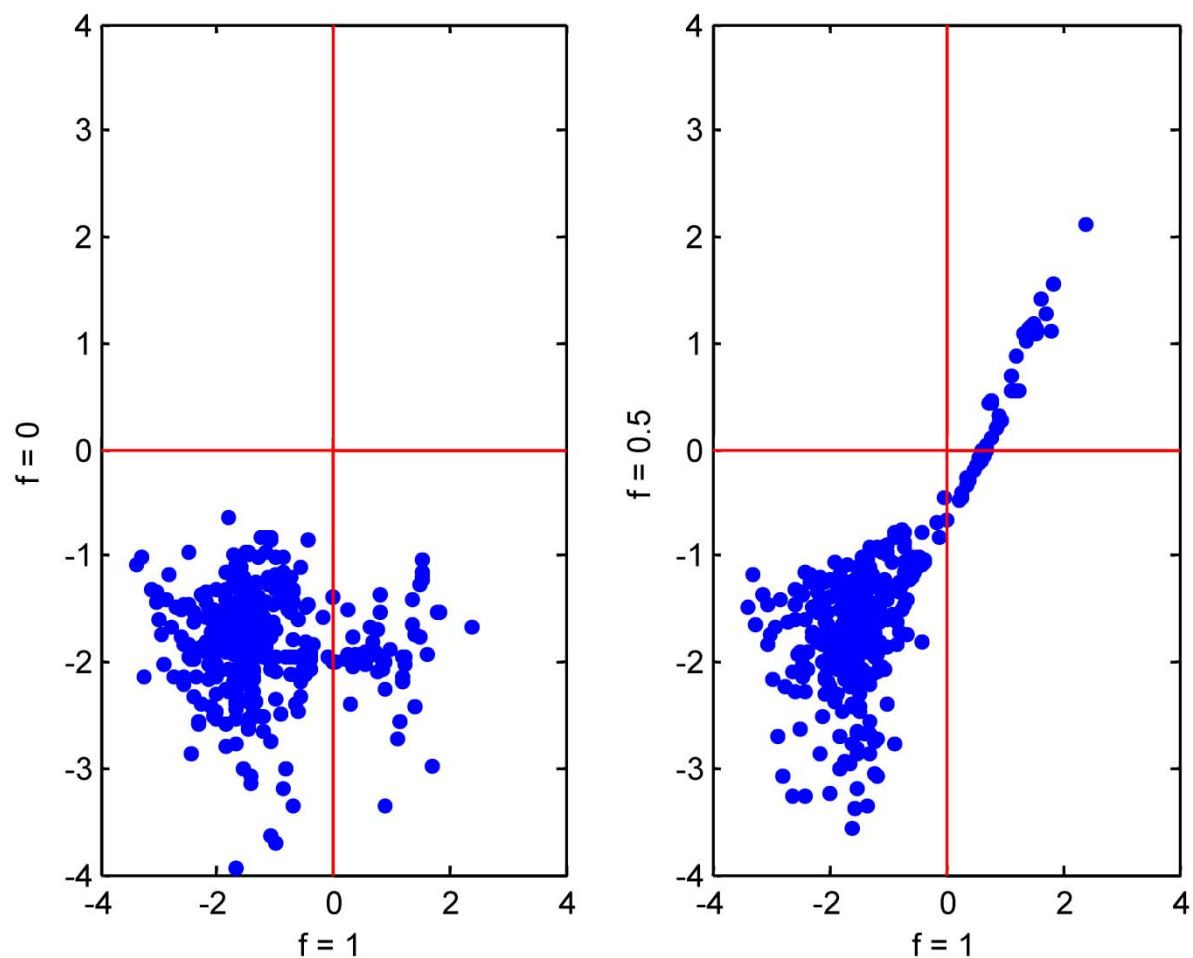
**Figure S2.**  
**ROC curve plots of *i*MM904 and *i*LL672 predictions using different analysis methods.**



**Figure S3.**

**Sensitivity analysis for reaction Z-scores with respect to magnitude (f) of secretion fluxes.**

Scatterplots indicate that the weighting magnitude of the extracellular metabolite secretion fluxes (i.e., between  $f=0.5$  and  $f=1$ ) does not generally affect reaction Z-scores calculations. While reaction Z-scores are sensitive to the addition of secretion flux constraints, the magnitude of the constraints does not significantly affect the scores.



**Figure S4.**  
**Sensitivity analysis of reaction Z-scores with respect to the percentage of the solution space sampled.**

X-axis in each plot shows the Z-scores obtained by sampling the upper 50% of the solution space relative to the maximum biomass production rate. (A) Y-axis: Z-scores obtained by sampling the range between 50-75% of maximum biomass production rate. (B) Y-axis: Z-scores obtained by sampling the upper 25% of the solution space. Reaction Z-scores are independent of either portion (i.e. lower 25% and upper 25%) of the solution space that was sampled between 50-100%; thus, Z-score results remain consistent across the sampled solution space irrespective of the biomass rate constraints.

