

Commensurate Distances and Motifs from Genetic Congruence and Protein Interaction Networks in Yeast

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1 Introduction.

Genetic interaction has contributed to the understanding of gene functions, as well as the networks and pathways in which gene products participate. Protein interactions can indicate correct network topology by linking proteins within the same pathway. The recent availability of high-throughput genetic interaction screens [4-5] and protein interaction screens [1-3,6] in the model organism *Saccharomyces cerevisiae* (budding yeast) provides a unique opportunity to investigate the genetic interaction network and protein interaction network both individually and jointly. Protein interaction data from high-throughput approaches are known to include false positive as well as physiologically relevant observations. Genetic interactions often reflect functional relationships that reach far beyond local protein interactions. However, information derived from these two types of networks can provide complementary data views important for developing our understanding of how genes function in specific biological pathways.

2 Results.

Graph theoretic approaches have been applied to study global properties of protein interaction networks and genetic interaction networks in yeast. However, no direct comparison of genetic and protein maps has been performed. Here, we present a global and local network investigation of the connections among genetic interaction, genetic congruence, and protein interaction networks for yeast. We define congruent genes as a pair of genes with similar sets of genetic interaction partners. Genetic congruence network can be constructed through linking congruent genes. We discovered that high genetic congruence values not only indicate direct protein interaction linkage but also exhibit commensurate distance with the protein interaction network. However, consistent distances are not observed between genetic and protein interaction networks. We also demonstrated that congruence and protein networks are enriched with motifs that indicate network transitivity, while the genetic network possesses intransitive types of motifs. Our study suggests that genetic congruence network inferred from direct genetic interactions is superior to genetic interaction in prediction of protein complex membership, and is likely to be a better predictor of physical interactions.

3 Figures

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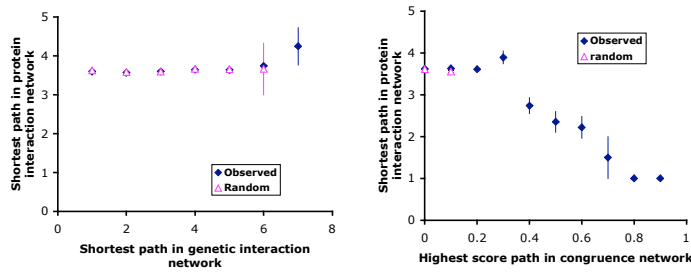


Figure 1: Genetic congruence but not genetic interaction is commensurate with physical interaction.

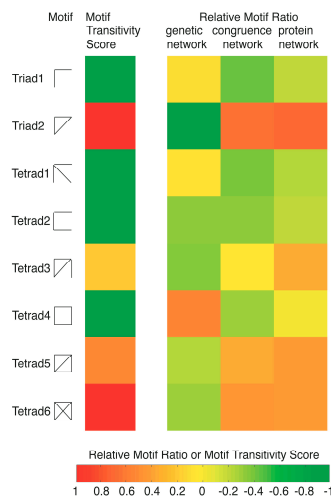


Figure 2: Motif characterization for genetic, congruence and protein networks.

4 References.

- [1] Gavin, A. C., Bosche, M., Krause, R., Grandi, P., Marzioch, M., Bauer, A., et al. 2002. Functional organization of the yeast proteome by systematic analysis of protein complexes. *Nature* 415:141-147.
- [2] Ho, Y., Gruhler, A., Heilbut, A., Bader, G. D., Moore, L., Adams, S. L., et al. 2002. Systematic identification of protein complexes in *Saccharomyces cerevisiae* by mass spectrometry. *Nature* 415:180-183.
- [3] Ito, T., Chiba, T., Ozawa, R., Yoshida, M., Hattori, M. and Sakaki, Y. 2001. A comprehensive two-hybrid analysis to explore the yeast protein interactome. *Proc Natl Acad Sci U S A* 98:4569-4574.
- [4] Pan, X., Yuan, D. S., Xiang, D., Wang, X., Sookhai-Mahadeo, S., Bader, J. S., et al. 2004. A robust toolkit for functional profiling of the yeast genome. *Mol Cell* 16:487-496.
- [5] Tong, A. H., Lesage, G., Bader, G. D., Ding, H., Xu, H., Xin, X., et al. 2004. Global mapping of the yeast genetic interaction network. *Science* 303:808-813.
- [6] Uetz, P., Giot, L., Cagney, G., Mansfield, T. A., Judson, R. S., Knight, J. R., et al. 2000. A comprehensive analysis of protein-protein interactions in *Saccharomyces cerevisiae*. *Nature* 403:623-627.