

Structural and Functional Characterization of Human Protein-Protein Interaction Network

¹Ryu, J.W., ¹Kang, A.R., ²Kim, T.K., ²Cho, Y.S., ³Yoo, J.S., ⁴Yoon, J.N., ⁴Han, S.K., and ¹Kim, H.Y.

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1. Introduction

Proteins bind to each other to form stable complex and to contribute cellular responses. At a complex system, proteins interact with other proteins weakly, transiently, or conditionally to form a biological module that serves a specific function in cells and systems as well [1, 2]. Therefore, many studies approach to construct protein network in yeast because of the abundance of protein information sources. Unfortunately, it is important to construct human protein network, although databases for human proteome and protein-protein interaction are insufficient. We, therefore, construct protein-protein interaction network from HPRD database (<http://www.hprd.org>). The human protein network is also shows scale free and hierarchical networks as if yeast system does [3].

2. Materials and methods

For each protein network investigated, nodes (proper proteins) and links (protein-protein interactions) were assembled and represented protein network as a graph using InterViewer program. Each link in the network was assigned a length of 1. In a basic principle, if a protein interacts with its partner, the link was designed as one. If, however, a protein does not interact with any proteins, zero was given in the link. For construction of network, the basic principle, therefore, follows adjacent matrix that is a matrix with rows and columns labeled by graph nodes with a 1 or 0 in position (i, j) according to whether i and j are adjacent or not. Protein complexes and modules are derived from clustering the protein interaction network.

¹Division of Life Sciences, Departments of ²Management Information Systems, ³Computer and Communication Engineering, and ⁴Physics, Chungbuk National University, Cheongju, 361-763, Korea

3. Results

Human protein interaction network was constructed from HPRD database (<http://www.hprd.org>) in January 2005 (protein: 5,139, interaction: 15,197). The largest core network (proteins: 4,837, interactions: 14,986, and clustering coefficient: 0.17721) showed characters of scale free network and hierarchical network as well. Because protein-protein interaction database generally contains false positives, filtration process of the data is required. To filter the database, we employed cellular localization and then reconstructed human protein network. To test robustness of the network, we removed largest 33 hub proteins from the network. Interestingly, the largest core network (proteins:

4,683, interactions: 12,653, and clustering coefficient: 0.16622) was still remained about 90.5% and also revealed characters of scale free and hierarchical networks. To find functional modules from the network, we propose a new technique that is based on motif-motif correlations in the human protein network. From the derived modules, we predicted and estimated tentative functions for unannotated proteins. It is important to construct protein-protein network in human systems. However, it is more important to derive the biological meaning and/or concepts, *e.g.* evolution from constructed structural network. For example, in protein network of human, several hub proteins, highly connected with other proteins, are essential to cell survival but several hub proteins are not. In same way, several linkers, only connected to two proteins, are lethal but several linkers are not. We couldn't find any consistent rule and/or any basic concept from the protein network. Wagner [4] suggests an idea to solve the problems, namely distributed robustness and redundancy. In future studies, we can consider to apply the concept and analytical method to human protein network.

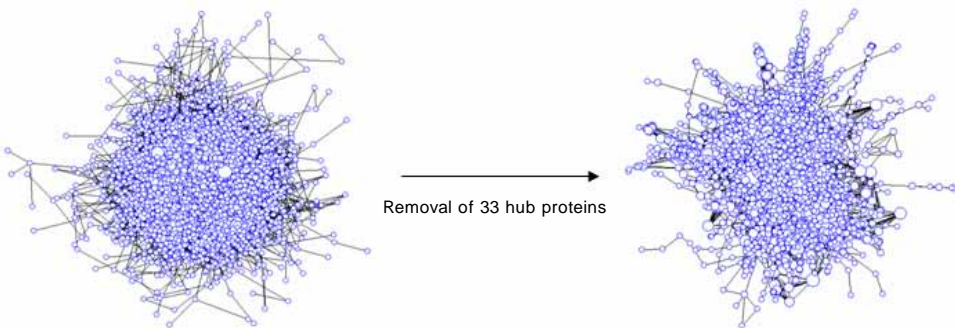


Figure 1. Largest core protein network (right-side) obtained from human protein network that was deleted largest 33 hub proteins and their linkers.

References

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