Additional File 2

1. Sugar uptake

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

(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]; \( v_{\text{max},i} \) and \( K_{S,i} \) are the maximum uptake rate and sugar saturation constant for the \( i^{\text{th}} \) 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).

\[ v_{S,i} = f \cdot \sum_i \alpha_i v'_{S,i} \]  

(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 \([\text{glucose}] < 20\text{g/L}\); \( \alpha = 0.5 \) for HXT3 and \( \alpha = 0.25 \) for HXT6 and HXT7 during the stationary phase.
2. Nitrogen uptake

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

(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

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

(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

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

(5)

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