

SUPPLEMENTARY METHODS

The Yeast Flux Balance Model

Details about Flux Balance Analysis (FBA) and its possible applications in system-level studies of cellular metabolism have been amply described¹⁻⁷. In particular, global-scale gene deletions *in silico* experiments were performed in yeast⁸⁻¹⁰ and *E. coli*¹¹⁻¹⁴. The yeast Flux Balance Analysis (FBA) model used in the present work is based on the stoichiometric reconstruction published in¹⁵, and available on the following web site:

- Genome Res. 2003 13: 244-253, Supplemental Research Data from¹⁵:
<http://www.genome.org/cgi/content/full/13/2/244/DC1>

The available data include the list of reactions (with gene names and EC numbers), the list of metabolites and the biomass composition. The Supplementary Information URL by Forster et al. (<http://www.cpb.dtu.dk/models/yeastmodel.html>) contains the same information in multiple formats, as well as a list of subsequent corrections, which were all implemented in our current model. The maintenance flux was implemented as described in⁹ and references therein. The additional constraints that have been used for generating the data presented in **Figs. 2** and **4** (“nominal” conditions) are shown in the Table below. Note that phosphate (PI), sulfur (SLF) and nitrogen (NH₃) are effectively unlimited resources under the carbon and oxygen regimes explored in the nominal run. Estimates of oxygen and glucose uptake fluxes are related to ranges reported in the literature¹⁶⁻¹⁸.

A complete list of reactions as used in the current study is available on-line at <http://www.cgr.harvard.edu/kishony/prism>.

Definition of flux bounds for Nominal condition (yellow: exchange fluxes; green: intracellular fluxes):

Flux (FBA name)	Lower , Upper bound mmol/(grDM·h)
Glucose (GLCxtI)	0 , 20
Acetate (AcxtI)	$-\infty$, 0
Oxygen (O2xtI)	0 , 5
Phosphate (PIxtI)	0 , 10
Sulfate (SLFxtI)	0 , 100
NH₃ (NH3xtI)	0 , 100
Histidine (HISxtI)	0 , 0.2
Leucine (LEUxtI)	0 , 0.2
Uracile (URAxI)	0 , 0.2
Threonine (THRxtI)	0 , 1.12
HIS3 (his3)	0 , 0
LEU2 (leu2)	0 , 0
URA3 (ura3)	0 , ∞
RIP1 (ctytr)	0 , 0

(For references, see **Supplementary References** online)