# Additional File 2

## 1. Sugar uptake

$$v'_{S,i} = \frac{v_{\max,i} \cdot S}{\left(1 + \frac{E}{K_E}\right) \cdot \left(K_{S,i} \cdot \left(1 + \frac{S}{K_{S,i}}\right) + S\right)} \quad (1)$$

where $v'_{S,i}$ are either glucose or fructose partial uptake rates for each of the 5 main hexose transporters i, expressed under anaerobic conditions [1]; $v_{\max,i}$ and $K_{S,i}$ are the maximum uptake rate and sugar saturation constant for the $i^{th}$ transporter; and $K_E$ is the ethanol inhibition constant (Table S1). Hexose transporters are active or inactive depending on the growth phase and glucose concentration in the medium. The uptake rates for glucose or fructose, $v_{S,i}$, are given by the weighted average of the uptake rates of the active transporters (Eq. 2).

$$v_{S,i} = f \cdot \sum_i \alpha_i v'_{S,i} \quad (2)$$

where $f$ is an empirical temperature-dependent efficiency factor for sugar transport that ranges from 0 to 1 [2].

Table S1: Kinetic parameters used for modeling sugar uptake rates [2]. The expression of hexose transporters during fermentation was set using weights, $\alpha$, corresponding to the relative abundance of each transporter in the given growth phase: $\alpha = 0.5$ for HXT1 and HXT3 in the exponential phase; $\alpha = 1$ for HXT3 from onset stationary phase until [glucose] < 20g/L; $\alpha = 0.5$ for HXT3 and $\alpha = 0.25$ for HXT6 and HXT7 during the stationary phase.

| Transporter | $V_{max}$ [ggDCW$^{-1}$·h$^{-1}$] | $K_g$ [gL$^{-1}$] | $K_f$ [gL$^{-1}$] |
|---|---|---|---|
| HXT1 | 7.45 | 18 | 54 |
| HXT3 | 2.7 | 10.8 | 22.3 |
| HXT6 | 1.31 | 0.18 | 0.47 |
| HXT7 | 1.31 | 0.36 | 0.83 |

## 2. Nitrogen uptake

$$v_{N,i} = \left( a\tan\left( \frac{n-0.2}{7.25e^{-3}} \right) \cdot \Pi + \frac{1}{2} \right) \cdot \frac{3e^{-4}}{N_i \cdot C_i} \tag{3}$$

Here, n represents total nitrogen content in the medium, $N_i$ is the number of nitrogen atoms in the i$^{th}$ nitrogen-containing substrate, and $C_i$ is the nitrogen-containing substrate i$^{th}$ with a concentration above 0.1mg/L in the extracellular medium.

## 3. Maintenance

$$v_{mATP} = \left[ \left( 0.17 \cdot N_{in} + 0.09 \right) + \left( \frac{0.26}{e^{\left( \frac{31.17-E}{7.3} \right)}} \right) \right] \cdot v_{S,i} \tag{4}$$

Here, $N_{in}$ represents the initial nitrogen concentration (i.e. summed across all N-compounds); $v_{S,i}$ is the sugar uptake rate and $E$ is the ethanol concentration in g/L.

## 4. Carbohydrates accumulation

$$v_{CARB,i} = e^{-\left(4.5+18 \cdot S^3 + 1.47 \cdot e^S\right)} \tag{5}$$

This function defines an UB in the LP. S represents the remaining sugar in the medium.

## 5. Biomass equation

| | | | Previous model | iFF708 | iIN800 | | IFV715 | |
|---|---|---|---|---|---|---|---|---|
| | | | Nitrogen limited | Carbon limited | Carbon limited | nitrogen limited | Carbon limited | nitrogen limited |
| Amino acids | | | 0.018287 | | | | | |
| | L-Alanine | ALA | | 0.4590 | 0.3570 | 0.2520 | 0.3570 | 0.2520 |
| | L-Arginine | ARG | | 0.1610 | 0.1360 | 0.0980 | 0.1360 | 0.0980 |
| | L-Asparagine | ASN | | 0.1020 | 0.1720 | 0.1530 | 0.1720 | 0.1530 |
| | L-Aspartate | ASP | | 0.2980 | 0.1720 | 0.1530 | 0.1720 | 0.1530 |
| | L-Cysteine | CYS | | 0.0070 | 0.0430 | 0.0440 | 0.0430 | 0.0440 |
| | L-Glutamate | GLU | | 0.3020 | 0.2680 | 0.2310 | 0.2680 | 0.2310 |
| | L-Glutamine | GLN | | 0.1050 | 0.2680 | 0.2310 | 0.2680 | 0.2310 |
| | Glycine | GLY | | 0.2900 | 0.3250 | 0.2780 | 0.3250 | 0.2780 |
| | L-Histidine | HIS | | 0.0660 | 0.0750 | 0.0710 | 0.0750 | 0.0710 |
| | L-Isoleucine | ILE | | 0.1930 | 0.1720 | 0.1420 | 0.1720 | 0.1420 |
| | L-Leucine | LEU | | 0.2960 | 0.2500 | 0.2070 | 0.2500 | 0.2070 |
| | L-Lysine | LYS | | 0.2860 | 0.2390 | 0.2040 | 0.2390 | 0.2040 |
| | L-Methionine | MET | | 0.0510 | 0.0500 | 0.0440 | 0.0500 | 0.0440 |
| | L-Phenylalanine | PHE | | 0.1340 | 0.1140 | 0.0920 | 0.1140 | 0.0920 |
| | L-Proline | PRO | | 0.1650 | 0.1290 | 0.1180 | 0.1290 | 0.1180 |
| | L-Serine | SER | | 0.1850 | 0.2540 | 0.2250 | 0.2540 | 0.2250 |
| | L-Threonine | THR | | 0.1910 | 0.1970 | 0.1600 | 0.1970 | 0.1600 |
| | L-Tryptophan | TRP | | 0.0280 | 0.0270 | 0.0280 | 0.0270 | 0.0280 |
| | L-Tyrosine | TYR | | 0.1020 | 0.0960 | 0.0680 | 0.0960 | 0.0680 |
| | Valine | VAL | | 0.2650 | 0.0000 | 0.0000 | 0.0000 | 0.0000 |
| Carbohydrates | | | 0.0154 | | | | | |
| | Glycogen | GLYCOGEN | | 0.5190 | 0.5190 | 0.6670 | 0.5190 | 0.6670 |
| | alpha,alpha-Trehalose | TRE | | 0.0234 | 0.0230 | 0.0850 | 0.0230 | 0.0850 |
| | Mannan | MANNAN | | 0.8080 | 0.8210 | 0.9940 | 0.8210 | 0.9940 |
| | 1,3-beta-D-Glucan | 13GLUCAN | | 1.1348 | 1.1360 | 0.9630 | 1.1360 | 0.9630 |
| RNA | | | 0.001651 | | | | | |
| | AMP | AMP | | 0.0460 | 0.0510 | 0.0400 | 0.0510 | 0.0400 |
| | GMP | GMP | | 0.0460 | 0.0510 | 0.0400 | 0.0510 | 0.0400 |
| | CMP | CMP | | 0.0450 | 0.0500 | 0.0390 | 0.0500 | 0.0390 |
| | UMP | UMP | | 0.0600 | 0.0670 | 0.0520 | 0.0670 | 0.0520 |
| DNA | | | 0.000161 | | | | | |
| | dAMP | DAMP | | 0.0040 | 0.0040 | 0.0040 | 0.0040 | 0.0040 |
| | dCMP | DCMP | | 0.0020 | 0.0020 | 0.0030 | 0.0020 | 0.0030 |
| | dTMP | DTMP | | 0.0040 | 0.0040 | 0.0040 | 0.0040 | 0.0040 |
| | dGMP | DGMP | | 0.0020 | 0.0020 | 0.0030 | 0.0020 | 0.0030 |
| Lipids | | | 0.001456 | | | | | |
| | Phosphatidylcholine | PC | | 0.00600 | 0.002884 | 0.001660 | 0.00309 | 0.00238 |
| | 1-Phosphatidyl-D-myo-inositol | PINS | | 0.00500 | 0.001531 | 0.001656 | 0.00153 | 0.00166 |
| | Phosphatidylserine | PS | | 0.00200 | 0.000373 | 0.000302 | 0.00037 | 0.00030 |
| | Phosphatidylethanolamine | PE | | 0.00400 | 0.000697 | 0.000083 | 0.00070 | 0.00008 |
| | Acyl_acids | ACYL | | | 0.000206 | 0.000723 | | |
| | Triacylglycerol | TAGLY | | 0.00700 | 0.000781 | 0.003618 | 0.00078 | 0.00362 |
| | Ergosterol-ester | ERGOSTE | | | 0.000812 | 0.004632 | | |
| | Ergosta-5,7,22,24(28)-tetraenol | ERTEOL | | | 0.000125 | 0.000167 | 0.00013 | 0.00017 |
| | Ergosterol | ERGOST | | 0.00100 | 0.005603 | 0.005155 | 0.00642 | 0.00532 |
| | Zymosterol | ZYMST | | 0.00200 | 0.000015 | 0.000051 | 0.00002 | 0.00005 |
| | Episterol | EPST | | | 0.000096 | 0.000062 | 0.00010 | 0.00006 |
| | Fecosterol | FEST | | | 0.000114 | 0.000068 | 0.00011 | 0.00007 |
| | Lanosterol | LNST | | | 0.000032 | 0.000074 | 0.00003 | 0.00007 |
| | 4,4-Dimethylzymosterol | DMZYMST | | | 0.000056 | 0.000046 | 0.00006 | 0.00005 |
| | Ceramide-I | CER1 | | | 0.000351 | 0.000075 | | |
| | Ceramide-II | CER2 | | | 0.000066 | 0.000009 | 0.00042 | 0.00008 |
| | Phosphatidate | PA | | 0.00100 | 0.000000 | 0.000000 | 0.00100 | 0.00000 |
| | Sulfate | SLF | | 0.02000 | | | 0.02000 | 0.02000 |
| | ATP | ATP | | 59.27600 | | | 59.276001 | 59.276001 |

Due to the unavailability of some lipid intermediates, some compounds were condensed into only one; Phosphatidylcholine and Acyl acids, ergosterol and ergosterol-ester and ceramide I and ceramide II were grouped into three compounds.

[1] Perez M, Luyten K, Michel R, Riou C, Blondin B: **Analysis of Saccharomyces cerevisiae hexose carrier expression during wine fermentation: both low- and high-affinity Hxt transporters are expressed.** *FEMS Yeast Res* 2005, **5:**351-361.

[2] Pizarro F, Varela C, Martabit C, Bruno C, Perez-Correa JR, Agosin E: **Coupling kinetic expressions and metabolic networks for predicting wine fermentations.** *Biotechnol Bioeng* 2007, **98:**986-998.