IDENTIFICATION OF KEY TRANSCRIPTION FACTORS IN GLUCOSE SENSING PATHWAY IN *SACCHAROMYCES CEREVISIAE*

by

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B.S., Chemical Engineering, Boğaziçi University, 2008

Submitted to the Institute for Graduate Studies in
Science and Engineering in partial fulfillment of
the requirements for the degree of
Master of Science

Graduate Program in Chemical Engineering
Boğaziçi University

2010

ACKNOWLEDGEMENTS

I would like to express my sincere gratitude and grateful thanks to my thesis advisor Prof. Betül Kırdar for her everlasting encouragement and support during my graduate studies. I also would like to thank my thesis jury, Assoc. Prof. Ebru Toksoy Öner and Assist. Prof. Elif Özkırımlı, for their critical comments on my thesis.

I am sincerely grateful to my friend Çisil Peşkircioğlu and my friends in Biosystems Engineering Research Group, especially to Şebnem Öç, Deniz Rende, Duygu Dikicioğlu, Ayça Cankorur, Elif Dereli, Esra Börklü Yücel, Dicle Hasdemir, Ceyda Kasavi, Erkan Karabekmez, Serpil Eraslan, Saliha Durmuş Tekir and Betül Kavun for their everlasting patience and support.

I would also like to thank my mother Nihal, my father Yaşar, my brother Ercüment and my sister Buket for their never ending love, support and encouragement through all my life. To them, I dedicate this thesis.

Last but certainly not the least I would like to thank with all my heart to my love, my husband, Feras Alazi for his everlasting love which makes everything bearable and beautiful.

This work was financially supported by Boğaziçi Research Fund through project Tubitak-106M444.

ABSTRACT

IDENTIFICATION OF KEY TRANSCRIPTION FACTORS IN GLUCOSE SENSING PATHWAY IN *SACCHAROMYCES CEREVISIAE*

In this study, a genome-scale transcriptional regulatory network (TRN) in *S. cerevisiae* was constructed and integrated with the transcriptome data available in literature for the mutants of the glucose signaling pathway of *S. cerevisiae* to identify key transcription factors (transcription factors around which a considerable collective change in the expression of the genes occur in response to environmental and genetic perturbations). Identification of key transcription factors demonstrates the regulatory mechanisms invoked in the cell and potential biomarkers, without *a priori* requirement of change in the transcription level of the transcription factors. Biologically meaningful key transcription factors identified with this approach shed light on the transcriptional regulatory mechanism controlling the glucose signaling in *S. cerevisiae*. For example, key transcription factors identified in *ΔSNF1* reveal the predicted role of Snf1p kinase, highlighting the effectiveness of the approach used and a large genome-scale TRN. In this study, after the key transcription factors were identified, the perturbation-responsive subnetworks were constructed by interconnecting key transcription factors and their differentially expressed target genes responsive to the same perturbation. Based on whether the key transcription factors have their differential expression changed significantly, it was investigated if the transcription factors are regulated mainly transcriptionally or mainly post-transcriptionally.

ÖZET

SACCHAROMYCES CEREVISIAE'DA GLİKOZ ALGILAMA YOLİZİNDEKİ ANAHTAR YAZILIM ETMENLERİNİN BELİRLENMESİ

Glikoz, *Saccharomyces cerevisiae*'da en çok tercih edilen karbon kaynağıdır. Bu çalışmada, *S. cerevisiae*'da genom ölçekli bir yazılım düzenleyici ağ oluşturulmuş ve bu ağ *S. cerevisiae*'nın glikoz algılama yolizi mutantlarının literatürde mevcut olan gen ekspresyonu verisi ile bütünleştirilerek anahtar yazılım etmenleri (etraflarındaki gen ekspresyonunda, çevresel ve genetik pertürbasyonlara tepki olarak önemli toplu bir değişim meydana gelen yazılım etmenleri) belirlenmiştir. Anahtar yazılım etmenlerinin belirlenmesi, hücrede başlatılan düzenleyici mekanizmaları ve olası biyolojik göstergeleri, yazılım etmenlerinin yazılım düzeylerinde değişim gözlenmese de gösterir. Kullanılan yaklaşımla belirlenmiş biyolojik olarak anlamlı anahtar yazılım etmenleri *S. cerevisiae*'nın glikoz algılamasını kontrol eden yazılım düzenleyici mekanizmaya ışık tutmuştur. Örneğin, *ΔSNF1*'da belirlenen anahtar yazılım etmenleri, kullanılan yaklaşımın ve geniş genom ölçekli bir yazılım düzenleyici ağın verimliliğini vurgulayarak, Snf1p'in öngörülen rolünü açığa çıkarmıştır. Bu çalışmada, anahtar yazılım etmenleri belirlendikten sonra, anahtar yazılım etmenleri ile onların aynı değişimlere istatistiksel olarak anlamlı yanıt veren hedef genleri birbirlerine bağlanarak, değişimlere yanıt veren altağlar da oluşturulmuştur. Anahtar yazılım etmenlerinin, değişimlere istatistiksel olarak anlamlı yanıt verip vermediklerine dayanarak, yazılım etmenlerinin başlıca yazılım sırasında mı yoksa başlıca yazılım sonrası mı düzenlendikleri araştırılmıştır.

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$<C>$	Average clustering coefficient of the network
$<k>$	Average degree of the network
b	Betweenness centrality
C	Clustering coefficient
f	Frequency
k	Degree
l	Number of interactions
N	Number of nodes
n	Cumulative distribution
P	Probability
p	p-value
Z	Z-score
γ	Power law exponent
$\Gamma(m, i, n)$	Number of the shortest paths between nodes N_m and N_n, passing through N_i
$\Gamma(m, n)$	Total number of paths between nodes N_m and N_n
μ	Mean
σ	Standard deviation
AER	Aerobic
AKG	α-ketoglutarate
AMP	Adenosine monophosphate
ANA	Anaerobic
ATP	Adenosine-5'-triphosphate
cAMP	Cyclic adenosine monophosphate
Clim	Carbon limitation regime
DNA	Deoxyribonucleic acid
FC	Fold change
GDP	Guanosine diphosphate

Gln	Glutamine
Glu	Glutamate
GO	The Gene Ontology
GPCR	G protein-coupled receptors
GTP	Guanosine-5'-triphosphate
GWLA	Genome-wide location analysis
MIPS	Munich Information Center for Protein Sequences
mRNA	Messenger ribonucleic acid
ORF	Open reading frame
PKA	Protein kinase A
PKB	Protein kinase B
PRS	Perturbation-responsive subnetwork
rDNA	Ribosomal deoxyribonucleic acid
RNA	Ribonucleic acid
S. cerevisiae	*Saccharomyces cerevisiae*
SF	Scale-free
SGD	*Saccharomyces* Genome Database
TF	Transcription factor
TOR	Target Of Rapamycin
TRN	Transcriptional regulatory network
tRNA	Transfer ribonucleic acid
YEASTRACT	Yeast Search for Transcriptional Regulators And Consensus Tracking

1. INTRODUCTION

1.1. Glucose Sensing and Signaling in *Saccharomyces cerevisiae*

Glucose is the preferred carbon and energy source for most cells and can act as a "growth hormone" to regulate several aspects of cell growth, metabolism, and development. Defects in glucose sensing, signaling, and metabolism cause severe and prevalent metabolic disorders in mammals known as diabetes (Özcan and Johnston, 1999).

Glucose is metabolized through glycolysis to pyruvate (Figure 1.1). In the presence of oxygen, most organisms convert pyruvate to carbon dioxide and water via the tricarboxylic acid cycle, generating 36 ATPs. Only when oxygen becomes limiting do most cells resort to fermentation, because it yields only two ATPs per molecule of glucose. *Saccharomyces cerevisiae* is one of the few organisms that prefer to ferment glucose, even when oxygen is abundant. The tendency of *S. cerevisiae* to carry out aerobic fermentation is called the 'Crabtree effect' (Johnston and Kim, 2005).

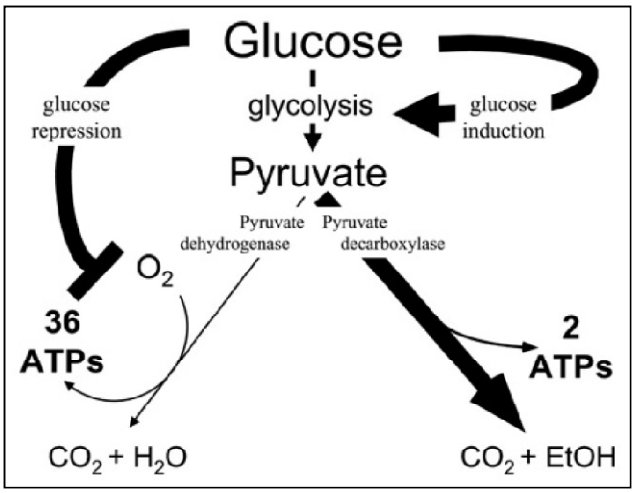

Figure 1.1. Simplified scheme of the glucose metabolism in yeast (Johnston and Kim, 2005)

Glucose, the most preferred carbon source of the budding yeast *S. cerevisiae*, elicits broad changes in the yeast cell that uses the sugar efficiently and exclusively. These changes include regulation of gene expression at the transcriptional, post-transcriptional, translational and post-translational levels (Kaniak *et al.,* 2004). However, the main effect of glucose takes place at the transcriptional level (Gancedo, 1998). For these adaptations to occur, the cell must sense glucose and transmit a signal to the appropriate targets.

Glucose induction and glucose repression are the two major constituents of glucose signaling. In glucose induction pathway, glucose has to be sensed so that glucose transporters can be transcribed and translated to transport glucose inside the cell. Glucose repression pathway becomes active after the glucose has been transported inside the cell and phosphorylated (Raghevendran *et al*., 2005). Although these two pathways show different characteristics, they are shown to be connected to each other by a regulatory network in *S. cerevisiae* (Kaniak *et al.,* 2004).

Zaman *et al.* have identified the glucose-mediated transcriptional response through the contribution of five distinct but interconnected pathways (Figure 1.2): Ras/PKA, Gpr1p/Gpa2p and Sch9p, playing significant roles in the early steps in signal transduction, and Snf1p, Rgt2p/Snf3p, members of the glucose repression and glucose induction pathways, respectively. Moreover, the heme-activated transcriptional regulators Hap1p and the Hap2p/3p/4p/5p complex regulate a significant fraction of the genes repressed independently of PKA (Santangelo, 2006; Zaman *et al.*, 2009).

1.1.1. Early Steps in Signal Transduction

The Ras/PKA pathway (Figure 1.3) is activated immediately in the presence of glucose; it responds to changes in glucose concentration and initiates the signaling processes that lead to cellular growth and division. Ras is a guanine nucleotide-binding protein which is inactive in the GDP-bound state and active when GTP is bound. The polypeptides encoded by the two RAS genes in *S. cerevisiae*, Ras1p and Ras2p, are about 70 per cent identical overall. In its GTP-bound state Ras activates adenylate cyclase (Cyr1p). Glucose addition to cells increases the level of GTP-bound Ras, yielding an increase in intracellular cAMP production by adenylate cyclase, to block the inhibitory

effect of the *BCY1*-encoded regulatory subunit on the catalytic subunits of PKA, encoded redundantly by *TPK1*, *TPK2*, and *TPK3*. The PKA catalytic subunits phosphorylate a variety of proteins involved in metabolism and transcription.

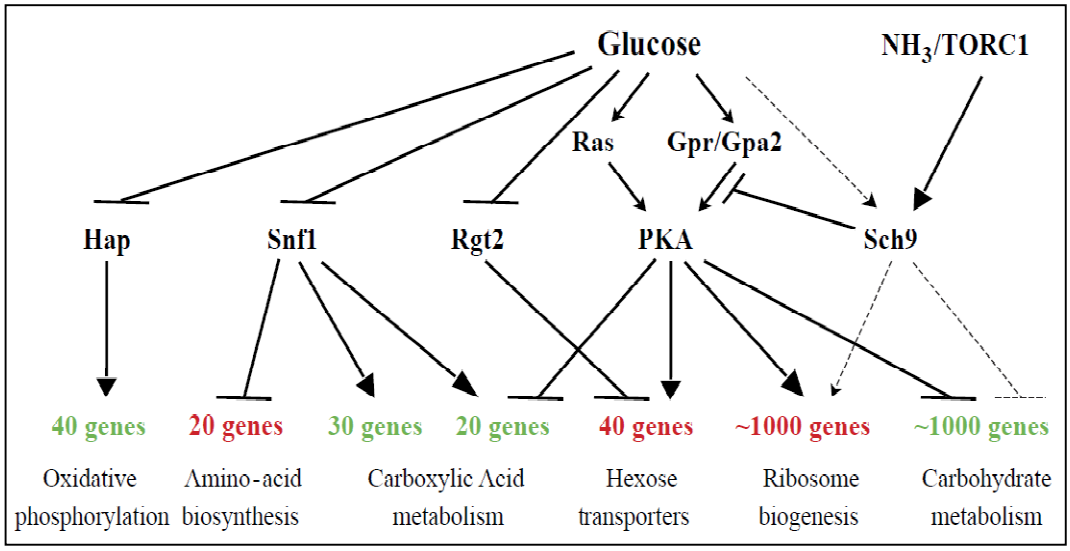

Figure 1.2. Diagram of the regulatory wiring connecting the addition of glucose to the transcriptional responses of the cell (Zaman *et al.*, 2009)

Gpr1p and Gpa2p represent a glucose sensing pathway that function in a similar manner to Ras to activate PKA. The GPCR-like seven-transmembrane protein located on the yeast cell surface, Gpr1p, stimulates the adenylate cyclase in response to glucose through its associated GTP-binding protein, Gpa2p (Santangelo, 2006; Zaman *et al.*, 2009).

Sch9p, an AGC family kinase, is the closest yeast homolog to the mammalian pro-survival Akt/PKB (a component of the mammalian insulin response pathway) as well as to the TOR regulated S6 kinase. *SCH9* overexpression suppresses lethality caused by the loss of PKA signaling (Toda *et al.*, 1988). It is still unknown whether the ability of Sch9p to compensate mutations in the Ras/PKA pathway reflects a convergence of Sch9p and PKA activities from different signaling paths or a direct participation of Sch9p in glucose signaling (Santangelo, 2006). Zaman *et al.* suggested that Sch9p does not contribute significantly to glucose signaling as does PKA but provides a parallel pathway to PKA for glucose-mediated transcriptional changes. They have also proposed a potential cross-talk

between the TOR and Gpa2p/PKA pathways by which diminished TOR signaling enhances the signaling response through the PKA pathway (Zaman *et al.*, 2009).

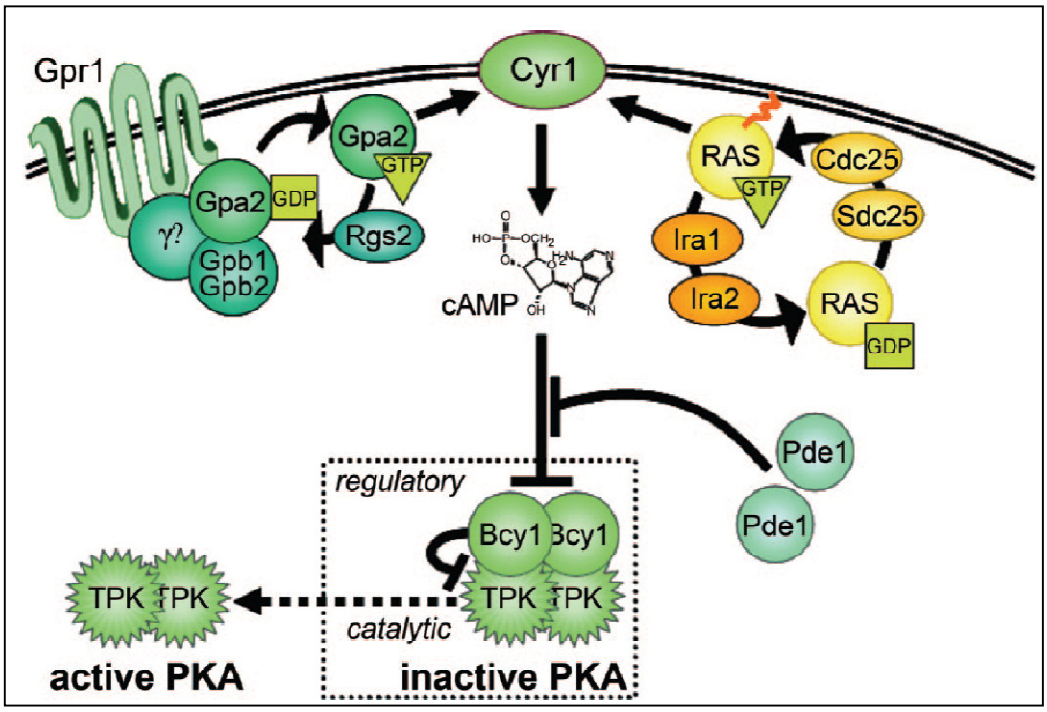

Figure 1.3. Cytoplasmic events in PKA signaling (Santangelo, 2006)

PKA and Snf1p cooperate in the regulation of many processes such as carboxylic acid metabolism, β-oxidation of fatty acids, stress response and filamentous growth; however they are activated by glucose excess or depletion, respectively (Figure 1.4). On the other hand, PKA and Tor1p are both active in response to the nutritional stimuli (glucose and nitrogen) thus function in parallel, to promote the growth (Zhang *et al.*, 2010).

1.1.2. Glucose Induction Pathway in *Saccharomyces cerevisiae*

The glucose induction (Figure 1.5) is initiated by two yeast membrane glucose sensors Snf3p and Rgt2p with very long cytoplasmic tails that sense low and high concentrations of glucose, respectively. When glucose binds to sensors, the sensors undergo a conformational change that activates the membrane-bound casein kinase, Yck1p. Two proteins, Mth1p and Std1p, which interact with the cytoplasmic tails in

glucose grown cells, are phosphorylated by Yck1p. Phosphorylated Mth1p and Std1p are ubiquitinated by the protein Grr1p. Ubiquitinated proteins are recognized by the proteasomal machinery and degraded. All the above-mentioned protein-protein interactions occur in the cytoplasm, resulting in a signal being sent to the nucleus, where the transcription factor Rgt1p becomes hyperphosphorylated. Once Rgt1p becomes hyperphosphorylated, it is believed that an unknown protein activates the transcription of the glucose-transporter-encoding *HXT* genes. In the absence of glucose, the proteins Mth1p and Std1p move to the nucleus, where they interact with the active Rgt1p protein and repress the transcription of *HXT* genes (Raghevendran *et al.*, 2005). Rgt1p activity is further influenced by the Snf1p and PKA pathways, and components of the Rgt system are subject to various positive and negative feedback loops (Kaniak *et al.*, 2004; Zaman *et al.*, 2009).

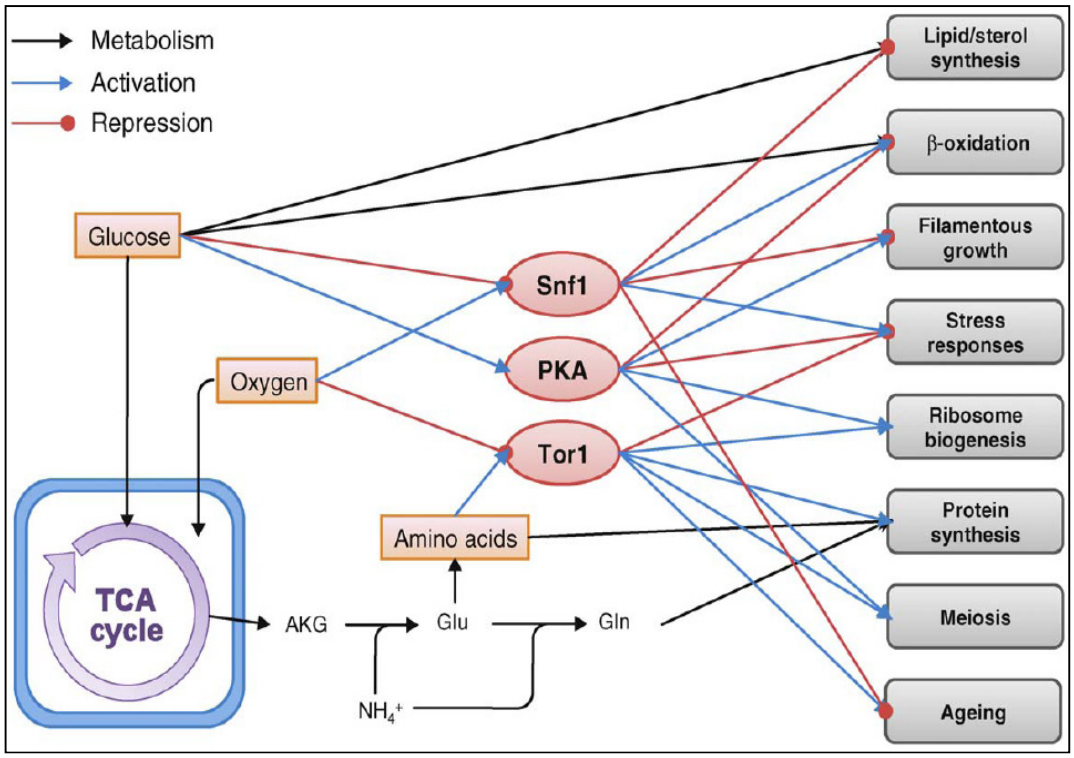

Figure 1.4. Interactions between Snf1p, Tor1p and PKA pathways in yeast (Zhang *et al.*, 2010)

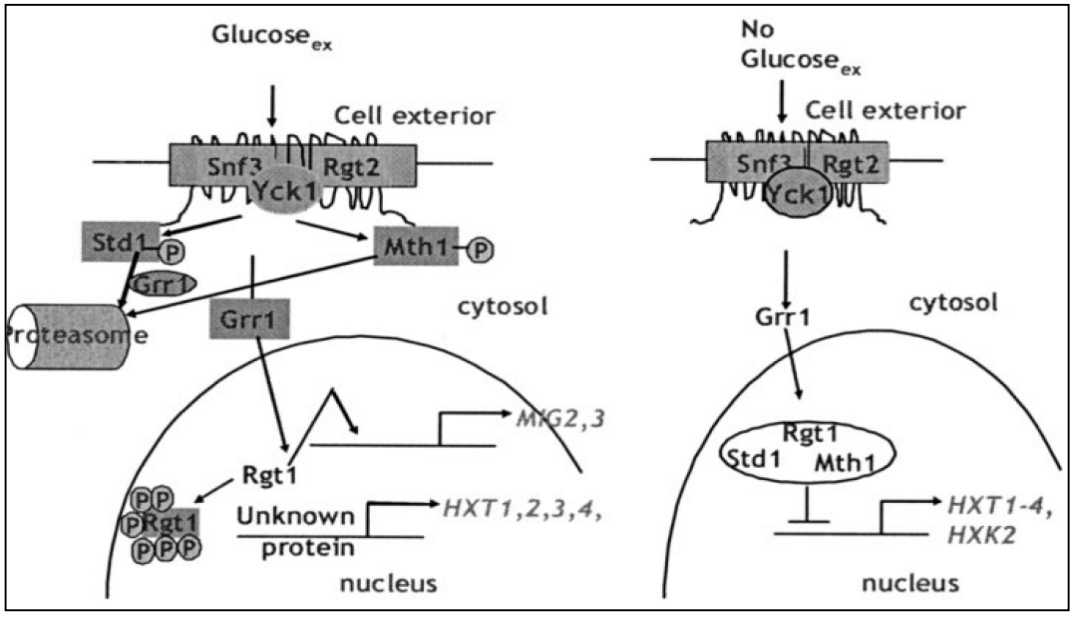

Figure 1.5. Glucose induction pathway in *S. cerevisiae* (Raghevendran *et al*., 2005)

1.1.3. Glucose Repression Pathway in *Saccharomyces cerevisiae*

In the presence of glucose, inactive Mig1p (a DNA-binding protein with Zinc finger domain) gets dephosphorylated by the Glc7p phosphatase via its regulatory subunit Reg1p. It is believed that the metabolic enzyme, hexokinase 2 (Hxk2p, it phosphorylates glucose in glycolysis) positively regulates this step either directly or indirectly. Active Mig1p (unphosphorylated) interacts with the co-repressors Ssn6p and Tup1p and binds to the promoters of various genes, including genes encoding enzymes of the tricarboxylic acid (TCA) cycle, electron transport chain, alternative carbon sources consumption, gluconeogenesis, and represses the transcription of those genes. *MIG1* expression is regulated by Mig2p. Snf1p, the yeast homolog of mammalian AMP-activated protein kinase, gets activated by three upstream kinases when the glucose becomes depleted, and activates genes that are repressed in glucose-containing media but are derepressed and needed for growth in the presence of nonfermentable carbon sources, such as glycerol and ethanol (Figure 1.6). Snf1p complex is a heterotrimer, composed of a catalytic α-subunit (Snf1p), a regulatory γ-subunit (Snf4p), and a scaffolding β-subunit (one of Sip1p, Sip2p or Gal83p). Active Snf1p enables the transcription of many genes responsible for oxidative growth through activation of the transcriptional activators Cat8p and Adr1p and inactivation of the Mig1p transcriptional repressor (Raghevendran *et al*., 2005). In the

presence of glucose, the Reg1p/Glc7p protein phosphatase 1 complex dephosphorylates and inactivates Snf1p (Sanz *et al.*, 2000).

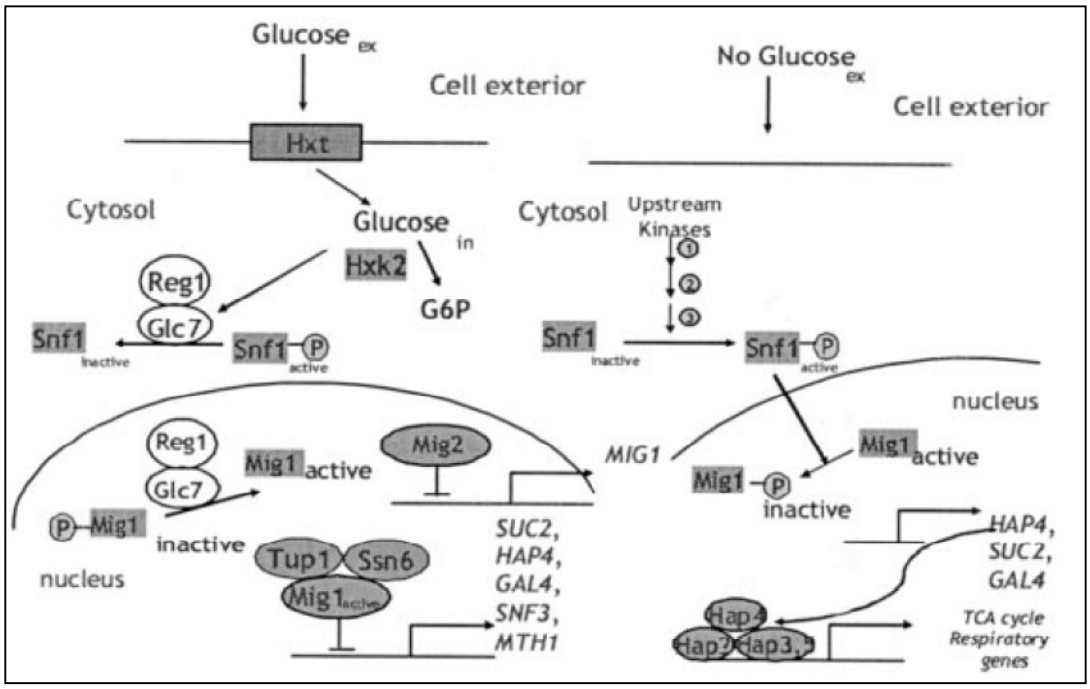

Figure 1.6. Glucose repression pathway in *S. cerevisiae* (Raghevendran *et al*., 2005)

1.2. Transcriptional Regulatory Networks

Gene expression is a carefully regulated and controlled process. Under a given condition or in a particular cell type, only a fraction of the genes are expressed. There is a complex transcriptional regulatory network (TRN) that controls which genes are expressed in response to various environmental and developmental signals (Palsson, 2006).

Transcription factors (TFs) determine which genes in a cell will be transcribed by recognizing and binding to short stretches of double-helical DNA of defined sequence. TFs may act as transcriptional activators or transcriptional repressors (Alberts *et al.*, 1994). The basic functional element of a TRN is the promoter region of a gene or operon that contains the regulatory binding sites for the relevant TFs regulating the expression of a particular gene. The locations and orientations of these binding sites, as well as the affinity of the TFs to particular variants of the site, determine the expression levels of a gene in response to

changes in the active TF concentrations inside the cell. In the light of the information given above, the TRN is defined by which TF binds to which promoters and what the integrated effect of all these TFs is on the expression of all the genes (Ptashne and Gann, 2002).

There are three types of intracellular biochemical reaction networks: metabolic, transcriptional regulatory and signaling networks. The ultimate goal of systems biology is to integrate all of these three to generate whole-cell models of microbes and other organisms. The major advantage of TRN reconstruction over other types of network reconstructions is the availability of high-throughput experimental data, such as genome-wide mRNA expression and genome-wide location analysis (GWLA), that is directly relevant to the TRN structure (Herrgard *et al.*, 2004).

For TRNs the number of TFs cannot be simply used to predict the complexity of the network, owing to the fact that TFs can have multiple target genes and can often act in synergistic combinations (Herrgard *et al*., 2004). However, the fraction of TF encoding genes tends to be higher in organisms that encounter a wider range of environmental conditions during their lifespans (Cases *et al*., 2003). This indicates that a number of TFs can only achieve a certain level of complexity. Well-studied organisms can be used to assess this complexity of TRNs in terms of the number of components, TFs and target genes, and regulatory interactions. For instance, in *S. cerevisiae*, a well studied model organism, the documented TFs (185) and their target genes (6297) are involved in 42609 interactions (YEASTRACT, taken on April 27th, 2009) (Teixeira *et al.*, 2006; Monteiro *et al.*, 2008). There are two other yeast TRNs available in literature. The study of Lee *et al.*, 2002 (updated at December 5, 2003) contains 4323 regulatory interactions between 106 TFs and 2343 target genes (p-value < 0.001) (Lee *et al*., 2002). The data on the yeast regulatory network constructed by Luscombe *et al.* consists of 7074 interactions between 142 TFs and 3420 target genes (Luscombe *et al.*, 2004).

1.2.1. Scale Free Networks

It is supposed that biological networks have a scale-free (SF) network structure instead of random network structure. Biological interaction networks are defined as sets of N nodes (N_i, i =1, . . ., N) linked together with interactions represented by l. The number of

links of a node is defined as the degree (k_i) of a node and <k> is the average degree of the network. In random networks each pair of nodes are connected with a probability that follows a Poisson distribution ($P(k) \sim e^{-k}$) peaking strongly at <k> and decaying exponentially for higher k values than <k>. SF networks are extremely heterogeneous where a few highly connected nodes are dominant by which rest of the less connected nodes are linked to network. Comparison between random networks and SF networks is illustrated in Figure 1.7. The degree distribution of a SF network follows power law, i.e. $f(k)=Ak^{-\gamma}$, with $2<\gamma<3$, where $f(k)$ is the frequency of the nodes with a degree of k and A is a constant. γ_c, the power law exponent of cumulative degree distribution, $n(k)$, and γ are related by:

$$\gamma = 1-\gamma_c \tag{1.1}$$

SF networks also exhibit power law correlations in clustering and betweenness vs. degree plots (Jeong *et al.,* 2000; Rodriguez-Caso *et al.*, 2005).

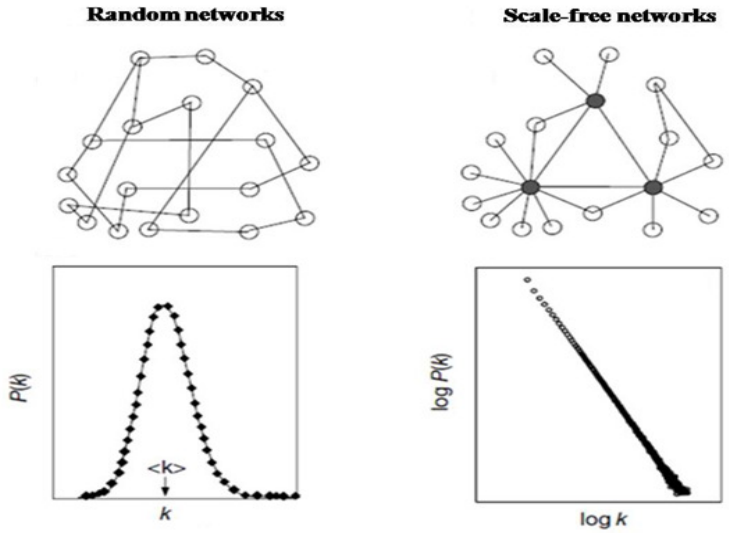

Figure 1.7. Representative structures of random and scale-free networks (Jeong *et al.,* 2000)

A SF network includes a small number of highly connected nodes (hubs) and a large number of poorly connected nodes (non-hubs) (He and Zhang, 2006). Hub nodes are generally distinguished by their degree but there is no consensus on how many interactions

a hub node should have. In the study of Hsing *et al.*, the hub selection criterion was based on the position of a sharp turn on an accumulative degree distribution plot, whereas Hwang *et al.* accepted the nodes having half of the maximum degree of the network as hubs (Hsing *et al.*, 2008; Hwang *et al.*, 2008). Betweenness measures the centrality of the nodes in networks and most of the shortest paths in a network go through the nodes with high betweenness. Hence, these nodes become the central nodes controlling the communication among other nodes in the network. In addition, Goh *et al.* have found that the betweenness of a node is correlated to its degree (Goh *et al.*, 2003; Yu *et al.*, 2007).

1.3. Key Transcription Factors and Reporter Features

The study of Luscombe *et al.* on the dynamics of the TRNs revealed that over half of the active interactions between TFs and their target genes are completely replaced by new ones when conditions are changed (Luscombe *et al.*, 2004). This result highlights the importance of the dynamics of a network, considering that significant changes occur in a network between two different conditions.

In previous studies, TRNs were studied by analyzing transcriptome data, assuming that there may be an all-to-all interaction among the studied genes, which leads to the identification of several false positives (Pe'er *et al.*, 2001; Segal *et al.*, 2003). However, the topology of TRN itself affects the regulatory response of the network following a perturbation. Integrating known biological interactions in the analysis of transcriptome data reduces the degrees of freedom in data analysis.

Many TFs do not respond at transcriptional level per se, but through post-translational regulation. Key TFs are TFs around which most significant transcriptional changes occur in response to environmental and genetic perturbations, where there is substantial regulation either to maintain homeostasis (i.e., a constant level of the expression of target genes) or adjust the expression levels of the target genes to another level required for proper functioning of the TRN (Patil and Nielsen, 2005). Identification of key TFs demonstrates a considerable collective change in the expression of the genes regulated by them when passing from one condition to another, the regulatory mechanisms

invoked in the cell and potential biomarkers, following a perturbation, without *a priori* requirement of change in the transcription level of the TFs.

Patil and Nielsen developed and implemented an algorithm for successful identification of reporter metabolites (metabolites around which the most significant transcriptional changes occur) in yeast by the integration of the genome-scale metabolic network with transcriptome data (Patil and Nielsen, 2005). Reporter metabolites algorithm has been generalized and extended to the reporter features algorithm in order to include reporter gene ontologies, reporter TFs, reporter proteins and reporter complexes (Oliveira *et al*., 2008). Reporter features algorithm has recently been used in many studies regarding yeast. Usaite *et al.* applied the algorithm to identify reporter TFs and regulatory proteins whose target genes were most significantly affected and responded as a group to genetic disruptions of the Snf1p complex (Usaite *et al*., 2009). Mo *et al.* have analyzed the intracellular flux distributions using reporter features algorithm to identify the dominant metabolic features that were collectively perturbed (Mo *et al.*, 2009). In a study of Cimini *et al.*, key proteins involved in the cellular response to *SDH3* deletion were identified (Cimini *et al*., 2009). The change in the activity of TFs can be positive or negative, however reporter features algorithm does not specify the direction of the change but only the significancy of the change.

1.4. The Aim of this Thesis

The aim of this thesis is to acquire a more detailed and comprehensive understanding of the transcriptional regulatory mechanism controlling the glucose signaling in yeast *S. cerevisiae* through the reconstruction of a genome-scale TRN in *S. cerevisiae* and analyzing its topology, and by integrating it with transcriptome data available in literature for the mutants of the glucose signaling pathway of *S. cerevisiae,* to identify the key TFs with the use of reporter features algorithm by Oliveira *et al*. (Oliveira *et al*., 2008).

2. METHODS

2.1. Construction of the Transcriptional Regulatory Network

A genome-scale TRN in baker's yeast *S. cerevisiae* was constructed by assembling regulatory interactions from different data sources (Lee *et al.*, 2002; Luscombe *et al.*, 2004; YEASTRACT (Teixeira *et al.*, 2006; Monteiro *et al.*, 2008)).

The documented regulations between all TFs and genes described in YEASTRACT, a freely accessible database available at http://www.yeastract.com/ and updated at April 27, 2009, include 42609 interactions between 185 TFs and 6297 target genes (Teixeira *et al.*, 2006; Monteiro *et al.*, 2008).

The publicly available datasets on the regulatory network of *S. cerevisiae* were downloaded from the supporting websites of the original publications of Lee *et al.*, 2002 updated at December 5, 2003 and Luscombe *et al.*, 2004 (Lee *et al.*, 2002; Luscombe *et al.*, 2004).

The regulatory interaction dataset of Lee *et al.* scores the interactions in terms of significance with *p*-value cut-offs of 0.001 or 0.005. The stricter option of 0.001 was selected and 4323 regulatory interactions were achieved with a *p*-value less than 0.001 between 106 TFs and 2343 target genes (Lee *et al.*, 2002). The data on the yeast regulatory network treated by Luscombe *et al.* consist of 7074 interactions between 142 TFs and 3420 target genes (Luscombe *et al.*, 2004).

If an interaction was present in any of the above three datasets, it was included to the TRN being constructed. The regulatory interactions, which were represented as two columns, are between TFs and non-TF target genes or between two TFs.

2.2. Topological Study of the Transcriptional Regulatory Network

The network was visualized using the program Cytoscape v2.6.3, a general purpose open source bioinformatics software capable of visualizing biomolecular interaction networks (Shannon *et al.*, 2003).

The degree distribution, betweenness centrality and clustering coefficient, which provide global information about the network, were obtained by using Networkx Module programming in Python v2.6.2, after self-interactions were excluded.

The clustering coefficient (C_i) of a node N_i is the number of neighboring of l_i links between nodes divided by the total number allowed by its degree, k_i (k_i –1),which shows the interconnection of the neighbors. The clustering coefficient of the whole network is,

$$<C>=\frac{1}{N}\sum_{i=1}^{N}\frac{2l_i}{k_i(k_i-1)} \tag{2.1}$$

The number of short paths connecting each pair of nodes that contain the node N_i is indicated as betweenness centrality (b_i) for a node N_i. It is defined as,

$$b_i=\sum_{m\neq n}\frac{\Gamma(m,\ i,\ n)}{\Gamma(m,\ n)} \tag{2.2}$$

where $\Gamma(m,\ i,\ n)$ is the number of the shortest paths between nodes N_m and N_n, passing through N_i, whereas $\Gamma(m,\ n)$ is the total number of paths between those two nodes. The ratio $\Gamma\ (m,\ i,\ n)\ /\ \Gamma\ (m,\ n)$ shows the significance of the node N_i in connecting N_m and N_n (Rodriguez-Caso *et al.*, 2005).

In order to analyze if the constructed TRN exhibits SF distribution, 1000 random networks were generated by assigning the same number of interactions among the same number of nodes as in the TRN. Degree and betweenness measures were taken as the basis for hub identification. Every node in the network was ranked according to its degree and betweenness, and the nodes at the intersection of the top 20 highest degree and top 20

highest betweenness nodes were selected as the hub nodes. The significant shared Gene Ontology (GO) biological process terms (p-value<0.01) associated with the selected hubs were found from the *Saccharomyces* Genome Database (SGD). Biological process refers to a biological objective that the gene or its product contributes (The Gene Ontology Consortium, 2000).

2.3. Identification of Key Transcription Factors

Differential gene expression data, in which two strains or two conditions were compared with multiple measurements for each strain, were used in the present study. For genetic perturbations the *ΔSNF1*, *ΔSNF4*, *ΔSNF1ΔSNF4*, *ΔMIG1*, *ΔMIG2*, *ΔMIG3*, *ΔMIG1ΔMIG2* and *ΔMIG1ΔMIG2ΔMIG3* mutants were compared with wild type strain and for environmental perturbation transcriptional data obtained under anaerobic and aerobic conditions for carbon limitation regime were used in the framework of this thesis (Tai *et al.*, 2005; Westholm *et al*., 2008; Usaite *et al.*, 2009).

The following steps were performed in order to identify key TFs responsive to each specific perturbation, after eliminating the nodes of the yeast TRN which were not quantified in the corresponding transcriptome data.

- p-value for each gene i in the TRN was calculated by using Student's t-test and converted into Z-score (Z_{ni}) using the inverse normal cumulative distribution function (θ^{-1}).

$$Z_{ni} = \theta^{-1}(1-p_i) \tag{2.3}$$

- Each TF was scored as the average of the Z-scores of its k neighboring genes.

$$Z_{TF} = \Sigma\, Z_{ni} / k \tag{2.4}$$

- Z_{TF} scores were corrected for the background distribution of Z-scores, by subtracting the mean, μ_k, and dividing by the standard deviation, σ_k, of 1000 sets of k

genes randomly selected from the graph. The MATLAB code performing $Z_{corrected,TF}$ calculations is given in Appendix B.

$$Z_{corrected,TF} = (Z_{TF} - \mu_k) / \sigma_k \quad (2.5)$$

• $Z_{corrected,TF}$ scores were converted back into *p*-values using the normal cumulative distribution function. TFs were ranked according their $Z_{corrected,TF}$ scores and TFs with a *p*-value less than 0.05 were defined as key TFs.

The GO biological process terms and definitions associated with each key TF and the significant shared GO biological process terms (*p*-value<0.01) associated with the key TFs responsive to each specific perturbation were found from the SGD (The Gene Ontology Consortium, 2000).

2.4. Identification of Perturbation-Responsive Subnetworks

Perturbation-responsive subnetworks (PRSs), composed of key TFs and their differentially expressed target genes (*p*-value<0.05) responsive to the same perturbation, were identified. The GO biological process terms significantly associated with the target genes for each PRS (*p*-value<0.01) were found from the SGD (The Gene Ontology Consortium, 2000).

2.5. Identification of Regulation of Key Transcription Factors

Regulation of key TFs was evaluated based on whether the TFs have their differential expression changed significantly (*p*-value<0.05). There are two possible cases (Oliveira *et al*., 2008):

(i) If the key TF is differently expressed, it is mainly transcriptionally governed.
(ii) If the key TF is not differentially expressed, it is mainly post-transcriptionally regulated.

3. RESULTS AND DISCUSSION

3.1. Topological Study of the Transcriptional Regulatory Network

The genome-scale transcriptional regulatory network in *S. cerevisiae* which contains 198 TFs and 6158 non-TF target genes was constructed and 44007 interactions between TFs and non-TF target genes or between two TFs were identified (Table A.4). An overview of the network produced in Cytoscape is displayed in Figure 3.1, where the network of interest was represented by 6356 nodes and 44007 edges.

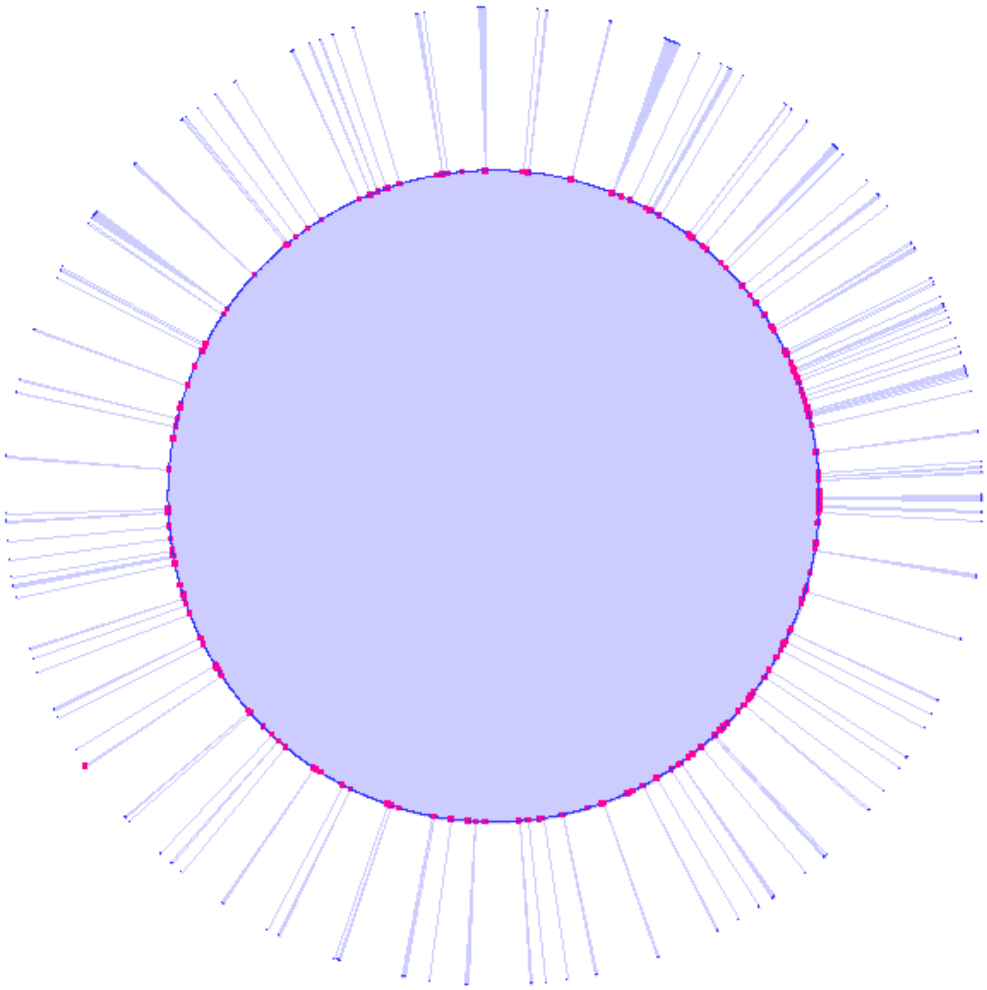

Figure 3.1. Representation of the reconstructed transcriptional regulatory network (pink and blue nodes represent TFs and non-TF target genes, respectively)

When self-interactions were excluded, the number of interactions between 6356 nodes reduced to 43922. Complete list of topological properties, i.e. degree (k), clustering coefficient (C) and betweenness (b), of individual nodes is given in Table A.1. The degree of the nodes of the TRN ranges from 1 to 2188, whereas for 1000 random networks the maximum degree was calculated to be 35. The average degree $<k>$, average clustering coefficient $<C>$ and average betweenness $<b>$ for the complete network were calculated to be 13.82, 0.24 and 10613, respectively. The average clustering coefficient for random networks was calculated to be 0.002 (Table 3.1). The remarkably higher average clustering coefficient than that of random networks implies that the network of interest is scale-free.

Table 3.1. Topological parameters of the yeast transcriptional regulatory network

Topological parameters	**Yeast transcriptional regulatory network**	**Random network**
N	6356	6356
l	43922	43922
$<k>$	13.82	13.82
$<C>$	0.24	0.002

The cumulative frequency, $n(k)$, and clustering coefficient, $C(k)$, distributions with respect to degree, k, followed power law, indicating that many nodes are linked to few nodes, but only a few of them are linked to many nodes (Figure 3.2 and Figure 3.3). The degree exponent of the network, γ, was found to be 2.012, which provides additional evidence that the constructed yeast TRN is scale-free and biologically significant. The cumulative frequency of nodes, $n(k)$, and clustering coefficients, $C(k)$, were presented in Table A.2 and Table A.3.

The average betweenness distribution was also well-characterized with power law scaling (Table A.3 and Figure 3.4), indicating that many nodes are located at the periphery and a few nodes at the centre, hence responsible for the communication within network.

3.1.1. Hub Nodes

In order to check that identified key TFs in the present study were size independent, hubs were first determined using both degree and betweenness measures as the basis for hub identification. 17 nodes which were at the intersection of the top 20 highest degree and

top 20 highest betweenness nodes were considered as hub nodes. (Table 3.2, Table 3.3, Figure 3.5, Figure 3.6)

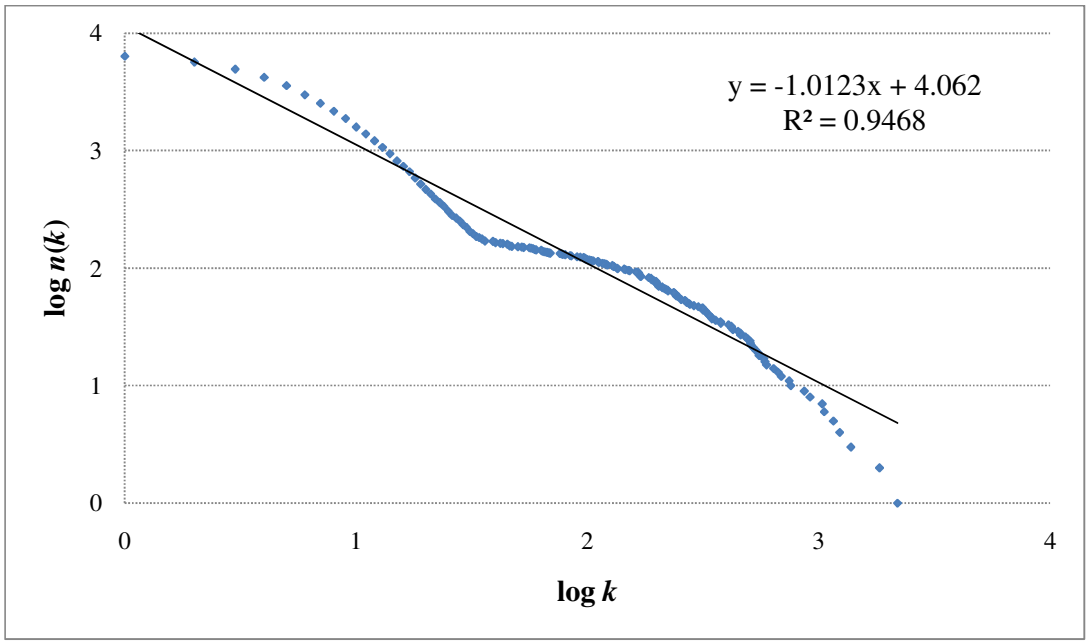

Figure 3.2. Cumulative degree distribution of the nodes of the yeast regulatory network

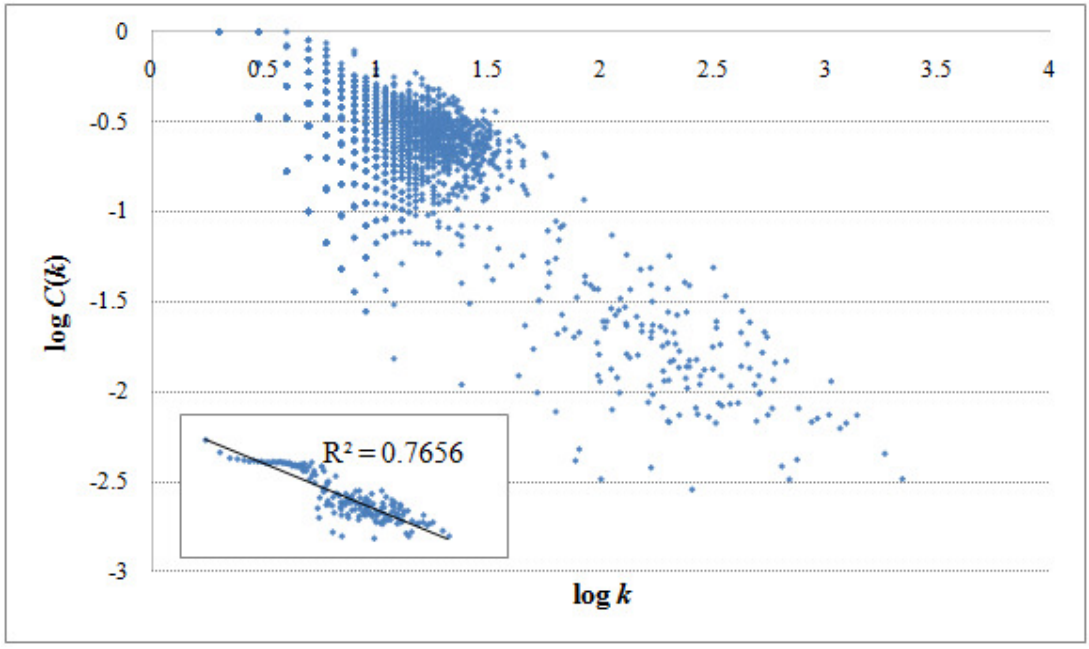

Figure 3.3. The distribution for clustering coefficient (power law fitting is presented in inset)

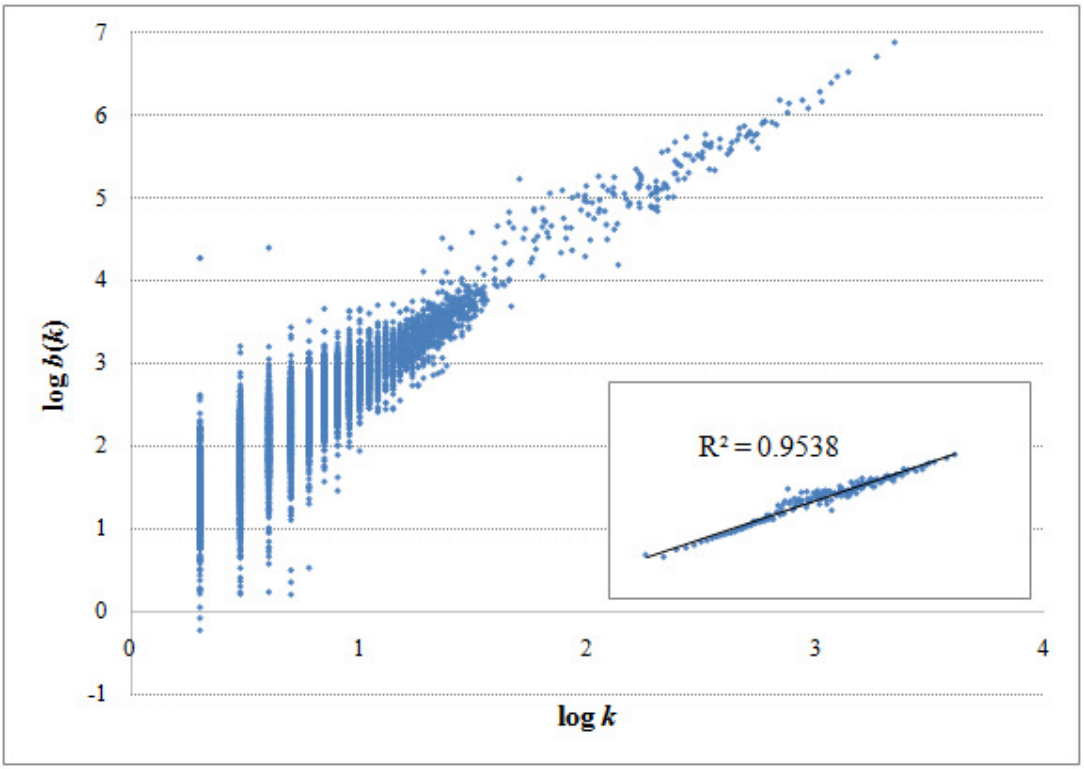

Figure 3.4. The distribution for betweenness (power law fitting is presented in inset)

All selected hubs were TFs. The degree (k) of these hub nodes ranges from 534 to 2188 with an average of 926 interactions, whereas the betweenness (b) ranges from 643610 to 7721326.

The highest degree and highest betweenness node of the constructed yeast TRN was found to be Sfp1p. Sfp1p is a TF and it has a role in the control of cell size and regulates ribosomal protein gene expression in response to nutrients and stress. The transcriptional control of ribosomal protein genes is crucial to alter the demand for protein biosynthetic capacity (Marion et al., 2004).

The significant shared GO biological process terms (p-value<0.01) associated with the selected hubs are listed in Table 3.4. Since all of the selected hubs were TFs, the GO terms with the lowest p-values were found to be "regulation of transcription" and "transcription", as expected. The hubs identified were found to be enriched significantly with very general GO biological process terms, such as "regulation of nitrogen compound metabolic process" and "regulation of macromolecule biosynthetic process". The

appearance of the terms “response to arsenic”, “response to inorganic substance”, “response to stimulus”, “response to chemical stimulus”, “response to heat” and “response to temperature stimulus” strengthens the idea that hubs are vital to control the communication among other nodes in the network in response to a disturbance in cellular homeostasis.

Table 3.2. Top 20 highest degree and top 20 highest betweenness nodes

k	**Top 20 highest degree nodes**		***b***	**Top 20 highest betweenness nodes**
2188	YLR403w		7721326	YLR403w
1829	YML007w		5162138	YML007w
1375	YHR084w		3379020	YHR084w
1230	YNL216w		2988666	YNL216w
1156	YNL103w		2489871	YNL103w
1055	YMR016c		1949936	YDL020c
1033	YDL020c		1544447	YKL112w
916	YMR037c		1540598	YPR104c
865	YPR104c		1491427	YMR016c
756	YGL071w		1414625	YGL071w
744	YPR199c		1230908	YMR037c
688	YKL112w		1094498	YPR199c
666	YGL013c		861633	YER111c
637	YOL108c		839314	YEL009c
594	YER111c		836047	YOL108c
585	YEL009c		804470	YGL073w
577	YGL073w		779413	YGL013c
552	YBL005w		752603	YML027w
547	YBR083w		705126	YOR028c
534	YKL043w		643610	YLR451w

Table 3.3. Hub nodes

ORF Name	**Gene Name**		**ORF Name**	**Gene Name**
YLR403w	SFP1		YGL071w	AFT1
YML007w	YAP1		YPR199c	ARR1
YHR084w	STE12		YKL112w	ABF1
YNL216w	RAP1		YGL013c	PDR1
YNL103w	MET4		YOL108c	INO4
YMR016c	SOK2		YER111c	SWI4
YDL020c	RPN4		YEL009c	GCN4
YMR037c	MSN2		YGL073w	HSF1
YPR104c	FHL1			

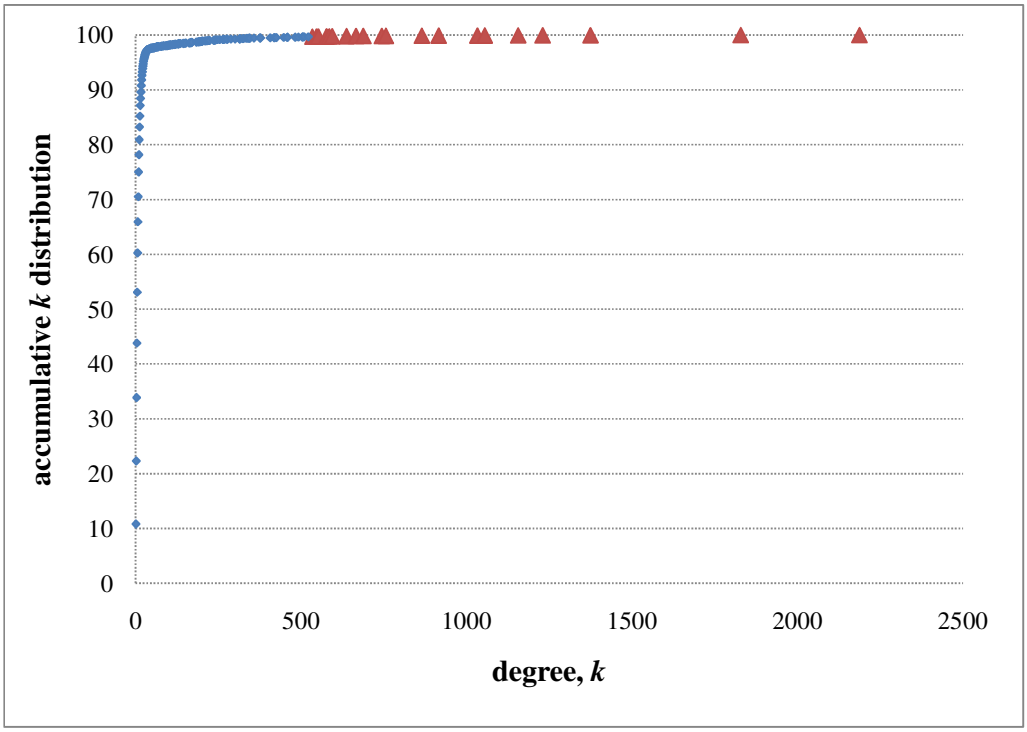

Figure 3.5. Accumulative percent distribution for degree (red triangles represent the hubs)

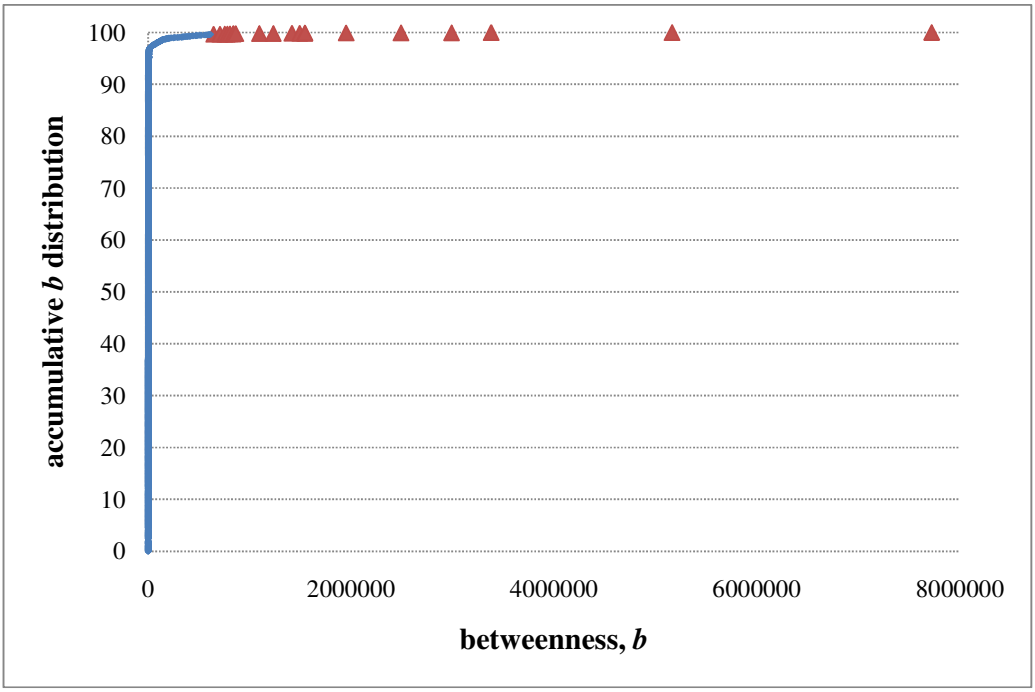

Figure 3.6. Accumulative percent distributions for betweenness (red triangles represent the hubs)

Table 3.4. Significant shared GO biological process terms of hubs

GO Term	*p*-value	Gene(s) annotated to the term
regulation of transcription	9.05E-15	RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
transcription	1.38E-14	RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	7.97E-14	RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
regulation of nitrogen compound metabolic process	8.45E-14	RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
regulation of gene expression	1.33E-13	RPN4,GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
regulation of macromolecule biosynthetic process	1.87E-13	RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
regulation of transcription, DNA-dependent	2.94E-13	GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
regulation of cellular biosynthetic process	3.05E-13	RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
regulation of biosynthetic process	3.30E-13	RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
regulation of RNA metabolic process	4.52E-13	GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
transcription, DNA-dependent	4.90E-13	GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
RNA biosynthetic process	5.16E-13	GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
positive regulation of transcription	6.38E-13	RPN4, GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1
positive regulation of gene expression	6.84E-13	RPN4, GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1
regulation of macromolecule metabolic process	8.57E-13	RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
positive regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	1.63E-12	RPN4, GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1
positive regulation of nitrogen compound metabolic process	1.63E-12	RPN4, GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1
regulation of primary metabolic process	1.95E-12	RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
positive regulation of macromolecule biosynthetic process	3.24E-12	RPN4, GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1
regulation of cellular metabolic process	3.48E-12	RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
positive regulation of cellular biosynthetic process	4.91E-12	RPN4, GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1
positive regulation of biosynthetic process	4.91E-12	RPN4, GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1
regulation of transcription from RNA polymerase II promoter	5.21E-12	GCN4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, INO4, FHL1, ARR1
regulation of metabolic process	6.76E-12	RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
biological regulation	8.43E-12	RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, SOK2, MSN2, MET4, RAP1, INO4, FHL1, ARR1
positive regulation of macromolecule metabolic process	1.33E-11	RPN4, GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1
positive regulation of cellular metabolic process	2.01E-11	RPN4, GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1
positive regulation of metabolic process	2.34E-11	RPN4, GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1
positive regulation of transcription, DNA-dependent	3.40E-11	GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1

Table 3.4. Significant shared GO biological process terms of hubs (continued)

GO Term	*p*-value	Gene(s) annotated to the term
positive regulation of RNA metabolic process	5.32E-11	GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1
positive regulation of cellular process	8.38E-11	RPN4, GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1
positive regulation of transcription from RNA polymerase II promoter	1.04E-10	GCN4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1
positive regulation of biological process	1.14E-10	RPN4, GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1
transcription from RNA polymerase II promoter	4.71E-10	GCN4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, INO4, FHL1, ARR1
regulation of cellular process	7.28E-10	RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
regulation of biological process	1.58E-09	RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
nucleic acid metabolic process	1.39E-08	RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
RNA metabolic process	1.90E-08	GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
cellular macromolecule biosynthetic process	3.58E-08	RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
macromolecule biosynthetic process	3.66E-08	RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	7.78E-08	RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
response to arsenic	3.22E-07	RPN4, YAP1, MET4, ARR1
gene expression	4.09E-07	RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
cellular nitrogen compound metabolic process	5.68E-07	RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
nitrogen compound metabolic process	7.13E-07	RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
cellular biosynthetic process	1.53E-06	RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
biosynthetic process	2.17E-06	RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, AP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
positive regulation of gene-specific transcription	0.0001	GCN4, SWI4, STE12, FHL1
cellular macromolecule metabolic process	0.00018	RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
response to inorganic substance	0.0002	RPN4, YAP1, MET4, ARR1
response to stimulus	0.00022	RPN4, PDR1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, ARR1
macromolecule metabolic process	0.00025	RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
response to chemical stimulus	0.00049	RPN4, PDR1, STE12, YAP1, MSN2, MET4, ARR1
regulation of gene-specific transcription	0.0006	GCN4, SWI4, STE12, FHL1
response to heat	0.00259	HSF1, YAP1, MSN2
negative regulation of transcription from RNA polymerase II promoter	0.00298	GCN4, PDR1, ABF1, FHL1
positive regulation of gene-specific transcription from RNA polymerase II promoter	0.00332	GCN4, STE12, FHL1
response to temperature stimulus	0.00373	HSF1, YAP1, MSN2
primary metabolic process	0.0054	RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1
negative regulation of transcription, DNA-dependent	0.00654	GCN4, PDR1, ABF1, RAP1, FHL1

Table 3.4. Significant shared GO biological process terms of hubs (continued)

GO Term	*p*-value	Gene(s) annotated to the term
negative regulation of RNA metabolic process	0.00671	GCN4, PDR1, ABF1, RAP1, FHL1
negative regulation of transcription	0.0078	GCN4, PDR1, ABF1, RAP1, FHL1
negative regulation of cellular process	0.00786	GCN4, PDR1, HSF1, ABF1, RAP1, FHL1
negative regulation of gene expression	0.00839	GCN4, PDR1, ABF1, RAP1, FHL1
negative regulation of biological process	0.00901	GCN4, PDR1, HSF1, ABF1, RAP1, FHL1

According to the reporter metabolites algorithm, Z_{TF} score of a TF should be calculated as the aggregated *Z*-scores of the neighboring genes of that TF divided by the square root of its degree (Patil and Nielsen, 2005). However, in reporter features algorithm, Z_{TF} score of a TF is defined as the average of the aggregated *Z*-scores of the neighboring genes of that TF, which, as proposed, assures that Z_{TF} score of each TF is size-independent (Oliveira *et al*., 2008). None of the selected hubs were found to be a key TF as it can be seen in Section 3.2. This result highlights that the $Z_{corrected,TF}$ score of each TF, which depends on the Z_{TF} score, was size-independent (independent of degree) and identified key TFs were not false-positive results because of their possible high degree.

3.2. Key Transcription Factors

3.2.1. Key TFs Responsive to Deletion of the Genes *SNF1* and *SNF4*

Budding yeast is able to utilize a wide variety of carbons other than glucose; alternative sugars such as galactose, sucrose, maltose, and melbiose as well as nonsugar carbons such as ethanol, lactate, glycerol, acetate, or oleate (Turcotte *et al*., 2009). When glucose becomes depleted (the AMP:ATP ratio is increased), Snf1p gets activated and enables the transcription of many genes responsible for oxidative growth through activation of the transcriptional activators Cat8p and Adr1p and inactivation of the Mig1p transcriptional repressor (Raghevendran *et al*., 2005). In addition, Snf1p complex regulates energy homeostasis by switching off ATP-consuming anabolic pathways, switching on ATP-producing catabolic pathways, such as fatty acid oxidation, and participating stress response and filamentous growth (Usaite *et al*., 2009). Snf1 protein kinase complex is a heterotrimer, composed of a catalytic α-subunit (Snf1p), a regulatory γ-subunit (Snf4p), and a scaffolding β-subunit (one of Sip1p, Sip2p or Gal83p).

In the presence of glucose, the Reg1p/Glc7p protein phosphatase 1 complex dephosphorylates and inactivates Snf1p and active Mig1p (unphosphorylated) represses the transcription of many genes, including genes encoding enzymes of the tricarboxylic acid (TCA) cycle, electron transport chain, alternative carbon sources consumption and gluconeogenesis (Sanz *et al.*, 2000).

Our aim in this part of the study was to test applicability and validity of the use of our larger TRN, consisting of only TFs and their target genes, and the reporter feature algorithm to predict the possible role of Snf1p kinase and compare the results with those which are reported by Usaite *at al*. using the integration of three level omics data (Usaite *et al*., 2009).

Key TFs responsive to the deletions of *SNF1*, *SNF4* and deletion of both *SNF1* and *SNF4* genes were identified using the triplicate transcriptome data of Usaite *et al.*. In the experiments of Usaite *et al*., Snf1p complex mutants (the deletion mutants of α and/or γ-subunits of the Snf1p complex, i.e., *ΔSNF1, ΔSNF4* and *ΔSNF1ΔSNF4*) and the wild type strain have been grown in carbon limited media, so that Snf1p complex is expected to be active in the wild type strain (Usaite *et al*., 2009).

When the nodes of the yeast TRN which were not quantified in these transcriptome data were eliminated, the number of the nodes, regulatory interactions and TFs reduced to 5457, 39522 and 192, respectively. By using reporter features algorithm, 33, 10 and 16 key TFs around which most transcriptional changes occur were identified as a response to deletions of *SNF1*, *SNF4* and deletion of both *SNF1* and *SNF4*, respectively (Table 3.5, Table 3.6 and Table 3.7). Key TFs were ranked from high to low $Z_{\text{corrected,TF}}$ score. $Z_{\text{corrected,TF}}$ scores, *p*-values and degrees for each key TF are represented in Table C.1, Table C.2 and Table C.3.

3.2.1.1. Response to the Deletion of *SNF1*. Thirty three key TFs around which most transcriptional changes occur were identified as a response to deletion of *SNF1* (Table 3.5).

Cat8p, Swi1p and Swi3p were identified to be key TFs as a response to the deletion of *SNF1* specifically. *CAT8* encodes a zinc-finger cluster protein that mediates

derepression of a number of genes during the diauxic shift. Snf1p is necessary for the activity of Cat8p, activating Cat8p directly by phosphorylation, as well as inactivating Mig1p, relieving the repression of *CAT8* expression, and allowing the Hap2p/3p/4p/5p complex to positively regulate the expression of *CAT8* (Hedges *et al.*, 1995; Turcotte *et al*., 2009). Swi1p and Swi3p are subunits of chromatin remodeling complex SWI/SNF and the transcriptional activator Cat8p requires the chromatin remodeling complex SWI/SNF for transcriptional activation (Biddick *et al*., 2008). Cat8p and Swi1p have also been identified as reporter effectors in *ΔSNF1* in the study of Usaite *et al*. (Usaite *et al*., 2009). In addition to Swi1p and Swi3p, the algorithm has also identified Hpc2p, Sin3p and Ada2p (Swi8), which are also involved in chromatin remodeling, as key TFs in this case.

The algorithm identified Opi1p as a key TF in *ΔSNF1* mutant. Sin3p is defined in SGD as component of the Sin3p-Rpd3p histone deacetylase complex, involved in transcriptional repression and activation of diverse processes, including mating-type switching and meiosis; involved in the maintenance of chromosomal integrity. Wagner *et al*. have demonstrated that Opi1p interacts with Sin3p affecting a large number of regulatory systems in yeast and higher eukaryotes (Wagner *et al*., 2001). The synthesis of phospholipids is a major activity throughout cell growth and Zhang *et al*. have suggested that Snf1p activates Opi1p, which represses phospholipid biosynthesis (Sreenivas and Carman, 2003; Zhang *et al*., 2010). Gis1p, which is reported to be involved in phospholipid metabolic process, was also identified as a key TF in *ΔSNF1*.

Oaf1p and Cst6p were also among the identified key TFs in *SNF1* deletion mutant. Cst6p is involved in the regulation of oleate responsive genes and Oaf1p is an oleate-activated TF, which activates genes involved in β-oxidation of fatty acids, peroxisome organization and biogenesis. This result is consistent with the fact that Snf1p regulates β-oxidation of fatty acids (Usaite *et al*., 2009). It has been reported that Snf1p is necessary for the activity of Adr1p in this regulation, although it is not known whether Snf1p activates Adr1p directly or indirectly. However, Adr1p was not identified as a key TF in any Snf1p complex mutants in the present study. Gene expression is under combinatorial control and many Adr1p dependent genes are activated by other transcription factors as well. For example, the promoters of genes encoding peroxisomal proteins and the enzymes

of β-oxidation bind both Adr1 and the heterodimeric, oleate-responsive transcription factors Oaf1p and Pip2p (Ratnakumar *et al.*, 2009).

Gsm1p, which is involved in the regulation of energy metabolism in yeast, was identified as a key TF in *ΔSNF1*. Gsm1p increases the expression of *HAP4*, which encodes the limiting and activating subunit of the Hap2p/3p/4p/5p complex, and the expression of *GSM1* is increased in nonfermentable carbons by the Hap2p/3p/4p/5p complex, providing a putative autoregulatory loop between *HAP4* and *GSM1* (Turcotte *et al*., 2009).

Although the expression products of *CAT8* and *GSM1* were identified as key TFs in *ΔSNF1*, which are positively controlled by Hap4p, Hap4p was not present among the identified key TFs.

In *ΔSNF1* mutant, the algorithm also identified Mig3p as a key TF as expected, since Mig3p is known to be regulated by Snf1p kinase, i.e., it is subject to Snf1p dependent phosphorylation and subsequent degradation in the absence of glucose. Westholm *et al.* have found that Mig3p downregulates *SIR2*, which counteracts aging in both yeast and animals, and suggested that this explains accelerated aging in yeast as a result of reduced Snf1p activity (Ashrafi *et al*., 2000; Westholm *et al.*, 2008).

However, Mig1p and Mig2p did not appear as key TFs in *ΔSNF1*. These results bring about the possibility that there are other proteins similar to Snf1p that might act on Mig1p and also Mig2p. In the absence of glucose, Mig1p, but not Mig2p, is inactivated by the Snf1p protein kinase. The nuclear localization of Mig1p is regulated by glucose, i. e., Snf1p action causes Mig1p to move to the cytoplasm, but Mig2p is located in the nucleus both in the presence and absence of glucose. The existence of a protein (possibly also a protein kinase) that regulates Mig2p activity in response to glucose has been previously suggested by Lutfiyya *et al.* (Lutfiyya *et al.*, 1998).

Imp2'p, which is involved in carbohydrate metabolic processes, was identified as a key TF in *ΔSNF1*. Imp2'p is required for the rapid glucose derepression of the maltose, galactose, raffinose and ethanol utilization pathways (Lodi *et al*., 1995). Snf1p complex activates genes encoding enzymes of alternative carbon sources consumption (Usaite *et al*.,

2009). Imp2'p has also been identified as a reporter effector in *ΔSNF1* in the study of Usaite *et al*. (Usaite *et al*., 2009).

Cst6p and Aca1p, which are also involved in utilization of nonoptimal carbon sources, were found to be key TFs in *ΔSNF1*. Garcia-Gimeno and Struhl suggest that Cst6p (Aca2p) and Snf1p possibly act in a common pathway of glucose repression and that Cst6p might be a substrate or transcriptional regulator of Snf1p. The fact that overexpression of Aca1p is found to suppress the inability of Δ*ACA2* mutant strains to grow on nonoptimal carbon sources may be the possible explanation for the considerable collective change in the expression of the genes regulated by Aca1p (Garcia-Gimeno and Struhl, 2000).

Pdc2p, which is involved in the regulation of glucose catabolic process to ethanol and in the regulation of thiamin biosynthetic process, was identified as a key TF indicating the role of Snf1p in the regulation of carbon metabolism. Gis1p, involved in the expression of genes during nutrient limitation, was also identified as a key TF in *ΔSNF1*. Pedruzzi *et al*. have proposed that Gis1p has a role in the RAS/cAMP pathway downstream of Rim15p controlling the transcription of a set of genes, such as *SSA3*, which are essential for long term survival following nutrient limitation (Pedruzzi *et al*., 2000).

Sfl1p, involved in repression of flocculation-related genes, and activation of stress responsive genes, was found to be a key TF in *ΔSNF1*. It is negatively regulated by cAMP-dependent protein kinase A subunit Tpk2p. This TF is required for normal cell surface assembly in vegetative growth and its null mutation shows pseudohyphal and invasive growth. Dig2p is involved in the invasive growth in response glucose limitation, and overexpression of *BYE1* and *SPS18* genes causes decreased vegetative growth. The identification of Sfl1p, Dig2p, Sps18p and Bye1p as key TFs indicate also a possible role of Snf1p in these processes. The key TFs Hmlalpha1p and Hmra1p are involved in mating-type specific regulation of transcription.

Sfl1p is negatively regulated by cAMP-dependent PKA subunit Tpk2p and Gis1p has a role in the RAS/cAMP pathway. Identification of Sfl1p and Gis1p as key TFs in response to *SNF1* deletion is logical, since PKA and Snf1p are reported to cooperate in the

regulation of many processes such as carboxylic acid metabolism, β-oxidation of fatty acids, stress response and filamentous growth (Zhang *et al*., 2010).

Rtg2p, which regulates the subcellular localization of Rtg1p and Rtg3p transcriptional activators of retrograde (RTG) and TOR pathways which is important in the regulation of cell growth in response to nutrients, and Elp6p, which is involved in protein urmylation, were identified as key TFs. Loss of urmylation pathway was reported to cause invasive growth and confers sensitivity to rapamycin due to genetic interactions with TOR pathway (Goehring et al., 2003). These observations indicate that Snf1p may possibly interacting/collaborating with TOR pathway to integrate the information related to nutritional state with energy and redox metabolism. These results agree with the study of Usaite *et al*. where an interactive role of Snf1p and Tor1p has also been suggested (Usaite *et al*., 2009).

Xbp1p, Pdr8p, Hot1p, Cup2p, Rlm1p, Sfl1p and Sut1p, which are involved in the regulation of stress response to different conditions, were identified as key TFs in *ΔSNF1*. These results are in good correlation with the previous observations that Snf1p complex regulates energy homeostasis also by participating stress response (Usaite *et al*., 2009).

To sum up, the algorithm identified key TFs that are involved in chromatin remodeling, phospholipid biosynthesis, β-oxidation of fatty acids, biogenesis, oxidative phosphorylation (energy metabolism), carbohydrate metabolic process, alternative carbon source consumption and stress response, as a response to *SNF1* deletion. These results are totally consistent with the predicted role of Snf1p kinase; such that loss of Snf1p kinase activity during carbon-limited growth affects significantly glucose repression related genes, fatty acid and lipid metabolism (mainly through posttranscriptional regulation), biogenesis, carnitine metabolism, stress response, nitrogen metabolism and energy metabolism (Usaite *et al*., 2009). Key TFs involved in processes, such as oleate response and protein urmylation, that have not previously been implicated as being regulated by Snf1p were also identified. Key TFs Gat4p, Rts2p and Yrm1p probably have roles in one or more of the processes mentioned above.

Table 3.5. Key TFs identified for *ΔSNF1* mutant

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
1	Hpc2p (YBR215w)	3	Subunit of the HIR complex, a nucleosome assembly complex involved in regulation of histone gene transcription; mutants display synthetic defects with subunits of FACT, a complex that allows passage of RNA Pol II through nucleosomes • DNA replication-independent nucleosome assembly • regulation of transcription involved in G1/S-phase of mitotic cell cycle • RNA elongation from RNA polymerase II promoter
2	Swi1p (YPL016w)	15	Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2; can form the prion [SWI+] • ATP-dependent chromatin remodeling • positive regulation of transcription, DNA-dependent • regulation of transcription from RNA polymerase II promoter
3	Swi3p (YJL176c)	9	Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2 • ATP-dependent chromatin remodeling • positive regulation of transcription, DNA-dependent
4	Elp6p (YMR312w)	7	Subunit of Elongator complex, which is required for modification of wobble nucleosides in tRNA; required for Elongator structural integrity • protein urmylation • regulation of transcription from RNA polymerase II promoter • tRNA wobble uridine modification
5	Pdc2p (YDR081c)	16	Transcription factor required for the synthesis of the glycolytic enzyme pyruvate decarboxylase, required for high level expression of both the THI and the PDC genes • glucose catabolic process to ethanol • positive regulation of gene-specific transcription from RNA polymerase II promoter • regulation of thiamin biosynthetic process
6	Pdr8p (YLR266c)	24	Transcription factor; targets include ATP-binding cassette (ABC) transporters, major facilitator superfamily transporters, and other genes involved in the pleiotropic drug resistance (PDR) phenomenon • positive regulation of transcription from RNA polymerase II promoter • response to stress
7	Rds3p (YPR094w)	8	Component of the SF3b subcomplex of the U2 snRNP, zinc cluster protein involved in pre-mRNA splicing and cycloheximide resistance • nuclear mRNA splicing, via spliceosome • response to xenobiotic stimulus • spliceosome assembly
8	Rtg2p (YGL252c)	9	Sensor of mitochondrial dysfunction; regulates the subcellular location of Rtg1p and Rtg3p, transcriptional activators of the retrograde (RTG) and TOR pathways; Rtg2p is inhibited by the phosphorylated form of Mks1p • extrachromosomal rDNA circle accumulation involved in replicative cell aging • intracellular signaling pathway • mitochondria-nucleus signaling pathway

Table 3.5. Key TFs identified for *ΔSNF1* mutant (continued)

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
9	Cup2p (YGL166w)	29	Copper-binding transcription factor; activates transcription of the metallothionein genes CUP1-1 and CUP1-2 in response to elevated copper concentrations • response to copper ion • transcription initiation from RNA polymerase II promoter
10	Gis1p (YDR096w)	187	JmjC domain-containing histone demethylase; transcription factor involved in expression of genes during nutrient limitation and in negative regulation of DPP1 and PHR1; activity is modulated by limited proteasome-mediated proteolysis • ascospore wall assembly • histone demethylation • phospholipid metabolic process
11	Mig3p (YER028c)	26	Probable transcriptional repressor involved in response to toxic agents such as hydroxyurea that inhibit ribonucleotide reductase; phosphorylation by Snf1p or the Mec1p pathway inactivates Mig3p, allowing induction of damage response genes • negative regulation of transcription from RNA polymerase II promoter • response to DNA damage stimulus • transcription initiation
12	Gat4p (YIR013c)	122	Protein containing GATA family zinc finger motifs • transcription
13	Hot1p (YMR172w)	73	Transcription factor required for the transient induction of glycerol biosynthetic genes GPD1 and GPP2 in response to high osmolarity; targets Hog1p to osmostress responsive promoters; has similarity to Msn1p and Gcr1p • hyperosmotic response • regulation of transcription from RNA polymerase II promoter
14	Yrm1p (YOR172w)	24	Zn2-Cys6 zinc-finger transcription factor that activates genes involved in multidrug resistance; paralog of Yrr1p, acting on an overlapping set of target genes • drug transmembrane transport • positive regulation of transcription from RNA polymerase II promoter
15	Xbp1p (YIL101c)	168	Transcriptional repressor that binds to promoter sequences of the cyclin genes, CYS3, and SMF2; expression is induced by stress or starvation during mitosis, and late in meiosis; member of the Swi4p/Mbp1p family; potential Cdc28p substrate • response to stress
16	Dig2p (YDR480w)	5	Regulatory protein of unknown function, pheromone-inducible, involved in the regulation of mating-specific genes and the invasive growth pathway, required for MAP-kinase imposed repression, inhibits pheromone-responsive transcription • invasive growth in response to glucose limitation
17	Cat8p (YMR280c)	126	Zinc cluster transcriptional activator necessary for derepression of a variety of genes under non-fermentative growth conditions, active after diauxic shift, binds carbon source responsive elements • positive regulation of gluconeogenesis • positive regulation of transcription from RNA polymerase II promoter
18	Bye1p (YKL005c)	24	Negative regulator of transcription elongation, contains a TFIIS-like domain and a PHD finger, multicopy suppressor of temperature-sensitive ess1 mutations, probably binds RNA polymerase II large subunit • negative regulation of transcription from RNA polymerase II promoter

Table 3.5. Key TFs identified for *ΔSNF1* mutant (continued)

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
19	Opi1p (YHL020c)	29	Transcriptional regulator of a variety of genes; phosphorylation by protein kinase A stimulates Opi1p function in negative regulation of phospholipid biosynthetic genes; involved in telomere maintenance • endoplasmic reticulum unfolded protein response • negative regulation of transcription from RNA polymerase II promoter • phospholipid biosynthetic process • positive regulation of transcription from RNA polymerase II promoter
20	Imp2'p (YIL154c)	7	Transcriptional activator involved in maintenance of ion homeostasis and protection against DNA damage caused by bleomycin and other oxidants, contains a C-terminal leucine-rich repeat • cellular carbohydrate metabolic process • DNA repair
21	Rts2p (YOR077w)	29	Basic zinc-finger protein, similar to human and mouse Kin17 proteins which are chromatin-associated proteins involved in UV response and DNA replication • biological process unknown
22	Ada2p (YDR448w)	8	Transcription coactivator, component of the ADA and SAGA transcriptional adaptor/HAT (histone acetyltransferase) complexes • chromatin modification • chromatin silencing at rDNA • chromatin silencing at telomere • positive regulation of histone acetylation • regulation of transcription from RNA polymerase II promoter
23	Sin3p (YOL004w)	31	Component of the Sin3p-Rpd3p histone deacetylase complex, involved in transcriptional repression and activation of diverse processes, including mating-type switching and meiosis; involved in the maintenance of chromosomal integrity • chromatin silencing at rDNA • chromatin silencing at silent mating-type cassette • chromatin silencing at telomere • double-strand break repair via nonhomologous end joining • histone deacetylation • negative regulation of transcription from RNA polymerase II promoter • negative regulation of transposition, RNA-mediated • positive regulation of gene-specific transcription from RNA polymerase II promoter • positive regulation of transcription from RNA polymerase II promoter
24	Gsm1p (YJL103c)	23	Putative zinc cluster protein of unknown function; proposed to be involved in the regulation of energy metabolism, based on patterns of expression and sequence analysis • oxidative phosphorylation
25	Sps18p (YNL204c)	63	Protein of unknown function, contains a putative zinc-binding domain; expressed during sporulation • sporulation resulting in formation of a cellular spore
26	Oaf1p (YAL051w)	248	Oleate-activated transcription factor, acts alone and as a heterodimer with Pip2p; activates genes involved in beta-oxidation of fatty acids and peroxisome organization and biogenesis • fatty acid metabolic process • negative regulation of transcription • peroxisome organization • positive regulation of transcription

Table 3.5. Key TFs identified for *ΔSNF1* mutant (continued)

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
27	Sfl1p (YOR140w)	55	Transcriptional repressor and activator; involved in repression of flocculation-related genes, and activation of stress responsive genes; negatively regulated by cAMP-dependent protein kinase A subunit Tpk2p • negative regulation of transcription from RNA polymerase II promoter
28	Aca1p (YER045c)	29	Basic leucine zipper (bZIP) transcription factor of the ATF/CREB family, may regulate transcription of genes involved in utilization of non-optimal carbon sources • transcription initiation from RNA polymerase II promoter
29	Cst6p (YIL036w)	187	Basic leucine zipper (bZIP) transcription factor of the ATF/CREB family, proposed to be a regulator of oleate responsive genes; involved in utilization of non-optimal carbon sources and chromosome stability • cellular response to oleic acid • DNA metabolic process • transcription initiation from RNA polymerase II promoter
30	Sut1p (YGL162w)	84	Transcription factor of the Zn[II]2Cys6 family involved in sterol uptake; involved in induction of hypoxic gene expression • regulation of transcription • regulation of transcription from RNA polymerase II promoter • sterol transport
31	Rlm1p (YPL089c)	180	MADS-box transcription factor, component of the protein kinase C-mediated MAP kinase pathway involved in the maintenance of cell integrity; phosphorylated and activated by the MAP-kinase Slt2p • fungal-type cell wall organization • positive regulation of transcription from RNA polymerase II promoter • response to acid • signal transduction
32	Hmlalpha1p (YCL066w)	18	Silenced copy of ALPHA1 at HML, encoding a transcriptional coactivator involved in the regulation of mating-type alpha-specific gene expression • regulation of transcription from RNA polymerase II promoter • regulation of transcription, mating-type specific
33	Hmra1p (YCR097w)	18	Silenced copy of a1 at HMR; homeobox corepressor that interacts with Alpha2p to repress haploid-specific gene transcription in diploid cells • regulation of transcription, mating-type specific

These key TFs identified as a response to deletion of *SNF1* were found to be enriched significantly with very general GO biological process terms, such as "regulation of nitrogen compound metabolic process" (p-value=1.76×10^{-14}) and "regulation of macromolecule biosynthetic process" (p-value=5.19×10^{-14}) (Table D.1). GO term with the lowest p-value was found to be "transcription" (p-value=1.69×10^{-18}), as expected.

3.2.1.2. Response to the Deletion of *SNF4*. Ten key TFs around which most transcriptional changes occur were identified as a response to deletion of *SNF4* (Table 3.6).

In *ΔSNF4* mutant, Gal80p, involved in galactose metabolic process, was identified as a key TF. *GAL* genes are repressed directly by Mig1p (Nehlin *et al*., 1991). Under low glucose condition, Mig1p is expected to be inactivated by Snf1p complex thus *GAL* genes are expected not to be repressed in wild type cells. Interestingly, Mig1p did not appear to be a key TF in *ΔSNF4* as in *ΔSNF1*. However, Mig2p did appear as a key TF in *ΔSNF4* mutant. Instead of Mig1p, Mig2p may repress *GAL80* in *ΔSNF4* mutant. In fact, Mig2p was shown to fine-tune glucose repression by targeting a subset of the Mig1p repressed genes (Westholm *et al*., 2008). Mig2p has also been identified as a reporter effector in *ΔSNF4* in the study of Usaite *et al*. (Usaite *et al*., 2009).

Haa1p, involved in adaptation to weak acid stress and in the transcription of *TPO2*, *YRO2*, and other genes putatively encoding membrane stress proteins, and Ndt80p, meiosis-specific transcription factor required for exit from pachytene and for full meiotic recombination, were among the key TFs identified as a response to deletion of *SNF4*.

Six key TFs (highlighted in Table 3.6) identified as a response to *SNF1* deletion were also determined as key TFs in the deletion of *SNF4*.

Table 3.6. Key TFs identified for *ΔSNF4* mutant

Rank	**TF (ORF Name)**	**degree (*k*)**	**SGD Definition & GO Biological Process Terms**
1	Imp2'p (YIL154c)	7	Transcriptional activator involved in maintenance of ion homeostasis and protection against DNA damage caused by bleomycin and other oxidants, contains a C-terminal leucine-rich repeat • cellular carbohydrate metabolic process • DNA repair
2	Rds3p (YPR094w)	8	Component of the SF3b subcomplex of the U2 snRNP, zinc cluster protein involved in pre-mRNA splicing and cycloheximide resistance • nuclear mRNA splicing, via spliceosome • response to xenobiotic stimulus • spliceosome assembly
3	Pdr8p (YLR266c)	24	Transcription factor; targets include ATP-binding cassette (ABC) transporters, major facilitator superfamily transporters, and other genes involved in the pleiotropic drug resistance (PDR) phenomenon • positive regulation of transcription from RNA polymerase II promoter • response to stress

Table 3.6. Key TFs identified for *ΔSNF4* mutant (continued)

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
4	Yrm1p (YOR172w)	24	Zn2-Cys6 zinc-finger transcription factor that activates genes involved in multidrug resistance; paralog of Yrr1p, acting on an overlapping set of target genes • drug transmembrane transport • positive regulation of transcription from RNA polymerase II promoter
5	Dig2p (YDR480w)	5	Regulatory protein of unknown function, pheromone-inducible, involved in the regulation of mating-specific genes and the invasive growth pathway, required for MAP-kinase imposed repression, inhibits pheromone-responsive transcription • invasive growth in response to glucose limitation
6	Hmlalpha1p (YCL066w)	18	Silenced copy of ALPHA1 at HML, encoding a transcriptional coactivator involved in the regulation of mating-type alpha-specific gene expression • regulation of transcription from RNA polymerase II promoter • regulation of transcription, mating-type specific
7	Mig2p (YGL209w)	61	Protein containing zinc fingers, involved in repression, along with Mig1p, of SUC2 (invertase) expression by high levels of glucose; binds to Mig1p-binding sites in SUC2 promoter • negative regulation of transcription from RNA polymerase II promoter by glucose
8	Gal80p (YML051w)	6	Transcriptional regulator involved in the repression of GAL genes in the absence of galactose; inhibits transcriptional activation by Gal4p; inhibition relieved by Gal3p or Gal1p binding • galactose metabolic process • negative regulation of kinase activity • positive regulation of transcription by galactose
9	Haa1p (YPR008w)	18	Transcriptional activator involved in the transcription of TPO2, YRO2, and other genes putatively encoding membrane stress proteins; involved in adaptation to weak acid stress • regulation of transcription, DNA-dependent • response to acid • transcription initiation from RNA polymerase II promoter
10	Ndt80p (YHR124w)	38	Meiosis-specific transcription factor required for exit from pachytene and for full meiotic recombination; activates middle sporulation genes; competes with Sum1p for binding to promoters containing middle sporulation elements (MSE) • meiosis • transcription

These key TFs identified as a response to deletion of *SNF4* were found to be enriched significantly with very general GO biological process terms, such as "nucleic acid metabolic process" (*p*-value=0.00036) and "regulation of nitrogen compound metabolic process" (*p*-value=0.00164), as well as with more specific GO biological process terms, such as "response to stimulus" (*p*-value=0.00105) and "response to chemical stimulus" (*p*-value=0.00255) (Table D.2). GO term with the lowest *p*-value was found to be "transcription" (*p*-value=0.00024), as expected.

3.2.1.3. Response to the Deletion of both *SNF1* and *SNF4*. Sixteen key TFs around which most transcriptional changes occur were identified as a response to deletion of both *SNF1* and *SNF4* (Table 3.7).

Cdc39p, Haa1p and War1p were among the key TFs identified for *ΔSNF1ΔSNF4*. Both Haa1p and War1p are involved in response to acid and Cdc39p is implemented in pseudohyphal growth.

Twelve key TFs (highlighted in Table 3.7) identified as a response to *SNF1* deletion were also determined as key TFs in the deletion of both *SNF1* and *SNF4*.

Table 3.7. Key TFs identified for *ΔSNF1ΔSNF4* mutant

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
1	Cdc39p (YCR093w)	9	Component of the CCR4-NOT complex, which has multiple roles in regulating mRNA levels including regulation of transcription and destabilizing mRNAs by deadenylation; basal transcription factor • negative regulation of transcription from RNA polymerase II promoter • nuclear-transcribed mRNA catabolic process, deadenylation-dependent decay • nuclear-transcribed mRNA poly(A) tail shortening • pseudohyphal growth • regulation of cell cycle • regulation of transcription from RNA polymerase II promoter • response to pheromone involved in conjugation with cellular fusion • RNA elongation from RNA polymerase II promoter
2	Rds3p (YPR094w)	8	Component of the SF3b subcomplex of the U2 snRNP, zinc cluster protein involved in pre-mRNA splicing and cycloheximide resistance • nuclear mRNA splicing, via spliceosome • response to xenobiotic stimulus • spliceosome assembly
3	Rtg2p (YGL252c)	9	Sensor of mitochondrial dysfunction; regulates the subcellular location of Rtg1p and Rtg3p, transcriptional activators of the retrograde (RTG) and TOR pathways; Rtg2p is inhibited by the phosphorylated form of Mks1p • extrachromosomal rDNA circle accumulation involved in replicative cell aging • intracellular signaling pathway • mitochondria-nucleus signaling pathway
4	Lys14p (YDR034c)	12	Transcriptional activator involved in regulation of genes of the lysine biosynthesis pathway; requires 2-aminoadipate semialdehyde as co-inducer • lysine biosynthetic process via aminoadipic acid

Table 3.7. Key TFs identified for *ΔSNF1ΔSNF4* mutant (continued)

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
5	Hpc2p (YBR215w)	3	Subunit of the HIR complex, a nucleosome assembly complex involved in regulation of histone gene transcription; mutants display synthetic defects with subunits of FACT, a complex that allows passage of RNA Pol II through nucleosomes • DNA replication-independent nucleosome assembly • regulation of transcription involved in G1/S-phase of mitotic cell cycle • RNA elongation from RNA polymerase II promoter
6	Haa1p (YPR008w)	18	Transcriptional activator involved in the transcription of TPO2, YRO2, and other genes putatively encoding membrane stress proteins; involved in adaptation to weak acid stress • regulation of transcription, DNA-dependent • response to acid • transcription initiation from RNA polymerase II promoter
7	Sps18p (YNL204c)	63	Protein of unknown function, contains a putative zinc-binding domain; expressed during sporulation • sporulation resulting in formation of a cellular spore
8	Gis1p (YDR096w)	187	JmjC domain-containing histone demethylase; transcription factor involved in expression of genes during nutrient limitation and in negative regulation of DPP1 and PHR1; activity is modulated by limited proteasome-mediated proteolysis • ascospore wall assembly • histone demethylation • phospholipid metabolic process
9	Cup2p (YGL166w)	29	Copper-binding transcription factor; activates transcription of the metallothionein genes CUP1-1 and CUP1-2 in response to elevated copper concentrations • response to copper ion • transcription initiation from RNA polymerase II promoter
10	Gat4p (YIR013c)	122	Protein containing GATA family zinc finger motifs • transcription
11	Hot1p (YMR172w)	73	Transcription factor required for the transient induction of glycerol biosynthetic genes GPD1 and GPP2 in response to high osmolarity; targets Hog1p to osmostress responsive promoters; has similarity to Msn1p and Gcr1p • hyperosmotic response • regulation of transcription from RNA polymerase II promoter
12	Ada2p (YDR448w)	8	Transcription coactivator, component of the ADA and SAGA transcriptional adaptor/HAT (histone acetyltransferase) complexes chromatin modification • chromatin silencing at rDNA • chromatin silencing at telomere • positive regulation of histone acetylation • regulation of transcription from RNA polymerase II promoter
13	Elp6p (YMR312w)	7	Subunit of Elongator complex, which is required for modification of wobble nucleosides in tRNA; required for Elongator structural integrity • protein urmylation • regulation of transcription from RNA polymerase II promoter • tRNA wobble uridine modification

Table 3.7. Key TFs identified for *ΔSNF1ΔSNF4* mutant (continued)

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
14	Cst6p (YIL036w)	187	Basic leucine zipper (bZIP) transcription factor of the ATF/CREB family, proposed to be a regulator of oleate responsive genes; involved in utilization of non-optimal carbon sources and chromosome stability • cellular response to oleic acid • DNA metabolic process • transcription initiation from RNA polymerase II promoter
15	Xbp1p (YIL101c)	168	Transcriptional repressor that binds to promoter sequences of the cyclin genes, CYS3, and SMF2; expression is induced by stress or starvation during mitosis, and late in meiosis; member of the Swi4p/Mbp1p family; potential Cdc28p substrate • response to stress
16	War1p (YML076c)	32	Homodimeric Zn2Cys6 zinc finger transcription factor; binds to a weak acid response element to induce transcription of PDR12 and FUN34, encoding an acid transporter and a putative ammonia transporter, respectively • response to acid

These key TFs identified as a response to deletion of both *SNF1* and *SNF4* were found to be enriched significantly with very general GO biological process terms, such as "nucleic acid metabolic process" (*p*-value=0.00398) and "cellular nitrogen compound metabolic process" (*p*-value=0.00538), as well as with a more specific GO biological process term, "response to chemical stimulus" (*p*-value=0.004) (Table D.3). GO term with the lowest *p*-value was found to be "transcription from RNA polymerase II promoter" (*p*-value=4.13×10^{-6}), as expected.

3.2.1.4. Comparison of the Responses to Deletions of *SNF1*, *SNF4* and both *SNF1* and *SNF4*. Comparison of the key TFs identified as a response to each deletion is shown in Figure 3.7. The number of key TFs can tell us how much transcriptional response occurs in a cell that was subjected to a specific genetic perturbation. The deletion of *SNF1* possibly is the cause of the largest perturbation at transcriptional response.

Regulator of Drug Sensitivity, Rds3p, is the only key TF that was identified for all three Snf1p complex mutants and was found to be regulated mainly post-transcriptionally (Table 3.14). It is defined in SGD as component of the SF3b subcomplex of the U2 snRNP, zinc cluster protein involved in pre-mRNA splicing and cycloheximide resistance. Two other TFs, Pdr8p and Yrm1p, were also identified for both *ΔSNF1* and *ΔSNF4* mutants, which regulate genes involved in the pleiotropic drug resistance (PDR)

phenomenon and genes involved in multidrug resistance, respectively. Nevertheless, the relationship of Snf1p with drug resistance needs further investigation.

Six key TFs identified for both *ΔSNF1* and *ΔSNF4* mutants are known to be involved in invasive growth in response glucose limitation (Dig2p), carbohydrate metabolic processes (Imp2'p), mating-type specific regulation of transcription (Hmlalpha1p) and stress response (Pdr8p). However, no significant shared GO biological process terms could be associated with them.

No significant shared GO biological process terms could be associated with the two key TFs (Haa1p, involved in response to acid, and Rds3p) identified for both *ΔSNF4* and *ΔSNF1ΔSNF4* mutants either.

As it can be seen in Table D.6, 12 key TFs identified for both *ΔSNF1* and *ΔSNF1ΔSNF4* mutants were found to be enriched significantly with very general GO biological process terms, such as "transcription from RNA polymerase II promoter" (p-value=7.81×10^{-5}), as expected. These key TFs are involved in several biological processes, i.e., utilization of nonoptimal carbon sources (Cst6p), chromatin remodeling (Ada2p, Hpc2p), stress response (Cup2p, Xbp1p and Hot1p), phospholipid biosynthesis (Gis1p); and Rtg2p and Elp6p collaborate with TOR pathway.

Significant shared GO biological process terms (p-value<0.01) of the key TFs identified only for each specific perturbation were also investigated.

Sixteen key TFs identified only for *ΔSNF1* mutant were found to be enriched significantly with very general GO biological process terms, such as "regulation of nitrogen compound metabolic process" (p-value= p-value=6.20×10^{-11}) and "regulation of macromolecule biosynthetic process" (p-value=1.22×10^{-10}) (Table D.4). GO term with the lowest p-value was found to be "regulation of transcription" (p-value=9.10×10^{-12}), as expected. These key TFs are involved in several biological processes, i.e., utilization of nonoptimal carbon sources (Cat8p, Aca1p), chromatin remodeling (Swi1p, Swi3p and Sin3p), stress response (Sut1p, Sfl1p and Rlm1p), phospholipid biosynthesis (Opi1p), β-

oxidation of fatty acids (Oaf1p), energy metabolism (Gsm1p) and regulation of glucose catabolic process to ethanol (Pdc2p).

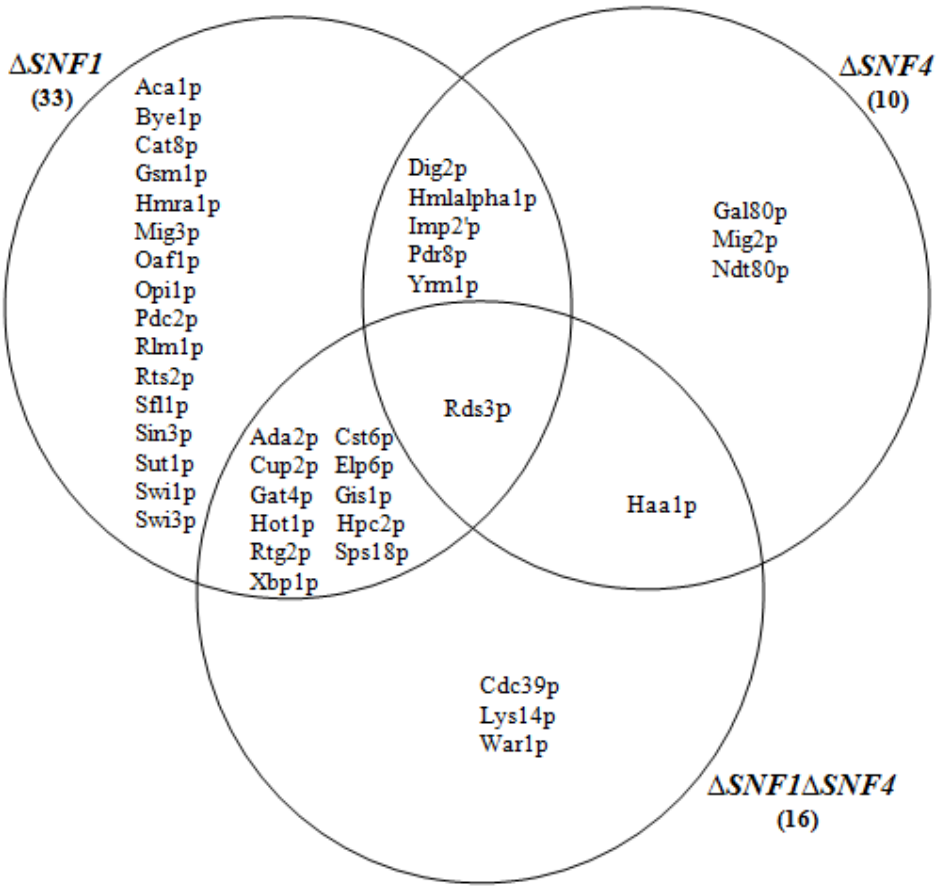

Figure 3.7. Comparison of the key TFs identified for *ΔSNF1*, *ΔSNF4* and *ΔSNF1ΔSNF4* mutants (the number of key TFs for each specific mutant is given in brackets)

The three key TFs identified only for *ΔSNF4* mutant (Gal80p, Mig2p, Ndt80p) were found to be enriched significantly with more specific GO biological process terms, such as "regulation of transcription by carbon catabolites" (*p*-value=0.00052), "cellular response to nutrient" (*p*-value=0.00087) and "response to nutrient" (*p*-value=0.00109) (Table D.5). Reporter metabolites algorithm by Patil and Nielsen has also been performed in the study of Usaite *et al.* to discover metabolic hot spots that significantly respond to the loss of Snf1p kinase activity, and they have found that deleting *SNF4* gene affects mainly only carbon metabolism (Patil and Nielsen, 2005; Usaite *et al.*, 2009). Our results is consistent with their findings, since two of these three key TFs in *ΔSNF4*, Gal80p and Mig2p, are

involved in carbon metabolism. In particular, TFs regulating chromatin remodeling, phospholipid biosynthesis, β-oxidation of fatty acids and energy metabolism were not identified for *ΔSNF4* mutant, but for *ΔSNF1* and/or *ΔSNF1ΔSNF4*.

Three TFs (Cdc39p, Lys14p and War1p) were identified only as a response specifically to the deletion of both *SNF1* and *SNF4* genes. However no significant GO biological process terms could be associated with this set. War1p is involved in response to acid and Cdc39p is implemented in pseudohyphal growth.

3.2.1.5. Perturbation-Responsive Subnetworks of *ΔSNF1*, *ΔSNF4* and *ΔSNF1ΔSNF4* Mutants. Perturbation responsive subnetworks (PRS) were constructed between the key TFs and their differentially expressed target genes (p-value<0.05) responsive to the same perturbation. The numbers of key TFs, their target genes and interactions in the perturbation-responsive subnetworks in *ΔSNF1*, *ΔSNF4* and *ΔSNF1ΔSNF4* mutants are given in Table 3.8. The overviews of these subnetworks produced in Cytoscape are displayed in Figure 3.8, Figure 3.9 and Figure 3.10, where the up- (green) or down-regulation (red) of the key TFs and their differentially expressed target genes in the corresponding mutants with respect to wild type strain are indicated. Key TFs indicated in black in these figures were found to be not significantly expressed in this study. Therefore they are considered to be post-transcriptionally regulated (Table 3.14). GO biological process terms significantly associated with the target genes in each PRS (p-value<0.01) were identified and represented in Table 3.9, Table 3.10 and Table 3.11.

Table 3.8. The numbers of TFs, their target genes and interactions for the PRSs of *ΔSNF1*, *ΔSNF4* and *ΔSNF1ΔSNF4* mutants

Mutant	Number of Key TFs	Number of Target Genes	Number of Interactions
ΔSNF1	33	542	961
ΔSNF4	10	86	97
ΔSNF1ΔSNF4	16	370	587

Table 3.9. Significantly associated GO biological process terms of the target genes of the PRS of *ΔSNF1* mutant

GO Term	Cluster frequency	*p*-value
small molecule catabolic process	42 out of 542 genes, 7.7 per cent	4.54E-12
monocarboxylic acid metabolic process	39 out of 542 genes, 7.2 per cent	1.07E-10
small molecule metabolic process	117 out of 542 genes, 21.6 per cent	5.46E-09
organic acid metabolic process	62 out of 542 genes, 11.4 per cent	4.81E-08
carboxylic acid metabolic process	61 out of 542 genes, 11.3 per cent	1.23E-07
oxoacid metabolic process	61 out of 542 genes, 11.3 per cent	1.23E-07
carbohydrate metabolic process	55 out of 542 genes, 10.1 per cent	4.40E-07
alcohol catabolic process	20 out of 542 genes, 3.7 per cent	4.58E-07
cellular ketone metabolic process	61 out of 542 genes, 11.3 per cent	7.39E-07
monosaccharide catabolic process	19 out of 542 genes, 3.5 per cent	1.08E-06
response to chemical stimulus	55 out of 542 genes, 10.1 per cent	2.48E-06
carbohydrate catabolic process	26 out of 542 genes, 4.8 per cent	2.89E-06
organic acid catabolic process	19 out of 542 genes, 3.5 per cent	3.43E-06
carboxylic acid catabolic process	19 out of 542 genes, 3.5 per cent	3.43E-06
cellular carbohydrate catabolic process	25 out of 542 genes, 4.6 per cent	6.81E-06
hexose catabolic process	17 out of 542 genes, 3.1 per cent	9.16E-06
alcohol metabolic process	42 out of 542 genes, 7.7 per cent	1.84E-05
cellular carbohydrate metabolic process	50 out of 542 genes, 9.2 per cent	2.15E-05
pyridine nucleotide metabolic process	17 out of 542 genes, 3.1 per cent	2.84E-05
hexose metabolic process	27 out of 542 genes, 5.0 per cent	3.63E-05
monosaccharide metabolic process	29 out of 542 genes, 5.4 per cent	4.16E-05
cellular response to chemical stimulus	40 out of 542 genes, 7.4 per cent	5.06E-05
catabolic process	81 out of 542 genes, 14.9 per cent	0.00044
glutamate metabolic process	9 out of 542 genes, 1.7 per cent	0.00096
coenzyme metabolic process	27 out of 542 genes, 5.0 per cent	0.00148
oxidoreduction coenzyme metabolic process	17 out of 542 genes, 3.1 per cent	0.00182
nicotinamide nucleotide metabolic process	14 out of 542 genes, 2.6 per cent	0.00285
glucose metabolic process	22 out of 542 genes, 4.1 per cent	0.00289
monohydric alcohol metabolic process	7 out of 542 genes, 1.3 per cent	0.00311
ethanol metabolic process	7 out of 542 genes, 1.3 per cent	0.00311

Table 3.10. Significantly associated GO biological process terms of the target genes of the PRS of *ΔSNF4* mutant

GO Term	Cluster frequency	*p*-value
positive regulation of spindle pole body separation	4 out of 86 genes, 4.7 per cent	0.00019
galactose catabolic process via UDP-galactose	3 out of 86 genes, 3.5 per cent	0.00048
regulation of spindle pole body separation	4 out of 86 genes, 4.7 per cent	0.00067
response to chemical stimulus	15 out of 86 genes, 17.4 per cent	0.00126
monosaccharide transport	5 out of 86 genes, 5.8 per cent	0.00227
hexose transport	5 out of 86 genes, 5.8 per cent	0.00227
spindle pole body separation	4 out of 86 genes, 4.7 per cent	0.00257
positive regulation of cell cycle process	4 out of 86 genes, 4.7 per cent	0.00257
cellular carbohydrate catabolic process	8 out of 86 genes, 9.3 per cent	0.00338
carbohydrate catabolic process	8 out of 86 genes, 9.3 per cent	0.0043
galactose catabolic process	3 out of 86 genes, 3.5 per cent	0.0094

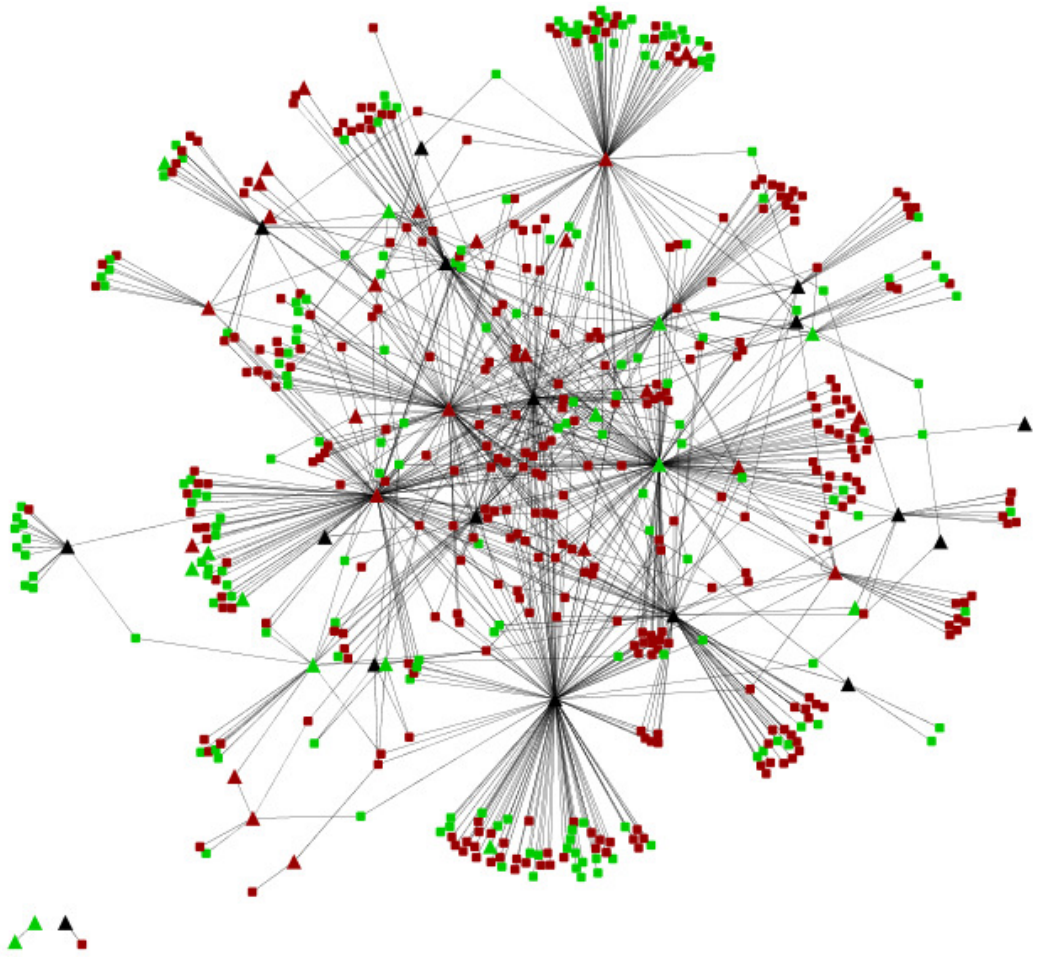

Figure 3.8. Representation of the PRS of *ΔSNF1* mutant (triangles and squares represent TFs and non-TF target genes, respectively)

Table 3.11. Significantly associated GO biological process terms of the target genes of the PRS of *ΔSNF1ΔSNF4* mutant

GO Term	Cluster frequency	*p*-value
carboxylic acid metabolic process	55 out of 370 genes, 14.9 per cent	9.9E-12
oxoacid metabolic process	55 out of 370 genes, 14.9 per cent	9.9E-12
organic acid metabolic process	55 out of 370 genes, 14.9 per cent	1.12E-11
small molecule metabolic process	94 out of 370 genes, 25.4 per cent	2.83E-11
cellular ketone metabolic process	55 out of 370 genes, 14.9 per cent	6.34E-11
small molecule catabolic process	28 out of 370 genes, 7.6 per cent	0.000000451
glutamate metabolic process	10 out of 370 genes, 2.7 per cent	0.00000104
alcohol metabolic process	35 out of 370 genes, 9.5 per cent	0.00000144
monocarboxylic acid metabolic process	26 out of 370 genes, 7.0 per cent	0.00000321
cellular amino acid and derivative metabolic process	37 out of 370 genes, 10.0 per cent	0.00000453
glutamine family amino acid metabolic process	14 out of 370 genes, 3.8 per cent	0.0000129
cellular amine metabolic process	34 out of 370 genes, 9.2 per cent	0.0000148
carbohydrate metabolic process	40 out of 370 genes, 10.8 per cent	0.0000169

Table 3.11. Significantly associated GO biological process terms of the target genes of the PRS of *ΔSNF1ΔSNF4* mutant (continued)

GO Term	Cluster frequency	*p*-value
cellular carbohydrate metabolic process	39 out of 370 genes, 10.5 per cent	0.0000184
amine metabolic process	36 out of 370 genes, 9.7 per cent	0.0000312
cellular amino acid metabolic process	31 out of 370 genes, 8.4 per cent	0.0000538
organic acid biosynthetic process	25 out of 370 genes, 6.8 per cent	0.0000544
carboxylic acid biosynthetic process	25 out of 370 genes, 6.8 per cent	0.0000544
monosaccharide metabolic process	23 out of 370 genes, 6.2 per cent	0.0000626
carbohydrate catabolic process	19 out of 370 genes, 5.1 per cent	0.00014
trehalose metabolic process	7 out of 370 genes, 1.9 per cent	0.00016
response to oxidative stress	18 out of 370 genes, 4.9 per cent	0.0002
small molecule biosynthetic process	40 out of 370 genes, 10.8 per cent	0.00025
cellular carbohydrate catabolic process	18 out of 370 genes, 4.9 per cent	0.00041
glutamine family amino acid biosynthetic process	10 out of 370 genes, 2.7 per cent	0.00042
cellular amino acid biosynthetic process	20 out of 370 genes, 5.4 per cent	0.00055
monosaccharide catabolic process	13 out of 370 genes, 3.5 per cent	0.00058
alcohol catabolic process	13 out of 370 genes, 3.5 per cent	0.00119
pentose catabolic process	5 out of 370 genes, 1.4 per cent	0.00127
amine biosynthetic process	20 out of 370 genes, 5.4 per cent	0.00169
hexose metabolic process	19 out of 370 genes, 5.1 per cent	0.0023
pyridine nucleotide metabolic process	12 out of 370 genes, 3.2 per cent	0.00239
carbohydrate transport	11 out of 370 genes, 3.0 per cent	0.00289
monohydric alcohol metabolic process	6 out of 370 genes, 1.6 per cent	0.00418
ethanol metabolic process	6 out of 370 genes, 1.6 per cent	0.00418
glycoside biosynthetic process	5 out of 370 genes, 1.4 per cent	0.00427
disaccharide biosynthetic process	5 out of 370 genes, 1.4 per cent	0.00427
trehalose biosynthetic process	5 out of 370 genes, 1.4 per cent	0.00427
arabinose metabolic process	4 out of 370 genes, 1.1 per cent	0.00434
arabinose catabolic process	4 out of 370 genes, 1.1 per cent	0.00434
D-xylose metabolic process	4 out of 370 genes, 1.1 per cent	0.00434
D-xylose catabolic process	4 out of 370 genes, 1.1 per cent	0.00434
glucose metabolic process	17 out of 370 genes, 4.6 per cent	0.00634
organic acid catabolic process	12 out of 370 genes, 3.2 per cent	0.00724
carboxylic acid catabolic process	12 out of 370 genes, 3.2 per cent	0.00724
nicotinamide nucleotide metabolic process	11 out of 370 genes, 3.0 per cent	0.00769
response to stress	54 out of 370 genes, 14.6 per cent	0.00816

By examining the biological process terms of PRSs identified for *ΔSNF1*, *ΔSNF4* and *ΔSNF1ΔSNF4* mutants it can be evaluated how much Snf1p and Snf4p contribute to the functions of the Snf1p kinase complex and whether they have additional functions.

Catabolic processes such as “alcohol catabolic process”, “carbohydrate catabolic process”, “monosaccharide catabolic process”, “organic acid catabolic process”, “small molecule catabolic process” are among the significantly associated GO terms of the PRSs

of *ΔSNF1* and *ΔSNF1ΔSNF4* mutants (Figure 3.11). This result is expected since active Snf1p complex switches on ATP-producing catabolic pathways (Usaite *et al*., 2009).

SNF4 deletion has very little effect compared to *SNF1* deletion (Figure 3.12). "Galactose catabolic process", "hexose transport", "monosaccharide transport" and "regulation of spindle pole body separation" are among the significantly associated GO terms found only for the PRS of *ΔSNF4* mutant.

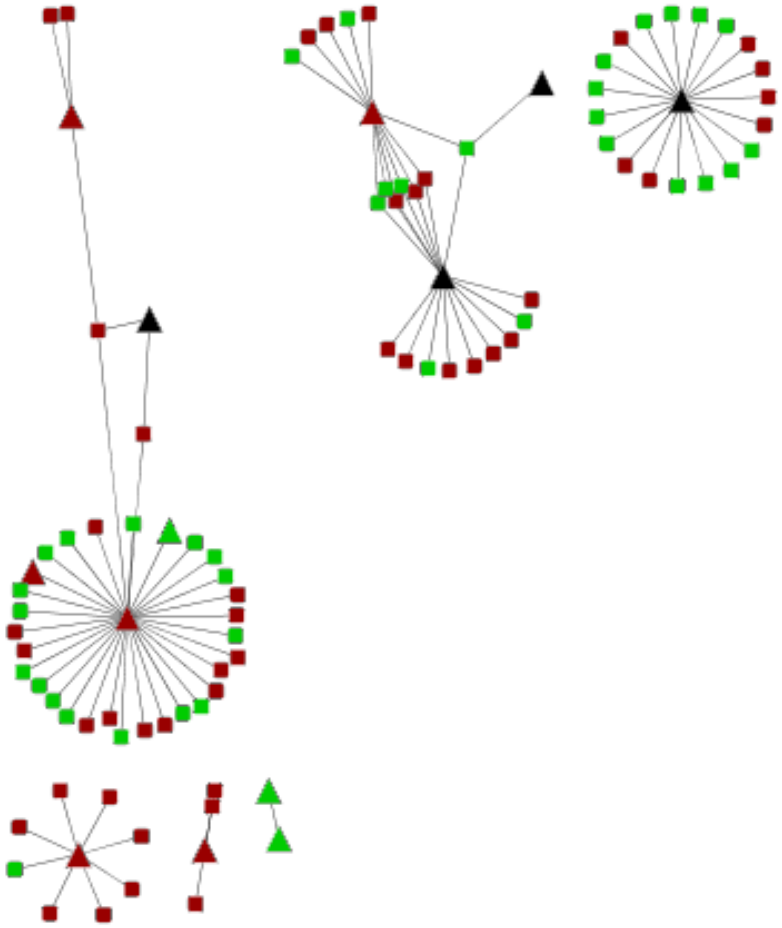

Figure 3.9. Representation of the PRS of *ΔSNF4* mutant (triangles and squares represent TFs and non-TF target genes, respectively)

Moreover, deletion of both *SNF1* and *SNF4* genes causes a significant change in the expression of the genes which are significantly associated with the processes "amine biosynthetic process", "amine metabolic process", "arabinose metabolic process", "D-xylose

metabolic process", "pentose catabolic process", "trehalose metabolic process", "carboxylic acid biosynthetic process", "cellular amino acid metabolic process", "glutamine family amino acid metabolic process" and "response to stress" (Table 3.12). These terms do not appear among the terms found for *ΔSNF1* and ΔSNF4 mutants. Change in the regulation of nitrogen metabolism in *ΔSNF1ΔSNF4* as a synergistic effect was also reported by Usaite *et al.* (Usaite *et al*., 2009).

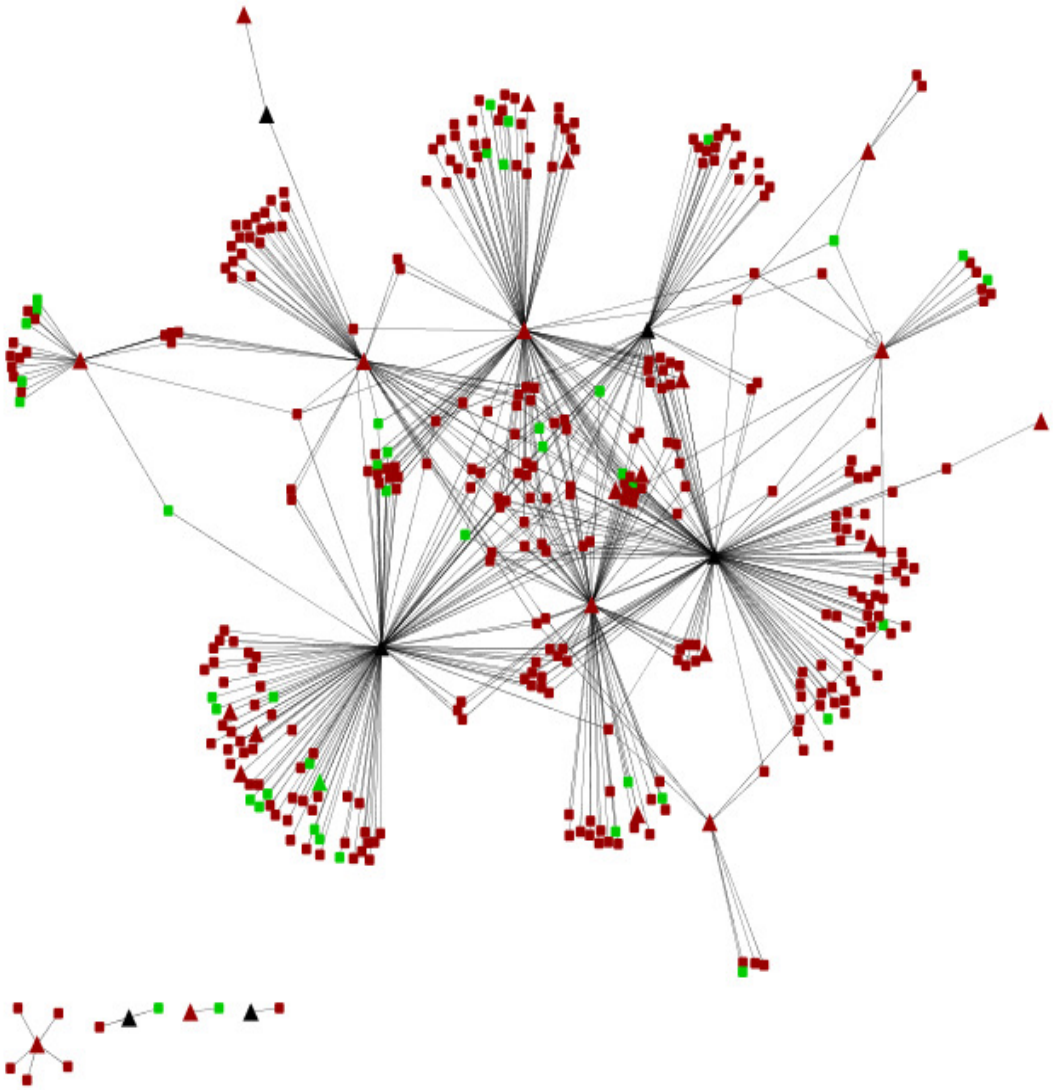

Figure 3.10. Representation of the PRS of *ΔSNF1ΔSNF4* mutant (triangles and squares represent TFs and non-TF target genes, respectively)

Table 3.12. Number of genes annotated to significantly associated GO biological process terms of the PRS of *ΔSNF1*, *ΔSNF4* and *ΔSNF1ΔSNF4* mutants

GO Term	*ΔSNF1*	*ΔSNF4*	*ΔSNF1ΔSNF4*
alcohol catabolic process	20	0	13
alcohol metabolic process	42	0	35
amine biosynthetic process	0	0	20
amine metabolic process	0	0	36
arabinose catabolic process	0	0	4
arabinose metabolic process	0	0	4
carbohydrate catabolic process	26	8	19
carbohydrate metabolic process	55	0	40
carbohydrate transport	0	0	11
carboxylic acid biosynthetic process	0	0	25
carboxylic acid catabolic process	19	0	12
carboxylic acid metabolic process	61	0	55
catabolic process	81	0	0
cellular amine metabolic process	0	0	34
cellular amino acid and derivative metabolic process	0	0	37
cellular amino acid biosynthetic process	0	0	20
cellular amino acid metabolic process	0	0	31
cellular carbohydrate catabolic process	25	8	18
cellular carbohydrate metabolic process	50	0	39
cellular ketone metabolic process	61	0	55
cellular response to chemical stimulus	40	0	0
coenzyme metabolic process	27	0	0
disaccharide biosynthetic process	0	0	5
D-xylose catabolic process	0	0	4
D-xylose metabolic process	0	0	4
ethanol metabolic process	7	0	6
galactose catabolic process	0	3	0
galactose catabolic process via UDP-galactose	0	3	0
glucose metabolic process	22	0	17
glutamate metabolic process	9	0	10
glutamine family amino acid biosynthetic process	0	0	10
glutamine family amino acid metabolic process	0	0	14
glycoside biosynthetic process	0	0	5
hexose catabolic process	17	0	0
hexose metabolic process	27	0	19
hexose transport	0	5	0
monocarboxylic acid metabolic process	39	0	26
monohydric alcohol metabolic process	7	0	6
monosaccharide catabolic process	19	0	13
monosaccharide metabolic process	29	0	23

Table 3.12. Number of genes annotated to significantly associated GO biological process terms of the PRS of *ΔSNF1*, *ΔSNF4* and *ΔSNF1ΔSNF4* mutants (continued)

GO Term	*ΔSNF1*	*ΔSNF4*	*ΔSNF1ΔSNF4*
monosaccharide transport	0	5	0
nicotinamide nucleotide metabolic process	14	0	11
organic acid biosynthetic process	0	0	25
organic acid catabolic process	19	0	12
organic acid metabolic process	62	0	55
oxidoreduction coenzyme metabolic process	17	0	0
oxoacid metabolic process	61	0	55
pentose catabolic process	0	0	5
positive regulation of cell cycle process	0	4	0
positive regulation of spindle pole body separation	0	4	0
pyridine nucleotide metabolic process	17	0	12
regulation of spindle pole body separation	0	4	0
response to chemical stimulus	55	15	0
response to oxidative stress	0	0	18
response to stress	0	0	54
small molecule biosynthetic process	0	0	40
small molecule catabolic process	42	0	28
small molecule metabolic process	117	0	94
spindle pole body separation	0	4	0
trehalose biosynthetic process	0	0	5
trehalose metabolic process	0	0	7

Interestingly, fatty acid and lipid metabolism did not appear among the terms significantly associated with the genes of any PRS. This might arise from the *p*-value threshold (0.05) used to identify significantly differentially expressed genes of the PRSs.

As a result, it can be proposed that, Snf1p and Snf4p as a complex are responsible for stress response and the metabolic processes of mono- and disaccharides. Snf4p, by its own, seems to affect sugar transport, and the catabolic processes that Snf1p kinase complex activates are likely because of the contribution of Snf1p.

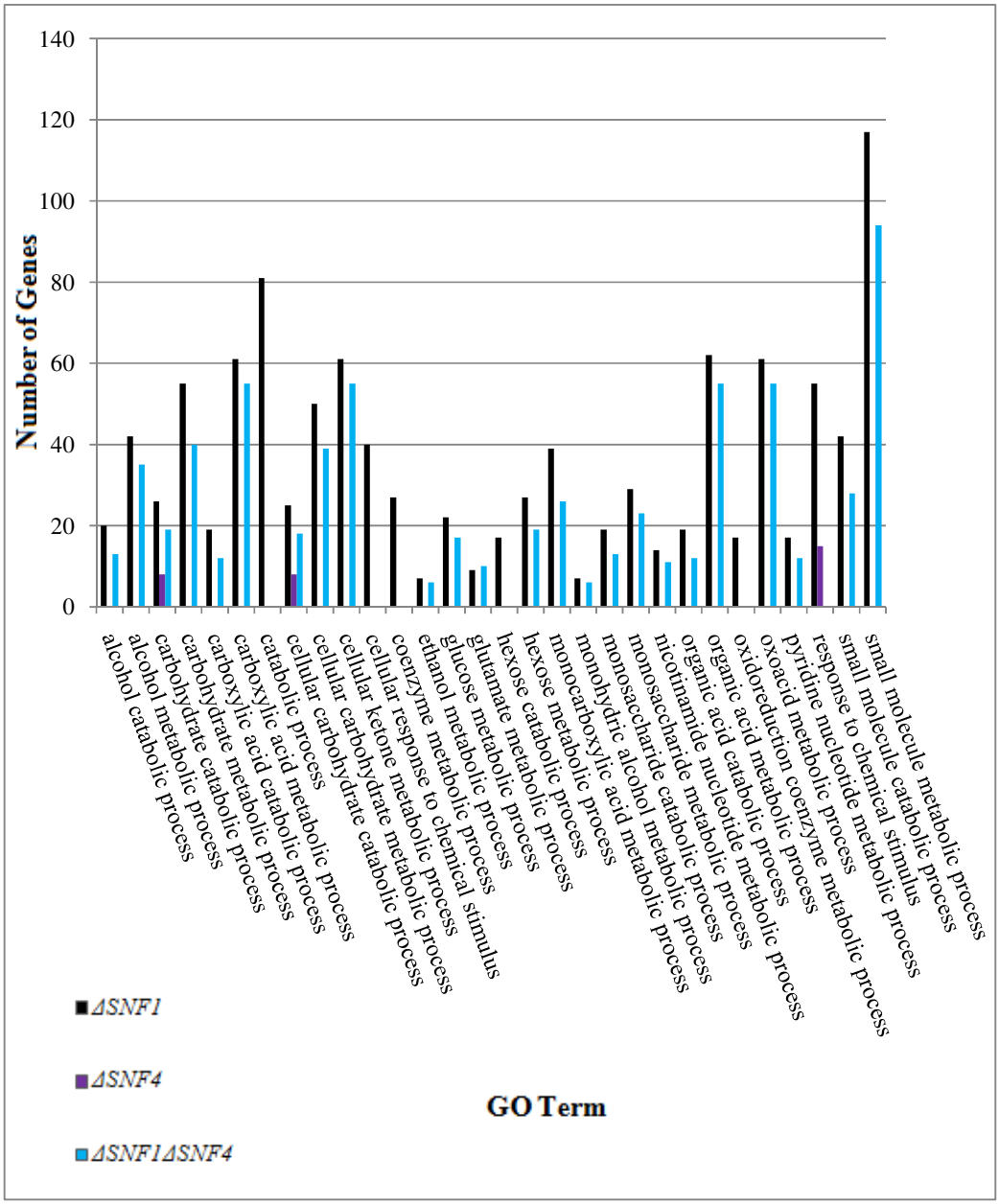

Figure 3.11. Significantly associated GO biological process terms of the target genes of the PRS of *ΔSNF1* mutant

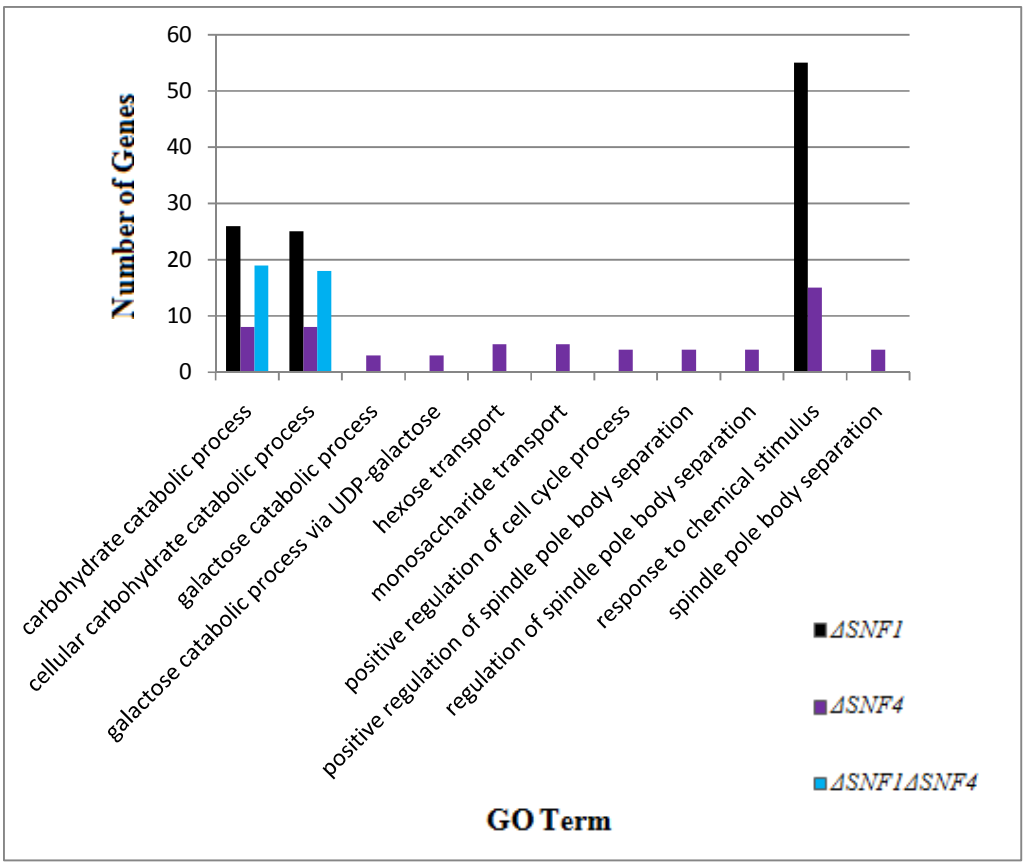

Figure 3.12. Significantly associated GO biological process terms of the target genes of the PRS of *ΔSNF4* mutant

3.2.1.6. Regulation of Key Transcription Factors of *ΔSNF1*, *ΔSNF4* and *ΔSNF1ΔSNF4* Mutants. Identification of key TFs demonstrates the change in TF activity when passing from one condition to another, without *a priori* requirement of change in the transcription level of the TFs, because many TFs do not respond at transcriptional level per se, but through post-translational regulation. Regulation of key TFs was evaluated based whether the key TFs are significantly differentially expressed, as described in Section 2.4. Most of the key TFs of *ΔSNF4* and *ΔSNF1ΔSNF4* mutants and almost half of the key TFs of *ΔSNF1* mutant were found to be regulated mainly transcriptionally (Table 3.13). In Table 3.14, regulation of each key TF is represented.

Table 3.13. Number of key TFs of *ΔSNF1*, *ΔSNF4* and *ΔSNF1ΔSNF4* mutants that were found to be mainly transcriptionally regulated (A) or mainly post-transcriptionally regulated (B)

Mutant	**Number of A**	**Number of B**
ΔSNF1	16	17
ΔSNF4	6	4
ΔSNF1ΔSNF4	10	6

Table 3.14. Regulation of key TFs of *ΔSNF1, ΔSNF4* and *ΔSNF1ΔSNF4* mutants

rank	***ΔSNF1***	**Case**	***ΔSNF4***	**Case**	***ΔSNF1ΔSNF4***	**Case**
1	Hpc2p	B	Imp2'p	A	Cdc39p	A
2	Swi1p	B	Rds3p	B	Rds3p	B
3	Swi3p	A	Pdr8p	A	Rtg2p	A
4	Elp6p	B	Yrm1p	B	Lys14p	A
5	Pdc2p	A	Dig2p	A	Hpc2p	B
6	Pdr8p	B	Hmlalpha1p	A	Haa1p	A
7	Rds3p	B	Mig2p	A	Sps18p	B
8	Rtg2p	B	Gal80p	B	Gis1p	B
9	Cup2p	A	Haa1p	A	Cup2p	A
10	Gis1p	A	Ndt80p	B	Gat4p	A
11	Mig3p	A			Hot1p	A
12	Gat4p	B			Ada2p	B
13	Hot1p	A			Elp6p	A
14	Yrm1p	A			Cst6p	B
15	Xbp1p	A			Xbp1p	A
16	Dig2p	A			War1p	A
17	Cat8p	B				
18	Bye1p	B				
19	Opi1p	A				
20	Imp2'p	A				
21	Rts2p	B				
22	Ada2p	B				
23	Sin3p	A				
24	Gsm1p	B				
25	Sps18p	B				
26	Oaf1p	B				
27	Sfl1p	B				
28	Aca1p	A				
29	Cst6p	A				
30	Sut1p	B				
31	Rlm1p	A				
32	Hmlalpha1p	B				
33	Hmra1p	A				

3.2.2. Key TFs Responsive to Deletion of the Genes *MIG1*, *MIG2* and *MIG3*

In the presence of glucose, inactive Mig1p gets dephosphorylated by the Glc7p phosphatase via its regulatory subunit Reg1p. Active Mig1p interacts with the co-repressors Ssn6p and Tup1p and binds to the promoters of various genes, including genes encoding enzymes of the tricarboxylic acid (TCA) cycle, electron transport chain, alternative carbon sources consumption, gluconeogenesis, and represses the transcription of those genes. Mig1p and Mig2p repress a largely overlapping set of genes on 2 per cent glucose and *MIG1* expression is regulated by Mig2p. Mig3p is proposed not to contribute much to the regulation of the genes that are regulated by Mig1p and Mig2p on 2 per cent glucose (Sanz *et al.*, 2000; Westholm *et al*., 2008).

In the absence of glucose, Mig1p, but not Mig2p, is inactivated by the Snf1p protein kinase. The nuclear localization of Mig1p is regulated by glucose, i. e., Snf1p action causes Mig1p to move to the cytoplasm, but Mig2p is located in the nucleus both in the presence and absence of glucose. The existence of a protein (possibly also a protein kinase) that regulates Mig2p activity in response to glucose has been previously suggested by Lutfiyya *et al.* (Lutfiyya *et al.*, 1998).

Key TFs responsive to the deletions of *MIG1*, *MIG2*, both *MIG1* and *MIG2*, *MIG3* and deletion of all *MIG1*, *MIG2* and *MIG3* genes were identified using the transcriptome data of Westholm *et al*.. In the experiments of Westholm *et al*., each of which was performed at least in triplicate, *ΔMIG1*, *ΔMIG2*, *ΔMIG1ΔMIG2*, *ΔMIG3* and *ΔMIG1ΔMIG2ΔMIG3* mutants and the wild type strain have been grown in the presence of 2 per cent glucose, so that Mig1p and Mig2p are expected to be active in the presence of glucose in the wild type strain (Westholm *et al*., 2008).

When the nodes of the yeast TRN which were not quantified in these transcriptome data were eliminated, the number of the nodes, regulatory interactions and TFs reduced to 5928, 41905 and 194, respectively. Reporter features algorithm identified 24, 14, 18, 15, 22 key TFs around which most transcriptional changes occur as a response to deletions of *MIG1*, *MIG2*, both *MIG1* and *MIG2*, *MIG3* and deletion of all *MIG1*, *MIG2* and *MIG3* genes, respectively (Table 3.15, Table 3.16, Table 3.17, Table 3.18, Table 3.19). Key TFs

were ranked from high to low $Z_{corrected,TF}$ score. $Z_{corrected,TF}$ scores, *p*-values and degrees for each key TF are represented in Table C.4, Table C.5, Table C.6, Table C.7 and Table C.8. The deletion of *MIG1* gene possibly is the cause of the largest perturbation at transcriptional response, as it can be concluded from the numbers of key TFs.

3.2.2.1. Response to the Deletion of *MIG1*. Twenty four key TFs around which most transcriptional changes occur were identified as a response to deletion of *MIG1* (Table 3.15).

Mig1p appeared as a key TF in *ΔMIG1* mutant as expected, since *MIG1* gene is deleted. The appearance of Mig2p as a key TF in *ΔMIG1* supports the idea that Mig2p acts in a redundant fashion with Mig1p and it can replace the function of Mig1p in case of its deletion. In fact, Mig2p was shown to fine-tune glucose repression by targeting a subset of the Mig1p repressed genes (Westholm *et al*., 2008).

Mig3p was identified as the top scoring key TF in *ΔMIG1* mutant, which suggest that Mig3p is somehow related to Mig1p and might has a role in glucose repression. Although the function of Mig3p is not well described, it has been reported that Mig3p binds also to the same DNA sequence and contributes modestly to glucose repression (Kaniak *et al*., 2004).

The algorithm also identified Nrg2p, described in SGD as a transcriptional repressor that mediates glucose repression and negatively regulates filamentous growth, as a key TF in *ΔMIG1* mutant. It was suggested that Nrg1p and Nrg2p are direct or indirect targets of the Snf1p kinase and function in glucose repression of a subset of Snf1p-regulated genes (Vyas *et al*., 2001). Nrg1p was identified as a third repressor required for glucose repression in addition to Mig1p and Mig2p (Zhou and Winston, 2001).

Rgt1p, which is involved in glucose metabolic process and regulation of glucose import, was also identified as a key TF in *ΔMIG1* mutant. Rgt1p has a role in the glucose induction pathway, in such a way that it functions as a transcriptional repressor in the absence of glucose, it is a transcriptional activator at high concentrations of glucose (4 per cent glucose), and it is neutral (neither represses nor activates transcription) in cells

growing on low levels of glucose (0.1 per cent glucose) (Özcan *et al*., 1996). Glucose repression interacts with the glucose induction pathway through Mig1p (and Mig2p) mediated repression of *MTH1* and *SNF3* expression, which reinforces the inhibitory effect of glucose on Mth1p function and ensures maximal glucose induction of Rgt1p repressed genes (*HXT* s, *MIG2* and *HXK2*) (Johnston and Kim, 2005; Palomino *et al*., 2005). Rgt1p repressor blocks transcription of glucose-induced genes only when glucose is absent (Johnston *et al.*, 1994).

Gal80p, involved in galactose metabolic process, was also identified as a key TF in response to deletion of *MIG1*. This result is expected, since *GAL* genes are repressed directly by Mig1p (Nehlin *et al*., 1991).

Mga2p, implemented in fatty acid metabolic process and response to cold, was also identified as a key TF in *ΔMIG1*. Sut1p is involved in stress response and Haa1p regulates the transcription of genes encoding membrane stress proteins. Mig1p sites and STRE motifs occur in the same promoters and it has been reported that dual control of many genes that contain STRE motifs by glucose repression and stress signalling is expected (Westholm *et al*., 2008).

Mdl2p was among the key TFs identified for *ΔMIG1* and its null mutation shows decreased resistance to oleate, decreased respiratory growth rate and decreased utilization of carbon source.

Twelve key TFs (highlighted in Table 3.15) identified as a response to *SNF1* deletion were also determined as key TFs in *ΔMIG1*.

The algorithm identified Imp2'p, which is required for the rapid glucose derepression of the maltose, galactose, raffinose and ethanol utilization pathways, as a key TF in *ΔMIG1* mutant. Alberti *et al*. have proposed that Imp2'p plays a dual role in the regulation of GAL gene expression, via Mig1p-dependent and Mig1p-independent pathways. The Mig1-independent role of Imp2'p depends on Nrg1p (Alberti *et al*., 2003).

Rds2p and Gsm1p, implicated in the use of nonfermentable carbon sources and target gluconeogenic genes, were identified as key TFs in *ΔMIG1*. Gluconeogenesis (generation of glucose from non-carbohydrate carbon substrates) is essential for the growth of yeast cells on nonfermentable carbon sources (Turcotte *et al*., 2009). In addition, Aca1p, which is involved in utilization of nonoptimal carbon sources, and Dig2p, involved in invasive growth in response glucose limitation, were found to be key TFs in *ΔMIG1*.

Three key TFs (Ada2p, Swi1p and Swi3p) that are involved in chromatin remodeling were also identified as key TFs in response to deletion of *MIG1*. Moreover, Regulator of Drug Sensitivity, Rds3p, and Rdr1p, controlling multidrug resistance, were among the identified key TFs.

Table 3.15. Key TFs identified for *ΔMIG1* mutant

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
1	Mig3p (YER028c)	26	Probable transcriptional repressor involved in response to toxic agents such as hydroxyurea that inhibit ribonucleotide reductase; phosphorylation by Snf1p or the Mec1p pathway inactivates Mig3p, allowing induction of damage response genes • negative regulation of transcription from RNA polymerase II promoter • response to DNA damage stimulus • transcription initiation
2	Imp2'p (YIL154c)	8	Transcriptional activator involved in maintenance of ion homeostasis and protection against DNA damage caused by bleomycin and other oxidants, contains a C-terminal leucine-rich repeat • cellular carbohydrate metabolic process • DNA repair
3	Dig2p (YDR480w)	5	Regulatory protein of unknown function, pheromone-inducible, involved in the regulation of mating-specific genes and the invasive growth pathway, required for MAP-kinase imposed repression, inhibits pheromone-responsive transcription • invasive growth in response to glucose limitation
4	Mig2p (YGL209w)	61	Protein containing zinc fingers, involved in repression, along with Mig1p, of SUC2 (invertase) expression by high levels of glucose; binds to Mig1p-binding sites in SUC2 promoter • negative regulation of transcription from RNA polymerase II promoter by glucose
5	Gsm1p (YJL103c)	25	Putative zinc cluster protein of unknown function; proposed to be involved in the regulation of energy metabolism, based on patterns of expression and sequence analysis • oxidative phosphorylation
6	Swi3p (YJL176c)	9	Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2 • ATP-dependent chromatin remodeling • positive regulation of transcription, DNA-dependent

Table 3.15. Key TFs identified for *ΔMIG1* mutant (continued)

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
7	Rds3p (YPR094w)	8	Component of the SF3b subcomplex of the U2 snRNP, zinc cluster protein involved in pre-mRNA splicing and cycloheximide resistance • nuclear mRNA splicing, via spliceosome • response to xenobiotic stimulus • spliceosome assembly
8	Swi1p (YPL016w)	15	Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2; can form the prion [SWI+] • ATP-dependent chromatin remodeling • positive regulation of transcription, DNA-dependent • regulation of transcription from RNA polymerase II promoter
9	Haa1p (YPR008w)	18	Transcriptional activator involved in the transcription of TPO2, YRO2, and other genes putatively encoding membrane stress proteins; involved in adaptation to weak acid stress • regulation of transcription, DNA-dependent • response to acid • transcription initiation from RNA polymerase II promoter
10	Rgt1p (YKL038w)	67	Glucose-responsive transcription factor that regulates expression of several glucose transporter (HXT) genes in response to glucose; binds to promoters and acts both as a transcriptional activator and repressor • glucose metabolic process • negative regulation of transcription • regulation of glucose import
11	Mig1p (YGL035c)	235	Transcription factor involved in glucose repression; sequence specific DNA binding protein containing two Cys2His2 zinc finger motifs; regulated by the SNF1 kinase and the GLC7 phosphatase • negative regulation of transcription from RNA polymerase II promoter by glucose
12	Rdr1p (YOR380w)	12	Transcriptional repressor involved in the control of multidrug resistance; negatively regulates expression of the PDR5 gene; member of the Gal4p family of zinc cluster proteins • response to xenobiotic stimulus
13	Gal80p (YML051w)	7	Transcriptional regulator involved in the repression of GAL genes in the absence of galactose; inhibits transcriptional activation by Gal4p; inhibition relieved by Gal3p or Gal1p binding • galactose metabolic process • negative regulation of kinase activity • positive regulation of transcription by galactose
14	Stp3p (YLR375w)	28	Zinc-finger protein of unknown function, possibly involved in pre-tRNA splicing and in uptake of branched-chain amino acids • biological process unknown
15	Nrg2p (YBR066c)	166	Transcriptional repressor that mediates glucose repression and negatively regulates filamentous growth; has similarity to Nrg1p • biofilm formation • invasive growth in response to glucose limitation • pseudohyphal growth

Table 3.15. Key TFs identified for *ΔMIG1* mutant (continued)

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
16	YPR015c (YPR015c)	59	Putative protein of unknown function; overexpression causes a cell cycle delay or arrest • biological process unknown
17	Aca1p (YER045c)	29	Basic leucine zipper (bZIP) transcription factor of the ATF/CREB family, may regulate transcription of genes involved in utilization of non-optimal carbon sources • transcription initiation from RNA polymerase II promoter
18	Mga2p (YIR033w)	35	ER membrane protein involved in regulation of OLE1 transcription, acts with homolog Spt23p; inactive ER form dimerizes and one subunit is then activated by ubiquitin/proteasome-dependent processing followed by nuclear targeting • fatty acid metabolic process • positive regulation of transcription from RNA polymerase II promoter • response to cold
19	Mdl2p (YPL270w)	7	Mitochondrial inner membrane half-type ATP-binding cassette (ABC) transporter, required for respiratory growth at high temperature; similar to human TAP1 and TAP2 implicated in bare lymphocyte syndrome and Wegener-like granulomatosis • oligopeptide transport
20	Rds2p (YPL133c)	45	Zinc cluster transcriptional activator involved in conferring resistance to ketoconazole • positive regulation of gluconeogenesis • response to xenobiotic stimulus
21	Gat4p (YIR013c)	129	Protein containing GATA family zinc finger motifs • transcription
22	Bye1p (YKL005c)	24	Negative regulator of transcription elongation, contains a TFIIS-like domain and a PHD finger, multicopy suppressor of temperature-sensitive ess1 mutations, probably binds RNA polymerase II large subunit • negative regulation of transcription from RNA polymerase II promoter
23	Sut1p (YGL162w)	84	Transcription factor of the Zn[II]2Cys6 family involved in sterol uptake; involved in induction of hypoxic gene expression • regulation of transcription • regulation of transcription from RNA polymerase II promoter • sterol transport
24	Ada2p (YDR448w)	8	Transcription coactivator, component of the ADA and SAGA transcriptional adaptor/HAT (histone acetyltransferase) complexes • chromatin modification • chromatin silencing at rDNA • chromatin silencing at telomere • positive regulation of histone acetylation • regulation of transcription from RNA polymerase II promoter

Key TFs identified in *ΔMIG1*, which are known to be involved in glucose derepression (Gal80p, Imp2'p, Rds2p, Gsm1p and Aca1p) are expected to be inactive in the wild type strain. Identification of them shows that most significant transcriptional changes occur around them, since they are not repressed any more or there are other very

high activity repressors suppressing the lack of the functions of Mig1p, respectively. Indeed, the former seems to be true, since deletion of the *MIG1* gene relieves glucose repression of numerous target genes (Santangelo, 2006).

To sum up, the algorithm identified key TFs that are involved in chromatin remodeling, fatty acid metabolic process, oxidative phosphorylation (energy metabolism), alternative carbon source consumption and stress response, as a response to *MIG1* deletion as in *ΔSNF1*. Key TFs involved in glucose repression and drug resistance were also identified. Key TFs Gat4p, Stp3p and YPR015c probably have roles in one or more of the processes mentioned above.

3.2.2.2. Response to the Deletion of *MIG2*. Fourteen key TFs around which most transcriptional changes occur were identified as a response to deletion of *MIG2* (Table 3.16).

Mig2p was not found to be a key TF in response to the deletion of the *MIG2* gene, which suggests that there are other factors functioning in place of Mig2p. In this particular case, this other factor is most probably Mig1p, which was not identified as a key TF in *ΔMIG2*. In fact, Westholm *et al*. have found that Mig1p and Mig2p regulate an overlapping set of genes on 2 per cent glucose, with Mig1p being the major regulator (Westholm *et al*., 2008).

Sin3p, involved in chromatin remodeling like Ada2p, Swi1p and Swi3p, and Hmlalpha1p, involved in mating-type specific regulation of transcription, were also identified as key TFs in response to *MIG2* deletion.

Although Mga2p, a key TF identified in *ΔMIG1*, did not appear to be a key TF in *ΔMIG2*, Spt23p, homolog of Mga2p, was identified as key TF in *ΔMIG2*. These TFs are involved in fatty acid metabolic process and response to cold.

Nine key TFs (highlighted in Table 3.16) identified as a response to *MIG1* deletion were also determined as key TFs in *ΔMIG2*.

Table 3.16. Key TFs identified for *ΔMIG2* mutant

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
1	Dig2p (YDR480w)	5	Regulatory protein of unknown function, pheromone-inducible, involved in the regulation of mating-specific genes and the invasive growth pathway, required for MAP-kinase imposed repression, inhibits pheromone-responsive transcription • invasive growth in response to glucose limitation
2	Gal80p (YML051w)	7	Transcriptional regulator involved in the repression of GAL genes in the absence of galactose; inhibits transcriptional activation by Gal4p; inhibition relieved by Gal3p or Gal1p binding • galactose metabolic process • negative regulation of kinase activity • positive regulation of transcription by galactose
3	Ada2p (YDR448w)	8	Transcription coactivator, component of the ADA and SAGA transcriptional adaptor/HAT (histone acetyltransferase) complexes • chromatin modification • chromatin silencing at rDNA • chromatin silencing at telomere • positive regulation of histone acetylation • regulation of transcription from RNA polymerase II promoter
4	Mig3p (YER028c)	26	Probable transcriptional repressor involved in response to toxic agents such as hydroxyurea that inhibit ribonucleotide reductase; phosphorylation by Snf1p or the Mec1p pathway inactivates Mig3p, allowing induction of damage response genes • negative regulation of transcription from RNA polymerase II promoter • response to DNA damage stimulus • transcription initiation
5	Haa1p (YPR008w)	18	Transcriptional activator involved in the transcription of TPO2, YRO2, and other genes putatively encoding membrane stress proteins; involved in adaptation to weak acid stress • regulation of transcription, DNA-dependent • response to acid • transcription initiation from RNA polymerase II promoter
6	Gsm1p (YJL103c)	25	Putative zinc cluster protein of unknown function; proposed to be involved in the regulation of energy metabolism, based on patterns of expression and sequence analysis • oxidative phosphorylation
7	Sin3p (YOL004w)	31	Component of the Sin3p-Rpd3p histone deacetylase complex, involved in transcriptional repression and activation of diverse processes, including mating-type switching and meiosis; involved in the maintenance of chromosomal integrity • chromatin silencing at rDNA • chromatin silencing at silent mating-type cassette • chromatin silencing at telomere • histone deacetylation • double-strand break repair via nonhomologous end joining • negative regulation of transcription from RNA polymerase II promoter • negative regulation of transposition, RNA-mediated • positive regulation of gene-specific transcription from RNA polymerase II promoter • positive regulation of transcription from RNA polymerase II promoter

Table 3.16. Key TFs identified for *ΔMIG2* mutant (continued)

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
8	Swi3p (YJL176c)	9	Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2 • ATP-dependent chromatin remodeling • positive regulation of transcription, DNA-dependent
9	Hmra2p (YCR096c)	27	Silenced copy of a2 at HMR; similarity to Alpha2p; required along with a1p for inhibiting expression of the HO endonuclease in a/alpha HO/HO diploid cells with an active mating-type interconversion system • biological process unknown
10	Swi1p (YPL016w)	15	Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2; can form the prion [SWI+] • ATP-dependent chromatin remodeling • positive regulation of transcription, DNA-dependent • regulation of transcription from RNA polymerase II promoter
11	Hmlalpha1p (YCL066w)	20	Silenced copy of ALPHA1 at HML, encoding a transcriptional coactivator involved in the regulation of mating-type alpha-specific gene expression • regulation of transcription from RNA polymerase II promoter • regulation of transcription, mating-type specific
12	Rgt1p (YKL038w)	67	Glucose-responsive transcription factor that regulates expression of several glucose transporter (HXT) genes in response to glucose; binds to promoters and acts both as a transcriptional activator and repressor • glucose metabolic process • negative regulation of transcription • regulation of glucose import
13	Spt23p (YKL020c)	57	ER membrane protein involved in regulation of OLE1 transcription, acts with homolog Mga2p; inactive ER form dimerizes and one subunit is then activated by ubiquitin/proteasome-dependent processing followed by nuclear targeting • fatty acid metabolic process • positive regulation of transcription from RNA polymerase II promoter • response to cold
14	Lys14p (YDR034c)	12	Transcriptional activator involved in regulation of genes of the lysine biosynthesis pathway; requires 2-aminoadipate semialdehyde as co-inducer • lysine biosynthetic process via aminoadipic acid

3.2.2.3. Response to the Deletion of both *MIG1* and *MIG2*. Eighteen key TFs around which most transcriptional changes occur were identified as a response to deletion of both *MIG1* and *MIG2* (Table 3.17).

Mig1p and Mig2p were found to be key TFs in response to the deletion of both *MIG1* and *MIG2* genes, as expected.

Hmlalpha1p and Hmlalpha2p, involved in mating-type specific regulation of transcription, were also identified as key TFs in response to *MIG1* and *MIG2* deletion. Hpc2p is involved in chromatin remodeling like Ada2p, Swi1p and Swi3p.

Thirteen key TFs (highlighted in Table 3.17) identified as a response to *MIG1* deletion were also determined as key TFs in *ΔMIG1ΔMIG2*, Mig3p being the top scoring key TF.

Table 3.17. Key TFs identified for *ΔMIG1ΔMIG2* mutant

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
1	Mig3p (YER028c)	26	Probable transcriptional repressor involved in response to toxic agents such as hydroxyurea that inhibit ribonucleotide reductase; phosphorylation by Snf1p or the Mec1p pathway inactivates Mig3p, allowing induction of damage response genes • negative regulation of transcription from RNA polymerase II promoter • response to DNA damage stimulus • transcription initiation
2	Mig2p (YGL209w)	61	Protein containing zinc fingers, involved in repression, along with Mig1p, of SUC2 (invertase) expression by high levels of glucose; binds to Mig1p-binding sites in SUC2 promoter • negative regulation of transcription from RNA polymerase II promoter by glucose
3	Hmlalpha1p (YCL066w)	20	Silenced copy of ALPHA1 at HML, encoding a transcriptional coactivator involved in the regulation of mating-type alpha-specific gene expression • regulation of transcription from RNA polymerase II promoter • regulation of transcription, mating-type specific
4	Swi1p (YPL016w)	15	Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2; can form the prion [SWI+] • ATP-dependent chromatin remodeling • positive regulation of transcription, DNA-dependent • regulation of transcription from RNA polymerase II promoter
5	Imp2'p (YIL154c)	8	Transcriptional activator involved in maintenance of ion homeostasis and protection against DNA damage caused by bleomycin and other oxidants, contains a C-terminal leucine-rich repeat • cellular carbohydrate metabolic process • DNA repair
6	Swi3p (YJL176c)	9	Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2 • ATP-dependent chromatin remodeling • positive regulation of transcription, DNA-dependent

Table 3.17. Key TFs identified for *ΔMIG1ΔMIG2* mutant (continued)

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
7	Gsm1p (YJL103c)	25	Putative zinc cluster protein of unknown function; proposed to be involved in the regulation of energy metabolism, based on patterns of expression and sequence analysis • oxidative phosphorylation
8	Hpc2p (YBR215w)	3	Subunit of the HIR complex, a nucleosome assembly complex involved in regulation of histone gene transcription; mutants display synthetic defects with subunits of FACT, a complex that allows passage of RNA Pol II through nucleosomes • DNA replication-independent nucleosome assembly • regulation of transcription involved in G1/S-phase of mitotic cell cycle • RNA elongation from RNA polymerase II promoter
9	Rdr1p (YOR380w)	12	Transcriptional repressor involved in the control of multidrug resistance; negatively regulates expression of the PDR5 gene; member of the Gal4p family of zinc cluster proteins • response to xenobiotic stimulus
10	Rpn10p (YHR200w)	9	Non-ATPase base subunit of the 19S regulatory particle (RP) of the 26S proteasome; N-terminus plays a role in maintaining the structural integrity of the RP; binds selectively to polyubiquitin chains; homolog of the mammalian S5a protein • ubiquitin-dependent protein catabolic process
11	Rgt1p (YKL038w)	67	Glucose-responsive transcription factor that regulates expression of several glucose transporter (HXT) genes in response to glucose; binds to promoters and acts both as a transcriptional activator and repressor • glucose metabolic process • negative regulation of transcription • regulation of glucose import
12	Mig1p (YGL035c)	235	Transcription factor involved in glucose repression; sequence specific DNA binding protein containing two Cys2His2 zinc finger motifs; regulated by the SNF1 kinase and the GLC7 phosphatase • negative regulation of transcription from RNA polymerase II promoter by glucose
13	Gat4p (YIR013c)	129	Protein containing GATA family zinc finger motifs • transcription
14	Rds3p (YPR094w)	8	Component of the SF3b subcomplex of the U2 snRNP, zinc cluster protein involved in pre-mRNA splicing and cycloheximide resistance • nuclear mRNA splicing, via spliceosome • response to xenobiotic stimulus • spliceosome assembly
15	Ada2p (YDR448w)	8	Transcription coactivator, component of the ADA and SAGA transcriptional adaptor/HAT (histone acetyltransferase) complexes • chromatin modification • chromatin silencing at rDNA • chromatin silencing at telomere • positive regulation of histone acetylation • regulation of transcription from RNA polymerase II promoter

Table 3.17. Key TFs identified for *ΔMIG1ΔMIG2* mutant (continued)

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
16	Gal80p (YML051w)	7	Transcriptional regulator involved in the repression of GAL genes in the absence of galactose; inhibits transcriptional activation by Gal4p; inhibition relieved by Gal3p or Gal1p binding • galactose metabolic process • negative regulation of kinase activity • positive regulation of transcription by galactose
17	Hmlalpha2p (YCL067c)	28	Silenced copy of ALPHA2 at HML; homeobox-domain protein that associates with Mcm1p in haploid cells to repress a-specific gene expression and interacts with a1p in diploid cells to repress haploid-specific gene expression • donor selection • regulation of transcription from RNA polymerase II promoter • regulation of transcription, mating-type specific
18	Hmra2p (YCR096c)	27	Silenced copy of a2 at HMR; similarity to Alpha2p; required along with a1p for inhibiting expression of the HO endonuclease in a/alpha HO/HO diploid cells with an active mating-type interconversion system • biological process unknown

3.2.2.4. Comparison of the Responses to Deletions of *MIG1*, *MIG2* and both *MIG1* and *MIG2*. The comparison between the key TFs identified in *ΔMIG1*, *ΔMIG2* and *ΔMIG1ΔMIG2* mutants is shown in Figure 3.13.

Seven key TFs were identified for all three mutants, namely Ada2p, Gal80p, Gsm1p, Mig3p, Rgt1p, Swi1p and Swi3p. These key TFs were found to be enriched significantly with very general GO biological process terms, such as "regulation of transcription" (*p*-value=3.05×10^{-5}), as expected (Table D.7). These key TFs are involved in several biological processes, i.e., galactose metabolic process (Gal80p), chromatin remodeling (Ada2p, Swi1 and Swi3), regulation of energy metabolism (Gsm1p) and regulation of glucose import (Rgt1p).

Nine (Aca1p, Bye1p, Mdl2p, Mga2p, Nrg2p, Rds2p, Stp3p, Sut1p and YPR015c) key TFs that were identified only as a response specifically to the deletion of *MIG1* are involved in several biological processes, i.e., glucose repression (Nrg2p), utilization of nonoptimal/nonfermentable carbon sources (Aca1p, Rds2p), fatty acid metabolic process (Mga2), oligopeptide transport (Mdl2p) and stress response (Sut1p, Mga2p). Three (Lys14p, Sin3p and Spt23p) key TFs that were identified only as a response specifically to the deletion of *MIG2* are involved in several biological processes, i.e., chromatin

remodeling (Sin3p), fatty acid metabolic process (Spt23p) and stress response (Spt23p). Three (Hmlalpha2p, Hpc2p and Rpn10p) key TFs that were identified only as a response specifically to the deletion of *MIG1* and *MIG2* are involved in mating-type specific regulation of transcription (Hmlalpha2p) and in chromatin remodeling (Hpc2p). However no significant GO biological process terms could be associated with these sets.

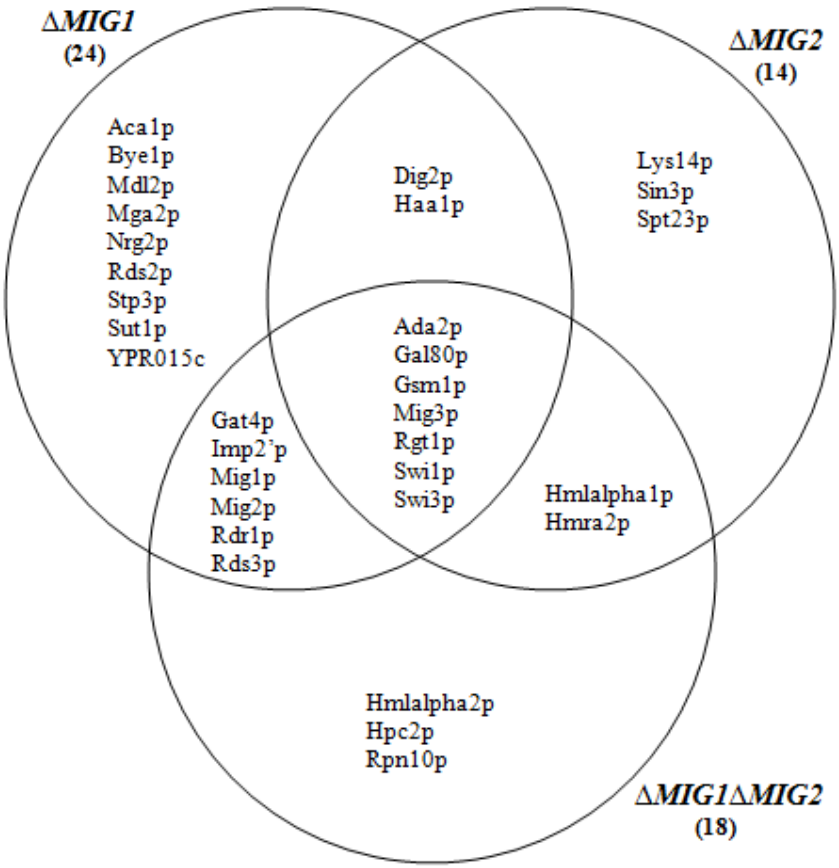

Figure 3.13. Comparison of the key TFs identified for *ΔMIG1*, *ΔMIG2* and *ΔMIG1ΔMIG2* mutants (the number of key TFs for each specific mutant is given in brackets)

When the significant shared GO biological process terms (p-value<0.01) of the key TFs identified for the overlaps of any two specific perturbations were further identified excluding the key TFs identified for all three mutants, no significant shared GO biological process terms could be associated with the two key TFs identified for both *ΔMIG1* and *ΔMIG2* mutants (Dig2p and Haa1p) and with the two key TFs identified for both *ΔMIG2* and *ΔMIG1ΔMIG2* mutants (Hmlalpha1p, Hmra2p). Dig2p is involved in invasive growth

in response glucose limitation, Haa1p regulates transcription of genes encoding membrane stress proteins, and Hmlalpha1p regulates mating-type specific regulation of transcription.

Six key TFs (Gat4p, Imp2'p, Mig1p, Mig2p, Rdr1p and Rds3p) identified for both *ΔMIG1* and *ΔMIG1ΔMIG2* mutants excluding the key TFs identified for all three mutants were found to be enriched significantly with more specific GO biological process terms, such as "negative regulation of transcription by glucose" (*p*-value=0.00065) and "cellular response to nutrient" (*p*-value=0.00657) (Table D.8). These key TFs are involved in biological processes carbohydrate metabolic processes (Imp2'p) and drug resistance (Rdr1p, Rd3p).

In particular, TFs regulating mating-type specific regulation of transcription did not appear as key TFs in *ΔMIG1* and TFs involved in drug resistance did not appear as key TFs in *ΔMIG2*.

3.2.2.5. Response to the Deletion of *MIG3*. Fifteen key TFs around which most transcriptional changes occur were identified as a response to deletion of *MIG3* (Table 3.18).

Mig3p was found to be a key TF in response to the deletion of *MIG3* gene, as expected.

Maltose fermentation protein, Mal13p, involved in cellular carbohydrate metabolic process, was also among the identified key TFs *ΔMIG3*.

Hmra1p, Hmlalpha1p and Hmlalpha2p, involved in mating-type specific regulation of transcription, were also identified as key TFs in response to *MIG3* deletion. Hpc2p is involved in chromatin remodeling like Ada2p, Swi1p and Swi3p.

Ten key TFs (highlighted in Table 3.18) identified as a response to *MIG1* deletion were also determined as key TFs in *ΔMIG3*.

Table 3.18. Key TFs identified for *ΔMIG3* mutant

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
1	Dig2p (YDR480w)	5	Regulatory protein of unknown function, pheromone-inducible, involved in the regulation of mating-specific genes and the invasive growth pathway, required for MAP-kinase imposed repression, inhibits pheromone-responsive transcription • invasive growth in response to glucose limitation
2	Mdl2p (YPL270w)	7	Mitochondrial inner membrane half-type ATP-binding cassette (ABC) transporter, required for respiratory growth at high temperature; similar to human TAP1 and TAP2 implicated in bare lymphocyte syndrome and Wegener-like granulomatosis • oligopeptide transport
3	Aca1p (YER045c)	29	Basic leucine zipper (bZIP) transcription factor of the ATF/CREB family, may regulate transcription of genes involved in utilization of non-optimal carbon sources • transcription initiation from RNA polymerase II promoter
4	Haa1p (YPR008w)	18	Transcriptional activator involved in the transcription of TPO2, YRO2, and other genes putatively encoding membrane stress proteins; involved in adaptation to weak acid stress • regulation of transcription, DNA-dependent • response to acid • transcription initiation from RNA polymerase II promoter
5	Ada2p (YDR448w)	8	Transcription coactivator, component of the ADA and SAGA transcriptional adaptor/HAT (histone acetyltransferase) complexes • chromatin modification • chromatin silencing at rDNA • chromatin silencing at telomere • positive regulation of histone acetylation • regulation of transcription from RNA polymerase II promoter
6	Hpc2p (YBR215w)	3	Subunit of the HIR complex, a nucleosome assembly complex involved in regulation of histone gene transcription; mutants display synthetic defects with subunits of FACT, a complex that allows passage of RNA Pol II through nucleosomes • DNA replication-independent nucleosome assembly • regulation of transcription involved in G1/S-phase of mitotic cell cycle • RNA elongation from RNA polymerase II promoter
7	Gal80p (YML051w)	7	Transcriptional regulator involved in the repression of GAL genes in the absence of galactose; inhibits transcriptional activation by Gal4p; inhibition relieved by Gal3p or Gal1p binding • galactose metabolic process • negative regulation of kinase activity • positive regulation of transcription by galactose
8	Hmlalpha2p (YCL067c)	28	Silenced copy of ALPHA2 at HML; homeobox-domain protein that associates with Mcm1p in haploid cells to repress a-specific gene expression and interacts with a1p in diploid cells to repress haploid-specific gene expression • donor selection • regulation of transcription from RNA polymerase II promoter • regulation of transcription, mating-type specific

Table 3.18. Key TFs identified for *ΔMIG3* mutant (continued)

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
9	Hmlalpha1p (YCL066w)	20	Silenced copy of ALPHA1 at HML, encoding a transcriptional coactivator involved in the regulation of mating-type alpha-specific gene expression • regulation of transcription from RNA polymerase II promoter • regulation of transcription, mating-type specific
10	Swi1p (YPL016w)	15	Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2; can form the prion [SWI+] • ATP-dependent chromatin remodeling • positive regulation of transcription, DNA-dependent • regulation of transcription from RNA polymerase II promoter
11	Gsm1p (YJL103c)	25	Putative zinc cluster protein of unknown function; proposed to be involved in the regulation of energy metabolism, based on patterns of expression and sequence analysis • oxidative phosphorylation
12	Swi3p (YJL176c)	9	Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2 • ATP-dependent chromatin remodeling • positive regulation of transcription, DNA-dependent
13	Mal13p (YGR288w)	12	MAL-activator protein, part of complex locus MAL1; nonfunctional in genomic reference strain S288C • cellular carbohydrate metabolic process • regulation of transcription, DNA-dependent
14	Mig3p (YER028c)	26	Probable transcriptional repressor involved in response to toxic agents such as hydroxyurea that inhibit ribonucleotide reductase; phosphorylation by Snf1p or the Mec1p pathway inactivates Mig3p, allowing induction of damage response genes • negative regulation of transcription from RNA polymerase II promoter • response to DNA damage stimulus • transcription initiation
15	Hmra1p (YCR097w)	20	Silenced copy of a1 at HMR; homeobox corepressor that interacts with Alpha2p to repress haploid-specific gene transcription in diploid cells • regulation of transcription, mating-type specific

3.2.2.6. Comparison of the Responses to Deletions of *MIG1*, *MIG2* and *MIG3*. The comparison between the key TFs identified in *ΔMIG1*, *ΔMIG2* and *ΔMIG3* mutants is shown in Figure 3.14.

Eight key TFs were identified for all three mutants, namely Ada2p, Dig2p, Gal80p, Gsm1p, Haa1p, Mig3p, Swi1p and Swi3p. These key TFs were found to be enriched significantly with very general GO biological process terms, such as "regulation of macromolecule biosynthetic process" (*p*-value=0.00039) (Table D.11). GO term with the

lowest *p*-value was found to be "regulation of transcription, DNA-dependent" (*p*-value=8.28×10^{-5}), as expected. These key TFs are involved in several biological processes, i.e., galactose metabolic process (Gal80p), chromatin remodeling (Ada2p, Swi1 and Swi3), regulation of energy metabolism (Gsm1p), invasive growth in response glucose limitation (Dig2p) and transcription of genes encoding membrane stress proteins (Haa1p).

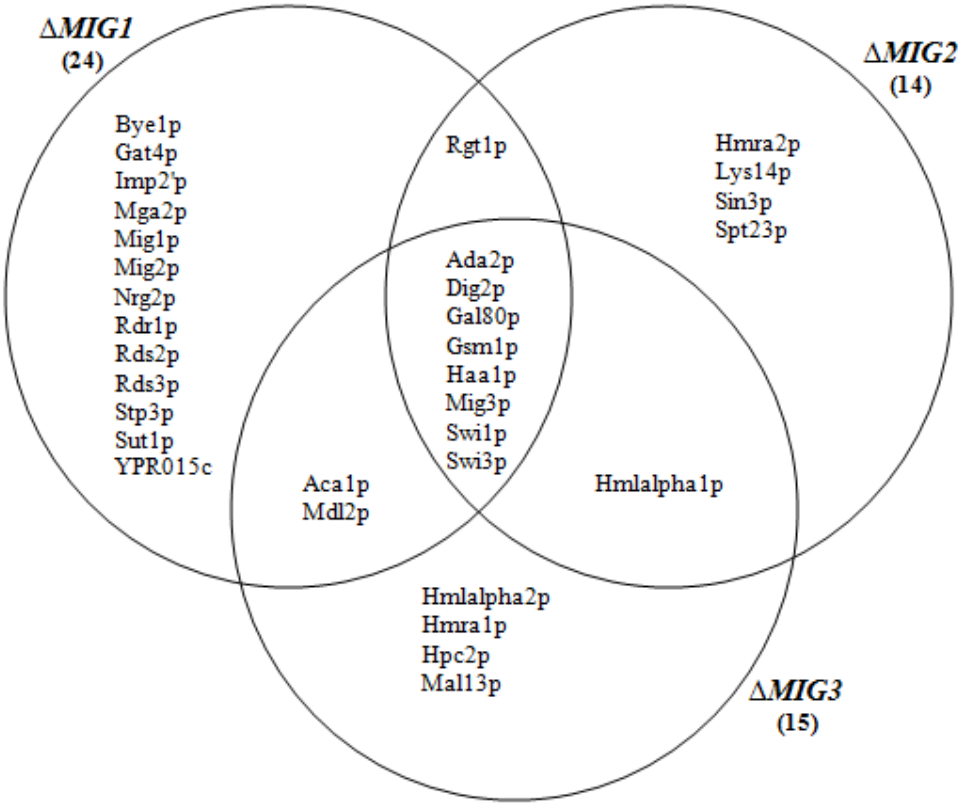

Figure 3.14. Comparison of the key TFs identified for *ΔMIG1*, *ΔMIG2* and *ΔMIG3* mutants (the number of key TFs for each specific mutant is given in brackets)

Thirteen key TFs were identified only as a response specifically to the deletion of *MIG1* and these key TFs were found to be enriched significantly with GO biological process terms related to glucose repression, such as "negative regulation of transcription by carbon catabolites" (*p*-value=0.00408) and "negative regulation of transcription by glucose" (*p*-value=0.00408) (Table D.9). These key TFs are involved in several biological processes, i.e., glucose repression (Nrg2p), carbohydrate metabolic processes (Imp2'p), use of nonfermentable carbon sources (Rds2p), fatty acid metabolic process (Mga2p), stress response (Mga2p, Sut1p) and drug resistance (Rdr1p, Rd3p).

No significant GO biological process terms could be associated with the four key TFs (Hmra2p, Lys14p, Sin3p and Spt23p) identified only as a response specifically to the deletion of *MIG2*. Sin3p is involved in chromatin remodeling and Spt23p is involved in fatty acid metabolic process and stress response.

Four key TFs (Hmlalpha2p, Hmra1p, Hpc2p and Mal13p) were identified only as a response specifically to the deletion of *MIG3* and these key TFs were found to be enriched significantly with general GO biological process terms, such as "regulation of macromolecule biosynthetic process" (p-value=0.00158), as well as with more specific GO biological process terms, such as "cell fate commitment" (p-value=0.00363), "sex determination" (p-value=0.00363) and "mating type determination" (p-value=0.00363) (Table D.10). Hmlalpha2p and Hmra1p regulate mating-type specific transcription and Mal13p is involved in cellular carbohydrate metabolic process.

When the significant shared GO biological process terms (p-value<0.01) of the key TFs identified for the overlaps of any two specific perturbations were further investigated excluding the key TFs identified for all three mutants, no significant shared GO biological process terms could be associated with the two key TFs identified for both *ΔMIG1* and *ΔMIG3* mutants (Aca1p and Mdl2p). Aca1p is involved in utilization of nonoptimal carbon sources and Mdl2p in oligopeptide transport.

Rgt1p, involved in glucose induction, was the only key TF identified for both *ΔMIG1* and *ΔMIG2* excluding the key TFs identified for all three mutants and Hmlalpha1p, regulating mating-type specific transcription, was the only key TF identified for both *ΔMIG1* and *ΔMIG3* excluding the key TFs identified for all three mutants.

In particular, TFs regulating mating-type specific regulation of transcription did not appear as key TFs in *ΔMIG1*, TFs involved in drug resistance did not appear as key TFs in *ΔMIG2* and *ΔMIG3*, and TFs involved in fatty acid metabolic process did not appear as key TFs in *ΔMIG3*.

3.2.2.7. Response to the Deletion of all *MIG1*, *MIG2* and *MIG3*. Twenty two key TFs around which most transcriptional changes occur were identified as a response to deletion of all *MIG1*, *MIG2* and *MIG3* genes (Table 3.19).

Mig1p, Mig2p and Mig3p were found to be key TFs in response to the deletion of *MIG1*, *MIG2* and *MIG3* genes, as expected.

Maltose fermentation protein, Mal13p, involved in cellular carbohydrate metabolic process, and Met32p, involved in sulfur amino acid metabolic process, were also among the identified key TFs in *ΔMIG3*.

Rtg2p, which regulates the subcellular localization of Rtg1p and Rtg3p transcriptional activators of retrograde (RTG) and TOR pathways which is important in the regulation of cell growth in response to nutrients was identified as a key TF.

Hmlalpha1p and Hmlalpha2p, involved in mating-type specific regulation of transcription, were also identified as key TFs in response to deletion of all *MIG1*, *MIG2* and *MIG3* genes. Hpc2p is involved in chromatin remodeling like Ada2p, Swi1p and Swi3p.

Thirteen key TFs (highlighted in Table 3.19) identified as a response to *MIG1* deletion were also determined as key TFs in *ΔMIG1ΔMIG2ΔMIG3*.

Table 3.19. Key TFs identified for *ΔMIG1ΔMIG2ΔMIG3* mutant

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
1	Hmlalpha1p (YCL066w)	20	Silenced copy of ALPHA1 at HML, encoding a transcriptional coactivator involved in the regulation of mating-type alpha-specific gene expression • regulation of transcription from RNA polymerase II promoter • regulation of transcription, mating-type specific
2	Hmra2p (YCR096c)	27	Silenced copy of a2 at HMR; similarity to Alpha2p; required along with a1p for inhibiting expression of the HO endonuclease in a/alpha HO/HO diploid cells with an active mating-type interconversion system • biological process unknown

Table 3.19. Key TFs identified for *ΔMIG1ΔMIG2ΔMIG3* mutant (continued)

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
3	Mig3p (YER028c)	26	Probable transcriptional repressor involved in response to toxic agents such as hydroxyurea that inhibit ribonucleotide reductase; phosphorylation by Snf1p or the Mec1p pathway inactivates Mig3p, allowing induction of damage response genes • negative regulation of transcription from RNA polymerase II promoter • response to DNA damage stimulus • transcription initiation
4	Mig2p (YGL209w)	61	Protein containing zinc fingers, involved in repression, along with Mig1p, of SUC2 (invertase) expression by high levels of glucose; binds to Mig1p-binding sites in SUC2 promoter • negative regulation of transcription from RNA polymerase II promoter by glucose
5	Imp2'p (YIL154c)	8	Transcriptional activator involved in maintenance of ion homeostasis and protection against DNA damage caused by bleomycin and other oxidants, contains a C-terminal leucine-rich repeat • cellular carbohydrate metabolic process • DNA repair
6	Gsm1p (YJL103c)	25	Putative zinc cluster protein of unknown function; proposed to be involved in the regulation of energy metabolism, based on patterns of expression and sequence analysis • oxidative phosphorylation
7	Hpc2p (YBR215w)	3	Subunit of the HIR complex, a nucleosome assembly complex involved in regulation of histone gene transcription; mutants display synthetic defects with subunits of FACT, a complex that allows passage of RNA Pol II through nucleosomes • DNA replication-independent nucleosome assembly • regulation of transcription involved in G1/S-phase of mitotic cell cycle • RNA elongation from RNA polymerase II promoter
8	Gal80p (YML051w)	7	Transcriptional regulator involved in the repression of GAL genes in the absence of galactose; inhibits transcriptional activation by Gal4p; inhibition relieved by Gal3p or Gal1p binding • galactose metabolic process • negative regulation of kinase activity • positive regulation of transcription by galactose
9	Rpn10p (YHR200w)	9	Non-ATPase base subunit of the 19S regulatory particle (RP) of the 26S proteasome; N-terminus plays a role in maintaining the structural integrity of the RP; binds selectively to polyubiquitin chains; homolog of the mammalian S5a protein • ubiquitin-dependent protein catabolic process
10	Rtg2p (YGL252c)	9	Sensor of mitochondrial dysfunction; regulates the subcellular location of Rtg1p and Rtg3p, transcriptional activators of the retrograde (RTG) and TOR pathways; Rtg2p is inhibited by the phosphorylated form of Mks1p • extrachromosomal rDNA circle accumulation involved in replicative cell aging • intracellular signaling pathway • mitochondria-nucleus signaling pathway

Table 3.19. Key TFs identified for *ΔMIG1ΔMIG2ΔMIG3* mutant (continued)

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
11	Haa1p (YPR008w)	18	Transcriptional activator involved in the transcription of TPO2, YRO2, and other genes putatively encoding membrane stress proteins; involved in adaptation to weak acid stress • regulation of transcription, DNA-dependent • response to acid • transcription initiation from RNA polymerase II promoter
12	Mal13p (YGR288w)	12	MAL-activator protein, part of complex locus MAL1; nonfunctional in genomic reference strain S288C • cellular carbohydrate metabolic process • regulation of transcription, DNA-dependent
13	Rgt1p (YKL038w)	67	Glucose-responsive transcription factor that regulates expression of several glucose transporter (HXT) genes in response to glucose; binds to promoters and acts both as a transcriptional activator and repressor • glucose metabolic process • negative regulation of transcription • regulation of glucose import
14	Hmlalpha2p (YCL067c)	28	Silenced copy of ALPHA2 at HML; homeobox-domain protein that associates with Mcm1p in haploid cells to repress a-specific gene expression and interacts with a1p in diploid cells to repress haploid-specific gene expression • donor selection • regulation of transcription from RNA polymerase II promoter • regulation of transcription, mating-type specific
15	Swi3p (YJL176c)	9	Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2 • ATP-dependent chromatin remodeling • positive regulation of transcription, DNA-dependent
16	Mig1p (YGL035c)	235	Transcription factor involved in glucose repression; sequence specific DNA binding protein containing two Cys2His2 zinc finger motifs; regulated by the SNF1 kinase and the GLC7 phosphatase • negative regulation of transcription from RNA polymerase II promoter by glucose
17	Gat4p (YIR013c)	129	Protein containing GATA family zinc finger motifs • transcription
18	Swi1p (YPL016w)	15	Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2; can form the prion [SWI+] • ATP-dependent chromatin remodeling • positive regulation of transcription, DNA-dependent • regulation of transcription from RNA polymerase II promoter

Table 3.19. Key TFs identified for *ΔMIG1ΔMIG2ΔMIG3* mutant (continued)

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
19	Kar4p (YCL055w)	47	Transcription factor required for gene regulation in response to pheromones; also required during meiosis; exists in two forms, a slower-migrating form more abundant during vegetative growth and a faster-migrating form induced by pheromone • G1 phase of mitotic cell cycle • karyogamy involved in conjugation with cellular fusion • meiosis • negative regulation of transcription from RNA polymerase II promoter by pheromones • positive regulation of transcription from RNA polymerase II promoter by pheromones
20	Ada2p (YDR448w)	8	Transcription coactivator, component of the ADA and SAGA transcriptional adaptor/HAT (histone acetyltransferase) complexes • chromatin modification • chromatin silencing at rDNA • chromatin silencing at telomere • positive regulation of histone acetylation • regulation of transcription from RNA polymerase II promoter
21	Mga2p (YIR033w)	35	ER membrane protein involved in regulation of OLE1 transcription, acts with homolog Spt23p; inactive ER form dimerizes and one subunit is then activated by ubiquitin/proteasome-dependent processing followed by nuclear targeting • fatty acid metabolic process • positive regulation of transcription from RNA polymerase II promoter • response to cold
22	Met32p (YDR253c)	99	Zinc-finger DNA-binding protein, involved in transcriptional regulation of the methionine biosynthetic genes, similar to Met31p • sulfur amino acid metabolic process

3.2.2.8. Perturbation-Responsive Subnetworks of *ΔMIG1*, *ΔMIG2*, *ΔMIG1ΔMIG2*, *ΔMIG3* and *ΔMIG1ΔMIG2ΔMIG3* mutants. Perturbation responsive subnetworks (PRS) were constructed between the key TFs and their differentially expressed target genes (p-value<0.05) responsive to the same perturbation. The numbers of key TFs, their target genes and interactions in the perturbation-responsive subnetworks in *ΔMIG1*, *ΔMIG2*, *ΔMIG1ΔMIG2*, *ΔMIG3* and *ΔMIG1ΔMIG2ΔMIG3* mutants are given in Table 3.20. The overviews of these subnetworks produced in Cytoscape are displayed in Figure 3.15, Figure 3.16, Figure 3.17, Figure 3.18 and Figure 3.19, where the up- (green) or down-regulation (red) of the key TFs and their differentially expressed target genes in the corresponding mutants with respect to wild type strain are indicated. Key TFs indicated in black in these figures were found to be not significantly expressed in this study. Therefore they are considered to be post-transcriptionally regulated (Table 3.27 and Table 3.28). GO

biological process terms significantly associated with the target genes in each PRS (*p*-value<0.01) were identified and represented in Table 3.21, Table 3.22, Table 3.23 and Table 3.24. No significant GO biological process terms could be associated with the target genes of the PRS of *ΔMIG2* mutant.

Table 3.20. The numbers of TFs, their target genes and interactions for the PRSs of *ΔMIG1*, *ΔMIG2*, *ΔMIG1ΔMIG2*, *ΔMIG3* and *ΔMIG1ΔMIG2ΔMIG3* mutants

Mutant	Number of Key TFs	Number of Target Genes	Number of Interactions
ΔMIG1	21	113	195
ΔMIG2	8	13	15
ΔMIG1ΔMIG2	15	143	209
ΔMIG3	4	4	4
ΔMIG1ΔMIG2ΔMIG3	19	166	234

Table 3.21. Significantly associated GO biological process terms of the target genes of the PRS of *ΔMIG1* mutant

GO Term	Cluster frequency	*p*-value
regulation of transcription by carbon catabolites	6 out of 113 genes, 5.3 per cent	0.0000117
monosaccharide transport	7 out of 113 genes, 6.2 per cent	0.000018
hexose transport	7 out of 113 genes, 6.2 per cent	0.000018
glucose transport	5 out of 113 genes, 4.4 per cent	0.0000345
carbohydrate transport	8 out of 113 genes, 7.1 per cent	0.0000595
carbohydrate metabolic process	19 out of 113 genes, 16.8 per cent	0.000066
cellular response to nutrient	6 out of 113 genes, 5.3 per cent	0.0000691
response to nutrient	6 out of 113 genes, 5.3 per cent	0.00014
hexose metabolic process	11 out of 113 genes, 9.7 per cent	0.00041
alcohol metabolic process	15 out of 113 genes, 13.3 per cent	0.0006
cellular carbohydrate metabolic process	17 out of 113 genes, 15.0 per cent	0.00087
fructose transport	3 out of 113 genes, 2.7 per cent	0.00123
regulation of transcription by glucose	4 out of 113 genes, 3.5 per cent	0.00126
monosaccharide metabolic process	11 out of 113 genes, 9.7 per cent	0.00142
glucose metabolic process	9 out of 113 genes, 8.0 per cent	0.00747

Table 3.22. Significantly associated GO biological process terms of the target genes of the PRS of *ΔMIG1ΔMIG2* mutant

GO Term	Cluster frequency	*p*-value
carbohydrate transport	11 out of 143 genes, 7.7 per cent	0.000000103
monosaccharide transport	9 out of 143 genes, 6.3 per cent	0.000000159
hexose transport	9 out of 143 genes, 6.3 per cent	0.000000159
glucose transport	6 out of 143 genes, 4.2 per cent	0.00000183
carbohydrate metabolic process	24 out of 143 genes, 16.8 per cent	0.00000203
cellular carbohydrate metabolic process	23 out of 143 genes, 16.1 per cent	0.00000492

Table 3.22. Significantly associated GO biological process terms of the target genes of the PRS of *ΔMIG1ΔMIG2* mutant (continued)

GO Term	Cluster frequency	*p*-value
alcohol metabolic process	20 out of 143 genes, 14.0 per cent	0.0000055
hexose metabolic process	14 out of 143 genes, 9.8 per cent	0.0000152
regulation of transcription by carbon catabolites	6 out of 143 genes, 4.2 per cent	0.0000604
monosaccharide metabolic process	14 out of 143 genes, 9.8 per cent	0.000076
response to chemical stimulus	22 out of 143 genes, 15.4 per cent	0.0001
cellular response to nutrient	6 out of 143 genes, 4.2 per cent	0.00035
response to nutrient	6 out of 143 genes, 4.2 per cent	0.00071
glucose metabolic process	11 out of 143 genes, 7.7 per cent	0.00154
fructose transport	3 out of 143 genes, 2.1 per cent	0.00314
regulation of transcription by glucose	4 out of 143 genes, 2.8 per cent	0.00404
cellular carbohydrate catabolic process	10 out of 143 genes, 7.0 per cent	0.00477
carbohydrate catabolic process	10 out of 143 genes, 7.0 per cent	0.00638

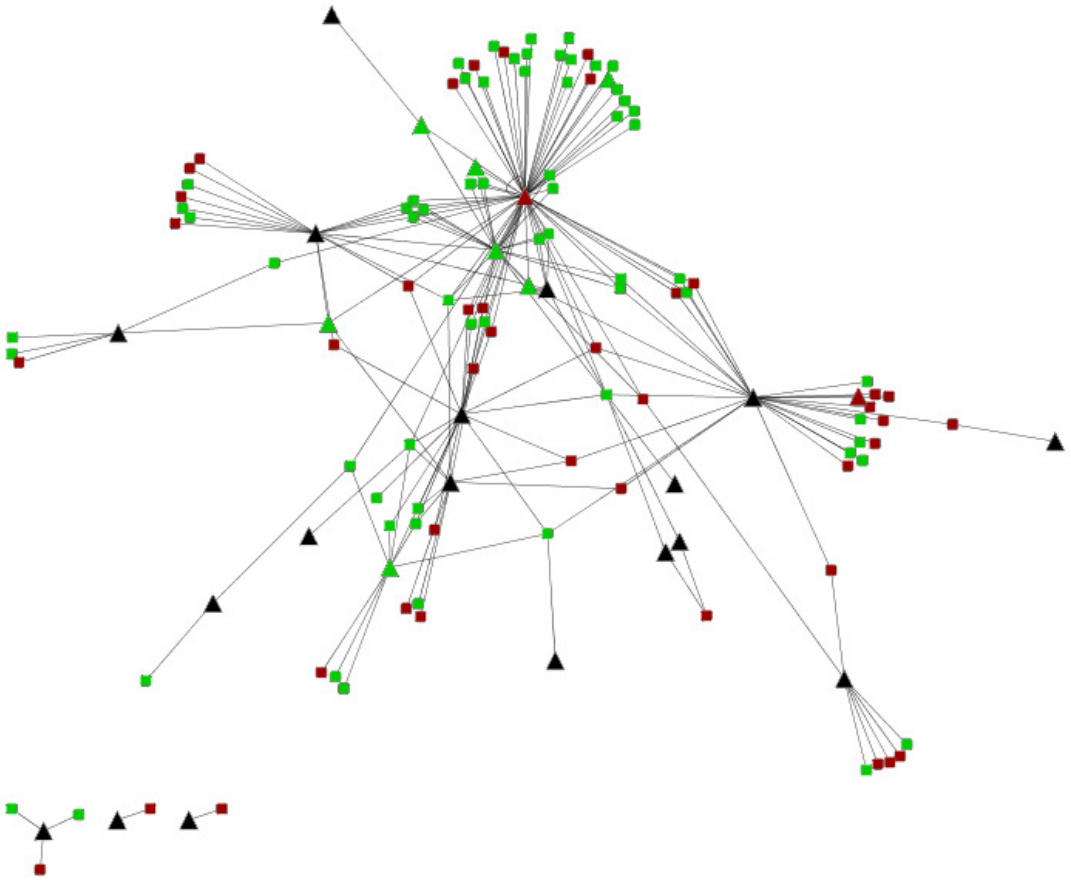

Figure 3.15. Representation of the PRS of *ΔMIG1* mutant (triangles and squares represent TFs and non-TF target genes, respectively)

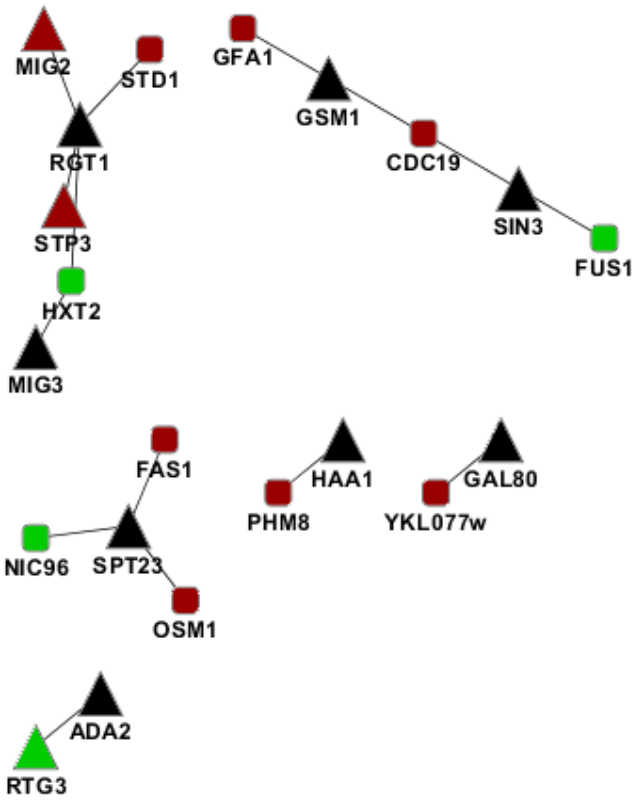

Figure 3.16. Representation of the PRS of *ΔMIG2* mutant (triangles and squares represent TFs and non-TF target genes, respectively)

Table 3.23. Significantly associated GO biological process terms of the target genes of the PRS of *ΔMIG3* mutant

GO Term	Cluster frequency	*p*-value
cellular process	2 out of 4 genes, 50.0 per cent	0

Table 3.24. Significantly associated GO biological process terms of the target genes of the PRS of *ΔMIG1ΔMIG2ΔMIG3* mutant

GO Term	Cluster frequency	*p*-value
carbohydrate transport	12 out of 166 genes, 7.2 per cent	3.01E-08
sulfur metabolic process	16 out of 166 genes, 9.6 per cent	1.89E-07
monosaccharide transport	9 out of 166 genes, 5.4 per cent	6.4E-07
hexose transport	9 out of 166 genes, 5.4 per cent	6.4E-07
glucose transport	6 out of 166 genes, 3.6 per cent	4.77E-06
carbohydrate metabolic process	24 out of 166 genes, 14.5 per cent	0.0000427
sulfur amino acid metabolic process	9 out of 166 genes, 5.4 per cent	0.000047
cellular carbohydrate metabolic process	23 out of 166 genes, 13.9 per cent	0.00009
regulation of transcription by carbon catabolites	6 out of 166 genes, 3.6 per cent	0.00016
alcohol metabolic process	19 out of 166 genes, 11.4 per cent	0.00034

Table 3.24. Significantly associated GO biological process terms of the target genes of the PRS of *ΔMIG1ΔMIG2ΔMIG3* mutant (continued)

GO Term	Cluster frequency	*p*-value
cellular response to nutrient	6 out of 166 genes, 3.6 per cent	0.00089
response to nutrient	6 out of 166 genes, 3.6 per cent	0.00178
small molecule metabolic process	40 out of 166 genes, 24.1 per cent	0.00208
hexose metabolic process	12 out of 166 genes, 7.2 per cent	0.00406
fructose transport	3 out of 166 genes, 1.8 per cent	0.00521
regulation of transcription by glucose	4 out of 166 genes, 2.4 per cent	0.00772
anion transport	6 out of 166 genes, 3.6 per cent	0.00944

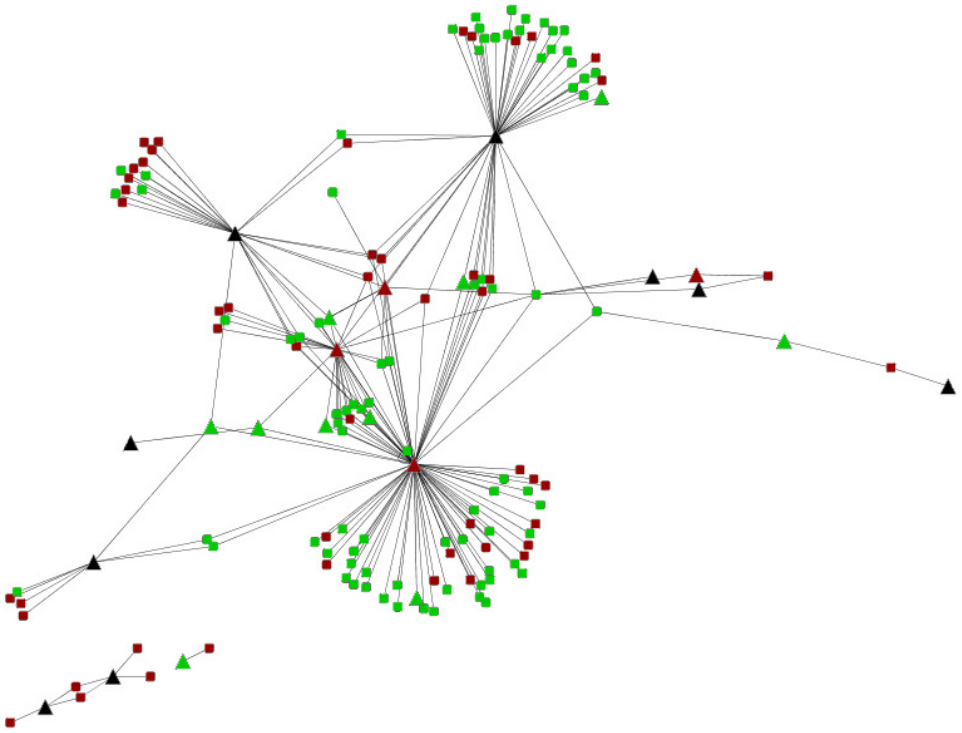

Figure 3.17. Representation of the PRS of *ΔMIG1ΔMIG2* mutant (triangles and squares represent TFs and non-TF target genes, respectively)

Figure 3.18. Representation of the PRS of *ΔMIG3* mutant (triangles and squares represent TFs and non-TF target genes, respectively)

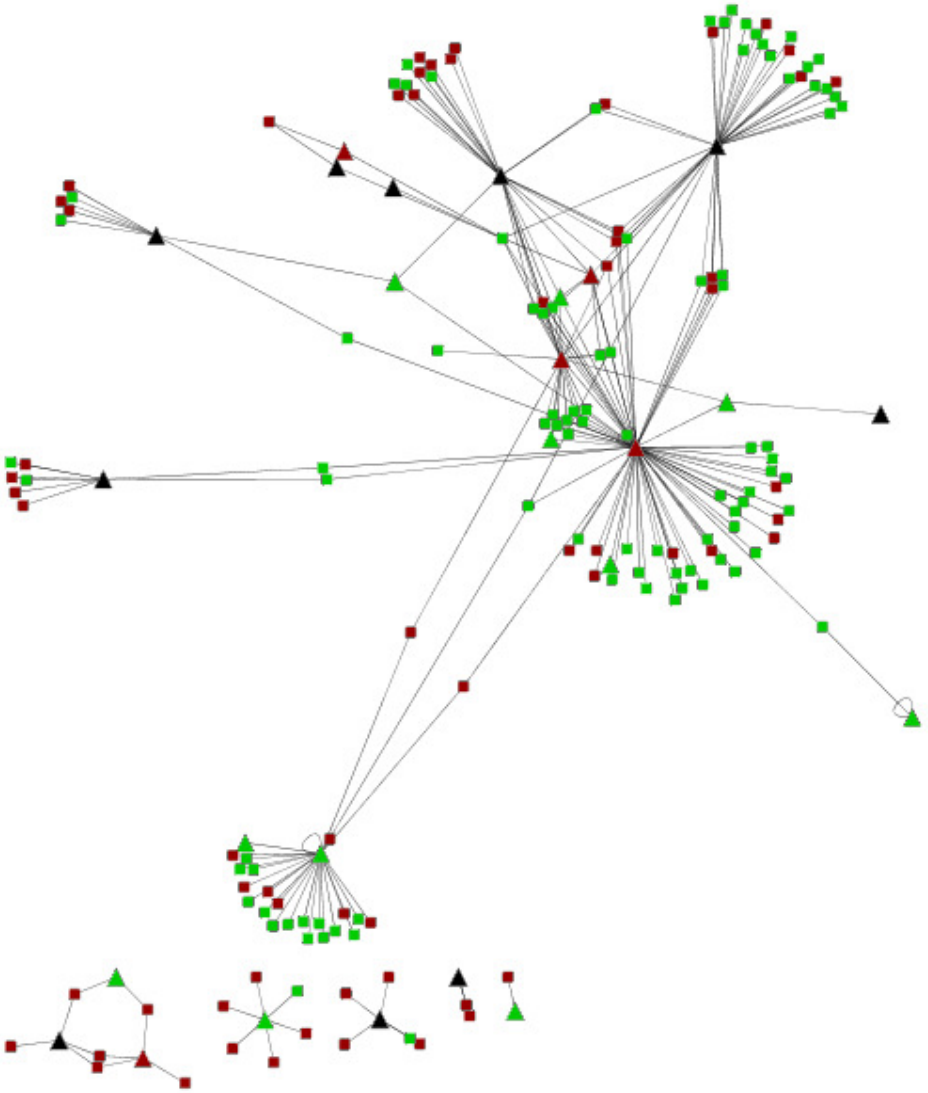

Figure 3.19. Representation of the PRS of *ΔMIG1ΔMIG2ΔMIG3* mutant (triangles and squares represent TFs and non-TF target genes, respectively)

The significantly associated GO terms of the PRSs of *ΔMIG1, ΔMIG1ΔMIG2* and *ΔMIG1ΔMIG2ΔMIG3* strains are very similar. "Regulation of transcription by carbon catabolites", "regulation of transcription by glucose", "cellular response to nutrient", "response to nutrient", "alcohol metabolic process", "carbohydrate transport", "cellular carbohydrate metabolic process", "glucose transport" and "fructose transport" were among the significantly associated GO terms of the PRSs of all three *MIG1* deletion mutants under investigation, almost with the same number of differentially expressed genes (Figure 3.20). This result is expected since Mig1p has a role in glucose repression pathway and represses

genes encoding enzymes of the tricarboxylic acid (TCA) cycle, electron transport chain, alternative carbon sources consumption, gluconeogenesis (Raghevendran *et al*., 2005).

MIG3 deletion has very little effect compared to *MIG1* deletion (Figure 3.20). The only GO term that was significantly associated only with the target genes of the PRS of *ΔMIG3* mutant was "cellular process".

Table 3.25. Number of genes annotated to significantly associated GO biological process terms of the PRS of *ΔMIG1*, *ΔMIG1ΔMIG2*, *ΔMIG3* and *ΔMIG1ΔMIG2ΔMIG3* mutants

GO Term	*ΔMIG1*	*ΔMIG1ΔMIG2*	*ΔMIG3*	*ΔMIG1ΔMIG2ΔMIG3*
alcohol metabolic process	15	20	0	19
anion transport	0	0	0	6
carbohydrate catabolic process	0	10	0	0
carbohydrate metabolic process	19	24	0	24
carbohydrate transport	8	11	0	12
cellular carbohydrate catabolic process	0	10	0	0
cellular carbohydrate metabolic process	17	23	0	23
cellular process	0	0	2	0
cellular response to nutrient	6	6	0	6
fructose transport	3	3	0	3
glucose metabolic process	9	11	0	0
glucose transport	5	6	0	6
hexose metabolic process	11	14	0	12
hexose transport	7	9	0	9
monosaccharide metabolic process	11	14	0	0
monosaccharide transport	7	9	0	9
regulation of transcription by carbon catabolites	6	6	0	6
regulation of transcription by glucose	4	4	0	4
response to chemical stimulus	0	22	0	0
response to nutrient	6	6	0	6
small molecule metabolic process	0	0	0	40
sulfur amino acid metabolic process	0	0	0	9
sulfur metabolic process	0	0	0	16

Deletion of all three *MIG1*, *MIG2* and *MIG3* genes causes a considerable collective change in the expression of the genes which are significantly associated with the processes "anion transport", "small molecule metabolic process", "sulfur amino acid metabolic process" and "sulfur metabolic process" (Table 3.25). These terms do not appear among the terms found for *ΔMIG1*, *ΔMIG3* and *ΔMIG1ΔMIG2* mutants. Moreover, deletion of

both *MIG1* and *MIG2* genes causes a significant change in the expression of the genes which are significantly associated with the processes "response to chemical stimulus", "carbohydrate catabolic process" and "cellular carbohydrate catabolic process", which do not appear among the terms found for *ΔMIG1* and *ΔMIG2* mutants.

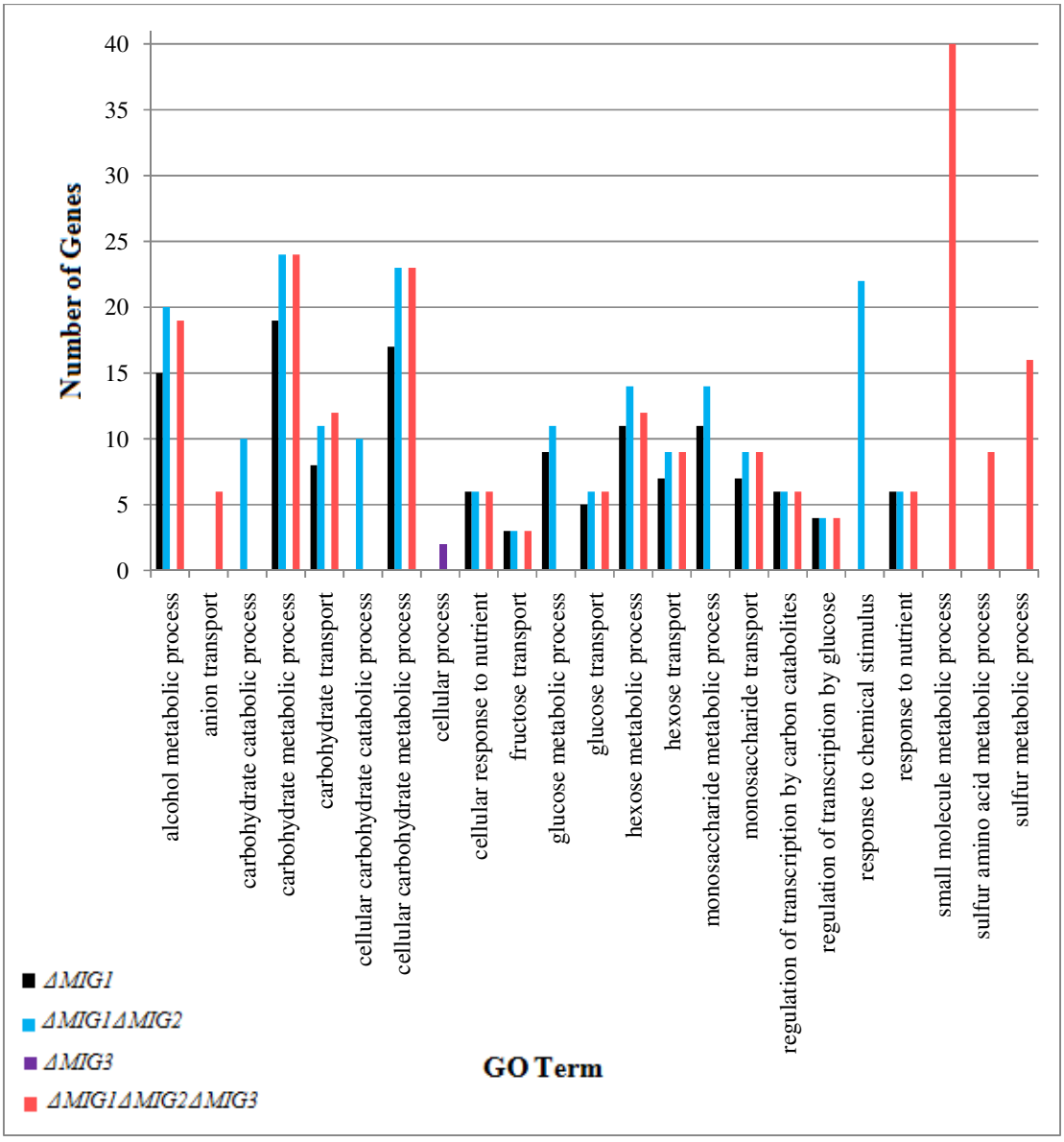

Figure 3.20. Significantly associated GO biological process terms of the target genes of the PRS of *ΔMIG1*, *ΔMIG1ΔMIG2*, *ΔMIG3* and *ΔMIG1ΔMIG2ΔMIG3* mutants

3.2.2.9. Regulation of Key Transcription Factors of *ΔMIG1*, *ΔMIG2*, *ΔMIG1ΔMIG2*, *ΔMIG3* and *ΔMIG1ΔMIG2ΔMIG3* mutants. Identification of key TFs demonstrates the

change in TF activity when passing from one condition to another, without *a priori* requirement of change in the transcription level of the TFs, because many TFs do not respond at transcriptional level per se, but through post-translational regulation. Regulation of key TFs was evaluated based whether the key TFs are significantly differentially expressed, as described in Section 2.4. Most of the key TFs of *ΔMIG1*, *ΔMIG2*, *ΔMIG3*, *ΔMIG1ΔMIG2* and *ΔMIG1ΔMIG2ΔMIG3* mutants were found to be regulated mainly post-transcriptionally (Table 3.26). In Table 3.27 and Table 3.28, regulation of each key TF is represented.

Table 3.26. Number of key TFs for *ΔMIG1, ΔMIG2, ΔMIG1ΔMIG2, ΔMIG3* and *ΔMIG1ΔMIG2ΔMIG3* mutants that were found to be mainly transcriptionally regulated (A) or mainly post-transcriptionally regulated (B)

Mutant	**Number of A**	**Number of B**
ΔMIG1	3	21
ΔMIG2	0	14
ΔMIG1ΔMIG2	6	12
ΔMIG3	1	14
ΔMIG1ΔMIG2ΔMIG3	10	12

Table 3.27. Regulation of key TFs of *ΔMIG1, ΔMIG2* and *ΔMIG1ΔMIG2* mutants

rank	***ΔMIG1***	**Case**	***ΔMIG2***	**Case**	***ΔMIG1ΔMIG2***	**Case**
1	Mig3p	B	Dig2p	B	Mig3p	A
2	Imp2'p	B	Gal80p	B	Mig2p	A
3	Dig2p	B	Ada2p	B	Hmlalpha1p	B
4	Mig2p	A	Mig3p	B	Swi1p	B
5	Gsm1p	B	Haa1p	B	Imp2'p	B
6	Swi3p	B	Gsm1p	B	Swi3p	A
7	Rds3p	B	Sin3p	B	Gsm1p	B
8	Swi1p	B	Swi3p	B	Hpc2p	B
9	Haa1p	B	Hmra2p	B	Rdr1p	A
10	Rgt1p	B	Swi1p	B	Rpn10p	B
11	Mig1p	A	Hmlalpha1p	B	Rgt1p	B
12	Rdr1p	B	Rgt1p	B	Mig1p	A
13	Gal80p	B	Spt23p	B	Gat4p	B
14	Stp3p	B	Lys14p	B	Rds3p	B
15	Nrg2p	B			Ada2p	B
16	YPR015c	A			Gal80p	A
17	Aca1p	B			Hmlalpha2p	B
18	Mga2p	B			Hmra2p	B

Table 3.27. Regulation of key TFs of *ΔMIG1, ΔMIG2* and *ΔMIG1ΔMIG2* mutants (continued)

rank	*ΔMIG1*	Case	*ΔMIG2*	Case	*ΔMIG1ΔMIG2*	Case
19	Mdl2p	B				
20	Rds2p	B				
21	Gat4p	B				
22	Bye1p	B				
23	Sut1p	B				
24	Ada2p	B				

Table 3.28. Regulation of key TFs of *ΔMIG3* and *ΔMIG1ΔMIG2ΔMIG3* mutants

rank	*ΔMIG3*	Case	*ΔMIG1ΔMIG2ΔMIG3*	Case
1	Dig2p	B	Hmlalpha1p	B
2	Mdl2p	B	Hmra2p	A
3	Aca1p	B	Mig3p	A
4	Haa1p	B	Mig2p	A
5	Ada2p	B	Imp2'p	B
6	Hpc2p	B	Gsm1p	B
7	Gal80p	B	Hpc2p	B
8	Hmlalpha2p	B	Gal80p	A
9	Hmlalpha1p	B	Rpn10p	B
10	Swi1p	B	Rtg2	B
11	Gsm1p	B	Haa1p	B
12	Swi3p	B	Mal13p	A
13	Mal13p	B	Rgt1p	B
14	Mig3p	A	Hmlalpha2p	A
15	Hmra1p	B	Swi3p	A
16			Mig1p	A
17			Gat4p	B
18			Swi1p	B
19			Kar4p	B
20			Ada2p	B
21			Mga2p	A
22			Met32p	A

3.2.3. Key TFs Responsive to Oxygen Availability Under Carbon Limitation Regime

Key TFs responsive to oxygen availability under carbon limitation regime (25 g L^{-1} glucose) were identified using the triplicate transcriptome data of Tai *et al.* (Tai *et al.*, 2005).

When the nodes of the yeast TRN which were not quantified in these transcriptome data were eliminated, the number of the nodes, regulatory interactions and TFs reduced to 5252, 37119 and 185, respectively. By using reporter features algorithm, 46 key TFs around which most transcriptional changes occur were identified as a response to oxygen availability under carbon limitation regime (Table 3.29). Key TFs were ranked from high to low $Z_{corrected,TF}$ score. $Z_{corrected,TF}$ scores, *p*-values and degrees for each key TF are represented in Table C.9.

Hap2p/3p/4p/5p complex was among the identified key TFs. The identification of Hap1p as a key TF responsible in cellular respiration is a meaningful result, since Hap1p was shown to be associated with the regulation of aerobiosis and is solely connected to the presence of oxygen. In addition, Hap4p, the regulatory subunit of the complex, has a role in both aerobic regulation and glucose derepression (Knijnenburg *et al.*, 2007).

Sut1p and Upc2p were also among the identified key TFs. These TFs have been shown to regulate anaerobically expressed genes in *S. cerevisiae* (Kwast *et al.*, 2002).

The algorithm also identified Rox1p and Cin5p as key TFs in response to oxygen availability (Clim). Rox1p, a heme-dependent transcriptional repressor of hypoxic genes, constitutes a multi-component TF loop together with Yap6p and Cin5p and these three TFs regulate each other (Knijnenburg *et al.*, 2007). Mot3p, involved in repression of a subset of hypoxic genes by Rox1p, repression of several DAN/TIR genes during aerobic growth, and repression of ergosterol biosynthetic genes, was also identified as a key TF.

Ume6p and Sin3p were found to be key TFs with very close scores. In fact, they are part of a complex formed by Ume6p, Sin3p and Rpd3p which regulates transcription of the phospholipid biosynthetic genes (Elkhaimi *et al.*, 2000).

There are twelve key TFs identified in both *ΔSNF1* and in response to oxygen availability under carbon limitation regime, but not in *ΔMIG1* (Cat8p, Cst6p, Elp6p, Gis1p, Hot1p, Oaf1p, Opi1p, Rtg2p, Sin3p, Sps18p, Xbp1p and Yrm1p) (Figure 3.21).

Cat8p and Adr1p were among the identified key TFs. In the study of Young *et al*. it was reported that Adr1p and Cat8p are active after diauxic transition in the glucose depletion, and when the energy generating metabolism has shifted to aerobic oxidation of non-fermentable carbon sources, which agrees well with the results of the present study (Young *et al*., 2003).

Oaf1p and Cst6p were also among the identified key TFs in response to oxygen availability (Clim). Oaf1p is an oleate-activated TF, which activates genes involved in β-oxidation of fatty acids, peroxisome organization and biogenesis (Usaite *et al*., 2009). Cst6p, which is also involved in the regulation of oleate responsive genes and in utilization of nonoptimal carbon sources, was also identified as a key TF.

Pip2p was also identified as a key TF. The promoters of genes encoding peroxisomal proteins and the enzymes of β-oxidation bind both Adr1 and the heterodimeric, oleate-responsive transcription factors Oaf1p and Pip2p (Ratnakumar *et al.*, 2009).

The algorithm identified Opi1p as a key TF. Wagner *et al*. have demonstrated that Opi1p interacts with Sin3p affecting a large number of regulatory systems in yeast and higher eukaryotes (Wagner *et al*., 2001). Zhang *et al*. have suggested that Snf1p activates Opi1p, which represses phospholipid biosynthesis (Sreenivas and Carman, 2003; Zhang *et al*., 2010). Gis1p, which is reported to be involved in phospholipid metabolic process and in expression of genes during nutrient limitation, was also identified as a key TF.

Rtg2p, which regulates the subcellular localization of Rtg1p and Rtg3p transcriptional activators of retrograde (RTG) and TOR pathways, and Elp6p, which is involved in protein urmylation, were identified as key TFs. Loss of urmylation pathway was reported to cause invasive growth and confers sensitivity to rapamycin due to genetic interactions with TOR pathway (Goehring et al., 2003). Elp6p may play a role in a pathway related to alternative carbon sources, since Δ*ELP6* strains were shown to be slow to adapt to a change in carbon source from glucose to galactose (Krogan and Greenblatt, 2001).

Xbp1p and Hot1p, TFs that are involved in stress response were also identified as key TFs. The algorithm has also identified Sin3p, which is involved in chromatin remodeling, as a key TF.

Although not identified in *ΔSNF1* as a key TF, Sip4p, activating the carbon source-responsive element (CSRE) of gluconeogenic genes, involved in the positive regulation of gluconeogenesis and regulated by Snf1p protein kinase, was identified as a key TF in response to oxygen availability.

There are six key TFs identified in both *ΔMIG1* and in response to oxygen availability under carbon limitation regime, but not in *ΔSNF1* (Mig1p, Nrg2p, Rdr1p, Rds2p, Stp3p and YPR015c) (Figure 3.21).

Mig1p, Nrg1p and Nrg2p were among the identified key TFs in response to oxygen availability (Clim). It was suggested that Nrg1p and Nrg2p are direct or indirect targets of the Snf1p kinase and function in glucose repression of a subset of Snf1p-regulated genes (Vyas *et al.*, 2001). Nrg1p was identified as a third repressor required for glucose repression in addition to Mig1p and Mig2p (Zhou and Winston, 2001).

Rds2p, involved in the use of nonfermentable carbon sources, and Rdr1p, controlling multidrug resistance, were also identified as key TFs.

Although not identified in *ΔMIG1* as a key TF, Sko1p, which forms a complex with Tup1p and Ssn6p to both activate and repress transcription and which is involved in oxidative stress responses, was identified as a key TF in response to oxygen availability. Active Mig1p interacts with the co-repressors Ssn6p and Tup1p and binds to the promoters of various genes, including genes encoding enzymes of the tricarboxylic acid (TCA) cycle, electron transport chain, alternative carbon sources consumption, gluconeogenesis, and represses the transcription of those genes (Sanz *et al.*, 2000).

There are seven key TFs identified in *ΔSNF1*, *ΔMIG1* and in response to oxygen availability under carbon limitation regime (Aca1p, Ada2p, Bye1, Gsm1p, Sut1p, Swi1p and Swi3p) (Figure 3.21).

The algorithm identified Gsm1p as a key TF, which is implicated in the use of nonfermentable carbon sources and target gluconeogenic genes. Gluconeogenesis (generation of glucose from non-carbohydrate carbon substrates) is essential for the growth of yeast cells on nonfermentable carbon sources (Turcotte *et al*., 2009). Moreover, Aca1p, involved in utilization of nonoptimal carbon sources, was also among the key TFs identified as a response to oxygen availability under carbon limitation regime (Garcia-Gimeno and Struhl, 2000).

Key TFs Ada2p, Swi1p and Swi3p are involved in chromatin remodeling, and Sut1p is involved in stress response.

The algorithm identified key TFs that are involved in cellular carbohydrate metabolic process (i.e., Adr1p, Hap2p/3p/4p/5p), phospholipid metabolic process (i.e., Gis1p, Opi1p), fatty acid metabolic process (i.e., Oaf1p, Pip2p), oxidative phosphorylation (i.e., Gsm1p), aerobic respiration (i.e., Hap1p) and response to stress (i.e., Xbp1p). Hap2p, Hap3p, Hap4p and Hap5p were counted as one TF because they form a complex. These findings are totally consistent with the study of Kwast *et al.* which showed that half of the anaerobically induced genes fit into four functional categories: cell wall related; lipid, fatty acid, and isoprenoid metabolism; carbohydrate metabolism; and cell stress.

To sum up, as a response to oxygen availability under carbon limitation regime key TFs known to be involved in regulation of aerobiosis/anaerobiosis were identified. In addition, TFs that are involved in glucose repression and derepression and TFs known to be positively regulated by Snf1p kinase (Cat8p, Adr1p and Opi1p) were identified as key TFs. In fact, Snf1p kinase is involved in the switch from fermentative/anaerobic to oxidative metabolism (Sutherland *et al.*, 2003). These results seem to contradict the results of Linde *et al*., who found that the majority of genes involved in respiratory sugar metabolism (e.g., those encoding enzymes of the tricarboxylic acid cycle or proteins involved in respiration) show little or no repression under anaerobic conditions in glucose-limited chemostat (Linde *et al*., 1999). On the other hand; even a direct comparison may not be valid, these results confirm the study of Kwast *et al*., who showed that the effect of oxygen availability (in growth on galactose) on respiratory and TCA cycle genes is exerted at the transcriptional level (Kwast *et al*., 2002).

Table 3.29. Key TFs identified responsive to oxygen availability under carbon limitation regime

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
1	Elp6p (YMR312w)	7	Subunit of Elongator complex, which is required for modification of wobble nucleosides in tRNA; required for Elongator structural integrity • protein urmylation • regulation of transcription from RNA polymerase II promoter • tRNA wobble uridine modification
2	Ada2p (YDR448w)	8	Transcription coactivator, component of the ADA and SAGA transcriptional adaptor/HAT (histone acetyltransferase) complexes • chromatin modification • chromatin silencing at rDNA • chromatin silencing at telomere • positive regulation of histone acetylation • regulation of transcription from RNA polymerase II promoter
3	Swi1p (YPL016w)	13	Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2; can form the prion [SWI+] • ATP-dependent chromatin remodeling • positive regulation of transcription, DNA-dependent • regulation of transcription from RNA polymerase II promoter
4	Swi3p (YJL176c)	8	Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2 • ATP-dependent chromatin remodeling • positive regulation of transcription, DNA-dependent
5	Cat8p (YMR280c)	126	Zinc cluster transcriptional activator necessary for derepression of a variety of genes under non-fermentative growth conditions, active after diauxic shift, binds carbon source responsive elements • positive regulation of gluconeogenesis • positive regulation of transcription from RNA polymerase II promoter
6	Pip2p (YOR363c)	131	Autoregulatory oleate-specific transcriptional activator of peroxisome proliferation, contains Zn(2)-Cys(6) cluster domain, forms heterodimer with Oaf1p, binds oleate response elements (OREs), activates beta-oxidation genes • fatty acid metabolic process • peroxisome organization • positive regulation of transcription
7	Aca1p (YER045c)	26	Basic leucine zipper (bZIP) transcription factor of the ATF/CREB family, may regulate transcription of genes involved in utilization of non-optimal carbon sources • transcription initiation from RNA polymerase II promoter

Table 3.29. Key TFs identified responsive to oxygen availability under carbon limitation regime (continued)

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
8	Sut1p (YGL162w)	77	Transcription factor of the Zn[II]2Cys6 family involved in sterol uptake; involved in induction of hypoxic gene expression • regulation of transcription • regulation of transcription from RNA polymerase II promoter • sterol transport
9	Xbp1p (YIL101c)	168	Transcriptional repressor that binds to promoter sequences of the cyclin genes, CYS3, and SMF2; expression is induced by stress or starvation during mitosis, and late in meiosis; member of the Swi4p/Mbp1p family; potential Cdc28p substrate • response to stress
10	Stp3p (YLR375w)	28	Zinc-finger protein of unknown function, possibly involved in pre-tRNA splicing and in uptake of branched-chain amino acids • biological process unknown
11	Gis1p (YDR096w)	173	JmjC domain-containing histone demethylase; transcription factor involved in expression of genes during nutrient limitation and in negative regulation of DPP1 and PHR1; activity is modulated by limited proteasome-mediated proteolysis • ascospore wall assembly • histone demethylation • phospholipid metabolic process
12	Nrg2p (YBR066c)	156	Transcriptional repressor that mediates glucose repression and negatively regulates filamentous growth; has similarity to Nrg1p • biofilm formation • invasive growth in response to glucose limitation • pseudohyphal growth
13	Oaf1p (YAL051w)	237	Oleate-activated transcription factor, acts alone and as a heterodimer with Pip2p; activates genes involved in beta-oxidation of fatty acids and peroxisome organization and biogenesis fatty acid metabolic process • negative regulation of transcription • peroxisome organization • positive regulation of transcription
14	Rds2p (YPL133c)	42	Zinc cluster transcriptional activator involved in conferring resistance to ketoconazole • positive regulation of gluconeogenesis • response to xenobiotic stimulus
15	Cst6p (YIL036w)	177	Basic leucine zipper (bZIP) transcription factor of the ATF/CREB family, proposed to be a regulator of oleate responsive genes; involved in utilization of non-optimal carbon sources and chromosome stability • cellular response to oleic acid • DNA metabolic process • transcription initiation from RNA polymerase II promoter
16	Sps18p (YNL204c)	58	Protein of unknown function, contains a putative zinc-binding domain; expressed during sporulation • sporulation resulting in formation of a cellular spore

Table 3.29. Key TFs identified responsive to oxygen availability under carbon limitation regime (continued)

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
17	Hot1p (YMR172w)	71	Transcription factor required for the transient induction of glycerol biosynthetic genes GPD1 and GPP2 in response to high osmolarity; targets Hog1p to osmostress responsive promoters; has similarity to Msn1p and Gcr1p • hyperosmotic response • regulation of transcription from RNA polymerase II promoter
18	Rtg2p (YGL252c9	9	Sensor of mitochondrial dysfunction; regulates the subcellular location of Rtg1p and Rtg3p, transcriptional activators of the retrograde (RTG) and TOR pathways; Rtg2p is inhibited by the phosphorylated form of Mks1p • extrachromosomal rDNA circle accumulation involved in replicative cell aging • intracellular signaling pathway • mitochondria-nucleus signaling pathway
19	Gsm1p (YJL103c)	23	Putative zinc cluster protein of unknown function; proposed to be involved in the regulation of energy metabolism, based on patterns of expression and sequence analysis • oxidative phosphorylation
20	Hap1p (YLR256w9	176	Zinc finger transcription factor involved in the complex regulation of gene expression in response to levels of heme and oxygen; the S288C sequence differs from other strain backgrounds due to a Ty1 insertion in the carboxy terminus • aerobic respiration • positive regulation of transcription from RNA polymerase II promoter
21	Mot3p (YMR070w)	131	Nuclear transcription factor with two Cys2-His2 zinc fingers; involved in repression of a subset of hypoxic genes by Rox1p, repression of several DAN/TIR genes during aerobic growth, and repression of ergosterol biosynthetic genes • negative regulation of transcription from RNA polymerase II promoter • transcription
22	Opi1p (YHL020c)	30	Transcriptional regulator of a variety of genes; phosphorylation by protein kinase A stimulates Opi1p function in negative regulation of phospholipid biosynthetic genes; involved in telomere maintenance • endoplasmic reticulum unfolded protein response • negative regulation of transcription from RNA polymerase II promoter • phospholipid biosynthetic process • positive regulation of transcription from RNA polymerase II promoter
23	Hap4p (YKL109w)	392	Subunit of the heme-activated, glucose-repressed Hap2p/3p/4p/5p CCAAT-binding complex, a transcriptional activator and global regulator of respiratory gene expression; provides the principal activation function of the complex • regulation of carbohydrate metabolic process • transcription
24	Bye1p (YKL005c)	23	Negative regulator of transcription elongation, contains a TFIIS-like domain and a PHD finger, multicopy suppressor of temperature-sensitive ess1 mutations, probably binds RNA polymerase II large subunit • negative regulation of transcription from RNA polymerase II promoter

Table 3.29. Key TFs identified responsive to oxygen availability under carbon limitation regime (continued)

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
25	Cdc14p (YFR028c)	60	Protein phosphatase required for mitotic exit; located in the nucleolus until liberated by the FEAR and Mitotic Exit Network in anaphase, enabling it to act on key substrates to effect a decrease in CDK/B-cyclin activity and mitotic exit • mitotic cell cycle • nucleolus organization • protein amino acid dephosphorylation • regulation of exit from mitosis
26	Nrg1p (YDR043c)	353	Transcriptional repressor that recruits the Cyc8p-Tup1p complex to promoters; mediates glucose repression and negatively regulates a variety of processes including filamentous growth and alkaline pH response • biofilm formation • glucose metabolic process • invasive growth in response to glucose limitation • pseudohyphal growth • regulation of transcription from RNA polymerase II promoter • response to pH
27	Hmra2p (YCR096c)	25	Silenced copy of a2 at HMR; similarity to Alpha2p; required along with a1p for inhibiting expression of the HO endonuclease in a/alpha HO/HO diploid cells with an active mating-type interconversion system • biological process unknown
28	Adr1p (YDR216w)	421	Carbon source-responsive zinc-finger transcription factor, required for transcription of the glucose-repressed gene ADH2, of peroxisomal protein genes, and of genes required for ethanol, glycerol, and fatty acid utilization • negative regulation of transcription from RNA polymerase II promoter by glucose • peroxisome organization • regulation of carbohydrate metabolic process • transcription
29	YPR015c (YPR015c)	55	Putative protein of unknown function; overexpression causes a cell cycle delay or arrest • Putative protein of unknown function; overexpression causes a cell cycle delay or arrest • biological process unknown
30	Upc2p (YDR213w)	194	Sterol regulatory element binding protein, induces transcription of sterol biosynthetic genes and of DAN/TIR gene products; Ecm22p homolog; relocates from intracellular membranes to perinuclear foci on sterol depletion • steroid metabolic process • sterol biosynthetic process
31	Rme1p (YGR044c)	204	Zinc finger protein involved in control of meiosis; prevents meiosis by repressing IME1 expression and promotes mitosis by activating CLN2 expression; directly repressed by a1-alpha2 regulator; mediates cell type control of sporulation • meiosis • negative regulation of transcription from RNA polymerase II promoter

Table 3.29. Key TFs identified responsive to oxygen availability under carbon limitation regime (continued)

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
32	Hap5p (YOR358w)	182	Subunit of the heme-activated, glucose-repressed Hap2/3/4/5 CCAAT-binding complex, a transcriptional activator and global regulator of respiratory gene expression; required for assembly and DNA binding activity of the complex • regulation of carbohydrate metabolic process • transcription
33	Sin3p (YOL004w)	27	Component of the Sin3p-Rpd3p histone deacetylase complex, involved in transcriptional repression and activation of diverse processes, including mating-type switching and meiosis; involved in the maintenance of chromosomal integrity • chromatin silencing at rDNA • chromatin silencing at silent mating-type cassette • chromatin silencing at telomere • double-strand break repair via nonhomologous end joining • histone deacetylation • negative regulation of transcription from RNA polymerase II promoter • negative regulation of transposition, RNA-mediated • positive regulation of gene-specific transcription from RNA polymerase II promoter • positive regulation of transcription from RNA polymerase II promoter
34	Ume6p (YDR207c)	227	Key transcriptional regulator of early meiotic genes, binds URS1 upstream regulatory sequence, couples metabolic responses to nutritional cues with initiation and progression of meiosis, forms complex with Ime1p, and also with Sin3p-Rpd3p • ascospore formation • chromosome organization • histone deacetylation • negative regulation of transcription, mitotic • positive regulation of gene-specific transcription from RNA polymerase II promoter • positive regulation of meiosis • reciprocal meiotic recombination
35	Sip4p (YJL089w)	104	C6 zinc cluster transcriptional activator that binds to the carbon source-responsive element (CSRE) of gluconeogenic genes; involved in the positive regulation of gluconeogenesis; regulated by Snf1p protein kinase; localized to the nucleus • invasive growth in response to glucose limitation • positive regulation of gluconeogenesis • regulation of transcription from RNA polymerase II promoter
36	Hap3p (YBL021c)	168	Subunit of the heme-activated, glucose-repressed Hap2p/3p/4p/5p CCAAT-binding complex, a transcriptional activator and global regulator of respiratory gene expression; contains sequences contributing to both complex assembly and DNA binding • regulation of carbohydrate metabolic process • transcription

Table 3.29. Key TFs identified responsive to oxygen availability under carbon limitation regime (continued)

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
37	Mig1p (YGL035c)	216	Transcription factor involved in glucose repression; sequence specific DNA binding protein containing two Cys2His2 zinc finger motifs; regulated by the SNF1 kinase and the GLC7 phosphatase • negative regulation of transcription from RNA polymerase II promoter by glucose
38	Rox1p (YPR065w)	339	Heme-dependent repressor of hypoxic genes; contains an HMG domain that is responsible for DNA bending activity • negative regulation of gene-specific transcription from RNA polymerase II promoter
39	Rdr1p (YOR380w)	9	Transcriptional repressor involved in the control of multidrug resistance; negatively regulates expression of the PDR5 gene; member of the Gal4p family of zinc cluster proteins • response to xenobiotic stimulus
40	Hms1p (YOR032c)	205	Basic helix-loop-helix (bHLH) protein with similarity to myc-family transcription factors; overexpression confers hyperfilamentous growth and suppresses the pseudohyphal filamentation defect of a diploid mep1 mep2 homozygous null mutant • pseudohyphal growth
41	Cin5p (YOR028c)	395	Basic leucine zipper (bZIP) transcription factor of the yAP-1 family, mediates pleiotropic drug resistance and salt tolerance; nuclearly localized under oxidative stress and sequestered in the cytoplasm by Lot6p under reducing conditions • regulation of transcription from RNA polymerase II promoter • response to drug • response to salt stress
42	Hap2p (YGL237c)	175	Subunit of the heme-activated, glucose-repressed Hap2p/3p/4p/5p CCAAT-binding complex, a transcriptional activator and global regulator of respiratory gene expression; contains sequences sufficient for both complex assembly and DNA binding • regulation of carbohydrate metabolic process • transcription
43	Mac1p (YMR021c)	92	Copper-sensing transcription factor involved in regulation of genes required for high affinity copper transport • cellular cadmium ion homeostasis • positive regulation of transcription from RNA polymerase II promoter • regulation of protein catabolic process
44	Stp2p (YHR006w9	293	Transcription factor, activated by proteolytic processing in response to signals from the SPS sensor system for external amino acids; activates transcription of amino acid permease genes • positive regulation of transcription from RNA polymerase II promoter
45	Sko1p (YNL167c)	309	Basic leucine zipper (bZIP) transcription factor of the ATF/CREB family, forms a complex with Tup1p and Ssn6p to both activate and repress transcription; cytosolic and nuclear protein involved in osmotic and oxidative stress responses • negative regulation of transcription from RNA polymerase II promoter

Table 3.29. Key TFs identified responsive to oxygen availability under carbon limitation regime (continued)

Rank	TF (ORF Name)	degree (*k*)	SGD Definition & GO Biological Process Terms
46	Yrm1p (YOR172w)	23	Zn2-Cys6 zinc-finger transcription factor that activates genes involved in multidrug resistance; paralog of Yrr1p, acting on an overlapping set of target genes • drug transmembrane transport • positive regulation of transcription from RNA polymerase II promoter

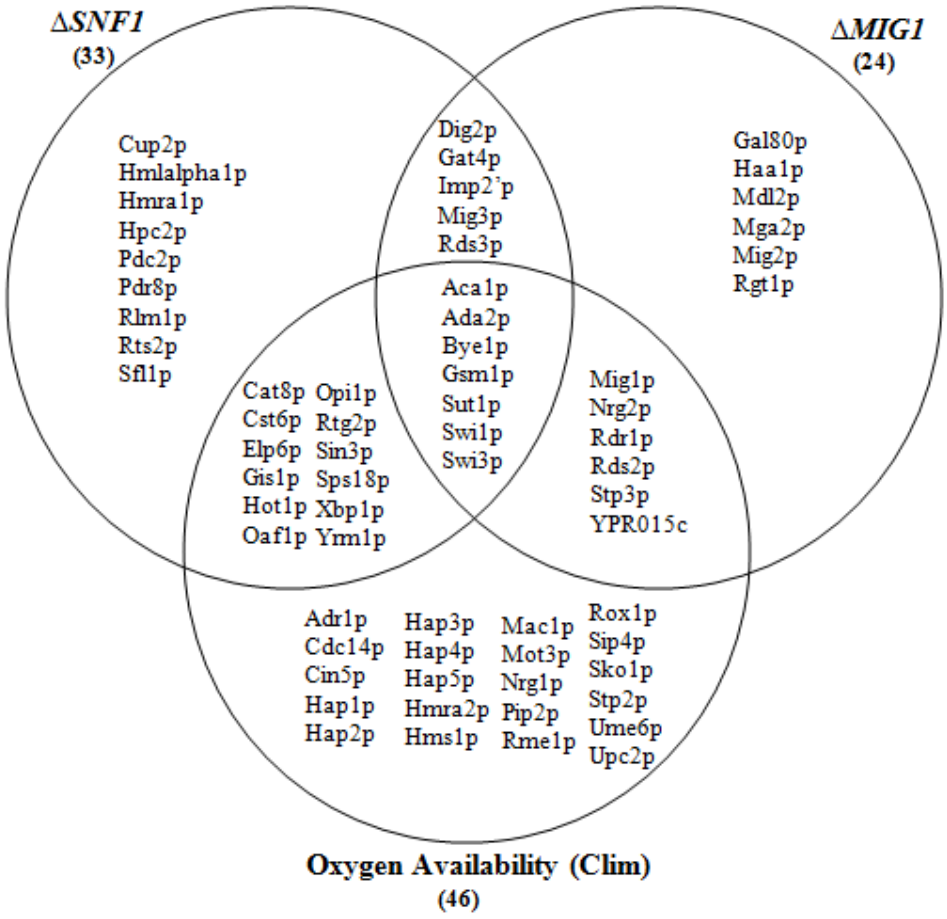

Figure 3.21. Comparison of the key TFs identified for *ΔSNF1*, *ΔMIG1* and as a response to oxygen availability under carbon limitation regime (the number of key TFs for each specific mutant is given in brackets)

Significant shared GO biological process terms (p-value<0.01) of 46 key TFs identified as a response to oxygen availability under carbon limitation regime were further identified (Table D.12). These key TFs were found to be enriched significantly with very general GO biological process terms, such as "regulation of cellular biosynthetic process"

(p-value=9.49x10^{-18}), as well as with a more specific GO biological process term, such as "positive regulation of gluconeogenesis" (p-value=0.00054), "positive regulation of cellular carbohydrate metabolic process" (p-value=0.00299) and "positive regulation of glucose metabolic process" (p-value=0.00299). GO term with the lowest p-value was found to be "transcription" (p-value=2.33x10^{-23}), as expected.

3.2.3.1. Perturbation-Responsive Subnetwork Responsive to Oxygen Availability (Clim).

Perturbation responsive subnetworks (PRS) were constructed between the key TFs and their differentially expressed target genes (p-value<0.05) responsive to the same perturbation. The numbers of key TFs, their target genes and interactions in the perturbation-responsive subnetwork responsive to oxygen availability under carbon limitation regime are given in Table 3.30. The overview of this subnetwork produced in Cytoscape is displayed in Figure 3.22, where the up- (green) or down-regulation (red) of the key TFs and their differentially expressed target genes in aerobic condition with respect to anaerobic condition are indicated. Key TFs indicated in black in this figure were found to be not significantly expressed in this study. Therefore they are considered to be post-transcriptionally regulated (Table 3.33). GO biological process terms significantly associated with the target genes in the PRS (p-value<0.01) were identified and represented in Table 3.31.

Table 3.30. The numbers of TFs, their target genes and interactions for the PRS responsive to oxygen availability (Clim)

Number of Key TFs	Number of Target Genes	Number of Interactions
46	873	2800

Table 3.31. Significantly associated GO biological process terms of the target genes of the PRS responsive to oxygen availability (Clim)

GO Term	Cluster frequency	p-value
small molecule metabolic process	201 out of 873 genes, 23.0 per cent	2.54E-21
monocarboxylic acid metabolic process	62 out of 873 genes, 7.1 per cent	2.63E-19
carboxylic acid metabolic process	107 out of 873 genes, 12.3 per cent	1.01E-18
oxoacid metabolic process	107 out of 873 genes, 12.3 per cent	1.01E-18
organic acid metabolic process	107 out of 873 genes, 12.3 per cent	1.3E-18
cellular ketone metabolic process	108 out of 873 genes, 12.4 per cent	1.17E-17
generation of precursor metabolites and energy	67 out of 873 genes, 7.7 per cent	1.57E-14
cofactor metabolic process	61 out of 873 genes, 7.0 per cent	3.84E-12
energy derivation by oxidation of organic compounds	54 out of 873 genes, 6.2 per cent	6.79E-12

Table 3.31. Significantly associated GO biological process terms of the target genes of the PRS responsive to oxygen availability (Clim) (continued)

GO Term	Cluster frequency	*p*-value
oxidative phosphorylation	27 out of 873 genes, 3.1 per cent	6.65E-11
small molecule biosynthetic process	87 out of 873 genes, 10.0 per cent	1.06E-09
cellular respiration	39 out of 873 genes, 4.5 per cent	4.35E-09
small molecule catabolic process	49 out of 873 genes, 5.6 per cent	4.78E-09
organic acid catabolic process	27 out of 873 genes, 3.1 per cent	6.67E-09
carboxylic acid catabolic process	27 out of 873 genes, 3.1 per cent	6.67E-09
electron transport chain	19 out of 873 genes, 2.2 per cent	9.3E-09
respiratory electron transport chain	19 out of 873 genes, 2.2 per cent	9.3E-09
ATP synthesis coupled electron transport	19 out of 873 genes, 2.2 per cent	9.3E-09
mitochondrial ATP synthesis coupled electron transport	19 out of 873 genes, 2.2 per cent	9.3E-09
oxidation reduction	19 out of 873 genes, 2.2 per cent	9.3E-09
coenzyme metabolic process	45 out of 873 genes, 5.2 per cent	4.57E-08
fatty acid metabolic process	24 out of 873 genes, 2.7 per cent	0.000000169
nucleoside phosphate metabolic process	45 out of 873 genes, 5.2 per cent	0.000000243
nucleotide metabolic process	45 out of 873 genes, 5.2 per cent	0.000000243
cellular nitrogen compound biosynthetic process	66 out of 873 genes, 7.6 per cent	0.000000659
fatty acid oxidation	10 out of 873 genes, 1.1 per cent	0.000000766
lipid oxidation	10 out of 873 genes, 1.1 per cent	0.000000766
fatty acid catabolic process	10 out of 873 genes, 1.1 per cent	0.000000766
alcohol metabolic process	60 out of 873 genes, 6.9 per cent	0.00000112
nicotinamide nucleotide metabolic process	22 out of 873 genes, 2.5 per cent	0.00000173
nucleobase, nucleoside and nucleotide metabolic process	50 out of 873 genes, 5.7 per cent	0.00000262
transmembrane transport	48 out of 873 genes, 5.5 per cent	0.00000548
fatty acid beta-oxidation	9 out of 873 genes, 1.0 per cent	0.00000634
pyridine nucleotide metabolic process	22 out of 873 genes, 2.5 per cent	0.00000802
lipid metabolic process	64 out of 873 genes, 7.3 per cent	0.0000107
ion transport	39 out of 873 genes, 4.5 per cent	0.0000128
cofactor catabolic process	13 out of 873 genes, 1.5 per cent	0.00011
organic acid transport	24 out of 873 genes, 2.7 per cent	0.00013
aerobic respiration	28 out of 873 genes, 3.2 per cent	0.00014
organic acid biosynthetic process	41 out of 873 genes, 4.7 per cent	0.00015
carboxylic acid biosynthetic process	41 out of 873 genes, 4.7 per cent	0.00015
NADH metabolic process	10 out of 873 genes, 1.1 per cent	0.00015
acetyl-CoA metabolic process	14 out of 873 genes, 1.6 per cent	0.00019
ion transmembrane transport	16 out of 873 genes, 1.8 per cent	0.00021
purine ribonucleotide biosynthetic process	16 out of 873 genes, 1.8 per cent	0.00021
acetyl-CoA catabolic process	11 out of 873 genes, 1.3 per cent	0.00023
tricarboxylic acid cycle	11 out of 873 genes, 1.3 per cent	0.00023
ribonucleotide biosynthetic process	17 out of 873 genes, 1.9 per cent	0.00025
carboxylic acid transport	23 out of 873 genes, 2.6 per cent	0.00043
oxidoreduction coenzyme metabolic process	23 out of 873 genes, 2.6 per cent	0.00043
catabolic process	117 out of 873 genes, 13.4 per cent	0.00051
coenzyme catabolic process	12 out of 873 genes, 1.4 per cent	0.00055
glutamate metabolic process	11 out of 873 genes, 1.3 per cent	0.00057
heterocycle metabolic process	48 out of 873 genes, 5.5 per cent	0.00074
lipid modification	14 out of 873 genes, 1.6 per cent	0.00123
cation transport	30 out of 873 genes, 3.4 per cent	0.00127

Table 3.31. Significantly associated GO biological process terms of the target genes of the PRS responsive to oxygen availability (Clim) (continued)

GO Term	Cluster frequency	*p*-value
NAD metabolic process	13 out of 873 genes, 1.5 per cent	0.00169
NADH oxidation	8 out of 873 genes, 0.9 per cent	0.00188
nucleotide biosynthetic process	23 out of 873 genes, 2.6 per cent	0.00376
cellular lipid metabolic process	50 out of 873 genes, 5.7 per cent	0.0048
purine nucleotide biosynthetic process	16 out of 873 genes, 1.8 per cent	0.00564
amine metabolic process	57 out of 873 genes, 6.5 per cent	0.00694
amine catabolic process	17 out of 873 genes, 1.9 per cent	0.00758
nucleobase, nucleoside and nucleotide biosynthetic process	26 out of 873 genes, 3.0 per cent	0.0087
nucleobase, nucleoside, nucleotide and nucleic acid biosynthetic process	26 out of 873 genes, 3.0 per cent	0.0087

As expected, “cellular respiration” and “aerobic respiration” are among the significantly associated GO terms of the PRS responsive to oxygen availability. In addition, the terms “respiratory electron transport chain” and “tricarboxylic acid cycle” are clearly related to the respiration. The appearance of the terms “fatty acid metabolic process” and “lipid metabolic process” is consistent with the study of Kwast *et al.*, which revealed that half of the anaerobically induced genes fit into four functional categories: cell wall related; lipid, fatty acid, and isoprenoid metabolism; carbohydrate metabolism; and cell stress (Kwast *et al.*, 2002).

3.2.3.2. Regulation of Key Transcription Factors Responsive to Oxygen Availability (Clim). Identification of key TFs demonstrates the change in TF activity when passing from one condition to another, without *a priori* requirement of change in the transcription level of the TFs, because many TFs do not respond at transcriptional level per se, but through post-translational regulation. Regulation of key TFs was evaluated based whether the key TFs are significantly differentially expressed. Half of the key TFs responsive to oxygen availability (Clim) were found to be regulated mainly transcriptionally (Table 3.32). In Table 3.33, regulation of each key TF is represented.

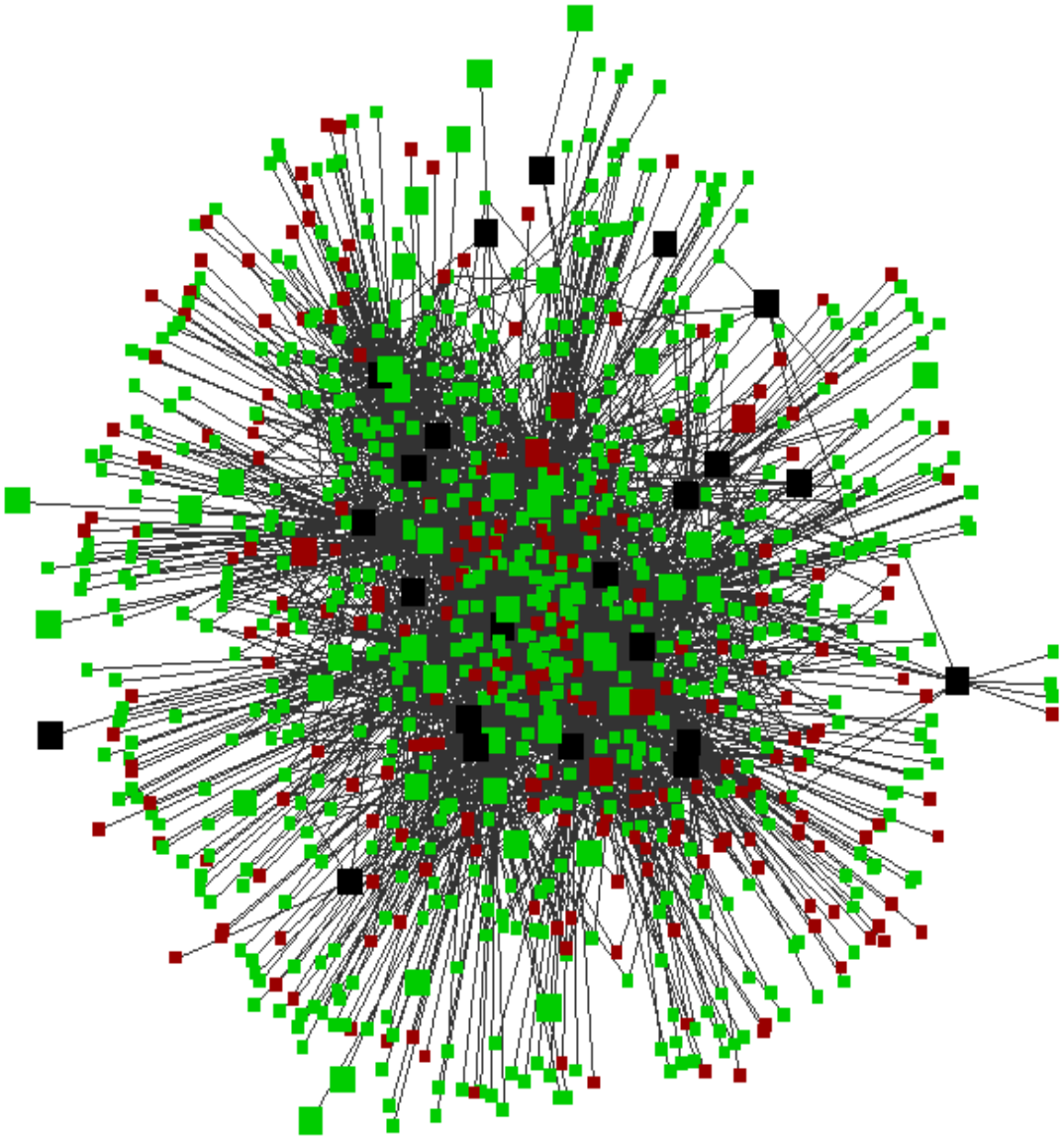

Figure 3.22. Representation of the PRS responsive to oxygen availability (Clim) (big and small squares represent TFs and non-TF target genes, respectively)

Table 3.32. Number of key TFs responsive to oxygen availability (Clim) that were found to be mainly transcriptionally regulated (A) or mainly post-transcriptionally regulated (B)

Mutant	Number of A	Number of B
AER vs. ANA (Clim)	23	23

Table 3.33. Regulation of key TFs responsive to oxygen availability (Clim)

rank	AER vs. ANA (Clim)	Case	rank	AER vs. ANA (Clim)	Case	rank	AER vs. ANA (Clim)	Case
1	Elp6p	A	17	Hot1p	B	33	Sin3p	B
2	Ada2p	B	18	Rtg2p	B	34	Ume6p	A
3	Swi1p	B	19	Gsm1p	A	35	Sip4p	A
4	Swi3p	A	20	Hap1p	B	36	Hap3p	A
5	Cat8p	A	21	Mot3p	A	37	Mig1p	A
6	Pip2p	A	22	Opi1p	A	38	Rox1p	A
7	Aca1p	A	23	Hap4p	B	39	Rdr1p	B
8	Sut1p	A	24	Bye1p	B	40	Hms1p	A
9	Xbp1p	A	25	Cdc14p	B	41	Cin5p	A
10	Stp3p	B	26	Nrg1p	A	42	Hap2p	B
11	Gis1p	B	27	Hmra2p	B	43	Mac1p	B
12	Nrg2p	A	28	Adr1p	A	44	Stp2p	A
13	Oaf1p	A	29	YPR015c	B	45	Sko1p	B
14	Rds2p	B	30	Upc2p	B	46	Yrm1p	B
15	Cst6p	B	31	Rme1p	B			
16	Sps18p	B	32	Hap5p	A			

4. CONCLUSIONS and RECOMMENDATIONS

4.1. Conclusions

It is concluded that key TFs (TFs around which a considerable collective change in the expression of the genes occur in response to environmental and genetic perturbations) can be identified using reporter features algorithm developed by Oliveira *et al.* (Oliveira *et al*., 2008). A genome-scale TRN in *S. cerevisiae* which contains 198 TFs, 6158 non-TF target genes and 44007 interactions was constructed and integrated with the transcriptome data available in literature for the mutants of the glucose signaling pathway of *S. cerevisiae*.

The constructed TRN was found to be scale free and none of the selected hubs (the intersection of the top 20 highest degree and top 20 highest betweenness nodes) were found to be a key TF, showing that identified key TFs were not false-positives resulting from their possible high degree.

Key TFs that are involved in chromatin remodeling, phospholipid biosynthesis, β-oxidation of fatty acids, biogenesis, oxidative phosphorylation (energy metabolism), carbohydrate metabolic process, alternative carbon source consumption and stress response, were identified as a response to *SNF1* deletion. These results are consistent with the predicted role of Snf1p kinase reported in the study of Usaite *et al*., where three level omics data (genome-wide mRNA, protein profiling and metabolite measurements) has been integrated with different networks (protein-protein interactions, protein-DNA interactions and metabolic reaction stoichiometry) using four computational tools. Key TFs involved in processes, such as oleate response and protein urmylation, were also identified. This result highlights the effectiveness of only using reporter features algorithm with a large genome-scale TRN to investigate the regulatory mechanisms invoked in the cell. The only disadvantage is that reporter features algorithm does not specify the direction of the change but only the significancy of the change.

Key TFs that are involved in chromatin remodeling, fatty acid metabolic process, oxidative phosphorylation (energy metabolism), alternative carbon source consumption and stress response, were identified as a response to *MIG1* deletion as in *ΔSNF1*. Key TFs involved in glucose repression and drug resistance were also identified.

As a response to oxygen availability under carbon limitation regime key TFs known to be involved in regulation of aerobiosis/anaerobiosis were identified, as expected. In addition, TFs that are involved in glucose repression and derepression and TFs known to be positively regulated by Snf1p kinase were identified as key TFs, providing further evidence to the role of Snf1p kinase in the switch from fermentative/anaerobic to oxidative metabolism.

Significant shared GO biological process terms of the key TFs identified as a response to each specific perturbation did not display the expected relationship of the key TFs with the corresponding specific perturbation, generally. However, when combined with the literature, it was observed that key TFs identified reveal the expected changes in response to each specific perturbation.

In this study, it was further showed that once the key TFs are identified, the perturbation-responsive subnetworks might be constructed by interconnecting key TFs and their differentially expressed target genes responsive to the same perturbation. PRSs of *ΔMIG1*, *ΔMIG1ΔMIG2*, *ΔMIG3* and *ΔMIG1ΔMIG2ΔMIG3* mutants do not contain all key TFs identified for each specific mutant, since some of these key TFs do not have significantly differentially expressed (p-value<0.05) target genes.

Significant shared GO biological process terms of the target genes in the PRSs display the expected relationship of the key TFs with the corresponding specific perturbation to some extent, but not fully. For example, fatty acid and lipid metabolism did not appear among the terms significantly associated with the genes of the PRSs of *ΔSNF1*, *ΔSNF4* and *ΔSNF1ΔSNF4*. This might arise from the approach used to construct PRSs, i. e., p-value threshold (0.05) used to identify significantly differentially expressed genes of the PRSs.

In this study, significant and biologically meaningful key TFs were identified which shed light on the transcriptional regulatory mechanism controlling the glucose signaling in *S. cerevisiae*. The results correlate with prior knowledge of glucose repression/derepression regulatory cascade studies, and they also provide a starting point for potential experimental studies to further investigate the relationships between the identified key TFs and the corresponding perturbations.

4.2. Recommendations

The approach used to construct PRSs may be improved or changed. To identify significantly differentially expressed genes a lover threshold value could be used and the larger effects of perturbations could be seen. Alternatively, a protein-protein interaction network could be constructed based on key TFs and differentially expressed target genes and this network could be enlarged by adding first neighbours of the nodes.

Key TFs responsive to carbon availability under aerobic regime could be identified, to further reveal the glucose sensing and signalling mechanism of yeast.

Although not information-preserving, the initial transcriptome data could be filtered to contain only up or down regulated genes. By this way, the identified key TFs can be used to enrich the information about the biological role of a perturbation without considering the directionality.

APPENDIX A: TOPOLOGICAL STUDY OF THE NETWORK

Table A.1. Topological parameters of individual nodes of the yeast TRN

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
A1	13	0.051	2799	snR17a	3	0.333	18	snR87	2	0.000	9
A2	1	0.000	0	snR17b	1	0.000	0	SRG1	1	0.000	0
ALD1	1	0.000	0	snR18	1	0.000	0	STA1	5	0.100	73
DEX2	6	0.667	20	snR189	1	0.000	0	STA2	9	0.222	245
MAL61	2	0.000	19053	snR190	21	0.081	2692	STA3	3	0.333	8
MAL62	2	0.000	19053	snR20	1	0.000	0	SUC6	1	0.000	0
MALR	4	0.000	25415	snR37	13	0.103	751	tA(AGC)D	1	0.000	0
MALS	1	0.000	0	snR4	2	0.000	18	tA(AGC)G	2	1.000	0
MALT	1	0.000	0	snR42	1	0.000	0	tA(AGC)K2	3	0.333	27
MEL1	2	1.000	0	snR44	2	0.000	6	tA(AGC)P	3	0.000	20
MPR1	2	1.000	0	snR45	5	0.200	168	tA(UGC)A	2	0.000	24
Q0010	2	0.000	15	snR46	2	0.000	44	tC(GCA)B	2	0.000	131
Q0045	3	0.333	17	snR47	5	0.000	286	tC(GCA)P1	1	0.000	0
Q0050	5	0.200	109	snR53	1	0.000	0	tC(GCA)P2	1	0.000	0
Q0055	4	0.667	21	snR54	1	0.000	0	tD(GUC)B	1	0.000	0
Q0060	2	0.000	13	snR55	4	0.000	42	tD(GUC)G1	1	0.000	0
Q0065	3	0.000	559	snR56	2	0.000	3	tD(GUC)J2	2	0.000	10
Q0070	4	0.000	84	snR57	15	0.171	2134	tD(GUC)K	1	0.000	0
Q0075	5	0.300	53	snR59	3	0.000	18	tD(GUC)L1	1	0.000	0
Q0080	7	0.429	128	snR6	9	0.056	857	tD(GUC)L2	1	0.000	0
Q0085	3	0.667	13	snR60	2	1.000	0	tE(CUC)D	9	0.111	1615
Q0105	4	0.333	77	snR61	9	0.056	534	tE(UUC)B	1	0.000	0
Q0110	2	1.000	0	snR63	2	1.000	0	tE(UUC)C	1	0.000	0
Q0115	5	0.700	48	snR64	1	0.000	0	tE(UUC)E2	1	0.000	0
Q0120	4	0.500	17	snR65	1	0.000	0	tE(UUC)E3	2	0.000	94
Q0130	2	0.000	21	snR66	3	0.333	47	tE(UUC)G1	1	0.000	0
Q0140	3	0.333	17	snR67	8	0.143	295	tE(UUC)J	1	0.000	0
Q0160	2	0.000	13	snR70	9	0.056	688	tE(UUC)P	2	1.000	0
Q0182	1	0.000	0	snR71	7	0.238	57	tF(GAA)B	1	0.000	0
Q0250	3	0.333	17	snR72	1	0.000	0	tF(GAA)D	2	1.000	0
Q0255	2	0.000	10	snR73	1	0.000	0	tF(GAA)F	1	0.000	0
Q0275	2	0.000	10	snR74	1	0.000	0	tF(GAA)H1	2	1.000	0
Q0297	2	0.000	10	snR75	1	0.000	0	tF(GAA)P2	1	0.000	0
RDN5	3	0.333	20	snR76	1	0.000	0	tG(GCC)F2	2	0.000	6
RPR1	2	0.000	9	snR77	1	0.000	0	tG(GCC)G2	1	0.000	0
snR128	3	0.000	67	snR78	1	0.000	0	tG(GCC)J1	2	0.000	131
snR13	2	0.000	24	snR7-S	1	0.000	0	tG(GCC)J2	1	0.000	0
snR14	2	0.000	123	snR8	2	0.000	13	tG(GCC)M	1	0.000	0

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
tG(GCC)P2	1	0.000	0	tP(UGG)O2	1	0.000	0	tY(GUA)M1	1	0.000	0
tG(UCC)G	2	0.000	64	tP(UGG)O3	1	0.000	0	tY(GUA)O	1	0.000	0
tG(UCC)O	1	0.000	0	tQ(CUG)M	2	0.000	367	YAL001c	5	0.100	408
tH(GUG)E1	6	0.133	212	tQ(UUG)D2	2	1.000	0	YAL002w	2	0.000	32
tH(GUG)G2	3	0.333	74	tQ(UUG)E1	4	0.000	719	YAL003w	15	0.390	928
tH(GUG)H	1	0.000	0	tQ(UUG)E2	1	0.000	0	YAL004w	4	0.000	60
tH(GUG)K	5	0.000	489	tR(ACG)D	1	0.000	0	YAL005c	28	0.243	6331
tK(CUU)D1	1	0.000	0	tR(ACG)K	1	0.000	0	YAL007c	6	0.467	78
tK(CUU)G3	1	0.000	0	tR(CCG)L	2	0.000	9	YAL008w	2	0.000	132
tK(CUU)J	3	0.000	23	tR(CCU)J	1	0.000	0	YAL009w	3	0.333	134
tK(CUU)K	1	0.000	0	tR(UCU)G2	1	0.000	0	YAL010c	4	0.333	306
tK(CUU)P	1	0.000	0	tS(AGA)D1	1	0.000	0	YAL011w	3	0.000	90
tK(UUU)D	2	1.000	0	tS(AGA)D2	1	0.000	0	YAL012w	12	0.303	646
tK(UUU)G1	1	0.000	0	tS(AGA)D3	2	0.000	92	YAL013w	7	0.333	277
tK(UUU)L	1	0.000	0	tS(AGA)J	1	0.000	0	YAL014c	4	0.333	97
tL(CAA)A	1	0.000	0	tS(CGA)C	1	0.000	0	YAL015c	6	0.200	199
tL(CAA)D	3	0.333	62	tS(GCU)L	2	0.000	9	YAL016w	5	0.100	87
tL(CAA)G1	3	0.000	13	tS(UGA)I	3	0.333	27	YAL017w	10	0.244	1111
tL(CAA)G2	1	0.000	0	tS(UGA)P	2	0.000	131	YAL018c	12	0.136	1559
tL(CAA)G3	2	0.000	9	tT(AGU)B	3	0.000	12	YAL019w	5	0.100	2780
tL(CAA)K	1	0.000	0	tT(AGU)H	2	0.000	4	YAL020c	5	0.300	162
tL(CAA)L	1	0.000	0	tT(AGU)J	12	0.076	1447	YAL021c	1	0.000	0
tL(CAA)M	2	1.000	0	tT(AGU)N1	2	0.000	34	YAL022c	18	0.176	2396
tL(GAG)G	1	0.000	0	tT(UGU)G1	1	0.000	0	YAL023c	7	0.048	984
tL(UAA)B1	1	0.000	0	tT(UGU)G2	7	0.048	515	YAL024c	3	0.333	30
tL(UAA)K	2	1.000	0	tT(UGU)P	3	0.000	32	YAL025c	9	0.139	1733
tL(UAG)L1	2	0.000	7	tV(AAC)E1	1	0.000	0	YAL026c	3	0.000	36
tM(CAU)C	1	0.000	0	tV(AAC)G1	1	0.000	0	YAL027w	4	0.167	29
tM(CAU)D	1	0.000	0	tV(AAC)J	1	0.000	0	YAL028w	9	0.444	482
tM(CAU)E	2	0.000	41	tV(AAC)K1	1	0.000	0	YAL029c	9	0.222	271
tM(CAU)J1	3	0.000	43	tV(AAC)K2	2	1.000	0	YAL030w	2	0.000	7
tM(CAU)J2	1	0.000	0	tV(AAC)L	3	0.000	699	YAL031c	4	0.667	60
tM(CAU)M	1	0.000	0	tV(AAC)O	1	0.000	0	YAL033w	2	1.000	0
tM(CAU)O2	2	0.000	10	tV(CAC)D	2	0.000	77	YAL034c	4	0.500	73
tM(CAU)P	1	0.000	0	tV(CAC)H	2	1.000	0	YAL034w-a	8	0.321	218
tN(GUU)F	1	0.000	0	tV(UAC)D	1	0.000	0	YAL035w	5	0.100	230
tN(GUU)L	1	0.000	0	tW(CCA)G1	4	0.167	252	YAL036c	6	0.267	140
tN(GUU)N1	1	0.000	0	tW(CCA)G2	4	0.000	78	YAL037c-a	2	0.000	34
tP(AGG)C	1	0.000	0	tW(CCA)J	12	0.015	1277	YAL037w	9	0.361	1033
tP(UGG)L	1	0.000	0	tW(CCA)K	3	0.000	12	YAL038w	25	0.247	9667
tP(UGG)M	1	0.000	0	tW(CCA)M	3	0.000	58	YAL039c	15	0.371	1579
tP(UGG)N1	1	0.000	0	tY(GUA)F1	1	0.000	0	YAL040c	23	0.360	2146
tP(UGG)O1	3	0.333	7	tY(GUA)J2	1	0.000	0	YAL041w	4	0.500	178

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YAL042w	4	0.167	332	YAR029w	5	0.100	113	YBL022c	9	0.389	600
YAL043c	3	0.000	396	YAR030c	1	0.000	0	YBL023c	7	0.381	169
YAL043c-a	1	0.000	0	YAR031w	4	0.000	103	YBL024w	2	0.000	28
YAL044c	11	0.327	891	YAR033w	3	0.667	19	YBL025w	3	0.000	130
YAL044w-a	1	0.000	0	YAR035w	16	0.300	1845	YBL026w	7	0.238	584
YAL045c	2	0.000	29	YAR042w	12	0.212	1595	YBL027w	11	0.455	358
YAL046c	2	0.000	25	YAR044w	1	0.000	0	YBL028c	12	0.379	472
YAL047c	1	0.000	0	YAR047c	7	0.286	542	YBL029c-a	19	0.444	1015
YAL048c	1	0.000	0	YAR050w	24	0.214	3248	YBL029w	39	0.216	19187
YAL049c	4	0.167	313	YAR053w	6	0.200	86	YBL030c	25	0.330	2001
YAL051w	264	0.008	174707	YAR060c	1	0.000	0	YBL031w	2	0.000	14
YAL053w	14	0.176	2643	YAR061w	5	0.400	102	YBL032w	5	0.400	203
YAL054c	18	0.190	3572	YAR062w	4	0.167	123	YBL033c	10	0.333	1420
YAL055w	2	1.000	0	YAR064w	5	0.700	18	YBL034c	4	0.167	109
YAL056w	2	0.000	48	YAR066w	8	0.321	103	YBL035c	3	0.333	53
YAL058c-a	1	0.000	0	YAR068w	13	0.244	981	YBL036c	5	0.400	135
YAL058w	2	1.000	0	YAR069c	3	0.000	72	YBL037w	4	0.500	64
YAL059w	5	0.300	82	YAR070c	5	0.400	129	YBL038w	5	0.100	726
YAL060w	13	0.359	1106	YAR071w	17	0.272	1260	YBL039c	12	0.288	1402
YAL061w	14	0.264	1095	YAR073w	10	0.444	1178	YBL041w	13	0.231	2127
YAL062w	27	0.171	5567	YAR075w	6	0.467	108	YBL042c	20	0.268	4609
YAL063c	22	0.281	3967	YBL001c	14	0.121	811	YBL043w	24	0.326	2225
YAL064c-a	14	0.440	838	YBL002w	12	0.182	1112	YBL044w	17	0.426	551
YAL064w	14	0.385	1876	YBL003c	7	0.238	407	YBL045c	14	0.385	295
YAL065c	5	0.100	107	YBL004w	8	0.286	465	YBL046w	3	0.333	259
YAL066w	1	0.000	0	YBL005w	552	0.007	407305	YBL047c	2	0.000	40
YAL067c	12	0.182	1113	YBL005w-a	4	0.333	38	YBL048w	4	0.167	60
YAL068c	10	0.178	625	YBL005w-b	2	1.000	0	YBL049w	16	0.225	2475
YAR002c-a	2	0.000	42	YBL006c	2	1.000	0	YBL050w	3	0.333	53
YAR002w	4	0.167	228	YBL007c	6	0.267	684	YBL051c	5	0.100	330
YAR003w	6	0.067	378	YBL008w	80	0.005	44543	YBL052c	1	0.000	0
YAR007c	8	0.214	1516	YBL009w	1	0.000	0	YBL053w	1	0.000	0
YAR008w	6	0.267	414	YBL010c	1	0.000	0	YBL054w	9	0.278	683
YAR009c	20	0.226	3656	YBL011w	11	0.400	330	YBL055c	1	0.000	0
YAR010c	3	0.000	41	YBL013w	6	0.333	205	YBL056w	5	0.100	457
YAR014c	4	0.667	33	YBL014c	5	0.400	56	YBL057c	5	0.100	268
YAR015w	11	0.436	520	YBL015w	12	0.515	481	YBL058w	4	0.500	46
YAR018c	5	0.500	67	YBL016w	11	0.473	994	YBL059c-a	3	0.000	90
YAR019c	7	0.286	592	YBL017c	6	0.600	283	YBL059w	10	0.089	842
YAR020c	7	0.381	211	YBL018c	7	0.143	1158	YBL060w	6	0.267	325
YAR023c	5	0.200	75	YBL019w	5	0.200	376	YBL061c	3	0.333	47
YAR027w	6	0.200	516	YBL020w	7	0.333	408	YBL063w	5	0.100	320
YAR028w	7	0.333	354	YBL021c	188	0.008	81126	YBL064c	12	0.288	630

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YBL066c	1	0.000	0	YBL105c	5	0.600	25	YBR033w	6	0.267	278
YBL067c	2	0.000	32	YBL106c	4	0.333	229	YBR034c	6	0.267	163
YBL068w	3	0.333	222	YBL107c	11	0.382	380	YBR035c	5	0.500	148
YBL069w	4	0.500	55	YBL107w-a	1	0.000	0	YBR036c	4	0.000	145
YBL070c	2	1.000	0	YBL108c-a	3	1.000	0	YBR037c	4	0.167	50
YBL071c	5	0.500	120	YBL108w	10	0.356	224	YBR038w	13	0.090	1654
YBL071c-b	2	0.000	9	YBL109w	23	0.186	2108	YBR039w	15	0.229	1002
YBL071w-a	2	0.000	9	YBL111c	20	0.221	1212	YBR040w	20	0.321	3739
YBL072c	7	0.619	139	YBL112c	14	0.209	912	YBR041w	6	0.067	517
YBL073w	6	0.133	369	YBL113c	12	0.167	371	YBR042c	3	0.000	128
YBL074c	3	0.000	27	YBR001c	4	0.500	117	YBR043c	7	0.143	656
YBL075c	18	0.248	2608	YBR002c	4	0.000	446	YBR044c	5	0.300	149
YBL076c	4	0.500	74	YBR003w	5	0.400	371	YBR045c	5	0.200	474
YBL077w	1	0.000	0	YBR004c	5	0.000	293	YBR046c	9	0.278	688
YBL078c	12	0.182	904	YBR005w	6	0.333	395	YBR047w	14	0.319	912
YBL079w	6	0.200	465	YBR006w	16	0.117	1469	YBR048w	16	0.267	2153
YBL080c	1	0.000	0	YBR007c	14	0.308	1325	YBR049c	324	0.007	465973
YBL081w	5	0.400	270	YBR008c	15	0.352	1582	YBR050c	14	0.154	1199
YBL082c	4	0.500	166	YBR009c	8	0.214	924	YBR051w	6	0.200	182
YBL083c	2	0.000	86	YBR010w	5	0.100	401	YBR052c	7	0.190	535
YBL085w	3	0.333	71	YBR011c	8	0.357	780	YBR053c	13	0.397	755
YBL086c	5	0.400	92	YBR012c	5	0.100	194	YBR054w	31	0.237	5667
YBL087c	15	0.314	1394	YBR012w-a	3	0.000	41	YBR055c	4	0.333	168
YBL088c	1	0.000	0	YBR012w-b	3	0.000	41	YBR056w	15	0.229	2642
YBL089w	3	0.333	50	YBR013c	6	0.333	590	YBR056w-a	6	0.400	281
YBL090w	1	0.000	0	YBR014c	5	0.300	120	YBR057c	11	0.073	498
YBL091c	1	0.000	0	YBR015c	5	0.400	248	YBR058c	1	0.000	0
YBL091c-a	3	0.333	241	YBR016w	6	0.333	444	YBR058c-a	1	0.000	0
YBL092w	10	0.422	848	YBR017c	4	0.000	399	YBR059c	1	0.000	0
YBL093c	9	0.361	693	YBR018c	10	0.289	766	YBR060c	7	0.238	634
YBL094c	1	0.000	0	YBR019c	20	0.116	5456	YBR061c	4	0.333	229
YBL095w	3	0.000	38	YBR020w	24	0.138	6512	YBR062c	5	0.500	434
YBL096c	1	0.000	0	YBR021w	10	0.244	1613	YBR063c	2	1.000	0
YBL097w	3	0.333	23	YBR022w	1	0.000	0	YBR065c	6	0.067	517
YBL098w	13	0.179	2002	YBR023c	4	0.333	59	YBR066c	166	0.049	134448
YBL099w	13	0.244	589	YBR024w	5	0.200	285	YBR067c	18	0.333	1820
YBL101c	5	0.400	109	YBR025c	14	0.264	499	YBR068c	13	0.205	1725
YBL101w-a	3	0.333	54	YBR026c	2	0.000	8	YBR069c	12	0.348	1036
YBL101w-b	3	0.000	92	YBR028c	3	0.000	137	YBR070c	8	0.321	314
YBL101w-c	1	0.000	0	YBR029c	8	0.250	1285	YBR071w	15	0.171	1401
YBL102w	3	0.000	40	YBR030w	5	0.200	413	YBR072w	56	0.209	16851
YBL103c	223	0.007	103327	YBR031w	8	0.536	848	YBR073w	6	0.333	120
YBL104c	4	0.167	35	YBR032w	4	0.000	94	YBR074w	9	0.250	942

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YBR075w	2	1.000	0	YBR116c	16	0.283	3421	YBR159w	9	0.111	285
YBR076w	9	0.222	708	YBR117c	30	0.232	4927	YBR160w	6	0.200	534
YBR077c	18	0.307	2061	YBR118w	10	0.489	437	YBR161w	6	0.200	297
YBR078w	23	0.269	3945	YBR119w	4	0.500	169	YBR162c	9	0.444	455
YBR079c	3	0.333	33	YBR120c	3	0.333	106	YBR162w-a	7	0.476	192
YBR080c	5	0.200	1067	YBR121c	5	0.300	698	YBR163w	7	0.095	513
YBR081c	7	0.286	551	YBR122c	1	0.000	0	YBR164c	5	0.100	564
YBR082c	13	0.372	1526	YBR123c	2	0.000	36	YBR165w	2	0.000	92
YBR083w	547	0.020	601548	YBR124w	1	0.000	0	YBR166c	8	0.107	302
YBR084c-a	6	0.533	121	YBR125c	2	1.000	0	YBR167c	20	0.142	2031
YBR084w	3	0.333	74	YBR126c	20	0.216	2917	YBR168w	17	0.147	1083
YBR085c-a	10	0.356	700	YBR127c	4	0.167	90	YBR169c	23	0.324	3270
YBR085w	17	0.294	2050	YBR128c	1	0.000	0	YBR170c	7	0.429	483
YBR086c	13	0.090	1479	YBR129c	6	0.333	373	YBR171w	4	0.500	217
YBR087w	11	0.091	1008	YBR130c	3	0.333	189	YBR172c	2	1.000	0
YBR088c	3	0.667	39	YBR131w	3	0.333	189	YBR173c	4	0.333	124
YBR089c-a	2	0.000	11	YBR132c	7	0.381	187	YBR174c	1	0.000	0
YBR089w	2	1.000	0	YBR133c	6	0.400	97	YBR175w	4	0.500	203
YBR090c	6	0.133	133	YBR134w	6	0.267	121	YBR176w	3	0.000	53
YBR091c	3	0.000	105	YBR135w	7	0.143	217	YBR177c	10	0.489	874
YBR092c	21	0.176	5045	YBR136w	2	0.000	12	YBR178w	1	0.000	0
YBR093c	24	0.130	7042	YBR137w	6	0.533	160	YBR179c	7	0.524	536
YBR094w	6	0.133	212	YBR138c	9	0.306	572	YBR180w	6	0.533	488
YBR095c	4	0.333	315	YBR139w	14	0.253	1520	YBR181c	5	0.500	98
YBR096w	4	0.167	305	YBR140c	2	0.000	7	YBR182c	167	0.020	88106
YBR097w	6	0.333	596	YBR141c	2	0.000	67	YBR182c-a	2	1.000	0
YBR098w	10	0.067	964	YBR142w	5	0.200	151	YBR183w	14	0.374	565
YBR099c	7	0.381	253	YBR143c	3	0.000	338	YBR184w	5	0.000	203
YBR101c	11	0.309	1165	YBR144c	7	0.476	251	YBR185c	3	0.333	41
YBR102c	9	0.222	436	YBR145w	17	0.279	2270	YBR186w	2	1.000	0
YBR103w	10	0.200	623	YBR146w	2	0.000	117	YBR187w	5	0.200	176
YBR104w	8	0.286	431	YBR147w	15	0.295	1636	YBR188c	7	0.333	958
YBR105c	16	0.267	2154	YBR148w	5	0.300	415	YBR189w	10	0.333	1359
YBR106w	7	0.143	429	YBR149w	11	0.273	553	YBR190w	9	0.389	439
YBR107c	2	0.000	11	YBR150c	6	0.333	153	YBR191w	9	0.472	377
YBR108w	4	0.000	154	YBR151w	10	0.222	794	YBR192w	1	0.000	0
YBR109c	9	0.167	1283	YBR152w	1	0.000	0	YBR194w	1	0.000	0
YBR110w	8	0.143	1235	YBR153w	3	0.000	66	YBR195c	4	0.333	319
YBR111c	5	0.500	113	YBR154c	4	0.167	445	YBR196c	10	0.156	677
YBR112c	8	0.464	1199	YBR155w	4	0.333	411	YBR196c-a	3	0.333	24
YBR113w	3	0.667	12	YBR156c	6	0.467	331	YBR196c-b	2	0.000	9
YBR114w	11	0.382	387	YBR157c	21	0.252	1717	YBR197c	4	0.167	54
YBR115c	10	0.289	547	YBR158w	18	0.333	1286	YBR198c	2	0.000	206

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YBR199w	3	0.667	97	YBR240c	85	0.040	102508	YBR284w	8	0.357	595
YBR200w	7	0.381	166	YBR241c	14	0.242	1151	YBR285w	15	0.276	831
YBR201w	6	0.200	367	YBR242w	1	0.000	0	YBR286w	15	0.229	2330
YBR202w	12	0.561	263	YBR243c	10	0.311	489	YBR287w	3	0.333	132
YBR203w	11	0.436	485	YBR244w	13	0.256	1310	YBR288c	3	0.000	90
YBR204c	2	0.000	2	YBR245c	1	0.000	0	YBR289w	4	0.000	201
YBR205w	2	0.000	2	YBR246w	1	0.000	0	YBR290w	3	0.000	248
YBR206w	2	0.000	2	YBR247c	10	0.244	594	YBR291c	8	0.357	940
YBR207w	7	0.286	610	YBR248c	11	0.218	1649	YBR293w	5	0.200	784
YBR208c	14	0.286	2382	YBR249c	9	0.444	472	YBR294w	16	0.208	2215
YBR209w	7	0.238	675	YBR250w	11	0.164	4093	YBR295w	9	0.306	1006
YBR210w	7	0.476	1075	YBR251w	2	1.000	0	YBR296c	28	0.164	4784
YBR211c	3	0.000	478	YBR253w	2	1.000	0	YBR297w	144	0.026	115072
YBR212w	3	0.000	277	YBR254c	5	0.000	174	YBR298c	8	0.464	423
YBR213w	6	0.200	306	YBR255c-a	1	0.000	0	YBR299w	16	0.292	2063
YBR214w	10	0.267	369	YBR255w	3	0.000	25	YBR300c	3	0.333	32
YBR215w	3	0.000	65	YBR256c	10	0.333	426	YBR301w	6	0.400	123
YBR216c	8	0.000	214	YBR257w	3	0.333	47	YBR302c	7	0.524	458
YBR217w	9	0.139	614	YBR258c	3	0.000	227	YCL001w	3	0.000	283
YBR218c	3	1.000	0	YBR259w	2	0.000	20	YCL001w-a	1	0.000	0
YBR219c	4	0.667	19	YBR260c	5	0.400	108	YCL002c	4	0.500	66
YBR220c	1	0.000	0	YBR261c	2	0.000	42	YCL004w	3	0.333	126
YBR221c	3	0.667	48	YBR262c	2	0.000	24	YCL005w	1	0.000	0
YBR222c	8	0.107	711	YBR263w	2	1.000	0	YCL007c	2	1.000	0
YBR223c	2	1.000	0	YBR264c	3	0.000	164	YCL008c	3	0.667	34
YBR224w	3	0.333	57	YBR265w	5	0.500	222	YCL009c	8	0.357	378
YBR225w	3	0.333	84	YBR266c	4	0.000	161	YCL010c	2	1.000	0
YBR226c	1	0.000	0	YBR267w	5	0.100	229	YCL011c	2	0.000	97
YBR227c	1	0.000	0	YBR268w	5	0.200	202	YCL012w	1	0.000	0
YBR228w	1	0.000	0	YBR269c	1	0.000	0	YCL014w	6	0.200	460
YBR229c	6	0.200	157	YBR270c	1	0.000	0	YCL016c	2	0.000	65
YBR230c	11	0.255	517	YBR271w	4	0.167	364	YCL017c	4	0.167	344
YBR230w-a	1	0.000	0	YBR272c	1	0.000	0	YCL018w	14	0.231	2236
YBR231c	3	0.333	92	YBR273c	4	0.333	133	YCL019w	3	0.667	10
YBR232c	2	1.000	0	YBR274w	2	0.000	25	YCL020w	3	0.333	185
YBR233w	4	0.500	314	YBR275c	14	0.099	645	YCL021w-a	2	1.000	0
YBR233w-a	4	0.500	257	YBR276c	1	0.000	0	YCL022c	1	0.000	0
YBR234c	2	0.000	39	YBR278w	1	0.000	0	YCL023c	1	0.000	0
YBR235w	4	0.167	171	YBR279w	3	0.000	167	YCL024w	11	0.218	1376
YBR236c	3	0.000	50	YBR280c	7	0.286	333	YCL025c	26	0.237	6432
YBR237w	3	0.000	50	YBR281c	3	1.000	0	YCL026c-a	13	0.282	1496
YBR238c	5	0.200	251	YBR282w	3	0.667	12	YCL026c-b	4	0.667	25
YBR239c	3	0.000	161	YBR283c	3	0.667	24	YCL027w	21	0.329	2826

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YCL028w	5	0.300	569	YCR001w	1	0.000	0	YCR039c	18	0.131	3141
YCL029c	5	0.500	232	YCR002c	3	0.667	42	YCR040w	18	0.137	2441
YCL030c	14	0.264	1724	YCR003w	1	0.000	0	YCR041w	13	0.103	1426
YCL031c	7	0.143	1038	YCR004c	6	0.533	123	YCR042c	3	0.000	96
YCL032w	4	0.000	351	YCR005c	30	0.161	6452	YCR043c	3	0.000	66
YCL033c	3	0.000	278	YCR006c	6	0.267	191	YCR044c	5	0.300	339
YCL034w	3	0.667	13	YCR007c	1	0.000	0	YCR045c	6	0.333	268
YCL035c	8	0.429	302	YCR008w	4	0.500	61	YCR046c	1	0.000	0
YCL036w	7	0.286	180	YCR009c	4	0.500	245	YCR047c	3	0.333	48
YCL037c	8	0.250	305	YCR010c	21	0.324	5008	YCR048w	4	0.500	49
YCL038c	1	0.000	0	YCR011c	6	0.400	358	YCR049c	1	0.000	0
YCL039w	6	0.400	378	YCR012w	14	0.330	1131	YCR050c	2	1.000	0
YCL040w	22	0.247	3802	YCR013c	2	0.000	15	YCR051w	1	0.000	0
YCL041c	6	0.200	257	YCR014c	2	1.000	0	YCR052w	4	0.167	183
YCL042w	18	0.353	2052	YCR015c	3	0.333	85	YCR053w	8	0.214	1172
YCL043c	12	0.364	1097	YCR016w	3	0.667	87	YCR057c	10	0.178	1313
YCL044c	5	0.300	364	YCR017c	5	0.800	103	YCR059c	5	0.400	356
YCL045c	3	0.333	8	YCR018c	64	0.021	54006	YCR060w	2	1.000	0
YCL046w	3	0.333	13	YCR018c-a	36	0.159	5881	YCR061w	14	0.341	1299
YCL047c	1	0.000	0	YCR019w	34	0.176	5868	YCR063w	12	0.288	1222
YCL048w	2	0.000	51	YCR020c	8	0.321	1037	YCR064c	7	0.333	128
YCL049c	11	0.345	1696	YCR020c-a	6	0.000	452	YCR065w	277	0.012	332117
YCL050c	9	0.389	710	YCR020w-b	5	0.400	164	YCR066w	2	0.000	13
YCL051w	3	0.333	42	YCR021c	39	0.247	10649	YCR067c	3	0.333	43
YCL052c	4	0.167	122	YCR022c	5	0.200	146	YCR068w	5	0.600	88
YCL054w	12	0.227	843	YCR023c	4	0.500	128	YCR069w	5	0.200	559
YCL055w	47	0.125	44124	YCR024c	7	0.429	110	YCR071c	1	0.000	0
YCL056c	9	0.222	1077	YCR024c-a	15	0.248	2020	YCR072c	8	0.071	1771
YCL057c-a	1	0.000	0	YCR024c-b	3	0.333	29	YCR073c	8	0.179	441
YCL057w	8	0.286	625	YCR025c	6	0.200	338	YCR073w-a	3	0.333	32
YCL058c	6	0.067	387	YCR026c	3	0.333	46	YCR075c	4	0.333	127
YCL059c	5	0.500	64	YCR027c	6	0.400	228	YCR075w-a	1	0.000	0
YCL061c	2	0.000	39	YCR028c	15	0.143	932	YCR076c	3	0.000	39
YCL063w	9	0.083	1424	YCR028c-a	3	0.000	102	YCR077c	3	0.333	34
YCL064c	25	0.157	5839	YCR030c	1	0.000	0	YCR079w	4	0.333	68
YCL065w	31	0.133	7428	YCR031c	12	0.409	1056	YCR081w	5	0.100	263
YCL066w	23	0.170	7574	YCR032w	9	0.167	478	YCR082w	7	0.143	1215
YCL067c	28	0.167	10786	YCR033w	2	1.000	0	YCR083w	5	0.600	47
YCL068c	6	0.200	165	YCR034w	4	0.000	245	YCR084c	2	0.000	35
YCL069w	8	0.214	340	YCR035c	3	0.333	191	YCR086w	3	0.000	114
YCL073c	1	0.000	0	YCR036w	3	0.333	191	YCR087c-a	5	0.500	105
YCL074w	9	0.250	575	YCR037c	5	0.000	397	YCR087w	2	0.000	16
YCL075w	3	0.333	10	YCR038c	2	0.000	1	YCR088w	5	0.500	306

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YCR089w	16	0.417	1295	YDL025c	5	0.400	157	YDL069c	1	0.000	0
YCR090c	1	0.000	0	YDL026w	4	0.333	219	YDL070w	11	0.145	2070
YCR091w	1	0.000	0	YDL027c	4	0.500	42	YDL071c	7	0.048	302
YCR092c	6	0.333	582	YDL028c	2	0.000	73	YDL072c	5	0.400	654
YCR093w	9	0.250	962	YDL029w	3	0.333	16	YDL073w	2	0.000	22
YCR094w	11	0.073	1362	YDL030w	4	0.167	188	YDL074c	4	0.000	216
YCR095c	11	0.091	661	YDL031w	5	0.300	185	YDL075w	23	0.213	3248
YCR096c	29	0.148	6399	YDL032w	4	0.167	181	YDL076c	9	0.194	504
YCR097w	25	0.120	25202	YDL033c	1	0.000	0	YDL078c	9	0.361	287
YCR097w-a	2	1.000	0	YDL034w	8	0.107	1244	YDL079c	8	0.286	309
YCR098c	17	0.279	2699	YDL035c	5	0.100	285	YDL080c	3	0.333	60
YCR099c	5	0.300	162	YDL036c	6	0.067	646	YDL081c	10	0.356	1508
YCR100c	7	0.238	600	YDL037c	17	0.257	1231	YDL082w	14	0.407	1087
YCR101c	3	0.333	69	YDL038c	25	0.173	3006	YDL083c	14	0.352	1186
YCR102c	20	0.358	1662	YDL039c	16	0.200	2477	YDL084w	10	0.156	1271
YCR102w-a	2	0.000	57	YDL040c	1	0.000	0	YDL085c-a	3	0.667	13
YCR104w	19	0.146	1840	YDL041w	2	0.000	9	YDL085w	10	0.133	2398
YCR105w	35	0.134	6420	YDL043c	2	0.000	14	YDL086w	4	0.000	361
YCR106w	58	0.052	31098	YDL044c	7	0.000	351	YDL087c	1	0.000	0
YCR107w	27	0.191	4047	YDL045w-a	5	0.000	257	YDL088c	4	0.167	204
YCR108c	2	1.000	0	YDL046w	7	0.143	584	YDL089w	8	0.214	565
YDL001w	16	0.067	2035	YDL047w	10	0.578	374	YDL090c	9	0.167	839
YDL003w	4	0.500	60	YDL048c	16	0.550	848	YDL091c	12	0.136	1228
YDL004w	8	0.250	241	YDL049c	15	0.324	998	YDL092w	7	0.095	596
YDL005c	2	0.000	12	YDL050c	2	0.000	15	YDL093w	2	1.000	0
YDL006w	3	0.000	68	YDL051w	5	0.300	219	YDL094c	4	0.000	68
YDL007w	7	0.619	160	YDL052c	8	0.107	873	YDL095w	2	0.000	26
YDL008w	2	0.000	32	YDL053c	4	0.333	158	YDL096c	1	0.000	0
YDL009c	1	0.000	0	YDL054c	3	0.333	222	YDL097c	3	1.000	0
YDL010w	7	0.381	583	YDL055c	17	0.471	854	YDL098c	3	0.333	128
YDL011c	1	0.000	0	YDL056w	506	0.010	605184	YDL099w	4	0.500	86
YDL012c	6	0.267	825	YDL057w	5	0.500	206	YDL100c	4	0.167	87
YDL013w	4	0.000	67	YDL058w	6	0.400	268	YDL101c	5	0.400	37
YDL014w	8	0.286	734	YDL059c	8	0.286	264	YDL102w	11	0.200	1253
YDL016c	1	0.000	0	YDL060w	11	0.345	428	YDL104c	2	0.000	12
YDL017w	9	0.083	1254	YDL061c	9	0.472	530	YDL105w	3	0.000	207
YDL018c	10	0.178	805	YDL062w	3	0.000	152	YDL106c	170	0.010	169704
YDL019c	6	0.333	1179	YDL063c	8	0.286	772	YDL107w	3	0.000	72
YDL020c	1033	0.007	1949936	YDL064w	4	0.167	381	YDL108w	3	0.333	25
YDL021w	26	0.280	2864	YDL065c	2	0.000	48	YDL109c	2	1.000	0
YDL022w	17	0.294	1523	YDL066w	9	0.250	195	YDL110c	15	0.200	1199
YDL023c	2	0.000	26	YDL067c	9	0.167	190	YDL111c	1	0.000	0
YDL024c	12	0.242	952	YDL068w	8	0.107	401	YDL112w	4	0.333	300

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YDL113c	2	0.000	48	YDL154w	9	0.028	588	YDL197c	3	0.333	130
YDL114w	8	0.250	629	YDL155w	12	0.182	1850	YDL198c	5	0.200	106
YDL115c	10	0.289	414	YDL156w	7	0.190	766	YDL199c	4	0.000	69
YDL116w	6	0.067	461	YDL157c	3	0.000	159	YDL201w	2	1.000	0
YDL117w	5	0.400	475	YDL158c	2	1.000	0	YDL202w	3	0.333	57
YDL118w	1	0.000	0	YDL159w	12	0.227	2088	YDL203c	1	0.000	0
YDL119c	4	0.000	78	YDL159w-a	4	0.333	38	YDL204w	13	0.449	854
YDL120w	6	0.333	287	YDL160c	11	0.200	1331	YDL205c	9	0.111	478
YDL121c	7	0.429	333	YDL161w	5	0.200	232	YDL206w	7	0.048	458
YDL122w	2	1.000	0	YDL164c	6	0.067	656	YDL207w	4	0.167	89
YDL123w	4	0.333	345	YDL165w	5	0.500	84	YDL208w	5	0.100	601
YDL124w	18	0.248	2471	YDL166c	4	0.500	47	YDL209c	3	0.000	225
YDL125c	9	0.194	855	YDL167c	6	0.467	147	YDL210w	14	0.242	1665
YDL126c	11	0.291	1215	YDL168w	9	0.500	256	YDL211c	8	0.321	784
YDL127w	14	0.516	550	YDL169c	7	0.476	232	YDL212w	2	0.000	7
YDL128w	7	0.333	273	YDL170w	122	0.033	125393	YDL213c	5	0.500	139
YDL129w	11	0.200	1198	YDL171c	11	0.164	1798	YDL214c	12	0.515	358
YDL130w	11	0.382	960	YDL172c	1	0.000	0	YDL215c	10	0.222	1479
YDL130w-a	7	0.190	1002	YDL173w	10	0.356	526	YDL216c	4	0.333	190
YDL131w	7	0.429	1003	YDL174c	19	0.257	1702	YDL217c	5	0.100	163
YDL132w	4	0.000	140	YDL175c	4	0.000	244	YDL218w	6	0.533	295
YDL133c-a	5	0.300	71	YDL176w	9	0.056	598	YDL219w	3	0.333	50
YDL133w	5	0.400	111	YDL177c	5	0.100	479	YDL220c	5	0.300	140
YDL134c	4	0.333	124	YDL178w	5	0.200	379	YDL221w	1	0.000	0
YDL135c	21	0.171	3141	YDL179w	4	0.167	50	YDL222c	16	0.333	913
YDL136w	12	0.303	1268	YDL180w	10	0.178	516	YDL223c	21	0.233	1811
YDL137w	11	0.182	2516	YDL181w	13	0.192	490	YDL224c	7	0.333	233
YDL138w	5	0.200	466	YDL182w	17	0.338	1924	YDL225w	6	0.133	313
YDL139c	4	0.500	28	YDL183c	12	0.439	791	YDL226c	4	0.167	123
YDL140c	5	0.500	315	YDL184c	10	0.356	837	YDL227c	22	0.203	7286
YDL141w	7	0.286	332	YDL185c-a	2	0.000	10	YDL228c	1	0.000	0
YDL142c	7	0.286	409	YDL185w	7	0.238	357	YDL229w	6	0.267	237
YDL143w	4	0.167	107	YDL186w	5	0.200	446	YDL230w	9	0.222	322
YDL144c	3	0.333	37	YDL187c	2	0.000	12	YDL231c	2	0.000	15
YDL145c	10	0.311	1102	YDL188c	4	0.333	315	YDL232w	2	0.000	88
YDL146w	5	0.100	207	YDL189w	6	0.067	676	YDL233w	5	0.200	292
YDL147w	7	0.476	890	YDL190c	4	0.500	357	YDL234c	5	0.000	189
YDL148c	6	0.400	421	YDL191w	11	0.291	916	YDL235c	4	0.333	85
YDL149w	11	0.091	896	YDL192w	10	0.289	654	YDL236w	1	0.000	0
YDL150w	2	0.000	145	YDL193w	10	0.089	972	YDL237w	7	0.333	580
YDL151c	3	0.333	35	YDL194w	4	0.333	272	YDL238c	7	0.333	723
YDL152w	2	0.000	5	YDL195w	2	0.000	9	YDL239c	8	0.214	416
YDL153c	3	0.333	45	YDL196w	5	0.300	92	YDL240w	6	0.533	110

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YDL241w	15	0.171	930	YDR034c-c	1	0.000	0	YDR076w	9	0.528	100
YDL242w	5	0.500	92	YDR034w-b	28	0.172	5741	YDR077w	43	0.244	8960
YDL243c	6	0.333	225	YDR035w	7	0.238	483	YDR078c	6	0.067	287
YDL244w	11	0.273	2198	YDR036c	6	0.533	180	YDR079w	7	0.190	275
YDL245c	16	0.292	1919	YDR037w	7	0.571	260	YDR080w	4	0.333	79
YDL246c	19	0.351	678	YDR038c	9	0.222	914	YDR081c	19	0.082	13056
YDL247w	6	0.133	381	YDR039c	9	0.222	634	YDR082w	1	0.000	0
YDL248w	8	0.321	1110	YDR040c	30	0.239	4332	YDR083w	9	0.167	676
YDR001c	12	0.197	1622	YDR041w	24	0.308	2230	YDR084c	31	0.118	5438
YDR002w	4	0.167	231	YDR042c	46	0.132	17451	YDR085c	11	0.236	998
YDR003w	9	0.194	4399	YDR043c	425	0.028	474296	YDR086c	11	0.200	1616
YDR004w	7	0.095	694	YDR044w	20	0.326	2612	YDR087c	1	0.000	0
YDR005c	1	0.000	0	YDR045c	5	0.000	198	YDR088c	5	0.200	2217
YDR006c	6	0.000	353	YDR046c	12	0.167	2089	YDR089w	15	0.381	2423
YDR007w	8	0.214	768	YDR047w	5	0.100	217	YDR090c	3	0.000	67
YDR008c	4	0.000	199	YDR048c	9	0.083	661	YDR091c	4	0.333	110
YDR009w	9	0.306	929	YDR049w	8	0.107	273	YDR092w	6	0.467	218
YDR010c	14	0.220	1115	YDR050c	11	0.291	1634	YDR093w	4	0.667	50
YDR011w	26	0.246	5038	YDR051c	3	0.333	95	YDR094w	1	0.000	0
YDR012w	9	0.500	619	YDR052c	6	0.133	150	YDR096w	194	0.022	76429
YDR013w	5	0.400	88	YDR053w	2	0.000	6	YDR097c	4	0.000	301
YDR014w	1	0.000	0	YDR054c	9	0.194	641	YDR098c	7	0.476	2454
YDR015c	2	1.000	0	YDR055w	19	0.281	1664	YDR098c-a	6	0.267	214
YDR016c	2	1.000	0	YDR056c	2	0.000	11	YDR098c-b	6	0.267	214
YDR017c	2	0.000	28	YDR057w	4	0.333	213	YDR099w	3	0.667	3
YDR018c	7	0.095	334	YDR058c	9	0.250	3626	YDR100w	6	0.200	441
YDR019c	9	0.389	759	YDR059c	3	0.000	44	YDR101c	7	0.143	771
YDR020c	3	0.333	62	YDR060w	5	0.500	109	YDR102c	7	0.190	426
YDR021w	4	0.500	89	YDR061w	8	0.179	536	YDR103w	11	0.145	1166
YDR022c	3	0.000	178	YDR062w	3	0.667	17	YDR104c	4	0.167	148
YDR023w	7	0.286	567	YDR063w	10	0.200	851	YDR105c	1	0.000	0
YDR024w	3	0.333	27	YDR064w	12	0.258	2418	YDR106w	2	0.000	31
YDR025w	9	0.222	621	YDR065w	9	0.222	798	YDR107c	5	0.200	112
YDR026c	3	0.000	105	YDR066c	4	0.167	127	YDR108w	2	0.000	86
YDR027c	3	0.000	326	YDR067c	12	0.167	1068	YDR109c	2	0.000	61
YDR028c	8	0.143	772	YDR068w	12	0.167	1068	YDR110w	5	0.100	387
YDR029w	4	0.000	372	YDR069c	2	1.000	0	YDR111c	6	0.467	148
YDR030c	19	0.187	1489	YDR070c	19	0.228	2064	YDR112w	2	1.000	0
YDR031w	15	0.124	757	YDR071c	4	0.000	72	YDR113c	9	0.278	2002
YDR032c	9	0.194	257	YDR072c	8	0.321	364	YDR114c	2	0.000	11
YDR033w	13	0.231	1365	YDR073w	8	0.429	179	YDR115w	4	0.167	45
YDR034c	12	0.288	664	YDR074w	15	0.200	1511	YDR117c	2	0.000	163
YDR034c-a	1	0.000	0	YDR075w	6	0.067	742	YDR118w	5	0.100	248

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YDR119w	3	0.333	110	YDR164c	3	0.000	158	YDR205w	1	0.000	0
YDR120c	2	0.000	10	YDR165w	6	0.267	519	YDR207c	266	0.015	339144
YDR121w	1	0.000	0	YDR166c	1	0.000	0	YDR208w	11	0.164	1580
YDR122w	4	0.333	67	YDR167w	2	0.000	175	YDR210c-c	3	0.667	6
YDR123c	168	0.021	77869	YDR168w	3	0.000	77	YDR210c-d	19	0.111	1533
YDR124w	7	0.333	251	YDR169c	8	0.393	423	YDR210w	10	0.289	760
YDR125c	6	0.200	385	YDR169c-a	3	0.667	31	YDR210w-c	2	1.000	0
YDR126w	3	0.000	51	YDR170c	4	0.333	50	YDR210w-d	5	0.300	92
YDR127w	10	0.178	598	YDR170w-a	3	0.333	31	YDR211w	5	0.500	100
YDR128w	3	0.333	47	YDR171w	30	0.260	6233	YDR212w	3	0.333	30
YDR129c	5	0.000	172	YDR172w	4	0.167	799	YDR213w	215	0.018	151526
YDR130c	2	1.000	0	YDR173c	2	1.000	0	YDR214w	11	0.218	1800
YDR131c	8	0.107	434	YDR174w	4	0.333	81	YDR215c	3	0.333	80
YDR132c	13	0.321	844	YDR175c	1	0.000	0	YDR216w	458	0.013	589228
YDR133c	9	0.333	292	YDR176w	2	0.000	19	YDR217c	2	1.000	0
YDR134c	12	0.379	387	YDR177w	1	0.000	0	YDR218c	3	0.667	8
YDR135c	8	0.393	504	YDR178w	10	0.222	557	YDR219c	2	0.000	33
YDR136c	5	0.700	97	YDR179c	22	0.126	2877	YDR220c	2	0.000	10
YDR137w	6	0.333	357	YDR179w-a	16	0.150	1603	YDR221w	3	1.000	0
YDR138w	5	0.400	144	YDR180w	2	0.000	1	YDR222w	11	0.218	1004
YDR139c	2	1.000	0	YDR181c	3	0.333	34	YDR223w	7	0.143	466
YDR140w	2	0.000	27	YDR182w	3	0.333	40	YDR224c	6	0.133	261
YDR141c	2	0.000	63	YDR182w-a	2	0.000	31	YDR225w	7	0.143	2504
YDR142c	3	0.000	52	YDR183w	12	0.121	1235	YDR226w	7	0.333	229
YDR143c	2	0.000	65	YDR184c	7	0.238	586	YDR227w	8	0.179	858
YDR144c	16	0.175	3404	YDR185c	5	0.500	204	YDR228c	5	0.200	149
YDR145w	14	0.110	1930	YDR186c	11	0.255	2334	YDR229w	6	0.400	133
YDR146c	240	0.028	286695	YDR187c	3	0.000	84	YDR231c	3	0.667	15
YDR147w	10	0.200	773	YDR188w	8	0.357	269	YDR232w	8	0.036	189
YDR148c	8	0.071	207	YDR189w	6	0.400	359	YDR233c	3	0.333	212
YDR150w	4	0.167	107	YDR190c	6	0.267	231	YDR234w	7	0.286	771
YDR151c	8	0.429	259	YDR191w	8	0.214	623	YDR235w	3	0.333	131
YDR152w	10	0.333	4641	YDR192c	6	0.267	122	YDR236c	2	1.000	0
YDR153c	3	0.333	18	YDR193w	1	0.000	0	YDR237w	2	1.000	0
YDR154c	12	0.333	874	YDR194c	3	0.000	135	YDR239c	2	0.000	89
YDR155c	16	0.158	2389	YDR195w	3	0.333	97	YDR240c	6	0.400	188
YDR156w	14	0.253	1769	YDR197w	3	0.333	213	YDR241w	1	0.000	0
YDR157w	9	0.194	561	YDR198c	1	0.000	0	YDR242w	4	0.167	63
YDR158w	12	0.227	884	YDR199w	1	0.000	0	YDR243c	2	0.000	15
YDR159w	3	0.000	99	YDR200c	2	1.000	0	YDR244w	14	0.099	5278
YDR160w	3	0.333	67	YDR201w	3	0.667	51	YDR245w	8	0.107	1258
YDR161w	5	0.300	196	YDR202c	1	0.000	0	YDR246w	9	0.306	854
YDR163w	3	1.000	0	YDR204w	2	0.000	15	YDR246w-a	4	0.500	21

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YDR247w	4	0.333	66	YDR290w	1	0.000	0	YDR332w	5	0.000	57
YDR248c	2	1.000	0	YDR291w	1	0.000	0	YDR333c	3	0.667	57
YDR249c	3	0.667	36	YDR292c	4	0.000	91	YDR334w	4	0.833	24
YDR250c	4	0.500	96	YDR293c	3	0.667	23	YDR335w	1	0.000	0
YDR251w	6	0.400	157	YDR294c	10	0.089	1213	YDR336w	1	0.000	0
YDR252w	1	0.000	0	YDR295c	1	0.000	0	YDR337w	2	0.000	8
YDR253c	102	0.024	31538	YDR296w	2	1.000	0	YDR338c	2	1.000	0
YDR254w	6	0.267	105	YDR297w	16	0.275	1877	YDR339c	3	0.000	325
YDR255c	2	0.000	19	YDR298c	9	0.222	168	YDR340w	2	0.000	37
YDR256c	13	0.154	1199	YDR299w	6	0.133	82	YDR341c	7	0.048	524
YDR257c	6	0.200	537	YDR300c	7	0.381	388	YDR342c	19	0.304	4026
YDR258c	17	0.324	2688	YDR301w	6	0.200	336	YDR343c	25	0.330	2492
YDR259c	358	0.034	219573	YDR302w	2	1.000	0	YDR345c	28	0.302	3768
YDR260c	6	0.467	297	YDR303c	3	0.333	44	YDR346c	1	0.000	0
YDR261c	11	0.291	292	YDR304c	1	0.000	0	YDR347w	1	0.000	0
YDR261w-b	1	0.000	0	YDR305c	1	0.000	0	YDR348c	2	1.000	0
YDR262w	7	0.429	239	YDR307w	2	0.000	77	YDR350c	2	1.000	0
YDR263c	8	0.250	238	YDR308c	4	0.500	43	YDR351w	3	0.333	42
YDR264c	5	0.700	83	YDR309c	26	0.286	3026	YDR352w	1	0.000	0
YDR265w	5	0.400	129	YDR310c	162	0.009	226036	YDR353w	9	0.500	253
YDR266c	6	0.267	1207	YDR311w	7	0.286	1679	YDR354w	10	0.400	566
YDR267c	4	0.167	203	YDR312w	9	0.278	1337	YDR355c	2	1.000	0
YDR268w	4	0.167	174	YDR313c	7	0.238	224	YDR356w	4	0.167	398
YDR270w	5	0.400	34	YDR314c	5	0.100	166	YDR357c	3	0.333	32
YDR271c	2	1.000	0	YDR315c	5	0.200	218	YDR358w	3	0.333	21
YDR272w	5	0.500	52	YDR316w	4	0.000	173	YDR359c	2	0.000	25
YDR273w	5	0.000	514	YDR316w-a	5	0.600	51	YDR360w	1	0.000	0
YDR274c	7	0.476	173	YDR316w-b	5	0.600	51	YDR361c	7	0.333	720
YDR275w	8	0.536	215	YDR317w	15	0.105	1682	YDR362c	1	0.000	0
YDR276c	5	0.300	120	YDR318w	1	0.000	0	YDR363w	2	0.000	15
YDR277c	90	0.039	110053	YDR319c	3	0.667	19	YDR363w-a	7	0.476	791
YDR278c	10	0.133	597	YDR320c	2	0.000	14	YDR364c	1	0.000	0
YDR279w	11	0.164	831	YDR321w	6	0.267	1163	YDR365c	3	0.333	152
YDR280w	3	0.000	157	YDR322c-a	7	0.238	127	YDR366c	3	0.333	7
YDR281c	6	0.333	381	YDR322w	2	1.000	0	YDR367w	5	0.300	119
YDR282c	13	0.115	1182	YDR323c	8	0.036	498	YDR368w	7	0.190	270
YDR283c	5	0.200	481	YDR324c	8	0.286	505	YDR369c	3	0.000	61
YDR284c	12	0.121	1352	YDR325w	6	0.200	542	YDR370c	13	0.090	2442
YDR285w	6	0.267	267	YDR326c	2	0.000	64	YDR371w	10	0.067	919
YDR286c	11	0.109	910	YDR327w	2	0.000	103	YDR372c	24	0.072	2904
YDR287w	9	0.111	768	YDR328c	5	0.100	242	YDR373w	17	0.147	1112
YDR288w	2	0.000	36	YDR329c	2	0.000	42	YDR374c	3	0.333	50
YDR289c	1	0.000	0	YDR330w	2	0.000	70	YDR375c	3	0.000	105

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YDR376w	6	0.067	241	YDR419w	4	0.000	1619	YDR463w	238	0.012	200667
YDR377w	13	0.103	738	YDR420w	4	0.333	271	YDR464w	3	0.000	147
YDR378c	6	0.267	420	YDR421w	99	0.011	91373	YDR465c	8	0.143	326
YDR379c-a	3	0.333	122	YDR422c	3	0.333	189	YDR466w	2	0.000	7
YDR379w	8	0.286	618	YDR423c	492	0.007	562971	YDR467c	1	0.000	0
YDR380w	22	0.212	4591	YDR424c	4	0.167	104	YDR468c	6	0.067	378
YDR381c-a	2	1.000	0	YDR425w	1	0.000	0	YDR469w	4	0.167	142
YDR381w	2	1.000	0	YDR426c	3	0.000	88	YDR470c	8	0.321	611
YDR382w	9	0.472	655	YDR427w	4	0.667	98	YDR471w	20	0.284	3248
YDR383c	3	0.333	17	YDR428c	1	0.000	0	YDR472w	7	0.143	521
YDR384c	20	0.237	5504	YDR429c	2	0.000	88	YDR473c	25	0.140	3953
YDR385w	13	0.321	1607	YDR430c	1	0.000	0	YDR474c	3	0.000	105
YDR386w	1	0.000	0	YDR432w	4	0.667	46	YDR475c	4	0.333	50
YDR387c	2	0.000	17	YDR433w	4	0.167	63	YDR476c	6	0.200	559
YDR388w	3	0.333	27	YDR434w	6	0.133	528	YDR477w	2	0.000	17
YDR389w	6	0.533	98	YDR435c	3	0.667	6	YDR478w	1	0.000	0
YDR390c	2	0.000	36	YDR436w	2	1.000	0	YDR479c	2	0.000	87
YDR391c	9	0.389	1501	YDR437w	2	0.000	22	YDR480w	5	0.300	648
YDR392w	2	0.000	23	YDR438w	5	0.300	142	YDR481c	8	0.286	977
YDR393w	9	0.111	668	YDR439w	5	0.300	341	YDR482c	4	0.333	115
YDR394w	5	0.600	74	YDR440w	1	0.000	0	YDR483w	5	0.100	298
YDR395w	3	0.000	140	YDR441c	26	0.317	2094	YDR484w	4	0.167	108
YDR396w	2	0.000	43	YDR442w	19	0.287	1112	YDR485c	1	0.000	0
YDR397c	2	0.000	47	YDR443c	2	0.000	26	YDR486c	7	0.286	591
YDR398w	4	0.500	23	YDR444w	2	0.000	189	YDR487c	8	0.500	472
YDR399w	10	0.378	325	YDR445c	1	0.000	0	YDR488c	4	0.167	94
YDR400w	3	0.333	27	YDR446w	8	0.357	247	YDR489w	2	0.000	9
YDR401w	1	0.000	0	YDR447c	10	0.444	392	YDR490c	3	0.333	32
YDR402c	12	0.167	1224	YDR448w	8	0.179	349	YDR491c	1	0.000	0
YDR403w	20	0.226	3717	YDR449c	12	0.288	802	YDR492w	13	0.154	973
YDR404c	5	0.300	360	YDR450w	10	0.356	913	YDR493w	3	0.667	19
YDR405w	6	0.333	492	YDR451c	326	0.023	443477	YDR494w	7	0.048	251
YDR406w	20	0.174	2926	YDR452w	17	0.287	1356	YDR495c	12	0.152	709
YDR407c	5	0.100	164	YDR453c	19	0.251	950	YDR496c	8	0.357	547
YDR408c	8	0.321	794	YDR454c	7	0.333	602	YDR497c	8	0.321	419
YDR409w	3	0.000	71	YDR455c	5	0.100	369	YDR498c	6	0.267	582
YDR410c	5	0.100	474	YDR456w	4	0.500	127	YDR499w	4	0.333	294
YDR411c	4	0.167	167	YDR457w	10	0.200	996	YDR500c	17	0.316	1902
YDR412w	4	0.333	202	YDR458c	1	0.000	0	YDR501w	210	0.015	363000
YDR415c	3	0.000	37	YDR459c	3	0.000	26	YDR502c	7	0.143	760
YDR416w	6	0.133	203	YDR460w	3	0.333	237	YDR503c	4	0.167	102
YDR417c	3	0.667	13	YDR461w	19	0.374	1769	YDR504c	3	0.667	2
YDR418w	11	0.382	1207	YDR462w	2	0.000	45	YDR505c	2	0.000	9

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YDR506c	3	0.000	36	YDR545w	28	0.183	2188	YEL041w	13	0.359	478
YDR507c	6	0.400	144	YEL001c	15	0.286	1715	YEL042w	5	0.100	132
YDR508c	17	0.279	1671	YEL002c	7	0.048	885	YEL043w	3	0.000	69
YDR509w	9	0.167	548	YEL003w	3	1.000	0	YEL044w	25	0.260	4523
YDR510w	21	0.290	2622	YEL004w	11	0.182	1312	YEL045c	22	0.208	3602
YDR511w	4	0.000	230	YEL005c	9	0.083	742	YEL046c	25	0.207	5077
YDR512c	7	0.095	337	YEL006w	1	0.000	0	YEL047c	11	0.291	547
YDR513w	5	0.600	37	YEL007w	19	0.433	1716	YEL048c	1	0.000	0
YDR514c	5	0.500	292	YEL008w	10	0.311	323	YEL049w	5	0.100	169
YDR515w	5	0.300	238	YEL009c	585	0.012	839314	YEL050c	12	0.227	971
YDR516c	14	0.374	843	YEL010w	8	0.143	173	YEL051w	3	0.667	11
YDR517w	4	0.333	63	YEL011w	21	0.400	1207	YEL052w	5	0.600	89
YDR518w	6	0.600	92	YEL012w	10	0.156	689	YEL053c	4	1.000	0
YDR519w	4	0.000	247	YEL013w	4	0.000	210	YEL054c	14	0.363	872
YDR520c	4	0.167	98	YEL014c	1	0.000	0	YEL055c	7	0.238	720
YDR521w	2	0.000	9	YEL015w	3	0.000	97	YEL056w	7	0.190	860
YDR522c	22	0.134	2395	YEL016c	6	0.133	562	YEL057c	8	0.357	466
YDR523c	17	0.221	5698	YEL017c-a	9	0.361	789	YEL058w	6	0.267	240
YDR524c	4	0.500	9	YEL017w	7	0.619	293	YEL059c-a	3	1.000	0
YDR524c-b	9	0.417	220	YEL018w	3	0.000	422	YEL059w	7	0.190	212
YDR524w-a	1	0.000	0	YEL019c	2	0.000	4	YEL060c	29	0.148	5192
YDR524w-c	1	0.000	0	YEL020c	3	0.333	96	YEL061c	5	0.300	661
YDR525w	9	0.111	255	YEL020w-a	10	0.444	441	YEL062w	14	0.220	1383
YDR525w-a	19	0.333	1810	YEL021w	18	0.248	2828	YEL063c	10	0.422	619
YDR526c	7	0.333	189	YEL022w	6	0.200	598	YEL064c	2	0.000	7
YDR527w	12	0.212	715	YEL023c	6	0.200	598	YEL065w	20	0.205	2595
YDR528w	15	0.238	990	YEL024w	15	0.238	834	YEL066w	2	1.000	0
YDR529c	9	0.139	254	YEL025c	8	0.071	234	YEL067c	3	0.333	119
YDR530c	5	0.300	225	YEL026w	7	0.524	177	YEL068c	2	0.000	20
YDR531w	7	0.381	355	YEL027w	4	0.167	148	YEL069c	11	0.418	517
YDR532c	2	0.000	48	YEL028w	1	0.000	0	YEL070w	22	0.316	1639
YDR533c	32	0.280	3844	YEL029c	2	0.000	36	YEL071w	22	0.294	2757
YDR534c	9	0.306	428	YEL030w	4	0.333	98	YEL072w	14	0.165	1155
YDR535c	5	0.100	139	YEL031w	3	0.000	138	YEL073c	10	0.267	742
YDR536w	17	0.147	1594	YEL032w	5	0.500	77	YEL074w	12	0.348	840
YDR537c	1	0.000	0	YEL033w	4	0.167	38	YEL075c	7	0.476	90
YDR538w	1	0.000	0	YEL034w	7	0.667	151	YEL076c	5	0.100	78
YDR539w	4	0.000	51	YEL035c	13	0.359	1005	YEL076c-a	6	0.133	134
YDR540c	5	0.300	229	YEL036c	6	0.733	32	YEL076w-c	2	0.000	2
YDR541c	10	0.200	464	YEL037c	4	0.333	314	YEL077c	5	0.100	85
YDR542w	21	0.214	3645	YEL038w	4	0.167	83	YER001w	25	0.247	3715
YDR543c	25	0.207	2146	YEL039c	19	0.275	1545	YER002w	12	0.227	1633
YDR544c	28	0.201	2430	YEL040w	30	0.264	5558	YER003c	4	0.667	50

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YER004w	7	0.333	362	YER044c-a	8	0.357	244	YER081w	12	0.212	5143
YER006w	9	0.278	831	YER045c	29	0.305	8796	YER082c	3	0.333	127
YER007c-a	19	0.088	1870	YER046w	14	0.374	1857	YER083c	2	0.000	7
YER007w	4	0.333	215	YER047c	4	0.333	189	YER084w	3	0.000	47
YER008c	1	0.000	0	YER048c	5	0.600	15	YER085c	3	0.333	28
YER009w	1	0.000	0	YER048w-a	7	0.095	510	YER086w	6	0.267	254
YER010c	9	0.361	407	YER049w	6	0.067	182	YER087c-a	1	0.000	0
YER011w	20	0.342	1602	YER050c	1	0.000	0	YER087c-b	3	0.000	26
YER012w	11	0.182	981	YER052c	9	0.333	621	YER087w	2	1.000	0
YER013w	17	0.066	3439	YER053c	18	0.275	1568	YER088c	269	0.007	551939
YER014w	5	0.400	124	YER053c-a	6	0.600	50	YER089c	9	0.472	507
YER015w	5	0.200	98	YER054c	13	0.308	551	YER090w	5	0.500	90
YER016w	2	0.000	28	YER055c	18	0.327	2610	YER091c	19	0.205	2226
YER017c	6	0.400	153	YER056c	8	0.536	328	YER091c-a	6	0.267	196
YER018c	9	0.278	461	YER056c-a	8	0.464	297	YER092w	13	0.179	2494
YER019c-a	5	0.700	28	YER057c	4	0.000	112	YER093c-a	3	0.333	50
YER019w	8	0.357	397	YER058w	2	1.000	0	YER094c	14	0.319	1161
YER020w	5	0.700	28	YER059w	4	0.333	105	YER095w	10	0.222	524
YER021w	6	0.400	408	YER060w	6	0.133	410	YER096w	19	0.316	1677
YER022w	4	0.167	198	YER060w-a	7	0.333	235	YER097w	2	0.000	26
YER023w	3	0.000	150	YER061c	5	0.400	93	YER098w	5	0.300	91
YER024w	10	0.178	745	YER062c	28	0.249	4741	YER099c	4	0.333	78
YER025w	5	0.200	176	YER063w	7	0.190	442	YER100w	7	0.333	227
YER026c	8	0.321	1010	YER064c	8	0.250	580	YER101c	6	0.600	153
YER027c	1	0.000	0	YER065c	13	0.256	2288	YER102w	11	0.491	729
YER028c	30	0.257	5256	YER066c-a	5	0.200	114	YER103w	30	0.216	5042
YER029c	4	0.500	73	YER066w	3	0.000	23	YER104w	3	0.667	94
YER030w	3	0.333	39	YER067w	14	0.297	1100	YER105c	3	0.333	253
YER031c	7	0.524	459	YER068w	45	0.057	68574	YER106w	5	0.400	518
YER032w	8	0.321	1242	YER069w	21	0.162	3459	YER107c	3	0.000	177
YER033c	13	0.436	798	YER070w	18	0.118	3038	YER109c	236	0.040	104710
YER034w	9	0.472	401	YER071c	3	0.333	100	YER110c	7	0.238	259
YER035w	12	0.318	1533	YER072w	15	0.295	1155	YER111c	594	0.014	861633
YER036c	5	0.300	143	YER073w	23	0.383	2090	YER112w	15	0.286	1404
YER037w	19	0.257	2389	YER074w	14	0.352	1230	YER114c	3	0.667	21
YER038c	5	0.400	113	YER074w-a	3	0.333	27	YER115c	1	0.000	0
YER039c	7	0.333	332	YER075c	8	0.500	144	YER116c	9	0.333	470
YER039c-a	3	0.000	119	YER076c	4	0.500	59	YER117w	11	0.473	773
YER040w	184	0.023	136327	YER077c	4	0.167	74	YER118c	3	0.333	24
YER041w	2	0.000	47	YER078c	14	0.297	836	YER119c	5	0.400	119
YER042w	5	0.200	94	YER078w-a	3	0.000	13	YER119c-a	1	0.000	0
YER043c	5	0.200	201	YER079w	18	0.222	1539	YER120w	5	0.400	72
YER044c	25	0.210	5928	YER080w	5	0.600	95	YER121w	6	0.600	86

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YER122c	1	0.000	0	YER162c	4	0.500	139	YFL010w-a	3	0.333	154
YER123w	6	0.133	223	YER163c	5	0.200	354	YFL011w	15	0.171	2837
YER124c	14	0.308	1752	YER164w	2	0.000	82	YFL012w	8	0.250	689
YER125w	9	0.417	681	YER165w	2	0.000	43	YFL013c	6	0.333	207
YER126c	6	0.333	133	YER166w	1	0.000	0	YFL013w-a	2	0.000	5
YER127w	3	0.333	33	YER167w	2	0.000	23	YFL014w	57	0.203	18951
YER128w	6	0.067	146	YER168c	3	1.000	0	YFL015c	2	1.000	0
YER129w	4	0.167	58	YER169w	96	0.019	94209	YFL016c	15	0.295	1196
YER130c	12	0.333	1273	YER170w	4	0.167	51	YFL017c	4	0.167	174
YER131w	14	0.385	1492	YER171w	3	0.000	33	YFL017w-a	4	0.167	273
YER132c	4	0.500	77	YER172c	3	0.333	38	YFL018c	9	0.167	690
YER133w	16	0.167	2202	YER173w	3	0.000	111	YFL020c	15	0.267	1218
YER134c	7	0.238	147	YER174c	9	0.278	178	YFL021w	167	0.039	200969
YER135c	4	0.167	76	YER175c	9	0.361	227	YFL022c	17	0.272	2888
YER136w	7	0.286	682	YER176w	10	0.200	416	YFL023w	14	0.209	1268
YER137c	6	0.333	221	YER177w	18	0.294	1354	YFL024c	13	0.218	869
YER137c-a	3	0.333	29	YER178w	2	1.000	0	YFL025c	4	0.333	75
YER138c	15	0.133	1711	YER179w	8	0.214	500	YFL026w	11	0.236	894
YER138w-a	7	0.333	119	YER180c	2	0.000	27	YFL027c	9	0.306	293
YER139c	6	0.267	188	YER180c-a	1	0.000	0	YFL028c	6	0.267	125
YER140w	6	0.400	198	YER181c	3	0.333	107	YFL029c	5	0.200	282
YER141w	10	0.200	939	YER182w	2	0.000	134	YFL030w	12	0.258	757
YER142c	11	0.218	497	YER183c	6	0.133	610	YFL031w	223	0.017	382509
YER143w	9	0.333	303	YER184c	6	0.267	293	YFL032w	1	0.000	0
YER144c	4	0.333	165	YER185w	9	0.167	786	YFL033c	4	0.167	967
YER145c	20	0.332	2177	YER186c	1	0.000	0	YFL034c-a	15	0.238	2518
YER146w	19	0.292	2373	YER187w	5	0.400	369	YFL034c-b	3	0.667	9
YER147c	4	0.167	184	YER188c-a	6	0.267	59	YFL034w	9	0.250	653
YER148w	4	0.167	541	YER188w	5	0.300	438	YFL036w	1	0.000	0
YER149c	10	0.267	472	YER189w	29	0.158	3910	YFL037w	6	0.200	797
YER150w	39	0.177	9189	YER190w	26	0.182	2789	YFL038c	3	0.000	276
YER151c	1	0.000	0	YFL001w	1	0.000	0	YFL039c	10	0.356	577
YER152c	4	0.167	81	YFL002c	2	0.000	11	YFL040w	3	0.333	130
YER153c	9	0.222	356	YFL002w-a	1	0.000	0	YFL041w	5	0.300	297
YER154w	8	0.393	210	YFL002w-b	4	0.167	192	YFL042c	6	0.600	84
YER155c	17	0.279	2129	YFL003c	5	0.100	414	YFL044c	98	0.016	141988
YER156c	5	0.500	189	YFL004w	6	0.467	229	YFL045c	7	0.429	552
YER157w	4	0.167	121	YFL005w	6	0.400	111	YFL046w	1	0.000	0
YER158c	18	0.359	2277	YFL006w	1	0.000	0	YFL047w	7	0.286	830
YER159c	7	0.429	268	YFL007w	6	0.267	432	YFL048c	5	0.400	467
YER159c-a	3	0.667	69	YFL008w	3	0.000	91	YFL049w	2	1.000	0
YER160c	4	0.500	218	YFL009w	2	0.000	21	YFL050c	2	1.000	0
YER161c	24	0.065	6118	YFL010c	2	0.000	21	YFL051c	4	0.833	6

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YFL052w	5	0.300	217	YFR027w	2	0.000	14	YGL009c	13	0.282	934
YFL053w	10	0.267	709	YFR028c	77	0.004	125739	YGL010w	6	0.333	154
YFL054c	8	0.357	326	YFR029w	6	0.067	591	YGL011c	5	0.500	139
YFL055w	12	0.424	504	YFR030w	13	0.333	1473	YGL012w	11	0.255	771
YFL056c	9	0.361	315	YFR031c	1	0.000	0	YGL013c	666	0.015	779413
YFL057c	10	0.511	285	YFR031c-a	14	0.374	1747	YGL014w	2	1.000	0
YFL058w	10	0.178	1879	YFR032c	8	0.107	1026	YGL015c	6	0.067	572
YFL059w	13	0.244	1122	YFR032c-a	15	0.229	1310	YGL017w	2	0.000	17
YFL060c	11	0.036	770	YFR032c-b	2	0.000	9	YGL018c	1	0.000	0
YFL061w	4	0.167	134	YFR033c	15	0.248	1049	YGL021w	7	0.286	435
YFL062w	10	0.222	266	YFR034c	377	0.011	523332	YGL022w	1	0.000	0
YFL063w	11	0.218	664	YFR035c	7	0.143	324	YGL023c	2	0.000	17
YFL064c	10	0.400	322	YFR036w	4	0.167	108	YGL025c	1	0.000	0
YFL065c	4	0.667	33	YFR037c	6	0.133	353	YGL026c	4	0.500	70
YFL066c	3	0.000	34	YFR038w	5	0.300	243	YGL027c	2	0.000	35
YFL067w	5	0.100	114	YFR039c	6	0.200	521	YGL028c	10	0.422	364
YFL068w	1	0.000	0	YFR040w	4	0.333	139	YGL029w	8	0.357	298
YFR001w	9	0.222	2615	YFR041c	4	0.333	69	YGL030w	9	0.417	325
YFR002w	3	0.000	56	YFR042w	2	0.000	41	YGL031c	11	0.400	624
YFR003c	6	0.333	383	YFR043c	5	0.200	315	YGL032c	15	0.448	628
YFR004w	5	0.300	303	YFR044c	7	0.143	729	YGL033w	3	0.000	44
YFR005c	3	0.000	41	YFR045w	4	0.167	75	YGL034c	2	0.000	10
YFR006w	5	0.400	42	YFR047c	7	0.286	321	YGL035c	247	0.015	263790
YFR007w	10	0.089	612	YFR048w	2	1.000	0	YGL036w	7	0.524	115
YFR008w	4	0.167	43	YFR049w	3	0.333	110	YGL037c	20	0.279	1919
YFR009w	7	0.238	970	YFR050c	4	0.833	52	YGL038c	11	0.273	940
YFR010w	5	0.300	469	YFR051c	1	0.000	0	YGL039w	7	0.381	317
YFR011c	7	0.381	326	YFR052w	5	0.200	223	YGL040c	2	0.000	36
YFR012w	8	0.214	700	YFR053c	27	0.296	2857	YGL041c	1	0.000	0
YFR013w	1	0.000	0	YFR054c	6	0.200	207	YGL043w	4	0.500	55
YFR014c	2	1.000	0	YFR055w	8	0.393	548	YGL044c	2	0.000	36
YFR015c	23	0.233	5291	YFR056c	1	0.000	0	YGL045w	7	0.381	102
YFR016c	3	0.333	56	YFR057w	6	0.133	336	YGL046w	1	0.000	0
YFR017c	32	0.254	5615	YGL001c	40	0.147	8647	YGL047w	4	0.333	292
YFR018c	9	0.306	1259	YGL002w	2	0.000	17	YGL048c	5	0.600	505
YFR019w	6	0.133	201	YGL003c	4	0.167	433	YGL050w	3	0.000	94
YFR020w	5	0.500	248	YGL004c	4	0.167	26	YGL051w	1	0.000	0
YFR021w	1	0.000	0	YGL005c	4	0.000	1145	YGL052w	3	0.000	162
YFR022w	14	0.264	1956	YGL006w	7	0.143	345	YGL053w	12	0.364	683
YFR023w	13	0.115	1964	YGL006w-a	14	0.385	699	YGL054c	1	0.000	0
YFR024c-a	5	0.300	90	YGL007c-a	15	0.400	796	YGL055w	23	0.281	9792
YFR025c	5	0.400	183	YGL007w	15	0.162	1540	YGL056c	8	0.179	312
YFR026c	8	0.179	951	YGL008c	16	0.192	1487	YGL057c	1	0.000	0

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YGL058w	2	0.000	33	YGL104c	13	0.346	892	YGL151w	4	0.167	98
YGL059w	4	0.000	96	YGL105w	1	0.000	0	YGL152c	3	0.000	50
YGL060w	4	0.500	56	YGL106w	1	0.000	0	YGL153w	5	0.400	94
YGL061c	6	0.400	96	YGL107c	2	0.000	171	YGL154c	6	0.533	67
YGL062w	17	0.279	1083	YGL108c	4	0.333	167	YGL155w	1	0.000	0
YGL063w	7	0.190	608	YGL110c	1	0.000	0	YGL156w	21	0.181	4276
YGL064c	3	0.000	80	YGL111w	3	0.667	12	YGL157w	27	0.205	4561
YGL065c	2	0.000	17	YGL113w	1	0.000	0	YGL158w	17	0.338	1426
YGL066w	2	0.000	7	YGL114w	9	0.361	480	YGL159w	10	0.111	708
YGL067w	1	0.000	0	YGL115w	6	0.267	233	YGL160w	7	0.095	607
YGL068w	4	0.500	56	YGL116w	20	0.179	2954	YGL161c	5	0.200	252
YGL069c	1	0.000	0	YGL117w	17	0.250	2655	YGL162w	84	0.116	44305
YGL070c	4	0.333	116	YGL118c	2	0.000	36	YGL163c	11	0.455	393
YGL071w	756	0.008	1414625	YGL119w	4	0.167	88	YGL164c	1	0.000	0
YGL072c	6	0.400	174	YGL120c	5	0.400	133	YGL165c	1	0.000	0
YGL073w	577	0.008	804470	YGL121c	22	0.216	4057	YGL166w	30	0.115	8658
YGL074c	4	0.667	17	YGL122c	2	1.000	0	YGL167c	8	0.393	636
YGL075c	3	0.333	54	YGL123w	10	0.378	703	YGL169w	2	0.000	16
YGL076c	9	0.472	291	YGL124c	5	0.400	110	YGL170c	1	0.000	0
YGL077c	7	0.143	795	YGL125w	14	0.297	1310	YGL171w	10	0.200	1909
YGL078c	5	0.500	64	YGL126w	9	0.333	854	YGL172w	2	1.000	0
YGL079w	4	0.000	198	YGL127c	5	0.300	193	YGL173c	5	0.300	401
YGL080w	2	0.000	54	YGL128c	7	0.286	512	YGL174w	4	0.500	100
YGL081w	2	0.000	11	YGL130w	2	0.000	158	YGL175c	3	0.333	92
YGL083w	4	0.167	80	YGL131c	2	1.000	0	YGL176c	1	0.000	0
YGL084c	3	0.667	17	YGL133w	12	0.136	956	YGL177w	6	0.200	158
YGL085w	1	0.000	0	YGL134w	11	0.073	904	YGL178w	6	0.733	35
YGL087c	1	0.000	0	YGL135w	20	0.142	3252	YGL179c	9	0.472	264
YGL088w	4	0.500	36	YGL136c	10	0.244	836	YGL180w	10	0.267	1382
YGL089c	10	0.244	842	YGL137w	1	0.000	0	YGL181w	69	0.022	46596
YGL091c	2	0.000	22	YGL138c	4	0.000	367	YGL182c	6	0.267	310
YGL092w	1	0.000	0	YGL139w	3	0.000	211	YGL183c	4	0.000	207
YGL093w	3	0.000	57	YGL140c	3	0.333	32	YGL184c	21	0.233	3021
YGL094c	3	0.333	70	YGL141w	5	0.200	230	YGL185c	3	0.667	121
YGL095c	4	0.667	62	YGL142c	3	0.667	18	YGL186c	9	0.250	1362
YGL096w	326	0.024	594587	YGL143c	7	0.238	147	YGL187c	14	0.220	756
YGL097w	5	0.600	25	YGL144c	4	0.167	513	YGL188c	10	0.356	573
YGL098w	2	1.000	0	YGL145w	14	0.341	1090	YGL188c-a	2	0.000	9
YGL099w	4	0.500	115	YGL146c	6	0.333	181	YGL189c	11	0.455	524
YGL100w	5	0.700	60	YGL147c	13	0.372	1007	YGL190c	5	0.000	180
YGL101w	8	0.214	372	YGL148w	10	0.200	840	YGL191w	12	0.121	1280
YGL102c	5	0.000	203	YGL149w	1	0.000	0	YGL192w	118	0.012	70076
YGL103w	9	0.556	294	YGL150c	1	0.000	0	YGL193c	10	0.267	344

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YGL194c	16	0.117	2986	YGL239c	1	0.000	0	YGR019w	14	0.209	1375
YGL195w	7	0.286	1302	YGL240w	4	0.667	43	YGR020c	4	0.167	193
YGL196w	8	0.143	863	YGL241w	2	0.000	46	YGR021w	3	0.333	57
YGL197w	6	0.200	190	YGL242c	5	0.300	297	YGR022c	2	0.000	76
YGL198w	5	0.200	145	YGL243w	2	1.000	0	YGR024c	6	0.467	193
YGL199c	2	0.000	14	YGL244w	3	0.000	72	YGR025w	1	0.000	0
YGL200c	4	0.333	64	YGL245w	5	0.100	533	YGR026w	11	0.091	933
YGL201c	5	0.400	54	YGL246c	4	0.167	374	YGR027c	8	0.429	445
YGL202w	8	0.286	694	YGL247w	4	0.167	169	YGR028w	6	0.333	142
YGL203c	1	0.000	0	YGL248w	8	0.500	404	YGR029w	2	0.000	26
YGL204c	2	1.000	0	YGL249w	6	0.000	162	YGR030c	2	0.000	30
YGL205w	13	0.128	1072	YGL250w	5	0.100	615	YGR031c-a	1	0.000	0
YGL206c	3	0.667	156	YGL251c	3	0.333	65	YGR031w	4	0.500	68
YGL207w	6	0.200	357	YGL252c	9	0.139	362	YGR032w	20	0.226	3145
YGL208w	4	0.000	107	YGL253w	14	0.264	1679	YGR033c	5	0.600	65
YGL209w	66	0.082	39033	YGL254w	104	0.023	89297	YGR034w	7	0.381	4655
YGL210w	2	0.000	14	YGL255w	29	0.180	6227	YGR035c	21	0.262	2428
YGL213c	1	0.000	0	YGL256w	13	0.154	1387	YGR035w-a	4	0.833	6
YGL214w	1	0.000	0	YGL257c	7	0.143	170	YGR036c	5	0.100	111
YGL215w	4	0.333	280	YGL258w	16	0.283	2564	YGR037c	4	0.667	70
YGL216w	1	0.000	0	YGL259w	10	0.222	382	YGR038c-a	6	0.467	301
YGL217c	2	0.000	54	YGL260w	4	0.333	29	YGR038c-b	2	1.000	0
YGL218w	1	0.000	0	YGL261c	13	0.295	566	YGR038w	1	0.000	0
YGL219c	3	0.333	66	YGL262w	1	0.000	0	YGR039w	6	0.267	110
YGL220w	1	0.000	0	YGL263w	7	0.095	674	YGR040w	11	0.327	435
YGL221c	2	0.000	35	YGR001c	1	0.000	0	YGR041w	15	0.381	1474
YGL222c	2	0.000	80	YGR002c	2	1.000	0	YGR042w	1	0.000	0
YGL223c	3	0.000	89	YGR003w	2	0.000	151	YGR043c	30	0.214	7926
YGL224c	6	0.267	198	YGR004w	1	0.000	0	YGR044c	247	0.014	168884
YGL225w	7	0.143	321	YGR005c	3	0.333	38	YGR045c	9	0.250	277
YGL226c-a	6	0.267	279	YGR006w	2	0.000	205	YGR046w	3	0.333	51
YGL226w	8	0.321	277	YGR007w	3	0.000	226	YGR047c	2	0.000	12
YGL227w	12	0.182	997	YGR008c	13	0.256	897	YGR048w	4	0.500	53
YGL228w	8	0.214	527	YGR009c	9	0.444	424	YGR049w	10	0.289	751
YGL229c	6	0.133	274	YGR010w	8	0.393	222	YGR050c	17	0.294	1087
YGL230c	8	0.250	1390	YGR011w	9	0.361	438	YGR051c	3	0.333	26
YGL231c	5	0.100	148	YGR012w	8	0.250	732	YGR052w	32	0.264	5059
YGL232w	2	0.000	57	YGR013w	4	0.500	60	YGR053c	5	0.200	259
YGL234w	12	0.212	1404	YGR014w	11	0.455	662	YGR054w	2	0.000	14
YGL235w	4	0.167	52	YGR015c	6	0.133	549	YGR055w	12	0.182	1897
YGL236c	5	0.400	123	YGR016w	8	0.107	957	YGR056w	2	0.000	171
YGL237c	201	0.007	70496	YGR017w	2	0.000	22	YGR057c	4	0.167	223
YGL238w	4	0.167	167	YGR018c	4	0.000	144	YGR058w	5	0.000	905

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YGR059w	12	0.076	1658	YGR105w	2	1.000	0	YGR146c	18	0.333	1275
YGR060w	20	0.300	3181	YGR106c	7	0.190	484	YGR146c-a	2	0.000	26
YGR061c	8	0.143	1157	YGR107w	6	0.200	225	YGR147c	3	0.000	122
YGR063c	1	0.000	0	YGR108w	21	0.314	2622	YGR148c	15	0.286	1569
YGR065c	11	0.327	513	YGR109c	11	0.127	1054	YGR149w	15	0.286	1298
YGR066c	14	0.143	1065	YGR109w-a	6	0.267	141	YGR150c	6	0.133	292
YGR067c	14	0.253	971	YGR109w-b	5	0.400	97	YGR151c	3	0.667	20
YGR068c	3	0.000	137	YGR110w	13	0.218	838	YGR152c	9	0.306	1095
YGR069w	5	0.300	88	YGR111w	4	0.500	84	YGR153w	5	0.500	83
YGR070w	7	0.333	507	YGR112w	7	0.238	1131	YGR154c	10	0.156	1336
YGR071c	12	0.106	623	YGR113w	6	0.267	346	YGR155w	10	0.267	1627
YGR072w	13	0.154	1296	YGR115c	1	0.000	0	YGR156w	4	0.500	55
YGR073c	4	0.000	107	YGR116w	4	0.167	256	YGR157w	12	0.258	2032
YGR074w	1	0.000	0	YGR117c	8	0.571	218	YGR158c	2	0.000	94
YGR075c	6	0.000	388	YGR118w	13	0.282	3171	YGR159c	9	0.333	449
YGR076c	2	0.000	26	YGR119c	2	0.000	47	YGR160w	2	0.000	14
YGR077c	2	1.000	0	YGR120c	6	0.133	602	YGR161c	27	0.291	4157
YGR078c	8	0.143	436	YGR121c	12	0.303	1418	YGR161w-a	2	0.000	51
YGR079w	19	0.164	2817	YGR121w-a	3	1.000	0	YGR161w-b	1	0.000	0
YGR080w	3	0.000	45	YGR122w	5	0.300	76	YGR161w-c	1	0.000	0
YGR081c	4	0.333	100	YGR123c	9	0.250	623	YGR162w	7	0.429	163
YGR082w	3	0.333	27	YGR124w	11	0.164	1343	YGR163w	1	0.000	0
YGR084c	9	0.250	1047	YGR125w	8	0.250	356	YGR164w	1	0.000	0
YGR085c	9	0.444	361	YGR126w	4	0.167	221	YGR165w	6	0.133	413
YGR086c	17	0.309	1168	YGR127w	9	0.222	1066	YGR166w	8	0.036	771
YGR087c	16	0.200	1550	YGR128c	5	0.300	674	YGR168c	7	0.190	174
YGR088w	45	0.191	10227	YGR129w	4	0.000	522	YGR169c	2	0.000	70
YGR089w	9	0.278	214	YGR130c	10	0.400	502	YGR169c-a	1	0.000	0
YGR090w	4	0.667	43	YGR131w	6	0.467	66	YGR170w	9	0.083	960
YGR091w	5	0.200	146	YGR132c	3	0.333	21	YGR171c	3	0.000	55
YGR092w	14	0.319	1221	YGR133w	4	0.500	44	YGR172c	2	0.000	121
YGR093w	3	0.000	396	YGR134w	5	0.500	428	YGR173w	6	0.067	660
YGR094w	6	0.333	1069	YGR135w	7	0.238	673	YGR174c	2	1.000	0
YGR095c	3	0.333	37	YGR136w	4	0.167	184	YGR174w-a	1	0.000	0
YGR096w	2	1.000	0	YGR137w	4	0.333	110	YGR175c	16	0.233	1415
YGR097w	5	0.900	3	YGR138c	13	0.244	1331	YGR176w	9	0.250	373
YGR098c	9	0.139	744	YGR139w	3	0.333	26	YGR177c	11	0.164	804
YGR099w	8	0.107	1029	YGR140w	8	0.571	127	YGR178c	3	0.333	62
YGR100w	2	0.000	8	YGR141w	5	0.400	221	YGR179c	4	0.333	112
YGR101w	2	1.000	0	YGR142w	21	0.224	3403	YGR180c	24	0.373	2167
YGR102c	1	0.000	0	YGR143w	10	0.311	355	YGR181w	6	0.800	41
YGR103w	13	0.128	1258	YGR144w	14	0.308	2160	YGR182c	2	0.000	47
YGR104c	1	0.000	0	YGR145w	6	0.467	90	YGR183c	15	0.152	1582

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YGR184c	5	0.200	230	YGR229c	8	0.250	456	YGR271w	13	0.179	480
YGR185c	3	0.333	274	YGR230w	10	0.356	707	YGR272c	7	0.190	246
YGR186w	1	0.000	0	YGR231c	5	0.100	651	YGR273c	5	0.000	362
YGR187c	7	0.286	547	YGR232w	6	0.133	819	YGR274c	2	1.000	0
YGR188c	17	0.096	1779	YGR233c	18	0.261	2097	YGR275w	3	0.333	142
YGR189c	19	0.269	2707	YGR234w	34	0.212	7972	YGR276c	3	0.333	310
YGR190c	4	0.000	95	YGR235c	4	0.000	202	YGR277c	4	0.000	73
YGR191w	12	0.409	450	YGR236c	8	0.179	464	YGR278w	4	0.000	73
YGR192c	21	0.333	4028	YGR237c	4	0.333	63	YGR279c	14	0.396	628
YGR193c	5	0.500	24	YGR238c	13	0.321	795	YGR280c	9	0.389	355
YGR194c	5	0.200	114	YGR239c	5	0.400	143	YGR281w	10	0.156	698
YGR195w	3	0.333	41	YGR240c	11	0.309	851	YGR282c	11	0.182	819
YGR196c	3	0.333	98	YGR240c-a	1	0.000	0	YGR283c	10	0.311	524
YGR197c	12	0.197	1496	YGR241c	6	0.467	187	YGR284c	3	0.667	57
YGR198w	7	0.333	849	YGR242w	3	0.333	33	YGR285c	3	0.333	66
YGR199w	6	0.267	538	YGR243w	11	0.218	686	YGR286c	10	0.378	372
YGR200c	5	0.100	574	YGR244c	10	0.200	944	YGR287c	17	0.265	1009
YGR201c	8	0.286	258	YGR245c	6	0.467	95	YGR288w	11	0.182	929
YGR202c	4	0.667	183	YGR246c	4	0.333	100	YGR289c	9	0.306	861
YGR203w	8	0.214	926	YGR247w	4	0.500	306	YGR292w	10	0.200	1214
YGR204c-a	1	0.000	0	YGR248w	45	0.231	10533	YGR294w	5	0.300	132
YGR204w	17	0.235	3260	YGR249w	316	0.049	365525	YGR295c	16	0.250	972
YGR205w	4	0.167	190	YGR250c	11	0.345	697	YGR296w	19	0.228	1132
YGR206w	2	0.000	11	YGR251w	10	0.444	1002	YHL001w	14	0.264	1863
YGR208w	4	0.500	80	YGR252w	2	0.000	126	YHL002w	3	0.333	29
YGR209c	11	0.309	319	YGR253c	14	0.319	1595	YHL003c	1	0.000	0
YGR210c	6	0.533	83	YGR254w	25	0.217	3498	YHL004w	3	0.000	54
YGR211w	9	0.444	392	YGR255c	6	0.333	325	YHL005c	2	0.000	93
YGR212w	4	0.333	173	YGR256w	22	0.229	4368	YHL006c	3	0.000	165
YGR213c	13	0.231	940	YGR257c	1	0.000	0	YHL007c	2	0.000	19
YGR214w	14	0.308	2366	YGR258c	8	0.179	1013	YHL008c	5	0.100	569
YGR215w	4	0.333	228	YGR259c	2	0.000	27	YHL009c	43	0.012	29212
YGR216c	5	0.200	217	YGR260w	6	0.133	897	YHL009w-a	1	0.000	0
YGR217w	7	0.333	608	YGR261c	3	0.667	94	YHL010c	2	0.000	4
YGR218w	14	0.187	823	YGR263c	3	0.333	262	YHL011c	3	1.000	0
YGR220c	3	0.000	71	YGR264c	5	0.500	184	YHL012w	7	0.048	204
YGR221c	16	0.433	1549	YGR265w	3	0.000	42	YHL013c	9	0.250	325
YGR222w	10	0.511	332	YGR266w	4	0.167	129	YHL015w	18	0.327	1612
YGR223c	6	0.733	66	YGR267c	5	0.300	216	YHL015w-a	5	0.700	26
YGR224w	12	0.333	769	YGR268c	9	0.278	1548	YHL016c	19	0.257	3084
YGR225w	2	0.000	4	YGR269w	3	0.667	61	YHL017w	3	0.000	69
YGR226c	1	0.000	0	YGR270w	9	0.250	2199	YHL019c	1	0.000	0
YGR227w	2	0.000	10	YGR271c-a	4	0.167	147	YHL020c	30	0.124	3625

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YHL021c	16	0.342	1584	YHR011w	3	0.000	41	YHR050w	8	0.214	388
YHL022c	6	0.133	400	YHR012w	5	0.300	98	YHR050w-a	3	0.000	71
YHL023c	4	0.167	185	YHR013c	4	0.000	163	YHR051w	12	0.152	761
YHL024w	20	0.389	2203	YHR014w	7	0.190	620	YHR052w	10	0.267	3417
YHL025w	5	0.500	31	YHR015w	6	0.133	1117	YHR053c	13	0.205	1220
YHL026c	10	0.400	283	YHR016c	10	0.400	822	YHR054c	6	0.200	333
YHL027w	218	0.027	146339	YHR017w	2	0.000	11	YHR055c	13	0.167	973
YHL028w	29	0.276	5211	YHR018c	21	0.195	3035	YHR056c	24	0.040	12856
YHL029c	18	0.275	1931	YHR019c	8	0.286	562	YHR058c	5	0.000	289
YHL030w	10	0.244	689	YHR020w	7	0.429	475	YHR059w	3	0.000	32
YHL031c	3	0.000	57	YHR021c	10	0.400	454	YHR060w	3	0.667	22
YHL032c	10	0.267	1052	YHR021w-a	4	0.167	103	YHR061c	9	0.333	1076
YHL033c	9	0.528	233	YHR022c	14	0.385	1336	YHR062c	9	0.278	889
YHL034c	13	0.218	766	YHR022c-a	4	0.167	222	YHR063c	4	0.667	102
YHL035c	6	0.400	474	YHR023w	12	0.318	1673	YHR064c	4	0.500	233
YHL036w	19	0.222	3383	YHR024c	2	0.000	36	YHR065c	5	0.400	374
YHL037c	3	0.000	37	YHR025w	6	0.333	279	YHR066w	6	0.400	554
YHL038c	6	0.533	509	YHR026w	3	0.333	28	YHR067w	7	0.333	587
YHL039w	8	0.143	395	YHR027c	2	1.000	0	YHR068w	4	0.167	415
YHL040c	19	0.363	1987	YHR028c	10	0.111	927	YHR069c	1	0.000	0
YHL041w	7	0.286	117	YHR029c	13	0.346	748	YHR070w	6	0.333	197
YHL042w	9	0.417	451	YHR030c	5	0.100	71	YHR071w	18	0.320	2608
YHL043w	1	0.000	0	YHR031c	7	0.238	169	YHR072w	4	0.500	43
YHL044w	7	0.429	72	YHR032w	6	0.467	77	YHR072w-a	3	0.667	10
YHL045w	8	0.357	300	YHR033w	20	0.447	1088	YHR073w	3	0.667	31
YHL046c	15	0.267	1160	YHR034c	3	0.667	9	YHR074w	2	0.000	118
YHL047c	9	0.222	1252	YHR035w	6	0.200	108	YHR076w	3	0.000	70
YHL048w	20	0.200	1786	YHR036w	3	0.000	31	YHR077c	3	0.333	58
YHL049c	17	0.294	1467	YHR037w	11	0.145	805	YHR078w	4	0.667	54
YHL050c	6	0.400	234	YHR038w	2	0.000	30	YHR079c	3	0.000	187
YHR001w	14	0.121	1359	YHR039c	3	0.000	53	YHR079c-a	3	0.333	15
YHR001w-a	12	0.136	562	YHR039c-a	5	0.200	180	YHR080c	5	0.100	253
YHR002w	5	0.200	265	YHR040w	3	0.333	38	YHR081w	6	0.000	646
YHR003c	4	0.167	73	YHR041c	9	0.250	744	YHR082c	4	0.000	168
YHR004c	5	0.200	147	YHR042w	11	0.218	638	YHR083w	8	0.107	1116
YHR005c	10	0.467	658	YHR043c	9	0.222	537	YHR084w	1375	0.007	3379020
YHR005c-a	7	0.333	216	YHR044c	5	0.000	334	YHR085w	6	0.333	637
YHR006w	345	0.008	467778	YHR045w	2	0.000	30	YHR086w	9	0.333	756
YHR007c	17	0.397	1160	YHR046c	3	0.333	111	YHR087w	39	0.189	13913
YHR007c-a	3	0.000	100	YHR047c	11	0.309	1073	YHR088w	10	0.311	311
YHR008c	17	0.294	924	YHR048w	17	0.360	2271	YHR089c	6	0.333	351
YHR009c	4	0.500	49	YHR049c-a	1	0.000	0	YHR090c	5	0.100	931
YHR010w	9	0.417	1024	YHR049w	18	0.275	1725	YHR091c	25	0.173	2580

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YHR092c	25	0.307	3198	YHR135c	7	0.095	380	YHR178w	343	0.012	420044
YHR093w	2	0.000	2	YHR136c	27	0.188	5322	YHR179w	25	0.223	4314
YHR094c	32	0.226	7223	YHR137w	32	0.185	8960	YHR180w	3	0.000	69
YHR095w	8	0.179	670	YHR138c	25	0.147	6429	YHR181w	4	0.167	109
YHR096c	33	0.208	7296	YHR139c	21	0.238	2590	YHR182w	7	0.048	551
YHR097c	13	0.308	1414	YHR139c-a	4	0.333	288	YHR183w	8	0.250	1291
YHR098c	4	0.000	123	YHR140w	17	0.213	2628	YHR184w	9	0.528	1013
YHR099w	5	0.000	193	YHR141c	16	0.292	2574	YHR185c	6	0.067	1892
YHR100c	1	0.000	0	YHR142w	15	0.371	2201	YHR186c	6	0.267	456
YHR101c	1	0.000	0	YHR143w	10	0.244	419	YHR187w	1	0.000	0
YHR102w	1	0.000	0	YHR143w-a	4	0.333	83	YHR189w	3	0.000	50
YHR103w	4	0.500	166	YHR144c	5	0.500	162	YHR190w	24	0.185	2626
YHR104w	17	0.331	1205	YHR145c	6	0.267	196	YHR191c	5	0.300	482
YHR105w	2	0.000	29	YHR146w	5	0.200	211	YHR192w	5	0.400	132
YHR106w	1	0.000	0	YHR147c	4	0.000	330	YHR193c	19	0.111	1590
YHR107c	6	0.333	317	YHR148w	11	0.291	1510	YHR194w	18	0.098	907
YHR108w	4	0.333	119	YHR149c	10	0.400	503	YHR195w	7	0.000	321
YHR109w	3	0.333	76	YHR150w	8	0.500	105	YHR196w	8	0.500	259
YHR110w	5	0.200	426	YHR151c	9	0.333	539	YHR197w	4	0.667	17
YHR111w	6	0.267	290	YHR152w	16	0.300	2249	YHR198c	2	1.000	0
YHR112c	4	0.167	153	YHR153c	8	0.071	851	YHR199c	11	0.164	1640
YHR113w	4	0.167	87	YHR154w	10	0.111	1439	YHR200w	9	0.306	1277
YHR114w	2	0.000	31	YHR155w	19	0.058	3804	YHR201c	3	0.000	114
YHR115c	3	0.333	114	YHR156c	21	0.114	2351	YHR202w	8	0.286	519
YHR116w	5	0.200	344	YHR157w	18	0.157	2118	YHR203c	12	0.379	680
YHR117w	6	0.267	153	YHR159w	1	0.000	0	YHR204w	7	0.190	298
YHR118c	6	0.067	467	YHR160c	14	0.220	725	YHR205w	2	0.000	21
YHR119w	4	0.000	137	YHR161c	7	0.286	574	YHR206w	420	0.014	380453
YHR120w	4	0.167	139	YHR162w	9	0.250	851	YHR207c	5	0.500	72
YHR121w	5	0.200	385	YHR163w	2	1.000	0	YHR208w	10	0.400	549
YHR122w	5	0.400	225	YHR164c	4	0.333	127	YHR209w	13	0.295	1217
YHR123w	7	0.190	1168	YHR165c	2	0.000	139	YHR210c	13	0.308	975
YHR124w	40	0.050	46293	YHR166c	1	0.000	0	YHR211w	7	0.524	161
YHR126c	5	0.200	290	YHR167w	1	0.000	0	YHR212c	1	0.000	0
YHR127w	2	0.000	16	YHR169w	8	0.214	328	YHR212w-a	5	0.700	101
YHR128w	10	0.378	622	YHR170w	9	0.389	308	YHR213w	6	0.333	394
YHR129c	2	1.000	0	YHR171w	6	0.133	159	YHR213w-a	2	1.000	0
YHR130c	2	0.000	21	YHR172w	2	1.000	0	YHR213w-b	3	1.000	0
YHR131c	1	0.000	0	YHR173c	4	0.167	100	YHR214c-b	2	0.000	34
YHR132c	2	0.000	9	YHR174w	15	0.333	1470	YHR214c-c	1	0.000	0
YHR132w-a	1	0.000	0	YHR175w	8	0.179	424	YHR214w	7	0.333	68
YHR133c	4	0.333	66	YHR176w	6	0.267	182	YHR214w-a	9	0.278	472
YHR134w	7	0.524	471	YHR177w	3	1.000	0	YHR215w	15	0.133	1583

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YHR216w	8	0.429	754	YIL041w	5	0.100	95	YIL086c	1	0.000	0
YHR217c	2	1.000	0	YIL042c	6	0.267	675	YIL087c	8	0.429	198
YHR218w	4	0.333	54	YIL043c	2	0.000	11	YIL088c	5	0.300	254
YHR219w	3	0.333	37	YIL044c	4	0.167	119	YIL089w	4	0.500	20
YIL001w	4	0.667	18	YIL045w	11	0.200	723	YIL090w	4	0.333	172
YIL002c	2	1.000	0	YIL046w	11	0.345	955	YIL091c	9	0.306	453
YIL002w-a	6	0.267	242	YIL046w-a	5	0.400	123	YIL092w	2	1.000	0
YIL003w	21	0.124	5310	YIL047c	8	0.321	411	YIL094c	5	0.300	229
YIL004c	1	0.000	0	YIL048w	10	0.178	1018	YIL095w	5	0.500	64
YIL005w	1	0.000	0	YIL049w	2	1.000	0	YIL096c	9	0.444	4329
YIL006w	3	0.667	2	YIL050w	10	0.333	933	YIL097w	4	0.167	152
YIL008w	3	0.667	70	YIL051c	15	0.200	1877	YIL098c	7	0.238	236
YIL009c-a	3	0.333	60	YIL052c	13	0.295	1237	YIL099w	42	0.262	9463
YIL009w	10	0.444	280	YIL053w	21	0.267	2425	YIL100w	12	0.348	286
YIL010w	1	0.000	0	YIL054w	3	0.000	46	YIL101c	201	0.057	97533
YIL011w	18	0.359	1513	YIL055c	8	0.393	341	YIL102c	8	0.321	548
YIL012w	3	0.333	9	YIL056w	17	0.426	3136	YIL103w	3	1.000	0
YIL013c	18	0.412	1187	YIL057c	16	0.508	1405	YIL104c	4	0.500	48
YIL014c-a	3	0.667	6	YIL060w	2	0.000	26	YIL105c	2	0.000	11
YIL014w	7	0.143	152	YIL061c	2	0.000	16	YIL106w	6	0.400	139
YIL015c-a	2	0.000	9	YIL062c	3	0.667	24	YIL107c	9	0.278	390
YIL015w	16	0.283	4558	YIL063c	2	0.000	39	YIL108w	7	0.333	257
YIL016w	4	0.500	179	YIL064w	3	0.000	46	YIL109c	3	0.333	27
YIL018w	11	0.309	1331	YIL065c	5	0.400	64	YIL110w	2	0.000	75
YIL019w	14	0.308	1573	YIL066c	28	0.230	3927	YIL111w	11	0.182	975
YIL020c	7	0.190	710	YIL067c	1	0.000	0	YIL112w	6	0.200	264
YIL022w	4	0.333	206	YIL069c	13	0.321	1122	YIL113w	14	0.275	1808
YIL023c	6	0.067	382	YIL070c	5	0.200	110	YIL114c	7	0.381	257
YIL024c	3	0.333	38	YIL071c	1	0.000	0	YIL115c	4	0.333	41
YIL026c	5	0.400	175	YIL072w	9	0.250	582	YIL116w	13	0.359	860
YIL027c	1	0.000	0	YIL073c	4	0.333	106	YIL117c	28	0.238	4419
YIL029c	2	0.000	5	YIL074c	7	0.476	345	YIL118w	23	0.415	2509
YIL030c	7	0.429	437	YIL075c	8	0.571	183	YIL119c	34	0.360	4432
YIL031w	4	0.167	284	YIL076w	4	0.000	299	YIL120w	6	0.467	184
YIL032c	3	0.333	97	YIL077c	4	0.000	137	YIL121w	15	0.324	1643
YIL033c	8	0.393	249	YIL078w	3	0.667	14	YIL122w	111	0.029	185444
YIL034c	1	0.000	0	YIL079c	2	0.000	158	YIL123w	21	0.338	2159
YIL035c	5	0.000	386	YIL080w	2	1.000	0	YIL124w	7	0.190	584
YIL036w	199	0.028	117431	YIL082w	2	1.000	0	YIL125w	6	0.200	69
YIL037c	18	0.340	3478	YIL082w-a	2	0.000	16	YIL126w	4	0.333	156
YIL038c	4	0.167	100	YIL083c	4	0.333	165	YIL127c	4	0.333	103
YIL039w	1	0.000	0	YIL084c	2	0.000	62	YIL128w	3	0.667	5
YIL040w	4	0.167	297	YIL085c	1	0.000	0	YIL129c	7	0.143	421

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YIL130w	4	0.833	16	YIL175w	12	0.212	597	YIR038c	18	0.320	1942
YIL131c	242	0.010	199990	YIL176c	13	0.218	766	YIR039c	12	0.152	1034
YIL132c	4	0.333	38	YIL177c	17	0.309	1258	YIR040c	7	0.095	278
YIL133c	14	0.308	1793	YIR001c	2	0.000	19	YIR041w	11	0.236	725
YIL134w	2	0.000	94	YIR002c	5	0.600	83	YIR042c	7	0.238	621
YIL135c	7	0.143	801	YIR003w	5	0.400	95	YIR043c	5	0.500	127
YIL136w	23	0.316	2417	YIR004w	4	0.500	75	YIR044c	6	0.133	221
YIL137c	5	0.200	611	YIR005w	4	0.167	50	YJL001w	7	0.333	357
YIL138c	3	0.000	214	YIR006c	6	0.667	123	YJL002c	3	0.667	7
YIL139c	6	0.333	159	YIR007w	2	1.000	0	YJL003w	4	0.167	17
YIL140w	7	0.095	243	YIR008c	2	0.000	28	YJL004c	2	0.000	36
YIL141w	5	0.300	91	YIR009w	3	0.000	269	YJL005w	4	0.333	80
YIL142w	3	0.333	34	YIR010w	2	0.000	68	YJL006c	2	0.000	6
YIL143c	2	0.000	19	YIR011c	2	0.000	34	YJL007c	1	0.000	0
YIL144w	3	0.000	75	YIR012w	5	0.200	153	YJL008c	8	0.286	826
YIL145c	4	0.167	261	YIR013c	135	0.037	15803	YJL009w	1	0.000	0
YIL146c	1	0.000	0	YIR014w	7	0.429	148	YJL010c	2	0.000	36
YIL147c	2	0.000	27	YIR015w	4	0.333	57	YJL011c	4	0.167	104
YIL148w	8	0.429	365	YIR016w	10	0.333	1010	YJL012c	11	0.109	1682
YIL149c	9	0.333	564	YIR017c	63	0.088	45517	YJL012c-a	2	0.000	13
YIL150c	1	0.000	0	YIR018c-a	5	0.900	2	YJL013c	1	0.000	0
YIL152w	2	0.000	36	YIR018w	504	0.012	614058	YJL014w	2	1.000	0
YIL153w	6	0.533	119	YIR019c	31	0.314	3668	YJL016w	11	0.309	768
YIL154c	8	0.250	736	YIR020c	18	0.373	562	YJL017w	2	0.000	8
YIL155c	25	0.253	4466	YIR020w-a	1	0.000	0	YJL019w	1	0.000	0
YIL156w	4	0.667	85	YIR020w-b	10	0.489	89	YJL020c	3	1.000	0
YIL157c	1	0.000	0	YIR021w	15	0.590	363	YJL022w	6	0.067	169
YIL158w	9	0.139	454	YIR022w	2	0.000	17	YJL023c	10	0.200	953
YIL159w	7	0.286	288	YIR023w	254	0.003	248926	YJL024c	2	0.000	46
YIL160c	14	0.264	1711	YIR024c	2	0.000	31	YJL025w	5	0.200	277
YIL161w	2	1.000	0	YIR025w	3	0.000	242	YJL026w	19	0.398	1351
YIL162w	27	0.188	3473	YIR026c	7	0.286	1667	YJL027c	5	0.400	84
YIL164c	5	0.500	130	YIR027c	19	0.269	4591	YJL028w	6	0.333	257
YIL165c	4	0.833	16	YIR028w	14	0.220	3231	YJL029c	7	0.524	121
YIL166c	7	0.143	411	YIR029w	17	0.257	2615	YJL030w	6	0.400	180
YIL167w	4	0.500	32	YIR030c	6	0.067	388	YJL031c	9	0.278	390
YIL168w	9	0.472	166	YIR031c	14	0.198	1950	YJL032w	1	0.000	0
YIL169c	22	0.260	1945	YIR032c	17	0.184	2345	YJL033w	5	0.200	160
YIL170w	19	0.380	1504	YIR033w	35	0.062	11992	YJL034w	8	0.321	952
YIL171w	14	0.473	496	YIR034c	17	0.191	2194	YJL035c	3	1.000	0
YIL172c	17	0.485	783	YIR035c	5	0.100	251	YJL036w	2	1.000	0
YIL173w	8	0.250	632	YIR036c	6	0.400	125	YJL037w	6	0.200	572
YIL174w	11	0.236	439	YIR037w	1	0.000	0	YJL038c	7	0.190	560

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YJL041w	1	0.000	0	YJL083w	5	0.200	150	YJL126w	2	0.000	29
YJL042w	7	0.381	204	YJL084c	7	0.238	230	YJL127c	3	0.667	28
YJL043w	9	0.306	996	YJL085w	6	0.267	167	YJL127c-b	2	1.000	0
YJL044c	8	0.321	995	YJL086c	1	0.000	0	YJL129c	2	0.000	33
YJL045w	17	0.228	1845	YJL087c	1	0.000	0	YJL130c	6	0.533	113
YJL047c	1	0.000	0	YJL088w	24	0.210	3279	YJL131c	1	0.000	0
YJL047c-a	6	0.467	149	YJL089w	116	0.027	142180	YJL132w	4	0.500	45
YJL048c	15	0.267	1307	YJL090c	4	0.167	79	YJL133c-a	2	0.000	24
YJL049w	7	0.429	318	YJL091c	4	0.000	93	YJL133w	5	0.000	484
YJL050w	9	0.278	501	YJL092w	6	0.200	283	YJL134w	9	0.361	671
YJL051w	9	0.167	768	YJL093c	3	1.000	0	YJL135w	6	0.333	260
YJL052c-a	2	1.000	0	YJL094c	6	0.267	762	YJL136c	12	0.318	1069
YJL052w	17	0.176	1876	YJL095w	5	0.200	247	YJL136w-a	1	0.000	0
YJL053w	2	0.000	22	YJL096w	4	0.333	71	YJL137c	1	0.000	0
YJL054w	2	0.000	15	YJL097w	3	0.333	67	YJL138c	6	0.333	275
YJL055w	3	0.667	103	YJL098w	5	0.500	61	YJL139c	7	0.143	171
YJL056c	191	0.011	115335	YJL099w	2	0.000	82	YJL140w	4	0.333	70
YJL057c	7	0.238	1288	YJL100w	10	0.356	770	YJL141c	9	0.306	403
YJL058c	3	0.667	37	YJL101c	17	0.221	1926	YJL142c	5	0.100	105
YJL059w	1	0.000	0	YJL102w	5	0.100	2051	YJL143w	4	0.000	184
YJL060w	14	0.077	1108	YJL103c	23	0.123	9756	YJL144w	15	0.171	1497
YJL061w	3	0.000	35	YJL104w	9	0.194	1550	YJL145w	8	0.250	149
YJL062w	1	0.000	0	YJL105w	13	0.231	2763	YJL146w	3	0.000	72
YJL063c	2	1.000	0	YJL106w	18	0.242	2666	YJL147c	1	0.000	0
YJL064w	1	0.000	0	YJL107c	16	0.308	852	YJL148w	45	0.139	16159
YJL066c	2	0.000	13	YJL108c	5	0.100	896	YJL149w	12	0.182	1315
YJL067w	4	0.333	48	YJL109c	3	0.000	106	YJL150w	4	0.167	160
YJL068c	7	0.238	390	YJL110c	152	0.022	86457	YJL151c	9	0.278	774
YJL069c	5	0.200	524	YJL111w	2	0.000	139	YJL152w	8	0.250	360
YJL070c	2	1.000	0	YJL112w	6	0.333	543	YJL153c	27	0.154	7813
YJL071w	4	0.667	68	YJL113w	2	0.000	13	YJL154c	1	0.000	0
YJL072c	1	0.000	0	YJL114w	3	0.333	43	YJL155c	5	0.200	131
YJL073w	8	0.107	860	YJL115w	13	0.359	790	YJL156c	3	0.000	63
YJL074c	5	0.100	406	YJL116c	24	0.301	3231	YJL156w-a	2	1.000	0
YJL075c	3	0.333	12	YJL117w	5	0.400	128	YJL157c	7	0.429	53
YJL076w	7	0.381	510	YJL118w	4	0.000	113	YJL158c	21	0.290	2626
YJL077c	8	0.321	691	YJL119c	3	0.333	22	YJL159w	22	0.303	3531
YJL077w-b	4	0.333	18	YJL120w	1	0.000	0	YJL160c	12	0.242	582
YJL078c	17	0.390	1212	YJL121c	4	0.000	122	YJL161w	11	0.182	700
YJL079c	25	0.317	3664	YJL122w	4	0.500	50	YJL162c	5	0.400	1272
YJL080c	6	0.267	216	YJL123c	2	0.000	39	YJL163c	12	0.227	514
YJL081c	2	0.000	20	YJL124c	2	0.000	9	YJL164c	9	0.139	813
YJL082w	9	0.361	238	YJL125c	1	0.000	0	YJL165c	1	0.000	0

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YJL166w	9	0.111	656	YJL213w	12	0.288	1009	YJR035w	2	0.000	20
YJL167w	4	0.167	216	YJL214w	5	0.800	16	YJR036c	1	0.000	0
YJL168c	4	0.000	617	YJL215c	1	0.000	0	YJR038c	1	0.000	0
YJL169w	1	0.000	0	YJL216c	16	0.317	1439	YJR039w	2	0.000	40
YJL170c	17	0.434	761	YJL217w	13	0.154	1062	YJR040w	3	0.000	89
YJL171c	10	0.178	444	YJL218w	17	0.279	1868	YJR041c	7	0.190	614
YJL172w	10	0.200	878	YJL219w	20	0.347	1656	YJR042w	3	0.333	43
YJL173c	5	0.000	290	YJL220w	11	0.455	330	YJR043c	6	0.533	1050
YJL174w	2	0.000	110	YJL221c	19	0.480	1045	YJR044c	23	0.103	4296
YJL175w	4	0.333	200	YJL222w	4	0.000	268	YJR045c	7	0.143	859
YJL176c	9	0.306	692	YJL223c	14	0.187	1765	YJR046w	9	0.139	500
YJL177w	9	0.444	411	YJL225c	18	0.261	1184	YJR047c	12	0.379	576
YJL178c	4	0.333	35	YJR001w	3	0.000	227	YJR048w	19	0.234	2310
YJL179w	3	0.000	91	YJR002w	5	0.300	327	YJR049c	4	0.167	162
YJL180c	4	0.500	324	YJR003c	5	0.300	58	YJR050w	3	0.000	31
YJL183w	1	0.000	0	YJR004c	7	0.190	466	YJR051w	4	0.333	68
YJL184w	3	1.000	0	YJR005w	2	0.000	80	YJR052w	2	0.000	31
YJL185c	7	0.238	236	YJR006w	6	0.200	436	YJR053w	5	0.300	116
YJL186w	8	0.250	322	YJR007w	8	0.071	811	YJR054w	10	0.289	637
YJL187c	7	0.333	287	YJR008w	12	0.227	923	YJR055w	2	0.000	36
YJL188c	6	0.267	60	YJR009c	10	0.378	426	YJR056c	3	0.000	171
YJL189w	14	0.308	1262	YJR010c-a	2	0.000	12	YJR057w	3	0.000	76
YJL190c	14	0.297	1289	YJR010w	16	0.200	2691	YJR058c	4	0.167	235
YJL191w	11	0.291	1088	YJR011c	23	0.142	3858	YJR059w	7	0.381	199
YJL192c	10	0.244	456	YJR013w	4	0.167	307	YJR060w	334	0.009	432706
YJL194w	17	0.250	1549	YJR015w	6	0.067	321	YJR061w	8	0.357	509
YJL196c	21	0.200	2232	YJR016c	8	0.357	412	YJR062c	1	0.000	0
YJL197w	1	0.000	0	YJR017c	2	0.000	11	YJR063w	2	0.000	171
YJL198w	8	0.429	337	YJR018w	3	0.667	11	YJR064w	3	0.333	60
YJL199c	1	0.000	0	YJR019c	9	0.389	404	YJR065c	3	0.333	230
YJL200c	10	0.333	520	YJR020w	1	0.000	0	YJR066w	4	0.167	319
YJL201w	5	0.100	281	YJR021c	2	1.000	0	YJR067c	1	0.000	0
YJL202c	1	0.000	0	YJR022w	2	0.000	19	YJR068w	1	0.000	0
YJL203w	11	0.145	1243	YJR023c	2	1.000	0	YJR069c	3	0.333	34
YJL204c	11	0.073	946	YJR025c	12	0.439	1461	YJR070c	4	0.500	68
YJL205c	5	0.400	614	YJR026w	3	0.333	231	YJR071w	5	0.200	142
YJL206c	52	0.010	33077	YJR027w	4	0.333	285	YJR072c	1	0.000	0
YJL207c	4	0.667	5	YJR028w	3	0.333	231	YJR073c	11	0.255	1004
YJL208c	3	0.667	30	YJR029w	4	0.333	285	YJR074w	4	0.333	116
YJL209w	6	0.000	790	YJR030c	8	0.357	410	YJR075w	4	0.500	883
YJL210w	13	0.295	1379	YJR032w	1	0.000	0	YJR076c	1	0.000	0
YJL211c	1	0.000	0	YJR033c	4	0.500	58	YJR077c	7	0.048	341
YJL212c	13	0.205	1900	YJR034w	1	0.000	0	YJR078w	12	0.136	2811

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YJR079w	7	0.143	209	YJR121w	12	0.318	550	YKL004w	5	0.300	752
YJR080c	2	0.000	19	YJR122w	10	0.267	831	YKL005c	26	0.031	5471
YJR082c	5	0.000	92	YJR123w	13	0.397	1153	YKL006c-a	8	0.179	817
YJR083c	1	0.000	0	YJR124c	2	0.000	4	YKL006w	11	0.327	1850
YJR084w	1	0.000	0	YJR127c	68	0.084	115913	YKL007w	15	0.229	4247
YJR085c	5	0.200	323	YJR128w	5	0.000	436	YKL008c	16	0.217	3046
YJR086w	5	0.200	188	YJR129c	6	0.333	755	YKL009w	11	0.273	1186
YJR087w	2	0.000	7	YJR130c	2	1.000	0	YKL010c	5	0.200	391
YJR088c	9	0.278	320	YJR131w	3	0.667	20	YKL011c	3	0.333	222
YJR089w	10	0.311	586	YJR132w	6	0.467	124	YKL012w	1	0.000	0
YJR090c	4	0.000	71	YJR133w	4	0.167	419	YKL013c	3	0.000	162
YJR091c	10	0.222	527	YJR134c	3	0.667	33	YKL014c	4	0.167	488
YJR092w	8	0.286	296	YJR135c	6	0.133	628	YKL015w	170	0.023	186446
YJR093c	3	0.000	152	YJR135w-a	2	0.000	57	YKL016c	14	0.209	1124
YJR094c	45	0.180	51329	YJR136c	3	0.667	14	YKL017c	1	0.000	0
YJR094w-a	14	0.462	695	YJR137c	15	0.267	2393	YKL018w	1	0.000	0
YJR095w	19	0.310	2164	YJR138w	9	0.167	1106	YKL019w	5	0.400	105
YJR096w	18	0.288	2322	YJR139c	6	0.467	147	YKL020c	59	0.046	24449
YJR097w	5	0.200	196	YJR140c	2	0.000	17	YKL021c	2	0.000	88
YJR098c	7	0.095	825	YJR141w	2	1.000	0	YKL022c	1	0.000	0
YJR099w	4	0.000	178	YJR144w	13	0.154	1580	YKL023w	1	0.000	0
YJR100c	19	0.058	1426	YJR145c	18	0.412	1284	YKL024c	2	1.000	0
YJR101w	3	0.000	15	YJR146w	13	0.359	700	YKL025c	3	1.000	0
YJR102c	6	0.400	189	YJR147w	58	0.078	70404	YKL026c	8	0.464	687
YJR103w	8	0.286	624	YJR148w	19	0.333	2506	YKL027w	3	0.667	13
YJR104c	14	0.286	1585	YJR149w	6	0.133	91	YKL028w	6	0.333	447
YJR105w	9	0.250	899	YJR150c	11	0.291	598	YKL029c	19	0.374	2373
YJR106w	2	1.000	0	YJR151c	9	0.194	723	YKL030w	5	0.300	84
YJR107w	4	0.333	274	YJR151w-a	1	0.000	0	YKL031w	2	0.000	9
YJR108w	3	0.667	11	YJR152w	19	0.234	2565	YKL032c	129	0.024	135771
YJR109c	16	0.267	1532	YJR153w	6	0.800	3	YKL033w	5	0.400	261
YJR110w	11	0.273	922	YJR154w	7	0.286	333	YKL033w-a	4	0.000	106
YJR111c	4	0.333	170	YJR155w	7	0.571	181	YKL034w	5	0.300	367
YJR112w	5	0.200	277	YJR156c	16	0.242	4596	YKL035w	17	0.301	1270
YJR112w-a	1	0.000	0	YJR157w	11	0.473	350	YKL036c	2	0.000	15
YJR113c	5	0.500	92	YJR158w	21	0.405	1000	YKL037w	8	0.250	239
YJR114w	3	0.000	506	YJR159w	17	0.441	691	YKL038w	67	0.027	34011
YJR115w	14	0.341	1650	YJR160c	3	0.333	171	YKL039w	13	0.244	786
YJR116w	7	0.333	536	YJR161c	9	0.222	736	YKL040c	18	0.222	2054
YJR117w	1	0.000	0	YJR162c	1	0.000	0	YKL041w	2	0.000	76
YJR118c	4	0.167	145	YKL001c	15	0.286	1853	YKL042w	7	0.286	1193
YJR119c	5	0.400	130	YKL002w	3	0.333	48	YKL043w	534	0.021	578631
YJR120w	7	0.429	273	YKL003c	3	0.333	118	YKL044w	15	0.410	712

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YKL045w	13	0.359	738	YKL086w	18	0.235	2340	YKL128c	3	0.000	137
YKL046c	1	0.000	0	YKL087c	8	0.321	545	YKL129c	4	0.500	292
YKL047w	5	0.200	310	YKL088w	2	1.000	0	YKL130c	1	0.000	0
YKL048c	2	0.000	32	YKL089w	2	0.000	36	YKL131w	1	0.000	0
YKL049c	5	0.000	518	YKL090w	6	0.333	121	YKL132c	5	0.400	49
YKL050c	1	0.000	0	YKL091c	11	0.309	543	YKL133c	2	0.000	2
YKL051w	13	0.128	1405	YKL092c	2	0.000	27	YKL134c	3	0.333	88
YKL052c	9	0.222	890	YKL093w	6	0.333	244	YKL135c	4	0.333	425
YKL053c-a	3	0.333	48	YKL095w	7	0.524	334	YKL136w	1	0.000	0
YKL053w	1	0.000	0	YKL096c-b	8	0.464	144	YKL137w	1	0.000	0
YKL054c	5	0.700	41	YKL096w	34	0.273	7123	YKL138c	5	0.200	427
YKL055c	5	0.200	148	YKL096w-a	31	0.280	5872	YKL138c-a	6	0.000	304
YKL056c	3	0.667	13	YKL097c	21	0.324	3335	YKL139w	6	0.200	181
YKL057c	4	0.333	148	YKL098w	7	0.286	373	YKL140w	2	0.000	27
YKL058w	6	0.200	199	YKL099c	3	0.000	277	YKL141w	10	0.200	607
YKL059c	5	0.300	77	YKL100c	4	0.167	164	YKL142w	10	0.244	846
YKL060c	12	0.227	1492	YKL101w	11	0.382	465	YKL143w	9	0.194	1561
YKL061w	2	1.000	0	YKL102c	4	0.500	38	YKL144c	5	0.100	614
YKL062w	522	0.016	493176	YKL103c	27	0.225	5053	YKL145w	5	0.600	63
YKL063c	9	0.222	809	YKL104c	9	0.278	483	YKL146w	5	0.200	169
YKL064w	4	0.333	199	YKL105c	2	0.000	19	YKL147c	3	0.667	19
YKL065c	4	0.500	138	YKL106w	3	0.000	122	YKL148c	12	0.167	890
YKL066w	4	0.167	78	YKL107w	11	0.164	2618	YKL149c	2	0.000	27
YKL067w	8	0.357	412	YKL108w	2	0.000	23	YKL150w	15	0.352	762
YKL068w	7	0.524	320	YKL109w	448	0.018	510855	YKL151c	11	0.382	420
YKL068w-a	1	0.000	0	YKL110c	18	0.477	940	YKL152c	9	0.278	729
YKL069w	6	0.067	807	YKL111c	2	0.000	71	YKL153w	3	0.000	64
YKL070w	7	0.286	251	YKL112w	688	0.003	1544447	YKL154w	3	0.333	67
YKL071w	17	0.250	1390	YKL113c	5	0.400	30	YKL155c	2	0.000	20
YKL072w	10	0.067	1058	YKL114c	4	0.000	122	YKL156w	9	0.417	619
YKL073w	14	0.121	1370	YKL115c	2	0.000	14	YKL157w	14	0.308	1072
YKL074c	4	0.333	193	YKL116c	2	0.000	23	YKL159c	3	0.333	151
YKL075c	3	0.000	118	YKL117w	3	1.000	0	YKL160w	4	0.167	451
YKL076c	1	0.000	0	YKL118w	4	0.167	382	YKL161c	11	0.164	1271
YKL077w	10	0.133	1355	YKL119c	2	0.000	36	YKL162c	3	0.667	14
YKL078w	11	0.091	2393	YKL120w	15	0.114	1733	YKL162c-a	9	0.417	247
YKL079w	3	0.000	212	YKL121w	2	1.000	0	YKL163w	35	0.249	5275
YKL080w	4	0.500	77	YKL122c	5	0.600	122	YKL164c	16	0.358	865
YKL081w	9	0.417	572	YKL123w	2	0.000	73	YKL165c	10	0.200	4382
YKL082c	10	0.400	3137	YKL124w	4	0.000	222	YKL167c	4	0.333	165
YKL083w	3	0.667	23	YKL125w	2	0.000	163	YKL168c	2	1.000	0
YKL084w	10	0.200	768	YKL126w	1	0.000	0	YKL169c	1	0.000	0
YKL085w	10	0.156	801	YKL127w	3	0.667	3	YKL171w	1	0.000	0

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YKL172w	4	0.000	469	YKL217w	15	0.248	1180	YKR038c	6	0.267	287
YKL173w	4	0.167	276	YKL218c	8	0.357	817	YKR039w	25	0.273	2966
YKL174c	6	0.133	565	YKL219w	11	0.109	797	YKR040c	19	0.234	1739
YKL175w	3	0.333	15	YKL220c	22	0.221	4897	YKR041w	14	0.264	1249
YKL176c	6	0.333	286	YKL221w	17	0.199	2886	YKR042w	32	0.282	4862
YKL177w	13	0.231	2052	YKL222c	1	0.000	0	YKR043c	4	0.000	165
YKL178c	13	0.218	2315	YKL223w	4	0.500	10	YKR044w	5	0.100	311
YKL179c	21	0.205	4292	YKL224c	12	0.348	420	YKR045c	1	0.000	0
YKL180w	8	0.536	278	YKL225w	8	0.179	257	YKR046c	11	0.309	1028
YKL181w	5	0.600	74	YKR002w	1	0.000	0	YKR047w	1	0.000	0
YKL182w	17	0.250	2827	YKR003w	1	0.000	0	YKR048c	1	0.000	0
YKL183c-a	1	0.000	0	YKR004c	4	0.000	80	YKR049c	9	0.417	342
YKL183w	7	0.286	763	YKR005c	3	0.333	29	YKR051w	1	0.000	0
YKL184w	3	0.000	71	YKR006c	1	0.000	0	YKR052c	12	0.364	708
YKL185w	120	0.028	48262	YKR007w	2	0.000	31	YKR053c	11	0.255	1622
YKL186c	5	0.600	18	YKR008w	2	0.000	18	YKR054c	5	0.400	249
YKL187c	15	0.181	1141	YKR009c	13	0.167	1313	YKR055w	8	0.107	907
YKL188c	4	0.500	57	YKR010c	5	0.100	254	YKR056w	9	0.167	714
YKL189w	6	0.400	393	YKR011c	6	0.600	65	YKR057w	12	0.439	865
YKL190w	2	0.000	171	YKR012c	4	0.000	138	YKR058w	12	0.212	2059
YKL191w	2	0.000	77	YKR013w	10	0.333	452	YKR059w	8	0.286	1114
YKL192c	2	1.000	0	YKR014c	3	0.667	5	YKR060w	4	0.333	85
YKL193c	1	0.000	0	YKR015c	4	0.000	432	YKR061w	10	0.356	584
YKL194c	1	0.000	0	YKR016w	3	0.333	27	YKR062w	6	0.067	330
YKL195w	4	0.167	240	YKR018c	2	0.000	30	YKR063c	2	1.000	0
YKL196c	5	0.400	451	YKR019c	2	1.000	0	YKR064w	1	0.000	0
YKL197c	8	0.286	646	YKR020w	1	0.000	0	YKR065c	5	0.400	126
YKL198c	8	0.321	234	YKR021w	1	0.000	0	YKR066c	9	0.361	625
YKL201c	15	0.314	1357	YKR022c	4	0.167	307	YKR067w	9	0.306	684
YKL202w	2	0.000	14	YKR023w	3	0.000	187	YKR068c	6	0.267	678
YKL203c	7	0.143	714	YKR024c	8	0.464	313	YKR069w	6	0.200	166
YKL204w	5	0.400	211	YKR025w	3	0.667	22	YKR070w	6	0.533	406
YKL205w	5	0.400	133	YKR026c	9	0.139	1860	YKR071c	6	0.333	156
YKL207w	1	0.000	0	YKR027w	3	0.000	80	YKR072c	3	0.333	57
YKL208w	3	0.333	29	YKR028w	1	0.000	0	YKR073c	5	0.200	202
YKL209c	8	0.393	188	YKR029c	2	0.000	80	YKR074w	2	1.000	0
YKL210w	8	0.571	156	YKR030w	2	0.000	171	YKR075c	17	0.199	1849
YKL211c	7	0.238	839	YKR031c	3	0.667	5	YKR076w	14	0.253	1624
YKL212w	1	0.000	0	YKR033c	1	0.000	0	YKR077w	4	0.333	51
YKL213c	3	0.333	146	YKR034w	85	0.044	23689	YKR078w	2	0.000	160
YKL214c	2	0.000	30	YKR035w-a	1	0.000	0	YKR079c	4	0.500	92
YKL215c	1	0.000	0	YKR036c	2	0.000	10	YKR080w	13	0.256	961
YKL216w	18	0.203	3026	YKR037c	2	0.000	44	YKR081c	6	0.400	540

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YKR082w	1	0.000	0	YLL018c	7	0.238	870	YLL063c	7	0.429	236
YKR083c	5	0.400	192	YLL018c-a	7	0.095	547	YLL064c	10	0.178	423
YKR084c	3	0.333	251	YLL019c	12	0.333	977	YLL065w	23	0.202	2888
YKR085c	2	0.000	46	YLL020c	4	0.000	76	YLL066c	21	0.252	2191
YKR086w	3	0.000	101	YLL021w	2	0.000	35	YLL066w-b	2	1.000	0
YKR087c	4	0.500	91	YLL022c	2	1.000	0	YLL067c	24	0.268	3206
YKR088c	1	0.000	0	YLL023c	6	0.400	155	YLR001c	3	0.333	36
YKR089c	6	0.267	369	YLL024c	10	0.267	695	YLR002c	6	0.133	663
YKR090w	5	0.300	215	YLL025w	13	0.192	1934	YLR003c	5	0.300	466
YKR091w	13	0.244	694	YLL026w	26	0.271	5848	YLR004c	8	0.321	1324
YKR092c	16	0.250	1943	YLL027w	15	0.276	759	YLR005w	5	0.600	120
YKR093w	24	0.225	3466	YLL028w	17	0.287	1319	YLR006c	4	0.167	126
YKR094c	8	0.536	320	YLL029w	3	0.000	100	YLR007w	2	0.000	36
YKR095w	4	0.333	67	YLL030c	3	0.000	66	YLR008c	1	0.000	0
YKR095w-a	1	0.000	0	YLL032c	9	0.056	1194	YLR009w	8	0.214	368
YKR096w	10	0.244	862	YLL033w	12	0.136	1686	YLR010c	1	0.000	0
YKR097w	24	0.246	2906	YLL034c	15	0.067	1843	YLR011w	3	0.000	9
YKR098c	6	0.067	211	YLL035w	3	0.333	58	YLR012c	13	0.269	831
YKR099w	146	0.016	99176	YLL036c	1	0.000	0	YLR013w	200	0.012	79517
YKR100c	3	0.667	36	YLL037w	4	0.500	72	YLR014c	31	0.049	38866
YKR101w	10	0.622	190	YLL038c	2	0.000	19	YLR016c	2	0.000	90
YKR102w	20	0.300	2060	YLL039c	18	0.333	1215	YLR017w	2	1.000	0
YKR103w	5	0.200	58	YLL040c	4	0.000	357	YLR018c	2	0.000	12
YKR104w	1	0.000	0	YLL041c	6	0.200	327	YLR019w	3	0.333	28
YKR105c	8	0.286	471	YLL042c	3	0.667	37	YLR020c	5	0.300	130
YKR106w	6	0.200	142	YLL043w	9	0.250	575	YLR021w	2	0.000	6
YLL001w	15	0.152	1974	YLL045c	10	0.422	531	YLR022c	8	0.286	1435
YLL002w	3	0.667	22	YLL046c	5	0.300	169	YLR023c	16	0.267	1096
YLL004w	10	0.267	1457	YLL048c	7	0.238	768	YLR024c	3	0.333	109
YLL005c	11	0.218	1274	YLL049w	5	0.900	25	YLR025w	3	0.000	427
YLL006w	8	0.000	697	YLL050c	5	0.500	73	YLR026c	1	0.000	0
YLL006w-a	2	0.000	48	YLL051c	8	0.500	591	YLR027c	6	0.200	135
YLL007c	5	0.100	272	YLL052c	16	0.350	986	YLR028c	3	0.000	77
YLL008w	7	0.143	388	YLL053c	8	0.179	684	YLR029c	12	0.348	811
YLL009c	7	0.238	218	YLL054c	6	0.267	144	YLR030w	9	0.194	738
YLL010c	3	0.333	14	YLL055w	18	0.288	1793	YLR031w	6	0.000	840
YLL011w	12	0.333	1338	YLL056c	15	0.286	1491	YLR032w	6	0.133	247
YLL012w	5	0.300	434	YLL057c	11	0.218	1740	YLR033w	6	0.200	354
YLL013c	4	0.167	367	YLL058w	6	0.333	183	YLR034c	10	0.244	498
YLL014w	3	0.333	65	YLL059c	2	0.000	77	YLR035c	6	0.333	231
YLL015w	10	0.222	629	YLL060c	8	0.214	375	YLR035c-a	18	0.229	2136
YLL016w	4	0.000	40	YLL061w	12	0.182	1467	YLR037c	5	0.100	199
YLL017w	2	0.000	4	YLL062c	7	0.095	382	YLR038c	9	0.111	692

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YLR039c	2	1.000	0	YLR082c	9	0.028	1110	YLR126c	8	0.250	272
YLR040c	6	0.267	518	YLR083c	6	0.200	357	YLR127c	4	0.500	53
YLR041w	3	0.000	463	YLR084c	11	0.345	1405	YLR128w	3	0.333	111
YLR042c	25	0.300	2428	YLR086w	4	0.000	62	YLR129w	4	0.167	68
YLR043c	7	0.238	264	YLR087c	2	0.000	99	YLR130c	11	0.145	699
YLR044c	29	0.222	7571	YLR088w	1	0.000	0	YLR131c	169	0.032	148567
YLR045c	2	1.000	0	YLR089c	16	0.200	2830	YLR132c	2	1.000	0
YLR046c	10	0.133	1905	YLR090w	12	0.197	1139	YLR133w	5	0.400	148
YLR047c	20	0.205	1998	YLR091w	3	0.000	41	YLR134w	13	0.308	2365
YLR048w	19	0.275	1873	YLR092w	10	0.333	785	YLR136c	17	0.191	3276
YLR049c	9	0.194	445	YLR093c	4	0.500	71	YLR137w	9	0.389	462
YLR050c	4	0.167	215	YLR094c	4	0.167	238	YLR138w	1	0.000	0
YLR051c	6	0.333	217	YLR095c	3	0.333	181	YLR139c	7	0.286	567
YLR052w	4	0.000	89	YLR096w	3	0.667	38	YLR140w	4	0.000	88
YLR053c	9	0.389	237	YLR097c	4	0.000	109	YLR141w	10	0.178	732
YLR054c	9	0.111	432	YLR098c	100	0.003	63988	YLR142w	24	0.225	5080
YLR055c	8	0.214	699	YLR099c	10	0.089	1153	YLR143w	3	0.333	119
YLR056w	20	0.211	3651	YLR099w-a	1	0.000	0	YLR144c	3	0.333	114
YLR057w	2	0.000	17	YLR100w	4	0.500	52	YLR145w	4	0.333	74
YLR058c	17	0.279	2089	YLR102c	5	0.200	111	YLR146c	2	1.000	0
YLR059c	2	0.000	21	YLR103c	3	0.333	20	YLR147c	2	0.000	35
YLR060w	8	0.286	678	YLR104w	4	0.167	123	YLR148w	1	0.000	0
YLR061w	13	0.346	1861	YLR105c	13	0.192	1069	YLR149c	14	0.253	1591
YLR062c	3	0.333	203	YLR106c	8	0.250	704	YLR149c-a	2	0.000	19
YLR063w	3	0.000	140	YLR107w	10	0.133	1521	YLR150w	9	0.333	666
YLR064w	5	0.000	138	YLR108c	19	0.287	1734	YLR151c	3	0.000	84
YLR065c	7	0.048	1067	YLR109w	24	0.268	3005	YLR152c	8	0.179	404
YLR066w	8	0.107	1303	YLR110c	23	0.296	3116	YLR153c	12	0.212	967
YLR067c	3	0.000	18	YLR111w	9	0.194	671	YLR154c	11	0.309	658
YLR068w	1	0.000	0	YLR112w	13	0.269	1392	YLR154c-g	2	0.000	10
YLR069c	3	0.000	178	YLR113w	24	0.254	3907	YLR154w-c	1	0.000	0
YLR070c	6	0.200	127	YLR114c	5	0.000	364	YLR155c	7	0.000	280
YLR071c	2	0.000	254	YLR115w	4	0.000	217	YLR156w	4	0.500	86
YLR072w	4	0.500	84	YLR116w	1	0.000	0	YLR157c	4	0.000	56
YLR073c	9	0.361	459	YLR117c	1	0.000	0	YLR157c-a	1	0.000	0
YLR074c	12	0.409	665	YLR118c	3	0.333	112	YLR157c-b	1	0.000	0
YLR075w	12	0.455	732	YLR119w	1	0.000	0	YLR157w-c	2	1.000	0
YLR076c	6	0.133	576	YLR120c	17	0.176	2226	YLR158c	5	0.000	145
YLR077w	5	0.400	456	YLR121c	21	0.229	3191	YLR159w	4	0.167	77
YLR078c	3	0.333	230	YLR122c	3	0.000	60	YLR160c	6	0.133	604
YLR079w	3	0.000	51	YLR123c	3	0.333	83	YLR161w	3	0.000	39
YLR080w	14	0.198	1747	YLR124w	1	0.000	0	YLR162w	15	0.219	1585
YLR081w	11	0.236	1271	YLR125w	6	0.067	351	YLR162w-a	5	0.400	104

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YLR163c	4	0.167	307	YLR209c	4	0.167	221	YLR252w	7	0.381	182
YLR164w	9	0.333	336	YLR210w	6	0.067	188	YLR253w	2	0.000	19
YLR165c	1	0.000	0	YLR211c	2	0.000	23	YLR254c	10	0.378	957
YLR166c	8	0.357	1207	YLR212c	5	0.500	140	YLR255c	8	0.321	189
YLR167w	13	0.244	2650	YLR213c	13	0.308	1707	YLR256w	198	0.037	162005
YLR168c	10	0.178	763	YLR214w	27	0.205	5700	YLR256w-a	3	0.333	195
YLR169w	7	0.143	138	YLR215c	2	0.000	14	YLR257w	11	0.291	1448
YLR170c	2	0.000	7	YLR216c	10	0.333	446	YLR258w	18	0.288	2517
YLR171w	7	0.048	253	YLR217w	3	0.333	38	YLR259c	8	0.321	959
YLR172c	3	0.000	82	YLR218c	3	0.000	134	YLR260w	5	0.500	132
YLR173w	5	0.100	532	YLR219w	3	0.000	2	YLR261c	7	0.095	307
YLR174w	20	0.168	2747	YLR220w	8	0.214	132	YLR262c	9	0.139	320
YLR175w	5	0.400	174	YLR221c	3	0.000	125	YLR262c-a	2	0.000	33
YLR176c	199	0.007	126921	YLR222c	9	0.306	773	YLR263w	7	0.381	560
YLR177w	9	0.278	276	YLR223c	314	0.018	327148	YLR264c-a	1	0.000	0
YLR178c	32	0.192	6866	YLR224w	3	0.667	41	YLR264w	9	0.278	987
YLR179c	14	0.187	2097	YLR225c	6	0.133	674	YLR265c	4	0.500	36
YLR180w	17	0.243	1923	YLR226w	2	0.000	26	YLR266c	24	0.083	3128
YLR181c	1	0.000	0	YLR227c	6	0.333	166	YLR267w	15	0.114	2056
YLR182w	222	0.014	134248	YLR228c	275	0.011	205404	YLR268w	1	0.000	0
YLR183c	240	0.014	481010	YLR229c	3	0.000	180	YLR270w	10	0.356	493
YLR184w	3	0.000	33	YLR230w	2	0.000	118	YLR271w	1	0.000	0
YLR185w	14	0.308	1171	YLR231c	6	0.200	693	YLR272c	7	0.286	202
YLR186w	5	0.300	119	YLR232w	1	0.000	0	YLR273c	5	0.200	118
YLR187w	4	0.500	47	YLR233c	6	0.267	240	YLR274w	5	0.300	169
YLR188w	3	0.000	98	YLR234w	3	0.333	23	YLR275w	3	0.667	36
YLR189c	8	0.179	368	YLR235c	1	0.000	0	YLR276c	8	0.321	888
YLR190w	7	0.143	251	YLR236c	2	0.000	22	YLR277c	6	0.267	163
YLR191w	1	0.000	0	YLR237w	16	0.200	2193	YLR278c	5	0.300	110
YLR192c	7	0.476	497	YLR238w	5	0.100	320	YLR279w	1	0.000	0
YLR193c	2	0.000	42	YLR239c	1	0.000	0	YLR280c	2	0.000	63
YLR194c	10	0.333	666	YLR240w	2	0.000	24	YLR281c	7	0.286	400
YLR195c	3	0.333	41	YLR241w	3	0.333	96	YLR283w	3	0.000	46
YLR196w	3	0.333	34	YLR242c	4	0.333	174	YLR284c	8	0.143	721
YLR197w	7	0.476	237	YLR243w	3	0.333	208	YLR285w	7	0.286	853
YLR198c	2	1.000	0	YLR244c	2	0.000	27	YLR286c	19	0.298	2951
YLR199c	5	0.300	100	YLR245c	1	0.000	0	YLR287c	9	0.111	647
YLR200w	7	0.190	262	YLR246w	4	0.167	370	YLR287c-a	10	0.378	629
YLR203c	1	0.000	0	YLR247c	2	1.000	0	YLR288c	3	0.000	35
YLR205c	14	0.198	1284	YLR248w	3	0.333	75	YLR289w	3	0.333	19
YLR206w	13	0.218	941	YLR249w	7	0.381	326	YLR290c	3	0.333	38
YLR207w	6	0.333	385	YLR250w	5	0.500	219	YLR291c	1	0.000	0
YLR208w	1	0.000	0	YLR251w	11	0.218	1071	YLR292c	5	0.100	782

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YLR293c	3	0.000	207	YLR338w	3	0.333	29	YLR382c	3	0.000	51
YLR294c	9	0.222	137	YLR339c	5	0.400	170	YLR383w	1	0.000	0
YLR295c	8	0.286	80	YLR340w	9	0.472	413	YLR384c	5	0.100	836
YLR296w	6	0.067	23	YLR341w	5	0.100	240	YLR385c	2	0.000	32
YLR297w	18	0.281	2453	YLR342w	13	0.308	1195	YLR386w	3	0.000	141
YLR298c	3	0.667	42	YLR343w	7	0.286	552	YLR387c	8	0.536	264
YLR299w	16	0.267	1232	YLR344w	8	0.536	284	YLR388w	9	0.417	410
YLR300w	18	0.261	1836	YLR345w	6	0.267	263	YLR389c	2	1.000	0
YLR301w	13	0.179	1245	YLR346c	15	0.238	2104	YLR390w	4	0.500	15
YLR302c	10	0.244	475	YLR347c	6	0.467	461	YLR390w-a	6	0.467	117
YLR303w	15	0.362	1229	YLR348c	7	0.286	263	YLR392c	5	0.200	192
YLR304c	24	0.181	4185	YLR349w	5	0.200	615	YLR393w	3	0.667	8
YLR305c	2	0.000	30	YLR350w	11	0.091	867	YLR394w	3	0.333	42
YLR306w	5	0.300	276	YLR351c	4	0.167	401	YLR395c	9	0.083	294
YLR307w	7	0.095	1356	YLR352w	6	0.133	386	YLR396c	2	0.000	171
YLR308w	4	0.167	201	YLR353w	3	0.667	6	YLR397c	22	0.190	4100
YLR309c	3	0.000	169	YLR354c	7	0.238	368	YLR398c	1	0.000	0
YLR310c	3	0.333	38	YLR355c	7	0.429	212	YLR399c	11	0.364	1128
YLR311c	2	0.000	19	YLR356w	10	0.311	565	YLR400w	6	0.467	311
YLR312c	12	0.409	516	YLR357w	3	0.333	142	YLR401c	8	0.286	301
YLR312w-a	10	0.489	454	YLR358c	3	0.667	29	YLR402w	3	1.000	0
YLR313c	3	0.000	84	YLR359w	8	0.179	391	YLR403w	2188	0.003	7721326
YLR314c	3	0.667	171	YLR360w	3	0.333	8	YLR405w	1	0.000	0
YLR315w	1	0.000	0	YLR362w	4	0.167	216	YLR406c	11	0.400	929
YLR316c	2	0.000	20	YLR363c	6	0.200	3313	YLR406c-a	2	0.000	9
YLR317w	2	0.000	12	YLR364w	2	0.000	405	YLR407w	7	0.381	382
YLR318w	4	0.000	191	YLR365w	1	0.000	0	YLR408c	2	0.000	42
YLR320w	2	0.000	59	YLR366w	7	0.095	764	YLR409c	8	0.286	843
YLR322w	1	0.000	0	YLR367w	18	0.176	3598	YLR410w	4	0.167	330
YLR323c	3	0.667	8	YLR368w	4	0.333	80	YLR410w-a	5	0.000	165
YLR324w	3	0.667	12	YLR369w	2	0.000	23	YLR410w-b	4	0.000	108
YLR325c	7	0.238	836	YLR370c	1	0.000	0	YLR411w	6	0.467	139
YLR326w	6	0.267	741	YLR371w	3	0.667	22	YLR412c-a	5	0.800	15
YLR327c	19	0.257	2845	YLR372w	6	0.333	334	YLR412w	6	0.667	29
YLR328w	4	0.500	30	YLR373c	6	0.000	611	YLR413w	17	0.412	1050
YLR329w	5	0.200	433	YLR374c	1	0.000	0	YLR414c	11	0.218	845
YLR330w	7	0.429	274	YLR375w	28	0.082	9467	YLR415c	5	0.300	251
YLR332w	10	0.467	197	YLR376c	1	0.000	0	YLR416c	2	0.000	11
YLR333c	8	0.536	284	YLR377c	15	0.229	1236	YLR417w	10	0.267	934
YLR334c	2	0.000	15	YLR378c	2	0.000	7	YLR418c	3	0.333	146
YLR335w	6	0.267	134	YLR379w	2	1.000	0	YLR419w	5	0.100	400
YLR336c	2	1.000	0	YLR380w	4	0.000	203	YLR420w	8	0.214	742
YLR337c	3	0.333	39	YLR381w	2	1.000	0	YLR421c	4	0.833	31

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YLR422w	3	1.000	0	YLR466w	13	0.192	776	YML043c	4	0.333	120
YLR423c	5	0.000	190	YLR467w	23	0.233	815	YML045w	3	0.000	1373
YLR424w	3	0.333	1645	YML001w	3	0.000	43	YML045w-a	1	0.000	0
YLR425w	4	0.333	238	YML002w	4	0.333	118	YML046w	4	0.500	66
YLR426w	2	1.000	0	YML003w	4	0.500	31	YML047c	9	0.444	302
YLR427w	1	0.000	0	YML004c	14	0.308	1056	YML047w-a	2	0.000	14
YLR428c	9	0.167	850	YML005w	6	0.267	209	YML048w	2	1.000	0
YLR429w	5	0.200	226	YML006c	2	0.000	19	YML048w-a	1	0.000	0
YLR430w	8	0.179	422	YML007c-a	2	1.000	0	YML049c	3	0.000	46
YLR432w	3	0.667	26	YML007w	1829	0.004	5162138	YML050w	6	0.267	220
YLR435w	4	0.500	70	YML008c	16	0.325	1135	YML051w	7	0.286	543
YLR436c	5	0.200	474	YML009c	2	1.000	0	YML052w	16	0.150	1945
YLR437c	11	0.255	1315	YML010c-b	1	0.000	0	YML053c	11	0.164	820
YLR438c-a	13	0.282	829	YML010w	3	1.000	0	YML054c	22	0.234	1710
YLR438w	17	0.213	3562	YML011c	2	1.000	0	YML054c-a	2	1.000	0
YLR439w	24	0.192	4450	YML012w	2	1.000	0	YML055w	3	0.000	27
YLR440c	3	0.667	5	YML013c-a	1	0.000	0	YML056c	11	0.309	639
YLR441c	9	0.500	410	YML013w	5	0.300	393	YML057w	5	0.200	197
YLR442c	1	0.000	0	YML014w	2	0.000	9	YML058w	5	0.400	80
YLR443w	1	0.000	0	YML015c	1	0.000	0	YML058w-a	9	0.306	776
YLR444c	1	0.000	0	YML017w	2	0.000	36	YML059c	5	0.200	94
YLR445w	2	1.000	0	YML018c	4	0.167	202	YML060w	2	1.000	0
YLR446w	5	0.400	123	YML019w	3	0.333	34	YML061c	1	0.000	0
YLR447c	8	0.214	492	YML021c	1	0.000	0	YML062c	2	0.000	86
YLR448w	11	0.364	704	YML022w	2	1.000	0	YML063w	12	0.409	724
YLR449w	6	0.333	160	YML023c	1	0.000	0	YML064c	9	0.333	390
YLR450w	7	0.143	658	YML024w	9	0.472	413	YML065w	2	0.000	17
YLR451w	510	0.010	643610	YML025c	6	0.333	162	YML066c	2	1.000	0
YLR452c	13	0.410	1051	YML026c	11	0.382	581	YML067c	1	0.000	0
YLR453c	6	0.133	1369	YML027w	482	0.011	752603	YML068w	2	0.000	28
YLR454w	9	0.389	473	YML028w	18	0.190	1734	YML069w	2	0.000	36
YLR455w	2	1.000	0	YML029w	5	0.600	69	YML070w	9	0.389	356
YLR456w	4	0.167	43	YML030w	1	0.000	0	YML071c	3	0.333	20
YLR457c	5	0.700	82	YML032c	3	0.667	10	YML072c	7	0.048	141
YLR458w	3	0.333	83	YML034w	3	0.333	75	YML073c	11	0.400	622
YLR459w	2	0.000	46	YML035c	5	0.500	136	YML074c	4	0.500	163
YLR460c	18	0.235	2044	YML036w	1	0.000	0	YML075c	11	0.345	729
YLR461w	22	0.212	3286	YML037c	1	0.000	0	YML076c	33	0.042	14407
YLR462w	12	0.333	488	YML038c	2	0.000	16	YML077w	4	0.667	68
YLR463c	21	0.205	730	YML039w	2	0.000	34	YML078w	4	0.500	114
YLR464w	6	0.400	111	YML040w	3	0.333	59	YML081c-a	5	0.400	349
YLR465c	18	0.242	544	YML041c	6	0.333	150	YML081w	3	0.000	167
YLR466c-b	1	0.000	0	YML042w	14	0.209	1928	YML082w	6	0.333	171

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YML083c	11	0.091	557	YML124c	5	0.200	130	YMR035w	7	0.238	188
YML085c	1	0.000	0	YML125c	8	0.393	394	YMR036c	2	1.000	0
YML086c	4	0.833	10	YML126c	7	0.429	246	YMR037c	916	0.007	1230908
YML087c	7	0.429	59	YML128c	24	0.279	3149	YMR038c	6	0.267	164
YML088w	11	0.309	296	YML129c	4	0.000	243	YMR039c	6	0.133	1347
YML089c	9	0.111	302	YML130c	14	0.242	1197	YMR040w	11	0.109	954
YML090w	1	0.000	0	YML131w	23	0.360	2205	YMR041c	8	0.429	325
YML091c	13	0.385	284	YML132w	26	0.258	4009	YMR042w	106	0.024	57111
YML092c	5	0.400	110	YML133c	19	0.310	2076	YMR043w	407	0.009	345552
YML093w	6	0.333	188	YMR001c	7	0.238	318	YMR044w	2	0.000	7
YML094w	1	0.000	0	YMR001c-a	1	0.000	0	YMR045c	3	0.667	34
YML095c	1	0.000	0	YMR002w	4	0.333	83	YMR046c	3	1.000	0
YML096w	3	0.333	19	YMR003w	6	0.200	229	YMR046w-a	1	0.000	0
YML097c	3	0.000	15	YMR004w	7	0.333	797	YMR047c	4	0.333	57
YML098w	10	0.333	713	YMR005w	1	0.000	0	YMR048w	4	0.000	149
YML099c	97	0.012	19891	YMR006c	12	0.348	823	YMR049c	9	0.417	361
YML100w	29	0.241	4045	YMR007w	3	0.000	124	YMR050c	2	0.000	18
YML100w-a	5	0.200	123	YMR008c	14	0.352	2131	YMR051c	3	0.333	52
YML101c	17	0.235	1820	YMR009w	7	0.476	229	YMR052c-a	1	0.000	0
YML101c-a	2	0.000	9	YMR010w	3	0.000	34	YMR052w	7	0.429	451
YML102c-a	7	0.333	199	YMR011w	30	0.324	5097	YMR053c	4	0.167	172
YML102w	3	0.000	42	YMR012w	2	0.000	38	YMR054w	2	0.000	11
YML103c	2	0.000	13	YMR013c	8	0.429	198	YMR055c	3	0.000	90
YML104c	2	0.000	68	YMR013w-a	1	0.000	0	YMR056c	16	0.158	1483
YML105c	2	0.000	21	YMR014w	10	0.200	524	YMR057c	1	0.000	0
YML106w	4	0.500	182	YMR015c	12	0.379	597	YMR058w	16	0.317	914
YML107c	2	0.000	27	YMR016c	1055	0.011	1491427	YMR059w	1	0.000	0
YML108w	2	0.000	48	YMR017w	22	0.394	1537	YMR060c	2	0.000	65
YML109w	1	0.000	0	YMR018w	7	0.190	140	YMR061w	1	0.000	0
YML110c	9	0.167	577	YMR019w	17	0.199	2119	YMR062c	14	0.286	1639
YML111w	3	0.000	10	YMR020w	6	0.333	259	YMR063w	3	0.000	26
YML112w	3	0.667	5	YMR021c	112	0.008	74302	YMR064w	5	0.300	342
YML113w	2	1.000	0	YMR023c	2	0.000	35	YMR065w	11	0.236	1435
YML115c	5	0.800	2	YMR026c	5	0.300	531	YMR066w	4	0.333	217
YML116w	19	0.333	1836	YMR027w	2	0.000	85	YMR067c	5	0.500	88
YML116w-a	2	0.000	14	YMR028w	4	0.500	68	YMR068w	3	0.000	80
YML117w	1	0.000	0	YMR029c	5	0.600	156	YMR069w	9	0.194	427
YML118w	1	0.000	0	YMR030w	3	1.000	0	YMR070w	150	0.048	81167
YML119w	14	0.220	1167	YMR031c	9	0.306	351	YMR071c	7	0.333	182
YML120c	18	0.222	2398	YMR031w-a	1	0.000	0	YMR072w	5	0.300	71
YML121w	14	0.253	1029	YMR032w	7	0.238	743	YMR073c	1	0.000	0
YML122c	5	0.300	148	YMR033w	2	0.000	33	YMR074c	2	1.000	0
YML123c	28	0.169	4695	YMR034c	4	0.667	24	YMR075w	1	0.000	0

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YMR076c	9	0.167	363	YMR119w	7	0.333	561	YMR159c	1	0.000	0
YMR077c	3	0.333	44	YMR119w-a	6	0.333	373	YMR160w	1	0.000	0
YMR078c	5	0.400	400	YMR120c	12	0.258	967	YMR162c	4	0.167	52
YMR079w	9	0.194	1650	YMR121c	14	0.429	816	YMR163c	4	0.000	315
YMR080c	3	0.333	356	YMR122c	1	0.000	0	YMR164c	78	0.033	57802
YMR081c	13	0.244	1121	YMR122w-a	12	0.379	652	YMR165c	16	0.200	1015
YMR082c	2	0.000	8	YMR123w	3	0.667	28	YMR166c	3	0.000	117
YMR083w	16	0.342	2274	YMR124w	7	0.286	795	YMR167w	3	0.000	220
YMR084w	6	0.200	682	YMR125w	7	0.095	261	YMR169c	35	0.237	6563
YMR085w	7	0.143	720	YMR126c	5	0.000	192	YMR170c	6	0.267	112
YMR086c-a	11	0.145	893	YMR127c	1	0.000	0	YMR171c	4	0.167	43
YMR086w	6	0.133	317	YMR128w	8	0.357	812	YMR172c-a	15	0.333	1162
YMR087w	14	0.165	1743	YMR129w	2	1.000	0	YMR172w	76	0.020	22083
YMR088c	5	0.100	391	YMR130w	3	0.000	98	YMR173w	29	0.246	3749
YMR089c	5	0.700	52	YMR131c	6	0.067	538	YMR173w-a	12	0.394	267
YMR090w	14	0.363	1493	YMR132c	1	0.000	0	YMR174c	18	0.235	1578
YMR091c	1	0.000	0	YMR133w	6	0.133	376	YMR175w	17	0.250	4320
YMR092c	3	0.333	217	YMR134w	16	0.208	1687	YMR176w	5	0.000	399
YMR093w	5	0.600	479	YMR135c	21	0.419	1865	YMR177w	14	0.198	1914
YMR094w	3	0.000	118	YMR135w-a	25	0.180	4044	YMR178w	9	0.194	427
YMR095c	12	0.288	1079	YMR136w	28	0.320	3449	YMR179w	5	0.500	105
YMR096w	18	0.288	3604	YMR137c	5	0.400	56	YMR180c	2	0.000	16
YMR097c	2	1.000	0	YMR138w	6	0.200	507	YMR181c	5	0.300	122
YMR098c	13	0.179	745	YMR139w	4	0.167	129	YMR182c	134	0.015	49648
YMR099c	2	0.000	19	YMR140w	6	0.467	146	YMR182w-a	2	0.000	14
YMR100w	1	0.000	0	YMR141c	1	0.000	0	YMR183c	5	0.500	260
YMR101c	5	0.300	52	YMR142c	11	0.382	581	YMR184w	6	0.267	280
YMR102c	9	0.250	432	YMR143w	13	0.346	1065	YMR185w	8	0.214	482
YMR103c	11	0.309	463	YMR144w	12	0.227	1874	YMR186w	18	0.255	3685
YMR104c	4	0.667	40	YMR145c	14	0.352	617	YMR187c	8	0.143	1051
YMR105c	28	0.212	4181	YMR146c	3	0.667	57	YMR188c	6	0.333	111
YMR106c	1	0.000	0	YMR147w	6	0.200	372	YMR189w	18	0.301	2861
YMR107w	19	0.211	1668	YMR148w	1	0.000	0	YMR190c	1	0.000	0
YMR108w	9	0.333	618	YMR149w	2	0.000	19	YMR191w	5	0.400	145
YMR110c	6	0.333	253	YMR150c	2	1.000	0	YMR192w	9	0.028	735
YMR111c	1	0.000	0	YMR151w	2	1.000	0	YMR193c-a	2	0.000	9
YMR112c	1	0.000	0	YMR152w	4	0.833	2	YMR193w	28	0.161	4610
YMR113w	3	0.333	51	YMR153w	2	0.000	37	YMR194c-a	10	0.267	313
YMR114c	1	0.000	0	YMR154c	3	0.000	178	YMR194c-b	6	0.533	131
YMR115w	2	0.000	19	YMR155w	4	0.167	211	YMR194w	21	0.195	2926
YMR116c	10	0.467	531	YMR156c	1	0.000	0	YMR195w	28	0.270	4973
YMR117c	4	0.167	152	YMR157c	3	0.667	2	YMR196w	18	0.281	1353
YMR118c	9	0.167	901	YMR158w-b	1	0.000	0	YMR197c	6	0.267	572

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YMR198w	12	0.364	1200	YMR240c	7	0.476	204	YMR280c	128	0.029	117015
YMR199w	22	0.273	2871	YMR241w	6	0.467	365	YMR281w	4	0.000	103
YMR200w	5	0.500	299	YMR242c	8	0.536	278	YMR282c	2	1.000	0
YMR201c	6	0.467	109	YMR242w-a	2	0.000	9	YMR283c	4	0.000	88
YMR202w	9	0.444	262	YMR243c	4	0.000	85	YMR284w	2	0.000	7
YMR203w	2	1.000	0	YMR244c-a	6	0.667	48	YMR285c	1	0.000	0
YMR204c	2	0.000	24	YMR244w	6	0.467	152	YMR286w	2	1.000	0
YMR205c	8	0.536	200	YMR245w	3	0.333	27	YMR287c	2	0.000	17
YMR206w	7	0.286	406	YMR246w	10	0.267	502	YMR288w	2	0.000	17
YMR207c	2	0.000	36	YMR247c	4	0.500	50	YMR289w	2	0.000	8
YMR208w	2	0.000	76	YMR247w-a	2	1.000	0	YMR290c	7	0.286	338
YMR209c	1	0.000	0	YMR250w	27	0.222	3962	YMR290w-a	2	0.000	10
YMR210w	2	0.000	13	YMR251w	11	0.309	543	YMR291w	9	0.222	345
YMR211w	4	0.000	261	YMR251w-a	32	0.264	6818	YMR292w	2	0.000	122
YMR212c	1	0.000	0	YMR252c	11	0.273	871	YMR294w	1	0.000	0
YMR213w	2	0.000	37	YMR253c	5	0.300	225	YMR294w-a	1	0.000	0
YMR214w	8	0.107	538	YMR254c	1	0.000	0	YMR295c	3	1.000	0
YMR215w	11	0.127	865	YMR255w	5	0.200	111	YMR296c	3	0.667	171
YMR216c	4	0.167	449	YMR256c	14	0.176	1048	YMR297w	4	0.333	204
YMR217w	5	0.200	508	YMR257c	13	0.090	2019	YMR298w	2	0.000	18
YMR218c	3	0.333	51	YMR258c	25	0.157	2698	YMR299c	1	0.000	0
YMR219w	6	0.400	302	YMR259c	8	0.036	431	YMR300c	10	0.267	872
YMR220w	6	0.200	538	YMR260c	7	0.286	1101	YMR301c	6	0.333	351
YMR221c	6	0.400	239	YMR261c	10	0.156	831	YMR302c	6	0.467	139
YMR222c	2	0.000	26	YMR262w	4	0.000	57	YMR303c	16	0.225	1941
YMR223w	4	0.333	152	YMR263w	3	0.000	89	YMR304c-a	9	0.306	226
YMR224c	3	0.333	349	YMR264w	1	0.000	0	YMR304w	4	0.167	88
YMR225c	3	0.333	41	YMR265c	9	0.528	237	YMR305c	16	0.358	1311
YMR226c	4	0.333	183	YMR266w	12	0.500	405	YMR306c-a	6	0.133	98
YMR227c	7	0.190	135	YMR267w	5	0.200	415	YMR306w	12	0.364	302
YMR228w	7	0.238	92	YMR268c	1	0.000	0	YMR307w	11	0.145	809
YMR229c	31	0.120	5170	YMR269w	4	0.000	281	YMR308c	5	0.400	260
YMR230w	12	0.318	1633	YMR270c	4	0.167	126	YMR309c	4	0.333	162
YMR230w-a	3	0.667	9	YMR271c	9	0.250	325	YMR310c	2	1.000	0
YMR231w	12	0.197	2105	YMR272c	9	0.056	1472	YMR311c	1	0.000	0
YMR232w	5	0.400	84	YMR272w-b	1	0.000	0	YMR312w	7	0.571	172
YMR233w	2	0.000	36	YMR273c	1	0.000	0	YMR313c	3	0.000	190
YMR234w	2	0.000	48	YMR274c	1	0.000	0	YMR314w	3	1.000	0
YMR235c	7	0.333	760	YMR275c	7	0.429	939	YMR315w	14	0.242	942
YMR236w	3	0.333	152	YMR276w	9	0.389	1428	YMR316c-a	2	0.000	60
YMR237w	3	0.333	104	YMR277w	6	0.333	198	YMR316c-b	3	0.333	63
YMR238w	4	0.000	183	YMR278w	1	0.000	0	YMR316w	9	0.194	705
YMR239c	7	0.429	290	YMR279c	6	0.267	121	YMR317w	2	1.000	0

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YMR318c	9	0.222	668	YNL034w	3	0.000	35	YNL073w	6	0.467	363
YMR319c	24	0.341	3295	YNL035c	5	0.400	66	YNL074c	3	0.333	84
YMR320w	7	0.238	732	YNL036w	26	0.182	4558	YNL075w	5	0.400	122
YMR321c	1	0.000	0	YNL037c	23	0.138	3552	YNL076w	4	0.000	258
YMR322c	22	0.216	2992	YNL038w	4	0.000	51	YNL077w	10	0.289	591
YMR323w	7	0.286	125	YNL039w	2	0.000	9	YNL078w	13	0.385	662
YMR324c	10	0.111	469	YNL040w	5	0.400	101	YNL079c	9	0.417	270
YMR325w	18	0.137	2565	YNL041c	6	0.267	306	YNL080c	4	0.167	202
YMR326c	1	0.000	0	YNL042w	5	0.500	90	YNL081c	2	0.000	64
YNL001w	11	0.109	591	YNL042w-b	1	0.000	0	YNL082w	5	0.300	186
YNL002c	9	0.111	504	YNL043c	6	0.200	1052	YNL083w	1	0.000	0
YNL003c	2	0.000	1	YNL044w	6	0.333	712	YNL084c	3	0.333	159
YNL004w	5	0.300	440	YNL045w	8	0.214	596	YNL085w	4	0.167	642
YNL005c	5	0.300	664	YNL046w	4	0.667	52	YNL086w	3	0.333	310
YNL006w	7	0.190	421	YNL047c	2	0.000	16	YNL087w	16	0.433	1299
YNL007c	8	0.357	316	YNL048w	4	0.000	120	YNL088w	4	0.667	18
YNL008c	5	0.100	186	YNL049c	2	0.000	7	YNL089c	2	0.000	3
YNL009w	14	0.143	733	YNL050c	4	0.167	177	YNL090w	8	0.357	454
YNL010w	13	0.077	1330	YNL051w	4	0.833	14	YNL091w	9	0.306	1028
YNL011c	6	0.200	684	YNL052w	13	0.154	340	YNL092w	8	0.250	993
YNL012w	10	0.156	998	YNL053w	6	0.400	148	YNL093w	3	0.333	97
YNL013c	1	0.000	0	YNL054w	3	1.000	0	YNL094w	6	0.333	290
YNL014w	10	0.267	1183	YNL054w-a	3	0.667	8	YNL095c	3	0.000	97
YNL015w	14	0.275	1053	YNL054w-b	1	0.000	0	YNL096c	11	0.327	861
YNL016w	8	0.286	625	YNL055c	7	0.429	189	YNL097c	10	0.200	818
YNL017c	4	0.167	225	YNL056w	4	0.167	50	YNL097c-b	1	0.000	0
YNL018c	5	0.300	29	YNL057w	4	0.167	335	YNL098c	3	0.333	13
YNL019c	3	0.000	55	YNL058c	6	0.200	131	YNL100w	7	0.000	1437
YNL020c	2	0.000	54	YNL059c	4	0.167	300	YNL101w	12	0.227	1359
YNL021w	1	0.000	0	YNL061w	10	0.267	1187	YNL102w	11	0.109	1177
YNL022c	4	0.167	216	YNL062c	5	0.500	110	YNL103w	1156	0.006	2489871
YNL023c	1	0.000	0	YNL063w	5	0.300	172	YNL104c	11	0.255	1309
YNL024c	2	0.000	77	YNL064c	5	0.200	601	YNL105w	1	0.000	0
YNL024c-a	1	0.000	0	YNL065w	22	0.255	2876	YNL106c	1	0.000	0
YNL025c	5	0.000	319	YNL066w	10	0.289	935	YNL107w	3	0.000	124
YNL026w	1	0.000	0	YNL067w	13	0.385	1234	YNL108c	4	0.333	132
YNL027w	301	0.007	334676	YNL067w-a	1	0.000	0	YNL109w	1	0.000	0
YNL028w	5	0.200	173	YNL067w-b	2	1.000	0	YNL110c	3	0.333	45
YNL029c	4	0.333	91	YNL068c	315	0.013	309200	YNL111c	14	0.264	1596
YNL030w	13	0.205	1568	YNL069c	12	0.455	586	YNL112w	10	0.244	1810
YNL031c	11	0.273	1189	YNL070w	6	0.000	762	YNL113w	5	0.200	165
YNL032w	4	0.500	72	YNL071w	4	0.333	70	YNL114c	2	1.000	0
YNL033w	5	0.300	65	YNL072w	5	0.600	128	YNL115c	11	0.309	1221

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YNL116w	2	0.000	64	YNL159c	2	1.000	0	YNL203c	1	0.000	0
YNL117w	19	0.187	4427	YNL160w	33	0.184	7806	YNL204c	63	0.008	11439
YNL118c	7	0.095	1046	YNL161w	5	0.400	82	YNL205c	4	0.333	51
YNL119w	1	0.000	0	YNL162w	11	0.418	772	YNL206c	2	0.000	63
YNL121c	1	0.000	0	YNL162w-a	2	0.000	9	YNL207w	5	0.300	416
YNL122c	6	0.267	618	YNL163c	6	0.333	183	YNL208w	9	0.194	1091
YNL123w	3	0.333	27	YNL164c	4	0.333	371	YNL209w	6	0.333	219
YNL124w	9	0.556	434	YNL165w	3	0.667	30	YNL210w	5	0.400	679
YNL125c	7	0.524	352	YNL166c	4	0.500	51	YNL211c	4	0.333	455
YNL126w	4	0.000	79	YNL167c	339	0.018	226233	YNL212w	5	0.200	822
YNL127w	1	0.000	0	YNL168c	6	0.467	242	YNL213c	5	0.100	786
YNL128w	5	0.100	307	YNL169c	8	0.393	449	YNL214w	1	0.000	0
YNL129w	6	0.133	248	YNL170w	2	0.000	8	YNL216w	1230	0.007	2988666
YNL130c	7	0.286	274	YNL171c	4	0.167	118	YNL217w	5	0.600	44
YNL130c-a	1	0.000	0	YNL172w	5	0.000	148	YNL218w	5	0.300	196
YNL131w	1	0.000	0	YNL173c	8	0.286	253	YNL219c	2	1.000	0
YNL132w	9	0.556	403	YNL174w	6	0.200	429	YNL220w	10	0.267	1192
YNL133c	6	0.467	245	YNL175c	8	0.321	550	YNL221c	3	0.333	146
YNL134c	17	0.228	1792	YNL176c	5	0.300	245	YNL224c	5	0.400	147
YNL135c	7	0.286	632	YNL178w	22	0.403	2215	YNL225c	1	0.000	0
YNL136w	3	0.333	29	YNL179c	8	0.429	341	YNL226w	2	0.000	14
YNL137c	2	0.000	17	YNL180c	17	0.493	1062	YNL227c	1	0.000	0
YNL138w	3	0.667	39	YNL181w	3	0.000	161	YNL229c	3	0.000	37
YNL139c	3	0.000	467	YNL182c	9	0.194	678	YNL230c	5	0.200	141
YNL141w	11	0.182	1044	YNL183c	5	0.300	351	YNL231c	20	0.221	3051
YNL142w	13	0.346	1918	YNL185c	1	0.000	0	YNL232w	10	0.222	400
YNL143c	7	0.333	502	YNL186w	5	0.400	116	YNL233w	4	0.000	166
YNL144c	13	0.423	770	YNL187w	3	0.667	14	YNL234w	22	0.225	2644
YNL145w	20	0.321	3328	YNL188w	4	0.000	293	YNL235c	3	1.000	0
YNL146c-a	5	0.100	325	YNL189w	7	0.143	841	YNL236w	3	0.000	29
YNL146w	16	0.158	1892	YNL190w	7	0.333	609	YNL237w	14	0.363	545
YNL147w	6	0.000	362	YNL191w	4	0.333	283	YNL238w	2	1.000	0
YNL148c	6	0.267	248	YNL192w	16	0.250	1460	YNL239w	13	0.244	1954
YNL149c	7	0.333	576	YNL193w	5	0.500	87	YNL240c	6	0.267	356
YNL150w	2	1.000	0	YNL194c	20	0.284	1895	YNL241c	33	0.195	7065
YNL151c	5	0.300	348	YNL195c	14	0.352	695	YNL242w	2	0.000	88
YNL152w	2	0.000	55	YNL196c	4	0.000	84	YNL243w	3	0.333	190
YNL153c	3	0.333	154	YNL197c	1	0.000	0	YNL244c	4	0.500	398
YNL154c	5	0.700	68	YNL198c	1	0.000	0	YNL245c	1	0.000	0
YNL155w	9	0.444	344	YNL199c	189	0.013	78263	YNL246w	1	0.000	0
YNL156c	5	0.600	64	YNL200c	14	0.516	284	YNL247w	3	1.000	0
YNL157w	3	0.667	52	YNL201c	2	0.000	30	YNL248c	3	0.333	38
YNL158w	2	0.000	19	YNL202w	9	0.194	425	YNL249c	2	0.000	16

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YNL250w	2	0.000	38	YNL293w	6	0.267	269	YNL337w	35	0.173	6085
YNL251c	6	0.200	462	YNL294c	8	0.214	389	YNL338w	30	0.195	2838
YNL252c	2	0.000	14	YNL295w	4	0.333	93	YNL339c	30	0.221	3452
YNL253w	5	0.300	212	YNL296w	4	0.333	136	YNR001c	21	0.114	3252
YNL254c	5	0.500	69	YNL297c	2	1.000	0	YNR002c	11	0.291	802
YNL255c	23	0.075	33211	YNL298w	9	0.278	1283	YNR003c	4	0.167	253
YNL256w	4	0.167	69	YNL299w	6	0.200	169	YNR004w	5	0.100	206
YNL257c	3	0.000	33	YNL300w	9	0.194	537	YNR006w	3	0.000	25
YNL258c	6	0.133	1031	YNL301c	11	0.327	1244	YNR007c	1	0.000	0
YNL259c	9	0.167	886	YNL302c	8	0.536	225	YNR008w	4	0.000	167
YNL260c	7	0.190	508	YNL303w	1	0.000	0	YNR009w	9	0.278	419
YNL261w	2	0.000	16	YNL304w	2	0.000	11	YNR010w	2	0.000	36
YNL262w	5	0.200	494	YNL305c	7	0.476	227	YNR011c	4	0.333	167
YNL263c	2	0.000	7	YNL306w	6	0.200	335	YNR012w	6	0.333	278
YNL265c	3	0.000	27	YNL307c	5	0.100	355	YNR013c	9	0.306	960
YNL267w	3	0.333	123	YNL308c	6	0.467	107	YNR014w	22	0.273	3047
YNL268w	7	0.429	436	YNL309w	58	0.038	74754	YNR016c	14	0.242	1944
YNL269w	5	0.300	108	YNL310c	3	0.333	67	YNR017w	20	0.284	3223
YNL270c	11	0.273	813	YNL311c	4	0.500	68	YNR018w	15	0.343	1970
YNL271c	6	0.067	1028	YNL312w	8	0.286	814	YNR019w	12	0.227	1139
YNL272c	1	0.000	0	YNL313c	7	0.238	730	YNR020c	3	0.667	103
YNL273w	4	0.333	99	YNL314w	167	0.004	147336	YNR021w	1	0.000	0
YNL274c	16	0.250	1050	YNL315c	1	0.000	0	YNR022c	1	0.000	0
YNL275w	1	0.000	0	YNL317w	1	0.000	0	YNR024w	3	0.333	118
YNL276c	1	0.000	0	YNL318c	3	0.000	120	YNR025c	2	0.000	20
YNL277w	18	0.275	1697	YNL319w	1	0.000	0	YNR026c	3	0.000	166
YNL277w-a	2	0.000	9	YNL320w	1	0.000	0	YNR027w	5	0.200	333
YNL278w	9	0.194	798	YNL321w	6	0.267	611	YNR028w	12	0.394	459
YNL279w	21	0.352	3408	YNL322c	5	0.300	308	YNR029c	3	0.000	8
YNL280c	7	0.286	827	YNL323w	1	0.000	0	YNR030w	3	0.000	29
YNL281w	3	0.333	36	YNL324w	4	0.167	65	YNR031c	4	0.167	100
YNL282w	7	0.381	207	YNL325c	2	1.000	0	YNR032c-a	2	0.000	63
YNL283c	8	0.357	324	YNL326c	3	0.333	51	YNR032w	5	0.500	165
YNL284c	6	0.267	254	YNL327w	12	0.333	416	YNR033w	3	0.000	153
YNL284c-a	2	0.000	7	YNL328c	7	0.571	133	YNR034w	10	0.267	849
YNL285w	3	0.667	12	YNL329c	6	0.067	253	YNR034w-a	8	0.500	145
YNL286w	2	0.000	17	YNL330c	2	0.000	12	YNR035c	4	0.167	635
YNL287w	3	0.000	176	YNL331c	7	0.476	176	YNR036c	5	0.400	378
YNL288w	6	0.600	312	YNL332w	6	0.333	422	YNR037c	3	0.333	257
YNL289w	29	0.204	3470	YNL333w	12	0.333	874	YNR038w	3	0.000	268
YNL290w	6	0.200	208	YNL334c	6	0.333	284	YNR039c	6	0.067	692
YNL291c	1	0.000	0	YNL335w	11	0.236	950	YNR040w	7	0.000	829
YNL292w	3	0.333	32	YNL336w	17	0.213	1692	YNR041c	4	0.500	144

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YNR042w	1	0.000	0	YOL008w	1	0.000	0	YOL049w	5	0.500	101
YNR043w	8	0.357	370	YOL009c	1	0.000	0	YOL050c	4	0.167	123
YNR044w	24	0.290	3307	YOL010w	8	0.429	417	YOL052c	2	1.000	0
YNR045w	2	1.000	0	YOL011w	8	0.286	522	YOL052c-a	32	0.302	4625
YNR046w	5	0.100	420	YOL012c	7	0.286	352	YOL053w	2	0.000	8
YNR047w	4	0.333	122	YOL013c	6	0.467	150	YOL054w	2	0.000	8
YNR049c	6	0.267	162	YOL013w-a	5	0.000	215	YOL055c	7	0.381	908
YNR050c	19	0.246	2131	YOL014w	10	0.222	1379	YOL056w	4	0.333	89
YNR051c	4	0.333	101	YOL016c	9	0.306	630	YOL057w	8	0.357	320
YNR052c	1	0.000	0	YOL017w	3	0.333	70	YOL058w	35	0.217	7254
YNR053c	10	0.333	1056	YOL018c	4	0.667	70	YOL059w	9	0.250	439
YNR054c	11	0.145	1018	YOL019w	10	0.444	559	YOL060c	7	0.429	243
YNR055c	4	0.167	133	YOL019w-a	4	0.667	4	YOL061w	1	0.000	0
YNR056c	9	0.278	603	YOL020w	7	0.190	887	YOL063c	1	0.000	0
YNR057c	5	0.400	322	YOL021c	4	0.167	487	YOL064c	7	0.286	208
YNR058w	8	0.357	776	YOL022c	5	0.200	782	YOL065c	3	0.000	84
YNR059w	5	0.200	397	YOL023w	9	0.083	721	YOL066c	1	0.000	0
YNR060w	23	0.360	1183	YOL024w	12	0.030	1677	YOL067c	130	0.016	42378
YNR061c	3	0.000	27	YOL025w	1	0.000	0	YOL068c	3	0.333	274
YNR062c	7	0.143	485	YOL026c	4	0.000	294	YOL069w	1	0.000	0
YNR063w	3	0.000	160	YOL027c	3	0.667	13	YOL070c	1	0.000	0
YNR064c	13	0.218	2040	YOL028c	188	0.018	110219	YOL071w	5	0.300	65
YNR065c	6	0.267	156	YOL029c	5	0.200	165	YOL072w	2	1.000	0
YNR066c	3	0.000	94	YOL030w	10	0.311	657	YOL073c	3	0.333	58
YNR067c	13	0.359	534	YOL031c	10	0.356	621	YOL075c	6	0.200	1356
YNR068c	11	0.200	887	YOL032w	5	0.200	97	YOL076w	6	0.067	873
YNR069c	7	0.429	211	YOL033w	2	0.000	87	YOL077c	9	0.278	1432
YNR070w	6	0.267	369	YOL034w	7	0.143	494	YOL077w-a	7	0.286	289
YNR071c	16	0.125	1273	YOL035c	3	0.000	131	YOL078w	8	0.214	306
YNR072w	24	0.217	2859	YOL036w	1	0.000	0	YOL079w	7	0.095	448
YNR073c	8	0.536	183	YOL037c	2	0.000	14	YOL080c	7	0.190	475
YNR074c	2	1.000	0	YOL038c-a	3	0.667	30	YOL081w	9	0.417	290
YNR075c-a	2	1.000	0	YOL038w	8	0.500	932	YOL082w	14	0.308	2186
YNR075w	10	0.244	716	YOL039w	16	0.325	1959	YOL083w	14	0.176	1137
YNR076w	24	0.254	4122	YOL040c	15	0.381	1102	YOL084w	31	0.252	4654
YNR081w	1	0.000	0	YOL041c	8	0.321	945	YOL085c	5	0.300	117
YOL001w	9	0.167	343	YOL042w	7	0.143	457	YOL086c	22	0.299	4244
YOL002c	6	0.133	209	YOL043c	3	0.000	249	YOL087c	1	0.000	0
YOL003c	3	0.000	166	YOL044w	1	0.000	0	YOL088c	1	0.000	0
YOL004w	32	0.081	4363	YOL045w	2	1.000	0	YOL089c	111	0.013	68468
YOL005c	3	0.000	76	YOL046c	1	0.000	0	YOL090w	2	1.000	0
YOL006c	6	0.400	169	YOL047c	4	0.167	510	YOL091w	10	0.044	1046
YOL007c	9	0.250	450	YOL048c	5	0.300	141	YOL092w	4	0.500	91

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YOL093w	3	0.000	785	YOL137w	5	0.300	327	YOR010c	9	0.361	267
YOL095c	1	0.000	0	YOL138c	5	0.000	381	YOR011w	9	0.333	845
YOL096c	2	0.000	36	YOL139c	4	0.333	174	YOR012w	1	0.000	0
YOL097c	1	0.000	0	YOL140w	12	0.227	1436	YOR014w	3	0.333	26
YOL098c	2	1.000	0	YOL141w	4	0.167	48	YOR015w	2	0.000	22
YOL099c	1	0.000	0	YOL142w	4	0.000	156	YOR016c	1	0.000	0
YOL100w	5	0.400	165	YOL143c	6	0.467	229	YOR017w	4	0.000	116
YOL101c	14	0.154	1199	YOL144w	5	0.300	462	YOR018w	10	0.378	474
YOL102c	4	0.167	588	YOL145c	5	0.000	257	YOR019w	5	0.300	177
YOL103w	3	0.333	44	YOL146w	4	0.000	83	YOR020c	10	0.222	738
YOL103w-a	1	0.000	0	YOL147c	7	0.238	164	YOR020w-a	3	0.000	69
YOL103w-b	1	0.000	0	YOL148c	5	0.300	276	YOR021c	8	0.214	744
YOL104c	5	0.300	331	YOL149w	4	0.167	117	YOR022c	2	0.000	16
YOL105c	8	0.214	662	YOL150c	8	0.500	193	YOR023c	9	0.167	893
YOL106w	1	0.000	0	YOL151w	28	0.233	2919	YOR024w	3	0.000	83
YOL107w	5	0.400	303	YOL152w	14	0.418	1869	YOR025w	12	0.152	1636
YOL108c	637	0.004	836047	YOL153c	12	0.258	887	YOR026w	3	0.667	11
YOL109w	21	0.290	1829	YOL154w	24	0.236	2472	YOR027w	16	0.433	1792
YOL110w	10	0.422	503	YOL155c	31	0.228	5805	YOR028c	459	0.024	705126
YOL111c	3	0.000	69	YOL155w-a	3	1.000	0	YOR029w	6	0.467	67
YOL112w	6	0.533	121	YOL156w	29	0.239	3901	YOR030w	8	0.750	29
YOL113w	9	0.222	420	YOL157c	25	0.267	3185	YOR031w	8	0.179	456
YOL114c	9	0.222	420	YOL158c	16	0.308	1177	YOR032c	247	0.039	258854
YOL115w	6	0.133	153	YOL159c	15	0.171	1085	YOR032w-a	8	0.786	43
YOL116w	53	0.032	42977	YOL160w	8	0.250	472	YOR033c	2	0.000	84
YOL117w	8	0.250	1597	YOL161c	16	0.250	1507	YOR034c	4	0.500	52
YOL118c	2	0.000	156	YOL162w	6	0.067	741	YOR035c	7	0.143	1280
YOL119c	17	0.228	3461	YOL163w	5	0.100	233	YOR036w	8	0.250	2112
YOL120c	10	0.489	487	YOL164w	11	0.200	1018	YOR037w	3	0.333	247
YOL121c	19	0.246	2429	YOL164w-a	2	1.000	0	YOR038c	80	0.021	32991
YOL122c	9	0.333	372	YOL165c	8	0.250	438	YOR039w	5	0.200	229
YOL123w	5	0.000	218	YOL166c	4	0.333	44	YOR040w	8	0.321	369
YOL124c	9	0.278	550	YOL166w-a	1	0.000	0	YOR041c	1	0.000	0
YOL125w	12	0.106	880	YOR001w	3	0.667	35	YOR042w	5	0.300	157
YOL126c	27	0.199	7420	YOR003w	7	0.143	900	YOR043w	6	0.400	248
YOL127w	12	0.333	850	YOR004w	4	0.167	154	YOR044w	7	0.048	746
YOL128c	8	0.250	504	YOR005c	8	0.179	796	YOR045w	3	0.000	234
YOL130w	7	0.286	426	YOR006c	2	0.000	14	YOR046c	2	0.000	9
YOL131w	3	0.333	13	YOR007c	5	0.600	66	YOR047c	5	0.500	128
YOL132w	3	0.333	22	YOR008c	5	0.400	164	YOR048c	5	0.200	132
YOL133w	4	0.667	35	YOR008c-a	3	0.667	22	YOR049c	22	0.433	770
YOL135c	3	0.333	35	YOR008w-b	1	0.000	0	YOR050c	7	0.333	220
YOL136c	12	0.227	1332	YOR009w	11	0.309	1078	YOR051c	4	0.667	57

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YOR052c	16	0.275	1615	YOR097c	1	0.000	0	YOR140w	65	0.069	52553
YOR053w	1	0.000	0	YOR098c	7	0.190	638	YOR141c	2	0.000	88
YOR054c	5	0.200	208	YOR099w	8	0.250	458	YOR142w	2	0.000	15
YOR055w	1	0.000	0	YOR100c	19	0.257	1831	YOR142w-a	1	0.000	0
YOR056c	7	0.286	656	YOR101w	12	0.348	837	YOR143c	8	0.250	1018
YOR057w	4	0.333	346	YOR102w	1	0.000	0	YOR144c	3	0.333	101
YOR058c	13	0.179	1674	YOR103c	1	0.000	0	YOR145c	4	0.500	413
YOR059c	4	0.500	53	YOR104w	1	0.000	0	YOR146w	1	0.000	0
YOR060c	3	0.000	81	YOR105w	3	0.000	23	YOR147w	1	0.000	0
YOR061w	2	0.000	39	YOR106w	5	0.100	89	YOR148c	7	0.095	242
YOR062c	11	0.327	624	YOR107w	14	0.341	788	YOR149c	3	0.333	35
YOR063w	16	0.350	2353	YOR108w	8	0.357	468	YOR150w	3	0.000	52
YOR064c	8	0.107	219	YOR109w	3	0.333	27	YOR151c	3	0.667	12
YOR065w	15	0.143	798	YOR110w	5	0.700	73	YOR152c	9	0.222	596
YOR066w	7	0.476	308	YOR111w	4	0.000	158	YOR153w	30	0.193	6987
YOR067c	4	0.167	398	YOR112w	3	0.000	90	YOR154w	7	0.095	38
YOR068c	1	0.000	0	YOR113w	130	0.023	111303	YOR155c	2	0.000	17
YOR070c	4	0.167	153	YOR114w	2	1.000	0	YOR156c	1	0.000	0
YOR071c	8	0.321	700	YOR115c	7	0.143	381	YOR157c	6	0.400	622
YOR072w	3	0.000	298	YOR116c	6	0.467	504	YOR158w	3	0.667	23
YOR072w-b	1	0.000	0	YOR117w	7	0.238	1260	YOR159c	1	0.000	0
YOR073w	4	0.333	65	YOR118w	2	0.000	18	YOR160w	1	0.000	0
YOR074c	11	0.291	1244	YOR119c	5	0.100	142	YOR161c	21	0.310	1653
YOR075w	7	0.143	727	YOR120w	14	0.275	2050	YOR161c-c	3	0.667	9
YOR076c	3	0.333	74	YOR121c	1	0.000	0	YOR162c	97	0.037	109267
YOR077w	50	0.017	171958	YOR122c	4	0.333	115	YOR163w	5	0.300	146
YOR078w	6	0.133	470	YOR123c	1	0.000	0	YOR164c	3	0.667	24
YOR080w	2	1.000	0	YOR124c	4	0.500	66	YOR165w	2	0.000	22
YOR081c	4	0.333	91	YOR125c	5	0.300	121	YOR166c	2	0.000	23
YOR082c	4	0.167	73	YOR126c	4	0.333	211	YOR167c	8	0.536	877
YOR083w	3	0.000	76	YOR127w	3	0.333	64	YOR168w	3	0.667	30
YOR084w	12	0.182	1149	YOR128c	16	0.375	1437	YOR171c	1	0.000	0
YOR085w	2	1.000	0	YOR129c	6	0.267	177	YOR172w	24	0.011	950
YOR086c	7	0.238	687	YOR130c	5	0.900	13	YOR173w	29	0.185	6242
YOR087w	6	0.400	247	YOR131c	4	0.333	153	YOR174w	3	0.000	74
YOR089c	2	0.000	72	YOR132w	1	0.000	0	YOR175c	1	0.000	0
YOR090c	4	0.167	157	YOR133w	5	0.500	468	YOR176w	3	0.667	11
YOR091w	5	0.400	540	YOR134w	12	0.121	775	YOR177c	5	0.500	129
YOR092w	5	0.700	32	YOR135c	3	0.000	34	YOR178c	30	0.363	2670
YOR093c	12	0.182	1665	YOR136w	17	0.257	1466	YOR179c	12	0.439	845
YOR094w	11	0.182	963	YOR137c	4	0.167	192	YOR180c	8	0.393	171
YOR095c	16	0.358	1587	YOR138c	18	0.261	1995	YOR181w	6	0.600	75
YOR096w	13	0.410	1077	YOR139c	2	1.000	0	YOR182c	12	0.273	1180

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YOR183w	4	0.167	63	YOR224c	5	0.200	595	YOR268c	13	0.154	527
YOR184w	14	0.286	1253	YOR225w	6	0.267	137	YOR269w	13	0.192	752
YOR185c	3	0.667	9	YOR226c	16	0.358	978	YOR270c	3	0.667	63
YOR186w	8	0.179	639	YOR227w	12	0.348	545	YOR271c	2	0.000	35
YOR187w	7	0.429	171	YOR228c	3	0.000	23	YOR272w	8	0.286	387
YOR188w	3	0.000	73	YOR229w	7	0.190	290	YOR273c	26	0.240	4521
YOR189w	2	0.000	424	YOR230w	18	0.255	1799	YOR274w	9	0.222	1375
YOR190w	2	0.000	14	YOR231w	1	0.000	0	YOR275c	2	0.000	3
YOR191w	2	1.000	0	YOR232w	1	0.000	0	YOR276w	6	0.667	92
YOR192c	16	0.158	959	YOR233w	5	0.400	83	YOR279c	1	0.000	0
YOR192c-a	1	0.000	0	YOR234c	14	0.297	1447	YOR280c	7	0.238	430
YOR192c-b	1	0.000	0	YOR235w	11	0.218	852	YOR281c	1	0.000	0
YOR192c-c	2	1.000	0	YOR236w	20	0.263	4767	YOR282w	3	0.000	57
YOR193w	4	0.167	145	YOR237w	6	0.267	326	YOR283w	2	0.000	88
YOR194c	5	0.400	306	YOR238w	1	0.000	0	YOR284w	8	0.286	613
YOR195w	4	0.167	244	YOR239w	3	0.000	43	YOR285w	10	0.267	736
YOR196c	2	0.000	47	YOR241w	2	1.000	0	YOR287c	4	0.333	110
YOR197w	3	0.333	289	YOR242c	2	1.000	0	YOR288c	6	0.333	500
YOR198c	5	0.600	113	YOR243c	2	1.000	0	YOR289w	8	0.071	1123
YOR199w	1	0.000	0	YOR244w	2	0.000	10	YOR290c	3	0.000	52
YOR201c	3	0.333	71	YOR245c	6	0.333	147	YOR291w	6	0.067	251
YOR202w	12	0.182	1137	YOR246c	12	0.348	493	YOR292c	11	0.345	382
YOR203w	5	0.300	140	YOR247w	17	0.301	1553	YOR293w	13	0.410	1080
YOR204w	5	0.100	429	YOR248w	9	0.278	573	YOR294w	5	0.300	82
YOR205c	4	0.000	426	YOR249c	2	1.000	0	YOR295w	1	0.000	0
YOR206w	12	0.136	1652	YOR250c	3	0.667	130	YOR296w	5	0.100	278
YOR207c	4	0.167	358	YOR251c	6	0.067	532	YOR297c	8	0.107	956
YOR208w	6	0.267	358	YOR252w	4	0.333	226	YOR298c-a	9	0.333	912
YOR209c	7	0.143	1552	YOR253w	2	0.000	47	YOR298w	7	0.238	257
YOR210w	5	0.300	182	YOR254c	4	0.167	278	YOR299w	8	0.321	361
YOR211c	1	0.000	0	YOR255w	6	0.133	551	YOR300w	2	0.000	22
YOR212w	3	0.000	21	YOR256c	2	0.000	11	YOR301w	12	0.394	589
YOR213c	1	0.000	0	YOR257w	4	0.167	77	YOR302w	21	0.171	2627
YOR214c	4	0.000	455	YOR258w	5	0.400	174	YOR303w	27	0.199	4348
YOR215c	5	0.200	353	YOR259c	5	0.800	100	YOR304w	7	0.000	489
YOR216c	3	0.000	138	YOR260w	4	0.333	288	YOR305w	1	0.000	0
YOR217w	2	0.000	6	YOR261c	4	0.667	310	YOR306c	15	0.390	1102
YOR218c	1	0.000	0	YOR262w	6	0.333	216	YOR307c	4	0.500	99
YOR219c	4	0.333	268	YOR263c	1	0.000	0	YOR308c	1	0.000	0
YOR220w	9	0.333	626	YOR264w	5	0.300	151	YOR309c	6	0.467	541
YOR221c	3	0.000	132	YOR265w	5	0.200	198	YOR310c	9	0.333	987
YOR222w	9	0.250	894	YOR266w	3	0.000	124	YOR311c	3	0.333	94
YOR223w	3	0.000	32	YOR267c	4	0.500	147	YOR312c	9	0.500	551

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YOR313c	23	0.281	4379	YOR352w	1	0.000	0	YOR396w	2	0.000	7
YOR314w	14	0.242	1269	YOR353c	5	0.300	161	YPL001w	2	1.000	0
YOR315w	35	0.276	8609	YOR354c	14	0.242	1973	YPL002c	2	0.000	171
YOR316c	17	0.250	1284	YOR355w	13	0.231	1620	YPL003w	2	0.000	15
YOR316c-a	3	0.333	59	YOR356w	3	0.000	38	YPL004c	12	0.409	367
YOR317w	13	0.269	719	YOR357c	6	0.133	1148	YPL005w	7	0.238	518
YOR318c	16	0.217	2126	YOR358w	203	0.015	128658	YPL006w	3	0.333	23
YOR319w	23	0.269	3139	YOR359w	5	0.400	135	YPL007c	4	0.167	45
YOR320c	1	0.000	0	YOR360c	9	0.222	1195	YPL008w	3	0.333	200
YOR321w	2	1.000	0	YOR361c	5	0.500	214	YPL009c	3	0.333	54
YOR322c	4	0.333	387	YOR362c	4	0.667	65	YPL010w	3	0.000	288
YOR323c	5	0.400	140	YOR363c	152	0.023	88670	YPL011c	2	0.000	17
YOR324c	2	0.000	7	YOR365c	4	0.000	347	YPL012w	11	0.182	1082
YOR325w	4	0.167	102	YOR366w	3	0.333	218	YPL013c	4	0.167	382
YOR326w	6	0.267	601	YOR367w	5	0.100	674	YPL014w	10	0.244	828
YOR327c	7	0.333	278	YOR368w	6	0.267	477	YPL015c	8	0.143	807
YOR328w	14	0.220	1098	YOR369c	13	0.436	869	YPL016w	17	0.228	2308
YOR329c	3	0.333	32	YOR370c	3	1.000	0	YPL017c	16	0.275	1569
YOR330c	3	0.333	41	YOR371c	2	0.000	30	YPL018w	15	0.095	1394
YOR332w	6	0.133	394	YOR372c	376	0.008	411693	YPL019c	25	0.153	5483
YOR333c	3	0.000	46	YOR373w	5	0.200	190	YPL020c	2	0.000	4
YOR334w	1	0.000	0	YOR374w	24	0.250	2581	YPL021w	3	0.000	97
YOR335c	3	0.000	80	YOR375c	18	0.229	1970	YPL022w	2	0.000	37
YOR336w	7	0.095	603	YOR376w	5	0.000	284	YPL023c	2	1.000	0
YOR337w	4	0.500	108	YOR376w-a	3	1.000	0	YPL024w	17	0.353	913
YOR338w	12	0.242	2984	YOR377w	8	0.107	424	YPL025c	10	0.311	232
YOR339c	5	0.400	89	YOR378w	8	0.214	660	YPL026c	15	0.400	1083
YOR340c	8	0.179	442	YOR380w	12	0.348	619	YPL027w	3	0.667	16
YOR341w	10	0.222	746	YOR381w	7	0.286	262	YPL028w	6	0.200	407
YOR342c	13	0.385	958	YOR381w-a	1	0.000	0	YPL029w	3	0.000	132
YOR343c	6	0.467	205	YOR382w	30	0.237	5193	YPL030w	4	0.000	357
YOR343c-a	1	0.000	0	YOR383c	20	0.189	2321	YPL031c	6	0.000	494
YOR343c-b	1	0.000	0	YOR384w	6	0.333	159	YPL032c	4	0.167	171
YOR343w-a	3	0.667	13	YOR385w	7	0.333	298	YPL033c	4	0.000	79
YOR343w-b	2	0.000	13	YOR386w	9	0.083	430	YPL034w	15	0.181	3020
YOR344c	130	0.057	180916	YOR387c	10	0.222	1168	YPL036w	19	0.123	5863
YOR345c	1	0.000	0	YOR388c	18	0.216	2086	YPL037c	5	0.400	593
YOR346w	7	0.381	135	YOR389w	15	0.286	1146	YPL038w	121	0.010	32092
YOR347c	9	0.278	356	YOR390w	5	0.400	138	YPL039w	3	0.000	123
YOR348c	28	0.265	4009	YOR391c	26	0.135	4344	YPL040c	4	0.167	184
YOR349w	14	0.418	431	YOR393w	6	0.333	80	YPL041c	3	0.000	52
YOR350c	3	0.000	132	YOR394c-a	1	0.000	0	YPL042c	4	0.167	181
YOR351c	2	0.000	14	YOR394w	11	0.309	657	YPL043w	7	0.238	252

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YPL044c	2	0.000	16	YPL086c	5	0.200	282	YPL132w	3	0.667	9
YPL045w	2	0.000	13	YPL087w	4	0.000	363	YPL133c	46	0.023	4985
YPL046c	1	0.000	0	YPL088w	14	0.352	993	YPL134c	5	0.300	123
YPL047w	1	0.000	0	YPL089c	211	0.021	131344	YPL135w	20	0.232	1758
YPL048w	6	0.867	32	YPL090c	11	0.400	644	YPL137c	11	0.291	499
YPL049c	93	0.037	72774	YPL091w	5	0.100	83	YPL138c	2	0.000	163
YPL050c	5	0.200	75	YPL092w	13	0.167	1340	YPL139c	9	0.139	1319
YPL051w	10	0.178	1599	YPL093w	11	0.291	660	YPL140c	1	0.000	0
YPL052w	4	0.500	100	YPL094c	6	0.400	294	YPL141c	5	0.400	115
YPL053c	2	1.000	0	YPL095c	9	0.167	562	YPL142c	2	0.000	23
YPL054w	12	0.106	922	YPL096w	3	0.667	22	YPL143w	12	0.394	820
YPL055c	2	1.000	0	YPL097w	3	0.333	121	YPL144w	7	0.429	201
YPL056c	17	0.228	2661	YPL098c	4	0.167	170	YPL145c	6	0.467	153
YPL057c	15	0.267	1236	YPL100w	2	1.000	0	YPL146c	4	0.333	229
YPL058c	14	0.330	746	YPL101w	3	0.667	14	YPL147w	8	0.214	380
YPL059w	7	0.143	455	YPL102c	1	0.000	0	YPL148c	5	0.400	91
YPL060c-a	2	0.000	6	YPL103c	1	0.000	0	YPL149w	4	0.333	129
YPL060w	3	0.000	18	YPL106c	8	0.393	783	YPL150w	3	0.000	25
YPL061w	23	0.261	2942	YPL107w	2	0.000	14	YPL151c	4	0.167	124
YPL062w	5	0.400	54	YPL108w	3	0.333	42	YPL152w	2	1.000	0
YPL063w	1	0.000	0	YPL109c	3	0.333	24	YPL153c	7	0.286	263
YPL064c	3	0.667	12	YPL110c	3	0.333	27	YPL154c	15	0.248	1043
YPL065w	1	0.000	0	YPL111w	18	0.196	3100	YPL155c	5	0.300	304
YPL066w	5	0.300	47	YPL112c	3	0.333	44	YPL156c	16	0.275	1303
YPL067c	7	0.429	283	YPL113c	11	0.345	572	YPL157w	7	0.381	295
YPL068c	9	0.333	457	YPL114w	4	0.167	99	YPL158c	6	0.333	144
YPL069c	1	0.000	0	YPL115c	1	0.000	0	YPL159c	5	0.400	275
YPL070w	6	0.200	161	YPL116w	5	0.200	208	YPL160w	8	0.286	791
YPL071c	8	0.179	480	YPL117c	7	0.238	398	YPL161c	5	0.200	159
YPL072w	1	0.000	0	YPL118w	1	0.000	0	YPL162c	2	0.000	12
YPL073c	2	1.000	0	YPL119c	5	0.400	167	YPL163c	13	0.282	957
YPL074w	4	0.500	5	YPL120w	3	0.333	35	YPL164c	4	0.167	70
YPL075w	288	0.013	292968	YPL121c	3	0.000	40	YPL165c	2	0.000	6
YPL076w	3	0.333	276	YPL122c	11	0.073	865	YPL166w	3	0.000	108
YPL077c	1	0.000	0	YPL123c	13	0.256	1117	YPL167c	2	1.000	0
YPL078c	7	0.238	133	YPL124w	6	0.067	366	YPL168w	3	0.667	16
YPL079w	10	0.422	716	YPL125w	4	0.167	111	YPL169c	1	0.000	0
YPL080c	4	0.500	41	YPL126w	8	0.321	289	YPL170w	11	0.291	1370
YPL081w	12	0.273	1301	YPL127c	5	0.400	68	YPL171c	34	0.205	6825
YPL082c	10	0.356	487	YPL128c	3	0.667	36	YPL172c	8	0.393	571
YPL083c	1	0.000	0	YPL129w	4	0.167	452	YPL173w	5	0.100	277
YPL084w	5	0.400	502	YPL130w	9	0.194	1138	YPL174c	2	0.000	19
YPL085w	6	0.267	342	YPL131w	11	0.382	1787	YPL175w	4	0.000	221

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YPL176c	5	0.200	273	YPL219w	3	0.667	20	YPL264c	4	0.167	147
YPL177c	112	0.074	95575	YPL220w	6	0.800	53	YPL265w	20	0.279	1980
YPL178w	4	0.333	85	YPL221w	14	0.264	1552	YPL266w	8	0.179	700
YPL179w	2	1.000	0	YPL222w	9	0.250	917	YPL267w	6	0.467	331
YPL180w	7	0.095	1295	YPL223c	15	0.229	1366	YPL268w	11	0.218	944
YPL181w	6	0.333	273	YPL224c	1	0.000	0	YPL269w	5	0.200	220
YPL182c	3	0.000	152	YPL226w	7	0.286	488	YPL270w	5	0.000	41
YPL183c	3	0.333	42	YPL227c	4	0.167	224	YPL271w	9	0.250	146
YPL183w-a	3	0.667	13	YPL228w	2	0.000	53	YPL272c	5	0.400	60
YPL184c	1	0.000	0	YPL229w	4	0.333	390	YPL273w	7	0.286	331
YPL185w	1	0.000	0	YPL230w	63	0.055	76516	YPL274w	14	0.209	2230
YPL186c	8	0.536	169	YPL231w	9	0.278	904	YPL275w	7	0.143	897
YPL187w	21	0.186	4417	YPL232w	5	0.300	525	YPL276w	14	0.132	1320
YPL188w	8	0.000	646	YPL233w	2	0.000	141	YPL277c	17	0.309	2696
YPL189c-a	2	0.000	32	YPL235w	5	0.200	154	YPL278c	12	0.318	699
YPL189w	23	0.261	1773	YPL236c	4	0.167	143	YPL279c	3	0.333	30
YPL190c	5	0.200	250	YPL237w	1	0.000	0	YPL280w	19	0.228	1614
YPL191c	3	0.667	32	YPL238c	2	1.000	0	YPL281c	5	0.200	127
YPL192c	6	0.600	87	YPL239w	2	1.000	0	YPL282c	13	0.218	339
YPL193w	2	1.000	0	YPL240c	18	0.203	3927	YPL283c	22	0.277	1861
YPL195w	2	0.000	25	YPL241c	9	0.139	409	YPR001w	17	0.154	1160
YPL196w	3	0.000	40	YPL242c	12	0.227	1917	YPR002c-a	8	0.286	656
YPL197c	4	0.667	21	YPL243w	9	0.306	1218	YPR002w	12	0.242	827
YPL198w	17	0.265	3234	YPL244c	7	0.048	870	YPR003c	3	0.000	85
YPL199c	4	0.500	57	YPL245w	2	0.000	51	YPR004c	4	0.000	235
YPL200w	4	0.333	91	YPL246c	3	0.000	63	YPR005c	8	0.357	304
YPL201c	7	0.143	186	YPL247c	6	0.467	119	YPR006c	9	0.306	420
YPL202c	198	0.019	137677	YPL248c	165	0.011	139223	YPR007c	2	0.000	31
YPL203w	5	0.400	80	YPL249c	2	0.000	9	YPR008w	18	0.124	2639
YPL204w	5	0.200	135	YPL249c-a	13	0.218	2257	YPR009w	8	0.357	250
YPL206c	5	0.300	177	YPL250c	20	0.253	1930	YPR010c	10	0.378	633
YPL207w	8	0.000	179	YPL251w	18	0.111	2306	YPR011c	1	0.000	0
YPL208w	10	0.089	739	YPL252c	5	0.100	179	YPR013c	26	0.308	4659
YPL209c	6	0.200	144	YPL253c	23	0.138	4510	YPR014c	4	0.667	9
YPL210c	1	0.000	0	YPL254w	4	0.000	219	YPR015c	60	0.158	34950
YPL211w	7	0.429	595	YPL255w	6	0.400	183	YPR016c	5	0.600	37
YPL212c	7	0.429	269	YPL256c	11	0.255	715	YPR017c	2	0.000	103
YPL213w	5	0.000	284	YPL257w	4	0.333	70	YPR018w	3	0.333	241
YPL214c	5	0.200	267	YPL258c	7	0.333	321	YPR019w	6	0.333	594
YPL215w	4	0.167	393	YPL260w	1	0.000	0	YPR020w	9	0.167	115
YPL216w	7	0.238	170	YPL261c	1	0.000	0	YPR021c	4	0.333	157
YPL217c	7	0.190	339	YPL262w	8	0.179	291	YPR022c	2	1.000	0
YPL218w	4	0.333	129	YPL263c	4	0.333	118	YPR024w	4	0.333	122

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YPR025c	6	0.133	382	YPR068c	3	0.000	148	YPR114w	3	0.333	52
YPR026w	13	0.333	1192	YPR069c	5	0.500	460	YPR115w	3	0.333	47
YPR027c	10	0.244	839	YPR070w	2	0.000	99	YPR116w	4	0.333	191
YPR028w	7	0.143	473	YPR071w	3	0.000	137	YPR117w	1	0.000	0
YPR029c	5	0.300	315	YPR072w	8	0.107	2409	YPR118w	3	0.333	40
YPR030w	6	0.267	351	YPR073c	4	0.167	155	YPR119w	12	0.182	1010
YPR031w	1	0.000	0	YPR074c	13	0.333	1316	YPR120c	5	0.200	187
YPR032w	4	0.000	270	YPR075c	11	0.145	779	YPR121w	9	0.306	549
YPR033c	5	0.200	646	YPR076w	5	0.000	743	YPR122w	11	0.273	822
YPR034w	12	0.136	1979	YPR077c	1	0.000	0	YPR123c	2	0.000	119
YPR035w	18	0.248	3303	YPR078c	5	0.200	332	YPR124w	16	0.242	2312
YPR036w	15	0.295	1773	YPR079w	9	0.306	519	YPR125w	3	0.667	119
YPR036w-a	6	0.467	93	YPR080w	8	0.179	589	YPR126c	6	0.400	77
YPR037c	2	1.000	0	YPR081c	5	0.000	412	YPR127w	15	0.248	1170
YPR038w	6	0.333	218	YPR082c	2	0.000	22	YPR128c	6	0.333	420
YPR039w	6	0.333	218	YPR083w	2	0.000	22	YPR129w	3	0.000	367
YPR040w	8	0.321	479	YPR084w	2	0.000	18	YPR130c	1	0.000	0
YPR041w	2	0.000	130	YPR085c	3	0.000	57	YPR131c	5	0.300	59
YPR042c	2	0.000	31	YPR086w	3	0.333	47	YPR132w	10	0.422	702
YPR043w	9	0.444	2407	YPR088c	2	1.000	0	YPR133c	2	0.000	24
YPR044c	3	0.000	46	YPR089w	1	0.000	0	YPR133w-a	5	0.200	321
YPR045c	3	0.000	200	YPR091c	5	0.000	96	YPR134w	5	0.100	237
YPR046w	4	0.167	345	YPR093c	3	0.000	180	YPR135w	4	0.000	722
YPR047w	5	0.200	269	YPR094w	8	0.250	451	YPR137w	7	0.429	341
YPR048w	7	0.333	409	YPR095c	1	0.000	0	YPR138c	8	0.321	181
YPR049c	11	0.291	1115	YPR097w	1	0.000	0	YPR139c	7	0.048	621
YPR051w	3	0.333	107	YPR098c	1	0.000	0	YPR140w	6	0.067	486
YPR052c	3	0.000	80	YPR099c	4	0.833	7	YPR141c	6	0.533	131
YPR053c	2	0.000	7	YPR100w	2	1.000	0	YPR142c	2	0.000	27
YPR054w	4	0.167	500	YPR101w	6	0.600	101	YPR143w	5	0.400	80
YPR055w	6	0.267	391	YPR102c	13	0.346	1279	YPR144c	10	0.244	2571
YPR056w	5	0.200	314	YPR103w	8	0.286	577	YPR145w	20	0.189	5142
YPR057w	5	0.400	382	YPR104c	865	0.007	1540598	YPR146c	1	0.000	0
YPR058w	8	0.536	358	YPR105c	2	1.000	0	YPR148c	13	0.385	935
YPR059c	1	0.000	0	YPR106w	6	0.467	138	YPR149w	30	0.294	5067
YPR060c	5	0.400	363	YPR107c	12	0.197	1073	YPR151c	23	0.194	2168
YPR061c	8	0.321	237	YPR108w	16	0.142	2196	YPR152c	3	0.333	71
YPR062w	1	0.000	0	YPR108w-a	1	0.000	0	YPR153w	3	0.000	107
YPR063c	11	0.473	729	YPR109w	8	0.143	260	YPR154w	1	0.000	0
YPR064w	9	0.500	190	YPR110c	12	0.212	3168	YPR155c	5	0.200	103
YPR065w	419	0.021	397072	YPR111w	7	0.286	497	YPR156c	10	0.333	394
YPR066w	3	0.333	165	YPR112c	9	0.250	604	YPR157w	13	0.256	1687
YPR067w	6	0.400	426	YPR113w	8	0.214	415	YPR158c-c	5	0.200	88

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i	ORF Name	k_i	C_i	b_i
YPR158c-d	4	0.167	42	YPR173c	1	0.000	0	YPR191w	11	0.218	339
YPR158w	12	0.212	2156	YPR174c	7	0.333	339	YPR192w	9	0.444	287
YPR158w-a	5	0.200	82	YPR175w	7	0.429	217	YPR193c	4	0.333	33
YPR158w-b	5	0.200	82	YPR176c	1	0.000	0	YPR194c	27	0.137	6204
YPR159w	10	0.289	837	YPR177c	1	0.000	0	YPR195c	8	0.143	534
YPR160w	27	0.234	4692	YPR178w	1	0.000	0	YPR196w	11	0.182	1328
YPR161c	4	0.000	170	YPR179c	5	0.300	149	YPR197c	2	0.000	14
YPR162c	2	1.000	0	YPR180w	3	1.000	0	YPR198w	13	0.154	898
YPR163c	7	0.429	269	YPR181c	5	0.400	102	YPR199c	744	0.004	1094498
YPR164w	4	0.167	243	YPR182w	4	0.167	74	YPR200c	11	0.309	866
YPR165w	2	1.000	0	YPR183w	4	0.833	9	YPR201w	17	0.257	2155
YPR166c	5	0.300	150	YPR184w	20	0.311	1997	YPR202w	14	0.363	928
YPR167c	15	0.333	1145	YPR185w	3	0.000	23	YPR203w	10	0.311	360
YPR168w	7	0.095	226	YPR186c	4	0.000	604	YPR204w	3	0.333	16
YPR169w	5	0.500	351	YPR187w	4	0.167	342				
YPR170c	4	0.000	194	YPR188c	1	0.000	0				
YPR171w	6	0.200	215	YPR189w	1	0.000	0				
YPR172w	4	0.167	532	YPR190c	9	0.139	622				

Table A.2. The frequency, f(k), and the cumulative frequency of nodes, $n(k)$

k	f(k)	$n(k)$	k	f(k)	$n(k)$	k	f(k)	$n(k)$	k	f(k)	$n(k)$
2188	1	1	315	1	45	134	1	100	46	2	155
1829	1	2	314	1	46	130	3	103	45	5	160
1375	1	3	301	1	47	129	1	104	43	2	162
1230	1	4	288	1	48	128	1	105	42	1	163
1156	1	5	277	1	49	122	1	106	40	2	165
1055	1	6	275	1	50	121	1	107	39	4	169
1033	1	7	269	1	51	120	1	108	36	1	170
916	1	8	266	1	52	118	1	109	35	7	177
865	1	9	264	1	53	116	1	110	34	5	182
756	1	10	254	1	54	112	2	112	33	4	186
744	1	11	247	3	57	111	2	114	32	10	196
688	1	12	242	1	58	106	1	115	31	9	205
666	1	13	240	2	60	104	1	116	30	17	222
637	1	14	238	1	61	102	1	117	29	12	234
594	1	15	236	1	62	100	1	118	28	18	252
585	1	16	223	2	64	99	1	119	27	15	267
577	1	17	222	1	65	98	1	120	26	13	280
552	1	18	218	1	66	97	2	122	25	25	305
547	1	19	215	1	67	96	1	123	24	29	334
534	1	20	211	1	68	93	1	124	23	27	361
522	1	21	210	1	69	90	1	125	22	27	388

Table A.2. The frequency, f(k), and the cumulative frequency of nodes, $n(k)$ (continued)

k	f(k)	$n(k)$	k	f(k)	$n(k)$	k	f(k)	$n(k)$	k	f(k)	$n(k)$
510	1	22	203	1	70	85	2	127	21	39	427
506	1	23	201	2	72	84	1	128	20	40	467
504	1	24	200	1	73	80	2	130	19	53	520
492	1	25	199	2	75	78	1	131	18	65	585
482	1	26	198	2	77	77	1	132	17	77	662
459	1	27	194	1	78	76	1	133	16	73	735
458	1	28	191	1	79	69	1	134	15	82	817
448	1	29	189	1	80	68	1	135	14	123	940
425	1	30	188	2	82	67	1	136	13	126	1066
420	1	31	184	1	83	66	1	137	12	147	1213
419	1	32	170	2	85	65	1	138	11	174	1387
407	1	33	169	1	86	64	1	139	10	201	1588
377	1	34	168	1	87	63	3	142	9	287	1875
376	1	35	167	3	90	60	1	143	8	290	2165
358	1	36	166	1	91	59	1	144	7	362	2527
345	1	37	165	1	92	58	3	147	6	455	2982
343	1	38	162	1	93	57	1	148	5	590	3572
339	1	39	152	2	95	56	1	149	4	631	4203
334	1	40	150	1	96	53	1	150	3	735	4938
326	2	42	146	1	97	52	1	151	2	732	5670
324	1	43	144	1	98	50	1	152	1	686	6356
316	1	44	135	1	99	47	1	153			

Table A.3. Average clustering coefficient and betweenness values for each degree

k	$C(k)$	$b(k)$	k	$C(k)$	$b(k)$	k	$C(k)$	$b(k)$	k	$C(k)$	$b(k)$
1	0.000	0	50	0.017	171958	144	0.026	115072	324	0.007	465973
2	1.000	114	52	0.010	33077	146	0.016	99176	326	0.023	519032
3	0.479	90	53	0.032	42977	150	0.048	81167	334	0.009	432706
4	0.340	205	56	0.209	16851	152	0.022	87564	339	0.018	226233
5	0.324	243	57	0.203	18951	162	0.009	226036	343	0.012	420044
6	0.298	337	58	0.056	58752	165	0.011	139223	345	0.008	467778
7	0.279	485	59	0.046	24449	166	0.049	134448	358	0.034	219573
8	0.291	559	60	0.158	34950	167	0.021	145470	376	0.008	411693
9	0.277	693	63	0.050	44491	168	0.021	77869	377	0.011	523332
10	0.280	831	64	0.021	54006	169	0.032	148567	407	0.009	345552
11	0.258	979	65	0.069	52553	170	0.016	178075	419	0.021	397072
12	0.268	1109	66	0.082	39033	184	0.023	136327	420	0.014	380453
13	0.255	1240	67	0.027	34011	188	0.013	95672	425	0.028	474296
14	0.277	1363	68	0.084	115913	189	0.013	78263	448	0.018	510855
15	0.260	1477	69	0.022	46596	191	0.011	115335	458	0.013	589228
16	0.267	1843	76	0.020	22083	194	0.022	76429	459	0.024	705126
17	0.274	1928	77	0.004	125739	198	0.028	149841	482	0.011	752603

Table A.3. Average clustering coefficient and betweenness values for each degree (continued)

k	$C(k)$	$b(k)$	k	$C(k)$	$b(k)$	k	$C(k)$	$b(k)$	k	$C(k)$	$b(k)$
18	0.259	2163	78	0.033	57802	199	0.017	122176	492	0.007	562971
19	0.259	2375	80	0.013	38767	200	0.012	79517	504	0.012	614058
20	0.255	2817	84	0.116	44305	201	0.032	84015	506	0.010	605184
21	0.246	2882	85	0.042	63098	203	0.015	128658	510	0.010	643610
22	0.257	3180	90	0.039	110053	210	0.015	363000	522	0.016	493176
23	0.244	4747	93	0.037	72774	211	0.021	131344	534	0.021	578631
24	0.213	3811	96	0.019	94209	215	0.018	151526	547	0.020	601548
25	0.224	4900	97	0.025	64579	218	0.027	146339	552	0.007	407305
26	0.229	4281	98	0.016	141988	222	0.014	134248	577	0.008	804470
27	0.207	5012	99	0.011	91373	223	0.012	242918	585	0.012	839314
28	0.214	4857	100	0.003	63988	236	0.040	104710	594	0.014	861633
29	0.213	5393	102	0.024	31538	238	0.012	200667	637	0.004	836047
30	0.230	5254	104	0.023	89297	240	0.021	383853	666	0.015	779413
31	0.192	9174	106	0.024	57111	242	0.010	199990	688	0.003	1544447
32	0.233	5824	111	0.021	126956	247	0.022	230509	744	0.004	1094498
33	0.157	9144	112	0.041	84939	254	0.003	248926	756	0.008	1414625
34	0.245	6444	116	0.027	142180	264	0.008	174707	865	0.007	1540598
35	0.193	7457	118	0.012	70076	266	0.015	339144	916	0.007	1230908
36	0.159	5881	120	0.028	48262	269	0.007	551939	1033	0.007	1949936
39	0.207	13235	121	0.010	32092	275	0.011	205404	1055	0.011	1491427
40	0.099	27470	122	0.033	125393	277	0.012	332117	1156	0.006	2489871
42	0.262	9463	128	0.029	117015	288	0.013	292968	1230	0.007	2988666
43	0.128	19086	129	0.024	135771	301	0.007	334676	1375	0.007	3379020
45	0.160	31364	130	0.032	111532	314	0.018	327148	1829	0.004	5162138
46	0.078	11218	134	0.015	49648	315	0.013	309200	2188	0.003	7721326
47	0.125	44124	135	0.037	15803	316	0.049	365525			

Table A.4. TFs in the constructed yeast TRN

TF	ORF Name		TF	ORF Name		TF	ORF Name
Abf1p	YKL112w		Gat4p	YIR013c		Mal63p	MALR
Aca1p	YER045c		Gcn4p	YEL009c		Mata1p	A1
Ace2p	YLR131c		Gcr1p	YPL075w		Matalpha1p	YCR040w
Ada2p	YDR448w		Gcr2p	YNL199c		Mbp1p	YDL056w
Adr1p	YDR216w		Gis1p	YDR096w		Mcm1p	YMR043w
Aft1p	YGL071w		Gis2p	YNL255c		Mdl2p	YPL270w
Aft2p	YPL202c		Gln3p	YER040w		Met28p	YIR017c
Arg80p	YMR042w		Gsm1p	YJL103c		Met31p	YPL038w
Arg81p	YML099c		Gts1p	YGL181w		Met32p	YDR253c
Aro80p	YDR421w		Gzf3p	YJL110c		Met4p	YNL103w
Arr1p	YPR199c		Haa1p	YPR008w		Mga1p	YGR249w

Table A.4. TFs in the constructed yeast TRN (continued)

TF	ORF Name	TF	ORF Name	TF	ORF Name
Ash1p	YKL185w	Hmlalpha2p	YCL067c	Phd1p	YKL043w
Azf1p	YOR113w	Hmra1p	YCR097w	Pho2p	YDL106c
Bas1p	YKR099w	Hmra2p	YCR096c	Pho4p	YFR034c
Bye1p	YKL005c	Hms1p	YOR032c	Pip2p	YOR363c
Cad1p	YDR423c	Hms2p	YJR147w	Plm2p	YDR501w
Cat8p	YMR280c	Hot1p	YMR172w	Pog1p	YIL122w
Cbf1p	YJR060w	Hpc2p	YBR215w	Ppr1p	YLR014c
Cdc14p	YFR028c	Hsf1p	YGL073w	Put3p	YKL015w
Cdc39p	YCR093w	Ifh1p	YLR223c	Rap1p	YNL216w
Cha4p	YLR098c	Ime1p	YJR094c	Rdr1p	YOR380w
Cin5p	YOR028c	Ime4p	YGL192w	Rds1p	YCR106w
Crz1p	YNL027w	Imp2'p	YIL154c	Rds2p	YPL133c
Cst6p	YIL036w	Ino2p	YDR123c	Rds3p	YPR094w
Cup2p	YGL166w	Ino4p	YOL108c	Reb1p	YBR049c
Cup9p	YPL177c	Ixr1p	YKL032c	Rfx1p	YLR176c
Dal80p	YKR034w	Kar4p	YCL055w	Rgm1p	YMR182c
Dal81p	YIR023w	Leu3p	YLR451w	Rgt1p	YKL038w
Dal82p	YNL314w	Lys14p	YDR034c	Rim101p	YHL027w
Dig1p	YPL049c	Mac1p	YMR021c	Rlm1p	YPL089c
Dig2p	YDR480w	Mal13p	YGR288w	Rme1p	YGR044c
Dot6p	YER088c	Mal33p	YBR297w	Rox1p	YPR065w
Ecm22p	YLR228c	Mga2p	YIR033w	Rph1p	YER169w
Elp6p	YMR312w	Mig1p	YGL035c	Rpn10p	YHR200w
Fhl1p	YPR104c	Mig2p	YGL209w	Rpn4p	YDL020c
Fkh1p	YIL131c	Mig3p	YER028c	Rsc30p	YHR056c
Fkh2p	YNL068c	Mot2p	YER068w	Rsf2p	YJR127c
Flo8p	YER109c	Mot3p	YMR070w	Rtg1p	YOL067c
Fzf1p	YGL254w	Msn1p	YOL116w	Rtg2p	YGL252c
Gal4p	YPL248c	Msn2p	YMR037c	Rtg3p	YBL103c
Gal80p	YML051w	Msn4p	YKL062w	Rts2p	YOR077w
Gat1p	YFL021w	Mss11p	YMR164c	Sfl1p	YOR140w
Gat3p	YLR013w	Mth1p	YDR277c	Sfp1p	YLR403w
Hac1p	YFL031w	Ndd1p	YOR372c	Sin3p	YOL004w
Hal9p	YOL089c	Ndt80p	YHR124w	Sip4p	YJL089w
Hap1p	YLR256w	Nrg1p	YDR043c	Skn7p	YHR206w
Hap2p	YGL237c	Nrg2p	YBR066c	Sko1p	YNL167c
Hap3p	YBL021c	Oaf1p	YAL051w	Smp1p	YBR182c
Hap4p	YKL109w	Opi1p	YHL020c	Sok2p	YMR016c
Hap5p	YOR358w	Otu1p	YFL044c	Sps18p	YNL204c
Hcm1p	YCR065w	Pdc2p	YDR081c	Spt2p	YER161c
Hir1p	YBL008w	Pdr1p	YGL013c	Spt23p	YKL020c
Hir2p	YOR038c	Pdr3p	YBL005w	Srd1p	YCR018c
Hmlalpha1p	YCL066w	Pdr8p	YLR266c	Stb1p	YNL309w

Table A.4. TFs in the constructed yeast TRN (continued)

TF	ORF Name		TF	ORF Name		TF	ORF Name
Stb5p	YHR178w		Tec1p	YBR083w		Yap1p	YML007w
Ste12p	YHR084w		Thi2p	YBR240c		Yap3p	YHL009c
Stp1p	YDR463w		Tos4p	YLR183c		Yap5p	YIR018w
Stp2p	YHR006w		Tos8p	YGL096w		Yap6p	YDR259c
Stp3p	YLR375w		Tye7p	YOR344c		Yap7p	YOL028c
Sum1p	YDR310c		Uga3p	YDL170w		Yhp1p	YDR451c
Sut1p	YGL162w		Ume1p	YPL139c		YJL206c	YJL206c
Swi1p	YPL016w		Ume6p	YDR207c		Yox1p	YML027w
Swi3p	YJL176c		Upc2p	YDR213w		YPR015c	YPR015c
Swi4p	YER111c		Usv1p	YPL230w		Yrm1p	YOR172w
Swi5p	YDR146c		War1p	YML076c		Yrr1p	YOR162c
Swi6p	YLR182w		Xbp1p	YIL101c		Zap1p	YJL056c

APPENDIX B: THE MATLAB CODE PERFORMING $Z_{corrected,TF}$ CALCULATIONS

```
loadS;
loadTF;
loadZW1;

% ========================================================
% Z-Score Calculations
% ========================================================

ZT=zeros(size(TF));

for x=1:length(TF);
   a=TF(x);
   k=0;
   for y=1:length(S);
      if a==0;
         ZT(x)=0;
      else
         ZT(x)=ZT(x)+S(a,y)*ZW1(y);
         k=k+S(a,y);
      end
   end
   if a==0;
      ZT(x)=0;
   else
      if k==0
         k=100000000000;
      end
      ZT(x)=ZT(x)/k;
   end
```

```
end

% ==========================================================
% Normalization of Z-Scores
% ==========================================================

ZTN=zeros(length(TF),1000);

den=0;
for x=1:length(S)
    for y=1:length(S)
        den=den+S(x,y);
    end
end
den=den/(length(S)*length(S));

for j=1:1000
  j=j
  % Random Sparse Matrice Creation
  % ------------------------------------------------------------

  RND=sprand(length(S),length(S),den);
  for x=1:length(RND)
      x=x;
      for y=1:length(RND)
          if RND(x,y)>0
              RND(x,y)=1;
          end
      end
  end
  save RND RND;
  % z-score calculation for random matrice with the same sparcity
  % ------------------------------------------------------------
```

```
  for x=1:length(TF);
     a=TF(x);
     k=0;
     for y=1:length(RND);
        if a==0;
           ZTN(x,j)=0;
        else
           ZTN(x,j)=ZTN(x,j)+RND(a,y)*ZW1(y);
           k=k+RND(a,y);
        end
     end
     if a==0;
        ZTN(x,j)=0;
     else
           if k==0
           k=100000000000;
        end
        ZTN(x,j)=ZTN(x,j)/k;
     end
     save ZTN ZTN;
  end
end

% z-score normalization
% ---------------------------------------------------------
ZCMN=zeros(length(TF),1);
ZCSD=zeros(length(TF),1);
for x=1:length(TF)
  for j=1:1000
     ZCMN(x)=ZCMN(x)+ZTN(x,j);
  end
  ZCMN(x)=ZCMN(x)/1000;
  for j=1:1000
```

```
        ZCSD(x)=ZCSD(x)+(ZTN(x,j)-ZCMN(x))^2;
    end
    ZCSD(x)=ZCSD(x)/1000;
    ZT(x)=(ZT(x)-ZCMN(x))/ZCSD(x);
 end
ZCSD
save ZT ZT;
```

APPENDIX C: KEY TRANSCRIPTION FACTORS

Table C.1. Key TFs responsive to the deletion of *SNF1* gene

rank	$Z_{corrected,TF}$	*p*-value	degree, *k*	ORF Name	Gene Name
1	8.0161	0.0000	3	YBR215w	HPC2
2	5.1382	0.0000	15	YPL016w	SWI1
3	4.7341	0.0000	9	YJL176c	SWI3
4	4.1747	0.0000	7	YMR312w	ELP6
5	4.0770	0.0000	16	YDR081c	PDC2
6	3.9824	0.0000	24	YLR266c	PDR8
7	3.9666	0.0000	8	YPR094w	RDS3
8	3.6888	0.0001	9	YGL252c	RTG2
9	3.5973	0.0002	29	YGL166w	CUP2
10	3.2348	0.0006	187	YDR096w	GIS1
11	3.1634	0.0008	26	YER028c	MIG3
12	2.6040	0.0046	122	YIR013c	GAT4
13	2.5991	0.0047	73	YMR172w	HOT1
14	2.5640	0.0052	24	YOR172w	YRM1
15	2.4608	0.0069	168	YIL101c	XBP1
16	2.4290	0.0076	5	YDR480w	DIG2
17	2.3150	0.0103	126	YMR280c	CAT8
18	2.2530	0.0121	24	YKL005c	BYE1
19	2.2472	0.0123	29	YHL020c	OPI1
20	2.1611	0.0153	7	YIL154c	IMP2'
21	2.1158	0.0172	29	YOR077w	RTS2
22	2.0723	0.0191	8	YDR448w	ADA2
23	1.9656	0.0247	31	YOL004w	SIN3
24	1.9175	0.0276	23	YJL103c	GSM1
25	1.8321	0.0335	63	YNL204c	SPS18
26	1.7450	0.0405	248	YAL051w	OAF1
27	1.7147	0.0432	55	YOR140w	SFL1
28	1.7147	0.0432	29	YER045c	ACA1
29	1.6937	0.0452	187	YIL036w	CST6
30	1.6914	0.0454	84	YGL162w	SUT1
31	1.6685	0.0476	180	YPL089c	RLM1
32	1.6676	0.0477	18	YCL066w	HMLALPHA1
33	1.6645	0.0480	18	YCR097w	HMRA1

Table C.2. Key TFs responsive to the deletion of *SNF4* gene

rank	$Z_{corrected,TF}$	*p*-value	degree, *k*	ORF Name	Gene Name
1	5.2109	0.0000	7	YIL154c	IMP2'
2	4.1936	0.0000	8	YPR094w	RDS3
3	3.7235	0.0001	24	YLR266c	PDR8
4	3.4286	0.0003	24	YOR172w	YRM1
5	2.9887	0.0014	5	YDR480w	DIG2
6	2.7043	0.0034	18	YCL066w	HMLALPHA1
7	2.3051	0.0106	61	YGL209w	MIG2
8	2.1167	0.0171	6	YML051w	GAL80
9	1.8746	0.0304	18	YPR008w	HAA1
10	1.8196	0.0344	38	YHR124w	NDT80

Table C.3. Key TFs responsive to the deletion of *SNF1* and *SNF4* genes

rank	$Z_{corrected,TF}$	*p*-value	degree, *k*	ORF Name	Gene Name
1	6.1519	0.0000	9	YCR093w	CDC39
2	3.2725	0.0005	8	YPR094w	RDS3
3	3.2246	0.0006	9	YGL252c	RTG2
4	3.1312	0.0009	12	YDR034c	LYS14
5	3.1188	0.0009	3	YBR215w	HPC2
6	3.0224	0.0013	18	YPR008w	HAA1
7	2.5811	0.0049	63	YNL204c	SPS18
8	2.4386	0.0074	187	YDR096w	GIS1
9	2.3798	0.0087	29	YGL166w	CUP2
10	2.3702	0.0089	122	YIR013c	GAT4
11	2.1886	0.0143	73	YMR172w	HOT1
12	2.1507	0.0157	8	YDR448w	ADA2
13	2.0967	0.0180	7	YMR312w	ELP6
14	2.0167	0.0219	187	YIL036w	CST6
15	1.8408	0.0328	168	YIL101c	XBP1
16	1.6782	0.0467	32	YML076c	WAR1

Table C.4. Key TFs responsive to the deletion of *MIG1* gene

rank	$Z_{corrected,TF}$	*p*-value	degree, *k*	ORF Name	Gene Name
1	7.1489	0.0000	26	YER028c	MIG3
2	6.7006	0.0000	8	YIL154c	IMP2'
3	6.3679	0.0000	5	YDR480w	DIG2
4	5.4422	0.0000	61	YGL209w	MIG2
5	4.823	0.0000	25	YJL103c	GSM1
6	4.7076	0.0000	9	YJL176c	SWI3
7	4.5571	0.0000	8	YPR094w	RDS3
8	4.1502	0.0000	15	YPL016w	SWI1
9	4.0021	0.0000	18	YPR008w	HAA1

Table C.4. Key TFs responsive to the deletion of *MIG1* gene (continued)

rank	$Z_{corrected,TF}$	*p*-value	degree, *k*	ORF Name	Gene Name
10	3.7811	0.0001	67	YKL038w	RGT1
11	3.5519	0.0002	235	YGL035c	MIG1
12	3.3388	0.0004	12	YOR380w	RDR1
13	3.1162	0.0009	7	YML051w	GAL80
14	2.9408	0.0016	28	YLR375w	STP3
15	2.6248	0.0043	166	YBR066c	NRG2
16	2.5953	0.0047	59	YPR015c	YPR015c
17	2.5914	0.0048	29	YER045c	ACA1
18	2.1134	0.0173	35	YIR033w	MGA2
19	1.9391	0.0262	7	YPL270w	MDL2
20	1.9041	0.0284	45	YPL133c	RDS2
21	1.8428	0.0327	129	YIR013c	GAT4
22	1.8176	0.0346	24	YKL005c	BYE1
23	1.8098	0.0352	84	YGL162w	SUT1
24	1.6451	0.0500	8	YDR448w	ADA2

Table C.5. Key TFs responsive to the deletion of *MIG2* gene

rank	$Z_{corrected,TF}$	*p*-value	degree, *k*	ORF Name	Gene Name
1	10.363	0.0000	5	YDR480w	DIG2
2	7.1447	0.0000	7	YML051w	GAL80
3	4.6995	0.0000	8	YDR448w	ADA2
4	2.8404	0.0023	26	YER028c	MIG3
5	2.6282	0.0043	18	YPR008w	HAA1
6	2.5415	0.0055	25	YJL103c	GSM1
7	2.2851	0.0112	31	YOL004w	SIN3
8	2.2459	0.0124	9	YJL176c	SWI3
9	2.1419	0.0161	27	YCR096c	HMRA2
10	2.0158	0.0219	15	YPL016w	SWI1
11	1.9967	0.0229	20	YCL066w	HMLALPHA1
12	1.7916	0.0366	67	YKL038w	RGT1
13	1.7189	0.0428	57	YKL020c	SPT23
14	1.714	0.0433	12	YDR034c	LYS14

Table C.6. Key TFs responsive to the deletion of *MIG1* and *MIG2* genes

rank	$Z_{corrected,TF}$	*p*-value	degree, *k*	ORF Name	Gene Name
1	5.2316	0.0000	26	YER028c	MIG3
2	4.9745	0.0000	61	YGL209w	MIG2
3	4.6398	0.0000	20	YCL066w	HMLALPHA1
4	3.884	0.0001	15	YPL016w	SWI1
5	3.8808	0.0001	8	YIL154c	IMP2'
6	3.6314	0.0001	9	YJL176c	SWI3

Table C.6. Key TFs responsive to the deletion of *MIG1* and *MIG2* genes (continued)

rank	$Z_{corrected,TF}$	*p*-value	degree, *k*	ORF Name	Gene Name
7	3.2742	0.0005	25	YJL103c	GSM1
8	3.0904	0.0010	3	YBR215w	HPC2
9	2.8607	0.0021	12	YOR380w	RDR1
10	2.8331	0.0023	9	YHR200w	RPN10
11	2.6297	0.0043	67	YKL038w	RGT1
12	2.6013	0.0046	235	YGL035c	MIG1
13	2.537	0.0056	129	YIR013c	GAT4
14	2.5188	0.0059	8	YPR094w	RDS3
15	2.4911	0.0064	8	YDR448w	ADA2
16	2.2608	0.0119	7	YML051w	GAL80
17	2.1894	0.0143	28	YCL067c	HMLALPHA2
18	1.7096	0.0437	27	YCR096c	HMRA2

Table C.7. Key TFs responsive to the deletion of *MIG3* gene

rank	$Z_{corrected,TF}$	*p*-value	degree, *k*	ORF Name	Gene Name
1	10.252	0.0000	5	YDR480w	DIG2
2	8.1369	0.0000	7	YPL270w	MDL2
3	4.522	0.0000	29	YER045c	ACA1
4	4.4773	0.0000	18	YPR008w	HAA1
5	3.7234	0.0001	8	YDR448w	ADA2
6	3.5799	0.0002	3	YBR215w	HPC2
7	2.6916	0.0036	7	YML051w	GAL80
8	2.221	0.0132	28	YCL067c	HMLALPHA2
9	2.1896	0.0143	20	YCL066w	HMLALPHA1
10	2.1635	0.0153	15	YPL016w	SWI1
11	1.9957	0.0230	25	YJL103c	GSM1
12	1.9105	0.0280	9	YJL176c	SWI3
13	1.8609	0.0314	12	YGR288w	MAL13
14	1.8249	0.0340	26	YER028c	MIG3
15	1.8139	0.0348	20	YCR097w	HMRA1

Table C.8. Key TFs responsive to the deletion of *MIG1, MIG2* and *MIG3* genes

rank	$Z_{corrected,TF}$	*p*-value	degree, *k*	ORF Name	Gene Name
1	7.4385	0.0000	20	YCL066w	HMLALPHA1
2	6.8346	0.0000	27	YCR096c	HMRA2
3	5.9188	0.0000	26	YER028c	MIG3
4	4.384	0.0000	61	YGL209w	MIG2
5	4.1577	0.0000	8	YIL154c	IMP2'
6	3.8408	0.0001	25	YJL103c	GSM1
7	3.6134	0.0002	3	YBR215w	HPC2
8	3.3753	0.0004	7	YML051w	GAL80

Table C.8. Key TFs responsive to the deletion of *MIG1, MIG2* and *MIG3* genes (continued)

rank	$Z_{corrected,TF}$	*p*-value	degree, *k*	ORF Name	Gene Name
9	3.3462	0.0004	9	YHR200w	RPN10
10	2.8349	0.0023	9	YGL252c	RTG2
11	2.7067	0.0034	18	YPR008w	HAA1
12	2.6272	0.0043	12	YGR288w	MAL13
13	2.5118	0.0060	67	YKL038w	RGT1
14	2.5051	0.0061	28	YCL067c	HMLALPHA2
15	2.4187	0.0078	9	YJL176c	SWI3
16	2.4113	0.0079	235	YGL035c	MIG1
17	2.3196	0.0102	129	YIR013c	GAT4
18	2.3067	0.0105	15	YPL016w	SWI1
19	2.1271	0.0167	47	YCL055w	KAR4
20	1.9309	0.0267	8	YDR448w	ADA2
21	1.8191	0.0344	35	YIR033w	MGA2
22	1.7807	0.0375	99	YDR253c	MET32

Table C.9. Key TFs responsive to oxygen availability under carbon limitation regime

rank	$Z_{corrected,TF}$	*p*-value	degree, *k*	ORF Name	Gene Name
1	7.7254	0.000	7	YMR312w	ELP6
2	7.0418	0.000	8	YDR448w	ADA2
3	6.4163	0.000	13	YPL016w	SWI1
4	5.7943	0.000	8	YJL176c	SWI3
5	4.1035	0.000	126	YMR280c	CAT8
6	3.8557	0.000	131	YOR363c	PIP2
7	3.7905	0.000	26	YER045c	ACA1
8	3.6913	0.000	77	YGL162w	SUT1
9	3.4546	0.000	168	YIL101c	XBP1
10	3.3739	0.000	28	YLR375w	STP3
11	3.2688	0.001	173	YDR096w	GIS1
12	3.0767	0.001	156	YBR066c	NRG2
13	3.065	0.001	237	YAL051w	OAF1
14	3.0498	0.001	42	YPL133c	RDS2
15	2.9718	0.001	177	YIL036w	CST6
16	2.8665	0.002	58	YNL204c	SPS18
17	2.8489	0.002	71	YMR172w	HOT1
18	2.6323	0.004	9	YGL252c	RTG2
19	2.3279	0.010	23	YJL103c	GSM1
20	2.2971	0.011	176	YLR256w	HAP1
21	2.2433	0.012	131	YMR070w	MOT3
22	2.2432	0.012	30	YHL020c	OPI1
23	2.2259	0.013	392	YKL109w	HAP4

Table C.9. Key TFs responsive to oxygen availability under carbon limitation regime (continued)

rank	$Z_{corrected,TF}$	*p*-value	degree, *k*	ORF Name	Gene Name
24	2.1986	0.014	23	YKL005c	BYE1
25	2.1925	0.014	60	YFR028c	CDC14
26	2.1569	0.016	353	YDR043c	NRG1
27	2.1488	0.016	25	YCR096c	HMRA2
28	2.1221	0.017	421	YDR216w	ADR1
29	2.1046	0.018	55	YPR015c	YPR015c
30	2.0335	0.021	194	YDR213w	UPC2
31	2.0329	0.021	204	YGR044c	RME1
32	1.9108	0.028	182	YOR358w	HAP5
33	1.9059	0.028	27	YOL004w	SIN3
34	1.8781	0.030	227	YDR207c	UME6
35	1.8574	0.032	104	YJL089w	SIP4
36	1.8101	0.035	168	YBL021c	HAP3
37	1.7892	0.037	216	YGL035c	MIG1
38	1.7877	0.037	339	YPR065w	ROX1
39	1.7753	0.038	9	YOR380w	RDR1
40	1.7695	0.038	205	YOR032c	HMS1
41	1.7594	0.039	395	YOR028c	CIN5
42	1.7575	0.039	175	YGL237c	HAP2
43	1.7117	0.043	92	YMR021c	MAC1
44	1.6964	0.045	293	YHR006w	STP2
45	1.6953	0.045	309	YNL167c	SKO1
46	1.6842	0.046	23	YOR172w	YRM1

APPENDIX D: SIGNIFICANT SHARED GO BIOLOGICAL PROCESS TERMS OF KEY TRANSCRIPTION FACTORS

Table D.1. Significant shared GO biological process terms of the key TFs identified for *ΔSNF1* mutant

GO Term	Cluster frequency	*p*-value
transcription	25 out of 33 genes, 75.8 per cent	1.69E-18
transcription from RNA polymerase II promoter	21 out of 33 genes, 63.6 per cent	1.00E-16
transcription, DNA-dependent	23 out of 33 genes, 69.7 per cent	3.57E-16
RNA biosynthetic process	23 out of 33 genes, 69.7 per cent	3.86E-16
regulation of transcription	21 out of 33 genes, 63.6 per cent	8.29E-16
regulation of transcription from RNA polymerase II promoter	18 out of 33 genes, 54.5 per cent	2.03E-15
regulation of transcription, DNA-dependent	20 out of 33 genes, 60.6 per cent	6.21E-15
regulation of RNA metabolic process	20 out of 33 genes, 60.6 per cent	1.13E-14
regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	21 out of 33 genes, 63.6 per cent	1.62E-14
regulation of nitrogen compound metabolic process	21 out of 33 genes, 63.6 per cent	1.76E-14
regulation of gene expression	21 out of 33 genes, 63.6 per cent	3.29E-14
regulation of macromolecule biosynthetic process	21 out of 33 genes, 63.6 per cent	5.19E-14
regulation of cellular biosynthetic process	21 out of 33 genes, 63.6 per cent	1.01E-13
regulation of biosynthetic process	21 out of 33 genes, 63.6 per cent	1.12E-13
regulation of macromolecule metabolic process	21 out of 33 genes, 63.6 per cent	4.10E-13
regulation of primary metabolic process	21 out of 33 genes, 63.6 per cent	1.24E-12
regulation of cellular metabolic process	21 out of 33 genes, 63.6 per cent	2.72E-12
regulation of metabolic process	21 out of 33 genes, 63.6 per cent	6.64E-12
nucleic acid metabolic process	27 out of 33 genes, 81.8 per cent	9.58E-12
nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	27 out of 33 genes, 81.8 per cent	1.55E-10
RNA metabolic process	24 out of 33 genes, 72.7 per cent	1.79E-10
regulation of cellular process	21 out of 33 genes, 63.6 per cent	3.56E-09
cellular nitrogen compound metabolic process	27 out of 33 genes, 81.8 per cent	3.81E-09
nitrogen compound metabolic process	27 out of 33 genes, 81.8 per cent	5.49E-09
cellular macromolecule biosynthetic process	25 out of 33 genes, 75.8 per cent	7.83E-09
macromolecule biosynthetic process	25 out of 33 genes, 75.8 per cent	8.07E-09
regulation of biological process	21 out of 33 genes, 63.6 per cent	9.86E-09
positive regulation of macromolecule metabolic process	12 out of 33 genes, 36.4 per cent	9.91E-09
positive regulation of transcription	11 out of 33 genes, 33.3 per cent	1.01E-08
positive regulation of gene expression	11 out of 33 genes, 33.3 per cent	1.08E-08
positive regulation of cellular metabolic process	12 out of 33 genes, 36.4 per cent	1.53E-08

Table D.1. Significant shared GO biological process terms of the key TFs identified for *ΔSNF1* mutant (continued)

GO Term	Cluster frequency	*p*-value
positive regulation of metabolic process	12 out of 33 genes, 36.4 per cent	1.80E-08
positive regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	11 out of 33 genes, 33.3 per cent	2.51E-08
positive regulation of nitrogen compound metabolic process	11 out of 33 genes, 33.3 per cent	2.51E-08
gene expression	26 out of 33 genes, 78.8 per cent	2.68E-08
positive regulation of macromolecule biosynthetic process	11 out of 33 genes, 33.3 per cent	4.87E-08
positive regulation of cellular biosynthetic process	11 out of 33 genes, 33.3 per cent	7.27E-08
positive regulation of biosynthetic process	11 out of 33 genes, 33.3 per cent	7.27E-08
positive regulation of cellular process	12 out of 33 genes, 36.4 per cent	9.52E-08
positive regulation of biological process	12 out of 33 genes, 36.4 per cent	1.24E-07
positive regulation of transcription, DNA-dependent	10 out of 33 genes, 30.3 per cent	1.65E-07
positive regulation of RNA metabolic process	10 out of 33 genes, 30.3 per cent	2.55E-07
biological regulation	21 out of 33 genes, 63.6 per cent	4.22E-07
cellular biosynthetic process	25 out of 33 genes, 75.8 per cent	1.77E-06
biosynthetic process	25 out of 33 genes, 75.8 per cent	2.89E-06
positive regulation of transcription from RNA polymerase II promoter	8 out of 33 genes, 24.2 per cent	4.54E-06
cellular macromolecule metabolic process	27 out of 33 genes, 81.8 per cent	3.25E-05
macromolecule metabolic process	27 out of 33 genes, 81.8 per cent	5.27E-05
negative regulation of transcription from RNA polymerase II promoter	5 out of 33 genes, 15.2 per cent	0.00362
negative regulation of transcription	7 out of 33 genes, 21.2 per cent	0.00368
cellular metabolic process	28 out of 33 genes, 84.8 per cent	0.00377
negative regulation of gene expression	7 out of 33 genes, 21.2 per cent	0.00407
primary metabolic process	27 out of 33 genes, 81.8 per cent	0.00537
chromatin organization	7 out of 33 genes, 21.2 per cent	0.00693
metabolic process	28 out of 33 genes, 84.8 per cent	0.00695
negative regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	7 out of 33 genes, 21.2 per cent	0.00736
negative regulation of nitrogen compound metabolic process	7 out of 33 genes, 21.2 per cent	0.00736
negative regulation of macromolecule biosynthetic process	7 out of 33 genes, 21.2 per cent	0.00781

Table D.2. Significant shared GO biological process terms of the key TFs identified for *ΔSNF4* mutant

GO Term	Cluster frequency	*p*-value
transcription	7 out of 10 genes, 70.0 per cent	0.00024
nucleic acid metabolic process	9 out of 10 genes, 90.0 per cent	0.00036
regulation of transcription, DNA-dependent	6 out of 10 genes, 60.0 per cent	0.00048
regulation of RNA metabolic process	6 out of 10 genes, 60.0 per cent	0.00058
regulation of transcription	6 out of 10 genes, 60.0 per cent	0.0007

Table D.2. Significant shared GO biological process terms of the key TFs identified for *ΔSNF4* mutant (continued)

GO Term	Cluster frequency	*p*-value
nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	9 out of 10 genes, 90.0 per cent	0.00095
response to stimulus	7 out of 10 genes, 70.0 per cent	0.00105
regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	6 out of 10 genes, 60.0 per cent	0.0016
regulation of nitrogen compound metabolic process	6 out of 10 genes, 60.0 per cent	0.00164
regulation of gene expression	6 out of 10 genes, 60.0 per cent	0.00195
regulation of macromolecule biosynthetic process	6 out of 10 genes, 60.0 per cent	0.00222
response to chemical stimulus	5 out of 10 genes, 50.0 per cent	0.00255
regulation of cellular biosynthetic process	6 out of 10 genes, 60.0 per cent	0.00268
regulation of biosynthetic process	6 out of 10 genes, 60.0 per cent	0.00276
cellular nitrogen compound metabolic process	9 out of 10 genes, 90.0 per cent	0.00285
transcription, DNA-dependent	6 out of 10 genes, 60.0 per cent	0.00321
nitrogen compound metabolic process	9 out of 10 genes, 90.0 per cent	0.00324
RNA biosynthetic process	6 out of 10 genes, 60.0 per cent	0.00327
regulation of macromolecule metabolic process	6 out of 10 genes, 60.0 per cent	0.00397
regulation of primary metabolic process	6 out of 10 genes, 60.0 per cent	0.00543
regulation of cellular metabolic process	6 out of 10 genes, 60.0 per cent	0.00676
transcription from RNA polymerase II promoter	5 out of 10 genes, 50.0 per cent	0.00799
regulation of metabolic process	6 out of 10 genes, 60.0 per cent	0.0087

Table D.3. Significant shared GO biological process terms of the key TFs identified for *ΔSNF1ΔSNF4* mutant

GO Term	Cluster frequency	*p*-value
transcription from RNA polymerase II promoter	9 out of 16 genes, 56.2 per cent	4.13E-06
transcription	10 out of 16 genes, 62.5 per cent	1.03E-05
transcription, DNA-dependent	9 out of 16 genes, 56.2 per cent	9.74E-05
RNA biosynthetic process	9 out of 16 genes, 56.2 per cent	0.0001
regulation of transcription, DNA-dependent	7 out of 16 genes, 43.8 per cent	0.00161
regulation of transcription from RNA polymerase II promoter	6 out of 16 genes, 37.5 per cent	0.00182
regulation of RNA metabolic process	7 out of 16 genes, 43.8 per cent	0.00197
regulation of transcription	7 out of 16 genes, 43.8 per cent	0.00242
nucleic acid metabolic process	11 out of 16 genes, 68.8 per cent	0.00398
response to chemical stimulus	6 out of 16 genes, 37.5 per cent	0.004
RNA metabolic process	10 out of 16 genes, 62.5 per cent	0.00443
cellular nitrogen compound metabolic process	12 out of 16 genes, 75.0 per cent	0.00538
regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	7 out of 16 genes, 43.8 per cent	0.00618
nitrogen compound metabolic process	12 out of 16 genes, 75.0 per cent	0.00628
regulation of nitrogen compound metabolic process	7 out of 16 genes, 43.8 per cent	0.00633

Table D.3. Significant shared GO biological process terms of the key TFs identified for *ΔSNF1ΔSNF4* mutant (continued)

GO Term	Cluster frequency	*p*-value
regulation of gene expression	7 out of 16 genes, 43.8 per cent	0.00771
regulation of macromolecule biosynthetic process	7 out of 16 genes, 43.8 per cent	0.00889

Table D.4. Significant shared GO biological process terms of the key TFs identified only for *ΔSNF1* mutant

GO Term	Cluster frequency	*p*-value
regulation of transcription	13 out of 16 genes, 81.2 per cent	9.10E-12
transcription	14 out of 16 genes, 87.5 per cent	1.22E-11
regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	13 out of 16 genes, 81.2 per cent	5.90E-11
regulation of nitrogen compound metabolic process	13 out of 16 genes, 81.2 per cent	6.20E-11
regulation of gene expression	13 out of 16 genes, 81.2 per cent	9.21E-11
regulation of macromolecule biosynthetic process	13 out of 16 genes, 81.2 per cent	1.22E-10
regulation of cellular biosynthetic process	13 out of 16 genes, 81.2 per cent	1.87E-10
regulation of biosynthetic process	13 out of 16 genes, 81.2 per cent	2.00E-10
regulation of transcription, DNA-dependent	12 out of 16 genes, 75.0 per cent	2.19E-10
transcription, DNA-dependent	13 out of 16 genes, 81.2 per cent	2.87E-10
RNA biosynthetic process	13 out of 16 genes, 81.2 per cent	3.00E-10
regulation of RNA metabolic process	12 out of 16 genes, 75.0 per cent	3.15E-10
regulation of macromolecule metabolic process	13 out of 16 genes, 81.2 per cent	4.54E-10
regulation of primary metabolic process	13 out of 16 genes, 81.2 per cent	9.20E-10
regulation of cellular metabolic process	13 out of 16 genes, 81.2 per cent	1.51E-09
regulation of metabolic process	13 out of 16 genes, 81.2 per cent	2.67E-09
regulation of transcription from RNA polymerase II promoter	10 out of 16 genes, 62.5 per cent	4.46E-09
transcription from RNA polymerase II promoter	11 out of 16 genes, 68.8 per cent	5.74E-09
positive regulation of transcription	8 out of 16 genes, 50.0 per cent	6.41E-08
positive regulation of gene expression	8 out of 16 genes, 50.0 per cent	6.74E-08
positive regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	8 out of 16 genes, 50.0 per cent	1.25E-07
positive regulation of nitrogen compound metabolic process	8 out of 16 genes, 50.0 per cent	1.25E-07
regulation of cellular process	13 out of 16 genes, 81.2 per cent	1.52E-07
positive regulation of macromolecule biosynthetic process	8 out of 16 genes, 50.0 per cent	2.04E-07
positive regulation of cellular biosynthetic process	8 out of 16 genes, 50.0 per cent	2.75E-07
positive regulation of biosynthetic process	8 out of 16 genes, 50.0 per cent	2.75E-07
regulation of biological process	13 out of 16 genes, 81.2 per cent	2.95E-07
positive regulation of macromolecule metabolic process	8 out of 16 genes, 50.0 per cent	5.60E-07
positive regulation of cellular metabolic process	8 out of 16 genes, 50.0 per cent	7.53E-07
positive regulation of metabolic process	8 out of 16 genes, 50.0 per cent	8.39E-07
nucleic acid metabolic process	14 out of 16 genes, 87.5 per cent	1.83E-06
positive regulation of transcription, DNA-dependent	7 out of 16 genes, 43.8 per cent	2.10E-06
RNA metabolic process	13 out of 16 genes, 81.2 per cent	2.36E-06
positive regulation of cellular process	8 out of 16 genes, 50.0 per cent	2.59E-06
positive regulation of RNA metabolic process	7 out of 16 genes, 43.8 per cent	2.86E-06
positive regulation of biological process	8 out of 16 genes, 50.0 per cent	3.11E-06

Table D.4. Significant shared GO biological process terms of the key TFs identified only for *ΔSNF1* mutant (continued)

GO Term	Cluster frequency	*p*-value
biological regulation	13 out of 16 genes, 81.2 per cent	3.48E-06
cellular macromolecule biosynthetic process	14 out of 16 genes, 87.5 per cent	4.19E-06
macromolecule biosynthetic process	14 out of 16 genes, 87.5 per cent	4.27E-06
nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	14 out of 16 genes, 87.5 per cent	8.00E-06
gene expression	14 out of 16 genes, 87.5 per cent	3.33E-05
cellular nitrogen compound metabolic process	14 out of 16 genes, 87.5 per cent	4.37E-05
negative regulation of transcription from RNA polymerase II promoter	5 out of 16 genes, 31.2 per cent	5.24E-05
nitrogen compound metabolic process	14 out of 16 genes, 87.5 per cent	5.30E-05
cellular biosynthetic process	14 out of 16 genes, 87.5 per cent	0.0001
biosynthetic process	14 out of 16 genes, 87.5 per cent	0.00014
negative regulation of transcription	6 out of 16 genes, 37.5 per cent	0.00026
negative regulation of gene expression	6 out of 16 genes, 37.5 per cent	0.00028
positive regulation of transcription from RNA polymerase II promoter	5 out of 16 genes, 31.2 per cent	0.00036
negative regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	6 out of 16 genes, 37.5 per cent	0.00049
negative regulation of nitrogen compound metabolic process	6 out of 16 genes, 37.5 per cent	0.00049
negative regulation of macromolecule biosynthetic process	6 out of 16 genes, 37.5 per cent	0.00051
negative regulation of cellular biosynthetic process	6 out of 16 genes, 37.5 per cent	0.0007
negative regulation of biosynthetic process	6 out of 16 genes, 37.5 per cent	0.0007
negative regulation of macromolecule metabolic process	6 out of 16 genes, 37.5 per cent	0.00083
negative regulation of cellular metabolic process	6 out of 16 genes, 37.5 per cent	0.00113
negative regulation of metabolic process	6 out of 16 genes, 37.5 per cent	0.00124
negative regulation of transcription, DNA-dependent	5 out of 16 genes, 31.2 per cent	0.00444
negative regulation of RNA metabolic process	5 out of 16 genes, 31.2 per cent	0.00455
negative regulation of cellular process	6 out of 16 genes, 37.5 per cent	0.00515
cellular macromolecule metabolic process	14 out of 16 genes, 87.5 per cent	0.00569
negative regulation of biological process	6 out of 16 genes, 37.5 per cent	0.00571
macromolecule metabolic process	14 out of 16 genes, 87.5 per cent	0.0074

Table D.5. Significant shared GO biological process terms of the key TFs identified only for *ΔSNF4* mutant

GO Term	Cluster frequency	*p*-value
regulation of transcription by carbon catabolites	2 out of 3 genes, 66.7 per cent	0.00052
cellular response to nutrient	2 out of 3 genes, 66.7 per cent	0.00087
response to nutrient	2 out of 3 genes, 66.7 per cent	0.00109

Table D.6. Significant shared GO biological process terms of the key TFs identified for both *ΔSNF1* and *ΔSNF1ΔSNF4* mutants

GO Term	Cluster frequency	*p*-value
transcription from RNA polymerase II promoter	7 out of 12 genes, 58.3 per cent	7.81E-05
transcription	8 out of 12 genes, 66.7 per cent	7.85E-05
transcription, DNA-dependent	7 out of 12 genes, 58.3 per cent	0.00092
RNA biosynthetic process	7 out of 12 genes, 58.3 per cent	0.00094
regulation of transcription from RNA polymerase II promoter	5 out of 12 genes, 41.7 per cent	0.00394
nucleic acid metabolic process	9 out of 12 genes, 75.0 per cent	0.00551

Table D.7. Significant shared GO biological process terms of the key TFs identified for *ΔMIG1*, *ΔMIG2* and *ΔMIG1ΔMIG2* mutants

GO Term	Cluster frequency	*p*-value
regulation of transcription	6 out of 7 genes, 85.7 per cent	3.05E-05
regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	6 out of 7 genes, 85.7 per cent	7.22E-05
regulation of nitrogen compound metabolic process	6 out of 7 genes, 85.7 per cent	7.39E-05
regulation of gene expression	6 out of 7 genes, 85.7 per cent	8.87E-05
regulation of macromolecule biosynthetic process	6 out of 7 genes, 85.7 per cent	0.0001
regulation of cellular biosynthetic process	6 out of 7 genes, 85.7 per cent	0.00012
regulation of biosynthetic process	6 out of 7 genes, 85.7 per cent	0.00013
regulation of macromolecule metabolic process	6 out of 7 genes, 85.7 per cent	0.00019
transcription	6 out of 7 genes, 85.7 per cent	0.00021
regulation of primary metabolic process	6 out of 7 genes, 85.7 per cent	0.00026
regulation of cellular metabolic process	6 out of 7 genes, 85.7 per cent	0.00032
regulation of metabolic process	6 out of 7 genes, 85.7 per cent	0.00042
regulation of transcription, DNA-dependent	5 out of 7 genes, 71.4 per cent	0.00104
regulation of RNA metabolic process	5 out of 7 genes, 71.4 per cent	0.00121
positive regulation of macromolecule metabolic process	4 out of 7 genes, 57.1 per cent	0.00194
positive regulation of cellular metabolic process	4 out of 7 genes, 57.1 per cent	0.00225
positive regulation of metabolic process	4 out of 7 genes, 57.1 per cent	0.00238
regulation of cellular process	6 out of 7 genes, 85.7 per cent	0.00274
regulation of biological process	6 out of 7 genes, 85.7 per cent	0.00373
positive regulation of cellular process	4 out of 7 genes, 57.1 per cent	0.00418
positive regulation of biological process	4 out of 7 genes, 57.1 per cent	0.00458
transcription, DNA-dependent	5 out of 7 genes, 71.4 per cent	0.00519
RNA biosynthetic process	5 out of 7 genes, 71.4 per cent	0.00527

Table D.8. Significant shared GO biological process terms of the key TFs identified for both *ΔMIG1* and *ΔMIG1ΔMIG2* mutants excluding the key TFs identified for all three *ΔMIG1*, *ΔMIG2* and *ΔMIG1ΔMIG2* mutants

GO Term	Cluster frequency	*p*-value
negative regulation of transcription from RNA polymerase II promoter by glucose	2 out of 6 genes, 33.3 per cent	0.00065
negative regulation of transcription from RNA polymerase II promoter by carbon catabolites	2 out of 6 genes, 33.3 per cent	0.00065
negative regulation of transcription by carbon catabolites	2 out of 6 genes, 33.3 per cent	0.00065
negative regulation of transcription by glucose	2 out of 6 genes, 33.3 per cent	0.00065
response to xenobiotic stimulus	2 out of 6 genes, 33.3 per cent	0.00065
regulation of transcription from RNA polymerase II promoter by glucose	2 out of 6 genes, 33.3 per cent	0.00091
regulation of transcription from RNA polymerase II promoter by carbon catabolites	2 out of 6 genes, 33.3 per cent	0.00121
regulation of transcription by glucose	2 out of 6 genes, 33.3 per cent	0.00121
response to chemical stimulus	4 out of 6 genes, 66.7 per cent	0.00389
regulation of transcription by carbon catabolites	2 out of 6 genes, 33.3 per cent	0.00392
response to stimulus	5 out of 6 genes, 83.3 per cent	0.00565
cellular response to nutrient	2 out of 6 genes, 33.3 per cent	0.00657
response to nutrient	2 out of 6 genes, 33.3 per cent	0.00816

Table D.9. Significant shared GO biological process terms of the key TFs identified only for *ΔMIG1* (comparing *ΔMIG1*, *ΔMIG2* and *ΔMIG3* mutants)

GO Term	Cluster frequency	*p*-value
response to xenobiotic stimulus	3 out of 13 genes, 23.1 per cent	8.36E-06
negative regulation of transcription from RNA polymerase II promoter by glucose	2 out of 13 genes, 15.4 per cent	0.00408
negative regulation of transcription from RNA polymerase II promoter by carbon catabolites	2 out of 13 genes, 15.4 per cent	0.00408
negative regulation of transcription by carbon catabolites	2 out of 13 genes, 15.4 per cent	0.00408
negative regulation of transcription by glucose	2 out of 13 genes, 15.4 per cent	0.00408
regulation of transcription from RNA polymerase II promoter by glucose	2 out of 13 genes, 15.4 per cent	0.00571
regulation of transcription from RNA polymerase II promoter	5 out of 13 genes, 38.5 per cent	0.00734
regulation of transcription from RNA polymerase II promoter by carbon catabolites	2 out of 13 genes, 15.4 per cent	0.00761
regulation of transcription by glucose	2 out of 13 genes, 15.4 per cent	0.00761

Table D.10. Significant shared GO biological process terms of the key TFs identified only for *ΔMIG3* (comparing *ΔMIG1*, *ΔMIG2* and *ΔMIG3* mutants)

GO Term	Cluster frequency	*p*-value
regulation of transcription, mating-type specific	2 out of 4 genes, 50.0 per cent	0.00024
regulation of transcription, DNA-dependent	4 out of 4 genes, 100.0 per cent	0.00055

Table D.10. Significant shared GO biological process terms of the key TFs identified only for *ΔMIG3* (comparing *ΔMIG1*, *ΔMIG2* and *ΔMIG3* mutants) (continued)

GO Term	Cluster frequency	*p*-value
regulation of RNA metabolic process	4 out of 4 genes, 100.0 per cent	0.00062
regulation of transcription	4 out of 4 genes, 100.0 per cent	0.0007
regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	4 out of 4 genes, 100.0 per cent	0.00126
regulation of nitrogen compound metabolic process	4 out of 4 genes, 100.0 per cent	0.00128
regulation of gene expression	4 out of 4 genes, 100.0 per cent	0.00144
regulation of macromolecule biosynthetic process	4 out of 4 genes, 100.0 per cent	0.00158
regulation of cellular biosynthetic process	4 out of 4 genes, 100.0 per cent	0.0018
regulation of biosynthetic process	4 out of 4 genes, 100.0 per cent	0.00184
transcription, DNA-dependent	4 out of 4 genes, 100.0 per cent	0.00205
RNA biosynthetic process	4 out of 4 genes, 100.0 per cent	0.00208
regulation of macromolecule metabolic process	4 out of 4 genes, 100.0 per cent	0.00237
transcription	4 out of 4 genes, 100.0 per cent	0.00261
regulation of primary metabolic process	4 out of 4 genes, 100.0 per cent	0.00295
regulation of cellular metabolic process	4 out of 4 genes, 100.0 per cent	0.00344
cell fate commitment	2 out of 4 genes, 50.0 per cent	0.00363
sex determination	2 out of 4 genes, 50.0 per cent	0.00363
mating type determination	2 out of 4 genes, 50.0 per cent	0.00363
regulation of metabolic process	4 out of 4 genes, 100.0 per cent	0.00412

Table D.11. Significant shared GO biological process terms of the key TFs identified for *ΔMIG1*, *ΔMIG2* and *ΔMIG3* mutants

GO Term	Cluster frequency	*p*-value
regulation of transcription, DNA-dependent	6 out of 8 genes, 75.0 per cent	8.28E-05
regulation of RNA metabolic process	6 out of 8 genes, 75.0 per cent	9.92E-05
regulation of transcription	6 out of 8 genes, 75.0 per cent	0.00012
regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	6 out of 8 genes, 75.0 per cent	0.00028
regulation of nitrogen compound metabolic process	6 out of 8 genes, 75.0 per cent	0.00029
regulation of gene expression	6 out of 8 genes, 75.0 per cent	0.00034
regulation of macromolecule biosynthetic process	6 out of 8 genes, 75.0 per cent	0.00039
regulation of cellular biosynthetic process	6 out of 8 genes, 75.0 per cent	0.00048
regulation of biosynthetic process	6 out of 8 genes, 75.0 per cent	0.00049
transcription, DNA-dependent	6 out of 8 genes, 75.0 per cent	0.00058
RNA biosynthetic process	6 out of 8 genes, 75.0 per cent	0.00059
regulation of macromolecule metabolic process	6 out of 8 genes, 75.0 per cent	0.00071
transcription	6 out of 8 genes, 75.0 per cent	0.00082
regulation of primary metabolic process	6 out of 8 genes, 75.0 per cent	0.00098
regulation of cellular metabolic process	6 out of 8 genes, 75.0 per cent	0.00123
regulation of metabolic process	6 out of 8 genes, 75.0 per cent	0.0016

Table D.11. Significant shared GO biological process terms of the key TFs identified for *ΔMIG1*, *ΔMIG2* and *ΔMIG3* mutants (continued)

GO Term	Cluster frequency	*p*-value
positive regulation of macromolecule metabolic process	4 out of 8 genes, 50.0 per cent	0.00393
positive regulation of cellular metabolic process	4 out of 8 genes, 50.0 per cent	0.00455
positive regulation of metabolic process	4 out of 8 genes, 50.0 per cent	0.00481
positive regulation of cellular process	4 out of 8 genes, 50.0 per cent	0.00842
positive regulation of biological process	4 out of 8 genes, 50.0 per cent	0.00922

Table D.12. Significant shared GO biological process terms of the key TFs responsive to oxygen availability (Clim)

GO Term	Cluster frequency	*p*-value
transcription	33 out of 46 genes, 71.7 per cent	2.33E-23
regulation of primary metabolic process	32 out of 46 genes, 69.6 per cent	1.69E-21
regulation of metabolic process	32 out of 46 genes, 69.6 per cent	2.28E-20
regulation of transcription from RNA polymerase II promoter	24 out of 46 genes, 52.2 per cent	3.43E-20
regulation of transcription	27 out of 46 genes, 58.7 per cent	3.68E-19
transcription from RNA polymerase II promoter	26 out of 46 genes, 56.5 per cent	5.92E-19
regulation of cellular biosynthetic process	28 out of 46 genes, 60.9 per cent	9.49E-18
regulation of biosynthetic process	28 out of 46 genes, 60.9 per cent	1.09E-17
regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	27 out of 46 genes, 58.7 per cent	1.66E-17
regulation of nitrogen compound metabolic process	27 out of 46 genes, 58.7 per cent	1.84E-17
regulation of transcription, DNA-dependent	25 out of 46 genes, 54.3 per cent	3.43E-17
regulation of gene expression	27 out of 46 genes, 58.7 per cent	4.12E-17
regulation of RNA metabolic process	25 out of 46 genes, 54.3 per cent	7.27E-17
regulation of macromolecule biosynthetic process	27 out of 46 genes, 58.7 per cent	7.39E-17
regulation of biological process	33 out of 46 genes, 71.7 per cent	1.22E-16
biological regulation	35 out of 46 genes, 76.1 per cent	2.91E-16
transcription, DNA-dependent	27 out of 46 genes, 58.7 per cent	3.93E-16
RNA biosynthetic process	27 out of 46 genes, 58.7 per cent	4.30E-16
regulation of cellular metabolic process	28 out of 46 genes, 60.9 per cent	7.62E-16
regulation of macromolecule metabolic process	27 out of 46 genes, 58.7 per cent	1.03E-15
regulation of cellular process	29 out of 46 genes, 63.0 per cent	8.73E-13
nucleic acid metabolic process	33 out of 46 genes, 71.7 per cent	1.70E-11
positive regulation of cellular metabolic process	16 out of 46 genes, 34.8 per cent	3.03E-11
positive regulation of metabolic process	16 out of 46 genes, 34.8 per cent	3.75E-11
positive regulation of cellular biosynthetic process	15 out of 46 genes, 32.6 per cent	8.30E-11
positive regulation of biosynthetic process	15 out of 46 genes, 32.6 per cent	8.30E-11
cellular macromolecule biosynthetic process	33 out of 46 genes, 71.7 per cent	1.04E-10
macromolecule biosynthetic process	33 out of 46 genes, 71.7 per cent	1.08E-10
positive regulation of cellular process	16 out of 46 genes, 34.8 per cent	2.26E-10

Table D.12. Significant shared GO biological process terms of the key TFs responsive to oxygen availability (Clim) (continued)

GO Term	Cluster frequency	*p*-value
positive regulation of biological process	16 out of 46 genes, 34.8 per cent	3.48E-10
nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	33 out of 46 genes, 71.7 per cent	4.40E-10
positive regulation of transcription	13 out of 46 genes, 28.3 per cent	2.49E-09
positive regulation of gene expression	13 out of 46 genes, 28.3 per cent	2.70E-09
biosynthetic process	35 out of 46 genes, 76.1 per cent	3.99E-09
positive regulation of macromolecule metabolic process	14 out of 46 genes, 30.4 per cent	5.17E-09
positive regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	13 out of 46 genes, 28.3 per cent	7.28E-09
positive regulation of nitrogen compound metabolic process	13 out of 46 genes, 28.3 per cent	7.28E-09
gene expression	33 out of 46 genes, 71.7 per cent	9.86E-09
regulation of carbohydrate metabolic process	8 out of 46 genes, 17.4 per cent	1.42E-08
positive regulation of macromolecule biosynthetic process	13 out of 46 genes, 28.3 per cent	1.58E-08
cellular biosynthetic process	34 out of 46 genes, 73.9 per cent	1.58E-08
cellular nitrogen compound metabolic process	33 out of 46 genes, 71.7 per cent	1.77E-08
RNA metabolic process	27 out of 46 genes, 58.7 per cent	2.02E-08
nitrogen compound metabolic process	33 out of 46 genes, 71.7 per cent	2.69E-08
negative regulation of transcription from RNA polymerase II promoter	9 out of 46 genes, 19.6 per cent	1.85E-07
negative regulation of transcription	12 out of 46 genes, 26.1 per cent	4.23E-07
negative regulation of gene expression	12 out of 46 genes, 26.1 per cent	5.04E-07
positive regulation of transcription, DNA-dependent	11 out of 46 genes, 23.9 per cent	5.21E-07
positive regulation of RNA metabolic process	11 out of 46 genes, 23.9 per cent	8.34E-07
negative regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	12 out of 46 genes, 26.1 per cent	1.44E-06
negative regulation of nitrogen compound metabolic process	12 out of 46 genes, 26.1 per cent	1.44E-06
negative regulation of macromolecule biosynthetic process	12 out of 46 genes, 26.1 per cent	1.60E-06
negative regulation of cellular biosynthetic process	12 out of 46 genes, 26.1 per cent	2.93E-06
negative regulation of biosynthetic process	12 out of 46 genes, 26.1 per cent	2.93E-06
negative regulation of transcription, DNA-dependent	11 out of 46 genes, 23.9 per cent	3.78E-06
negative regulation of RNA metabolic process	11 out of 46 genes, 23.9 per cent	4.00E-06
negative regulation of macromolecule metabolic process	12 out of 46 genes, 26.1 per cent	4.11E-06
positive regulation of transcription from RNA polymerase II promoter	9 out of 46 genes, 19.6 per cent	6.03E-06
negative regulation of cellular metabolic process	12 out of 46 genes, 26.1 per cent	7.46E-06
negative regulation of metabolic process	12 out of 46 genes, 26.1 per cent	8.91E-06
cellular macromolecule metabolic process	34 out of 46 genes, 73.9 per cent	0.0001
negative regulation of cellular process	12 out of 46 genes, 26.1 per cent	0.00013
negative regulation of biological process	12 out of 46 genes, 26.1 per cent	0.00017
macromolecule metabolic process	34 out of 46 genes, 73.9 per cent	0.00018
positive regulation of gluconeogenesis	3 out of 46 genes, 6.5 per cent	0.00054
primary metabolic process	36 out of 46 genes, 78.3 per cent	0.00232

Table D.12. Significant shared GO biological process terms of the key TFs responsive to oxygen availability (Clim) (continued)

GO Term	Cluster frequency	*p*-value
positive regulation of cellular carbohydrate metabolic process	3 out of 46 genes, 6.5 per cent	0.00299
positive regulation of glucose metabolic process	3 out of 46 genes, 6.5 per cent	0.00299
positive regulation of carbohydrate metabolic process	3 out of 46 genes, 6.5 per cent	0.00299
metabolic process	37 out of 46 genes, 80.4 per cent	0.006

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