Supplementary Information

Reconstruction and logical modeling of glucose repression signaling pathways in *Saccharomyces cerevisiae*

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Additional File 2. Logical Equations

The applied logical equations are summarized and (when deemed relevant) commented below. Each equation corresponds to a hyperedge. More detailed references are given in Additional file 1. Cells marked in yellow indicate that the equation is not considered in the computation of logical steady state. In very few cases, for reactions ignored in logical steady state calculations, a coefficient of 2 is used. These edges lead to species with default values of 1. The coefficient 2 is used in the hope that it will at some time be possible to implement in CNA that a gene is always expressed at a basal level (1), but may be induced to a higher level (2). A note about the nomenclature: genes are referred in uppercase (e.g., MIG1), while proteins include ths suffix ‘p’ (e.g., Mig1p). In the main text, proteins are referred similarly but without the suffix (e.g., Mig1), and genes are in italic uppercase (e.g., MIG1).

Logical Equation	Notes on logical equations
1 glucose_ext + 1 SNF3 = 1 Snf3p	In this version Snf3 is assumed to be inactive under high concentrations of glucose due to transcriptional repression. This may be a too drastic interpretation. However, since basal level gene expression is difficult to represent in CNA, the only alternative would be to give *SNF3* a default value of 1, which would mean that the model could not me used to make predictions of changes in *SNF3* expression levels
1 !Mig1p + 1 !Mig2p = 1 SNF3	It is assumed that Mig1 or Mig2 alone is sufficient to repress *SNF3*
1 !Mig3p = 1 SNF3	Ignored for logical steady state calculations as Mig3 is not physiogically relevant
1 glucose_ext + 1 RGT2 = 1 Rgt2p	
1 YCK1/2 = 1 Yck1p	
1 GRR1 = 1 SCF_Grr1	
1 !Mig1p = 1 MTH1	It is not entirely clear to the author whether Mig2 is a significant factor in the repression of *MTH1*. Here it is supposed that either Mig1 or Mig2 should be inactive for the gene to be derepressed
1 !Mig2p = 1 MTH1	
1 !Mig3p = 1 MTH1	Ignored for logical steady state calculations as Mig3 is not physiogically relevant
1 !Rgt1p = 1 MTH1	Ignored in logical computations, cf. Kaniak et al. (2004)
1 Gal4p = 1 MTH1	Ignored in logical computations, cf. Kaniak et al. (2004)
1 MTH1 + 1 !Yck1p = Mth1p	
1 MTH1 + 1 !SCF_Grr1 = Mth1p	
1 MTH1 + 1 !Snf3p + 1 !Rgt2p = Mth1p	
1 !Rgt1p = 1 STD1	Ignored in logical computations since *STD1* is active per default

Logical Equation	**Notes on logical equations**
1 STD1 + 1 !Yck1p = Std1p	
1 STD1 + 1 !SCF_Grr1 = Std1p	
1 STD1 + 1 !Snf3p + 1 !Rgt2p = Std1p	
1 Mth1p + 1 RGT1 = 1 Rgt1p	Rgt1 only function as repressor when Mth1 OR Std1 is present. *RGT1* is active per default
1 Std1p + 1 RGT1 = 1 Rgt1p	Rgt1 only function as repressor when Mth1 OR Std1 is present
1 glucose_ext + 1 REG1 + 1 GLC7 = 1 Glc7Reg1	
1 !Glc7Reg1 + 1 SNF1 + 1 SNF4 = 1 Snf1p	
1 !Mig2p =2 MIG1	Ignored in logical computations: Mig1 and Mig2 are active at the same time. We thus expect Mig1 to be most active while it is repressed at the transcriptional level
1 !Mig3p =2 MIG1	Ignored for logical steady state calculations as Mig3 is not physiogically relevant
1 !Snf1p + 1 MIG1 = 1 Mig1p	
1 !Rgt1p = 1 MIG2	
1 MIG2 = 1 Mig2p	Assuming that Mig2 is not post-translationally regulated.
1 !Rgt1p = 1 MIG3	
1 MIG3 + 1 !Snf1p = Mig3p	Assuming that the repression by Rgt1 is significant
1 !Mig1p = 1 MALR	
1 maltose_int + 1 MALR = 1 MalRp	
1 !Mig1p + 1 MalRp = 2 MALT	Ignored in logical computations since *MALT* is active per default: This is chosen as a consequence of the setup of CNA rather than due to physiological data: There must be a basal level of *MALT* expression for the logical steady state analysis to reach a result, for which reason *MALT* is given the default value of 1. However, given this default value, *MALT* can never reach the 2 level, for which reason this edge will be ignored in any case.
1 MALT = 1 MalTp	
1 !glucose_ext = 1 MalTp	Assuming that MalT is inhibited by glucose, either directly or indirectly, on the protein level. It is not obvious that this interaction should be excluded in logical computations, and further elucidation is required to decide in the future whether to include this equation. The choice did not, however effect the result of the present evaluations in the present report
1 !Mig1p + 1 Gal4p = 1 GAL1	This choice is not obvious. The reader is referred to Lohr et al. (1995): Significant repression by each individual mechanism, but only total repression when all repression pathways are active
1 Gal11p = 1 GAL1	Excluded in logical computations: Gal11 probably forms a complex with Gal4. Δ*gal11* diminishes Gal1 and Gal2 expression 10-11 times. However, a significant galactose induction would still be seen
1 GAL1 = 1 Gal1p	
1 Gal4p = 2 GAL2	In the present model, a basal level of Gal2 must be assumed, since intracellular galactose is necessary for the induction of Gal3
1 !glucose_ext = 1 Gal2p	The extent of glucose inhibition of galactose transport is not obvious based on literary data
1 Gal11p = 2 GAL2	Excluded in logical computations: Gal11 probably forms a complex with Gal4. Δ*gal11* diminishes Gal1 and Gal2 expression 10-11 times. However, a significant galactose induction would still be seen
1 GAL2 = 1 Gal2p	
1 Gal4p = 1 GAL3	Ignored in logical computations: If Mig1 is present Gal3 is not expressed. When grown on glycerol, Gal3 is present even though Gal4 is not active
1 !Mig1p = 1 GAL3	
1 GAL3 + 1 galactose_int = 1 Gal3p	

Logical Equation	**Notes on logical equations**
1 !Mig1p = 1 GAL4	
1 GAL4 + 1 !Gal80p = Gal4p	
1 GAL11 = 1 Gal11p	
1 Gal4p = 2 GAL80	This interaction cannot not be critical for the expression of Gal80, since Gal4 is only active when Gal80 is not present. Additionally, we must include a basal level of expression from *GAL80* by setting a default value of 1, so this edge would in any case be ignored in the logical steady state calculation
2 !Gal1p + 1 !Gal3p + 1 GAL80 = Gal80p	Here it is stated that Gal1 must be present at level 2 (which it never reaches in the wild type) to inhibit Gal80. This is done to stress that Gal1 over-expression can complement a *GAL3* deletion, but that Gal1 is probably only plays a minor role in Gal80 inhibition in the WT. Additionally, applying simply a 1 !Gal1p + 1 !Gal3p relationship would result in ambiguities in terms of multiple possible logical steady state solutions for several of the products of the *GAL* gene family
1 !Mig1p = 1 CAT8	
1 CAT8 + 1 Snf1p = 1 Cat8p	
1 Cat8p = 1 SIP4	
1 SIP4 + 1 Snf1p = 1 Sip4p	
1 !Mig1p + 1 !Mig2p = 1 SUC2	It is assumed that both Mig1 and Mig2 should be absent for SUC2 to be expressed at high levels, cf. Lutfiyya et al. (1998) who found that single deletions on had low impact on *SUC2* expression level, whereas Δ*mig1*Δ*mig2* had great effect**.** Contrary to this Klein et al. (1999) found a large increase in *SUC2* expression in a Δ*mig1* strain and further increase by additional disruption of *MIG2*
1 !Rgt1p = 1 HXT1	
1 !Mth1p + 1 !Std1p = HXT1	According to Kim et al. (2006), either Std1 or Mth1 is required for Rgt1 repression of *HXT1*.
1 !Mig1p + 1 !Rgt1p = 1 HXT2	Here it is assumed that Rgt1 can act as a repressor in the presence of either Mth1 OR Std1 (Mth1 and Std1 are not part of the expression since Rgt1 is only active if at least one of the two is present)
1 !Mth1p = 1 HXT3	
1 !Rgt1p = 1 HXT3	
1 !Mth1p + 1 !Mig1p = 1 HXT4	According to Kim et al. (2006), Mth1, but not Std1, is involved in Rgt1 repression of *HXT1*
1 !Rgt1p + 1 !Mig1p = 1 HXT4	
1 !Rgt1p = 1 HXT5	
1 !Rgt1p = 1 HXT8	
1 !Rgt1 = 1 4ORFs	
1 !Mig1p + 1 MalRp = 1 MALS	
1 Gal4p = 1 GAL5	Doubtable, see note on the species
1 Gal4 = 1 GAL7	
1 Gal4 = 1 GAL10	
1 Gal4p = 1 MEL1	
1!Mig1p = 1 MEL1	
1 Cat8p = 1 ICL1	Here it assumed that either Cat8 or Sip4 can activate gene expression. However, Sip4 expression is controlled by Cat8 in wild type cell
1 Sip4p = 1 ICL1	
1 Cat8p = 1 FBP1	Here it assumed that either Cat8 or Sip4 can activate gene expression. However, Sip4 expression is controlled by Cat8 in wild type cells
1 Sip4p = 1 FBP1	
1 Cat8p = 1 PCK1	
1 Cat8p = 1 MLS1	Here it assumed that either Cat8 or Sip4 can activate gene expression. However, Sip4 expression is controlled by Cat8 in wild type cells
1 Sip4p = 1 MLS1	

Logical Equation	Notes on logical equations
1 Cat8p = 1 MDH2	Here it assumed that either Cat8 or Sip4 can activate gene expression. However, Sip4 expression is controlled by Cat8 in wild type cells
1 Sip4p = 1 MDH2	
1 Cat8p = 1 ACS1	
1 Cat8p = 1 SFC1	
1 Cat8p = 1 CAT2	
1 Cat8p = 1 IDP2	
1 Cat8p = 1 JEN1	
1 galactose_ext + 1 Gal2p = 1 galactose_int	
1 maltose_ext + 1 MalTp = 1 maltose_int	

References for Supplementary Information

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