

REPORTS

found in clusters 4 through 16 (10.3% versus 2.8%; $P < 0.002$). This set of nine contained genes involved in glycogen accumulation and

protein metabolism as well as several genes of unknown function (e.g., *YMR318C*, a gene shown in Fig. 3 to have strong mRNA and

protein responses to galactose induction) (24). As shown in Fig. 1, we suggest that Gal4p may regulate these genes by direct binding.

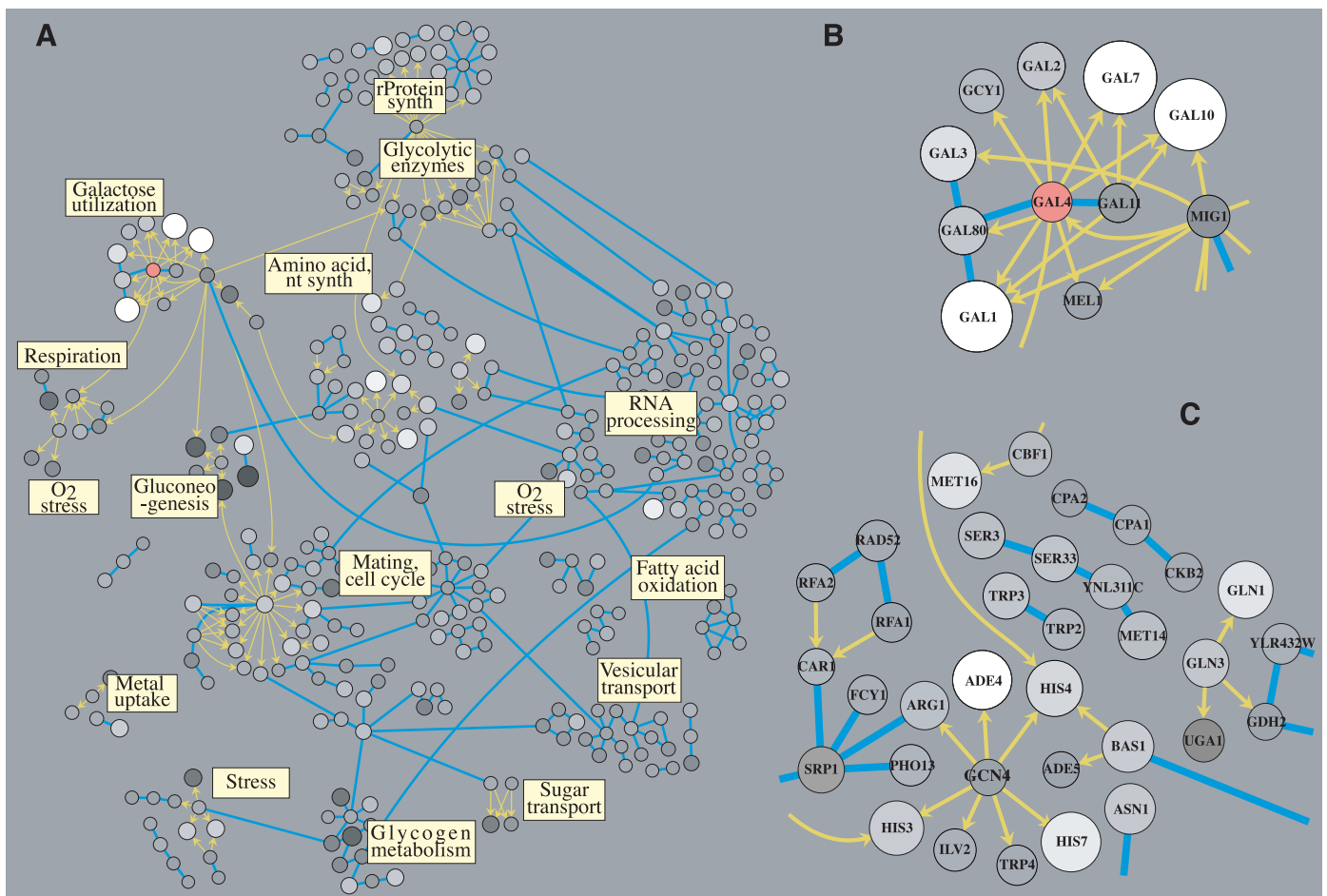


Fig. 4. Integrated physical-interaction network. Nodes represent genes, a yellow arrow directed from one node to another signifies that the protein encoded by the first gene can influence the transcription of the second by DNA binding (protein→DNA), and a blue line between two nodes signifies that the corresponding proteins can physically interact (protein-protein). Highly interconnected groups of genes tend to have common biological function and are labeled accordingly. (A) Effects of

gal4Δ+gal perturbation are superimposed on the network, with *GAL4* colored red and the gray scale intensity of other nodes, representing changes in mRNA as in Fig. 2 (node diameter also scales with the magnitude of change). Regions corresponding to (B) galactose utilization and (C) amino acid synthesis are detailed at right. Graphical layout and network display were performed automatically using software based on the *LEDA* toolbox (37). An enlarged version of (A) is provided in (20).

Fig. 5. Tree comparing gene-expression changes resulting from different perturbations to the GAL pathway. We used the *Neighbor* and *Drawtree* programs (38) to construct a hierarchical-clustering tree (39) based on Euclidean distance between perturbation profiles, where each profile consists of \log_{10} mRNA expression ratios over the set of 997 significantly affected genes. The closer two perturbations are to each other through the branches of the tree, the more similar their observed changes in gene expression. Leaves of the tree are labeled with the relevant genetic perturbation (wild-type or gene deletion) followed by the environmental perturbation (+/- gal). Twenty initial perturbations (solid branches) and three follow-up perturbations are shown (dotted branches). As in Fig. 2, profiles for all genetic perturbations are relative to that of the wild type, with both strains grown in identical media (+gal or -gal).

