

Human protein-protein interaction networks are small worlds

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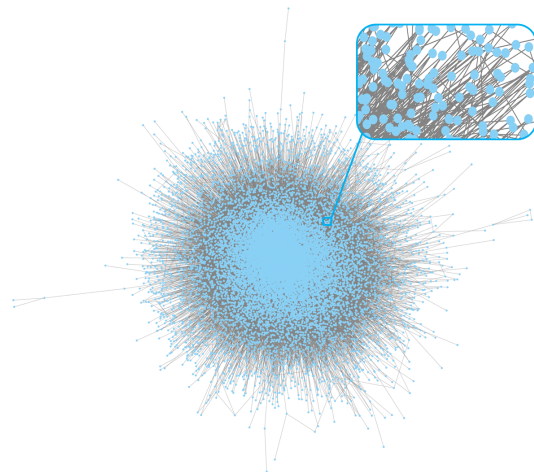
Abstract—Networks that meet the six degrees of separation requirement are called small worlds, as their elements are close to each other. Here, we count the separation degrees in the full-scale human protein-protein interaction network to show that human protein-protein interaction networks are small worlds.

Index Terms—Network science, six degrees of separation

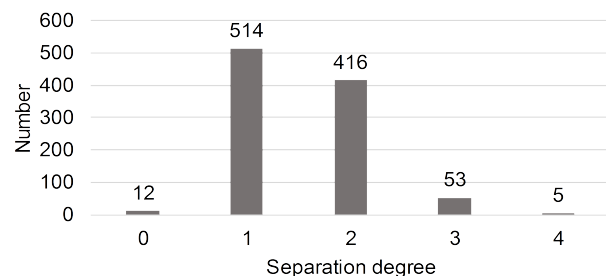
I. MAIN CONTENT

The six degrees of separation theory claims that all living things and everything else in the world are six or fewer steps away from each other [1]. Various types of networks meet this requirement, such as food webs [2], neural networks [3], scientific collaboration networks [4], and drug similarity networks [5]. Nevertheless, no one has analyzed the separation degrees of human protein-protein interaction networks to date, even though they are critical to understanding cell biology data [6]. We address this issue by counting the separation degrees in the full-scale human protein-protein interaction network.

The String database [7] is one of the most comprehensive databases of protein-protein interactions. Thus, we use the String data to generate the full-scale human protein-protein interaction network in Figure 1a (data file: 9606.protein.links.detailed.v10; this network was first used in our previous work of identifying elements of cancer-related signaling pathways [8]). There are 16,843 vertices and 1,736,922 edges in total. We randomly select 1000 pairs of proteins to obtain the sample data in Figure 1b. It can be seen that all the proteins are four or fewer steps away from each other, which means that human protein-protein interaction networks are small worlds. This discovery helps the further analyses on human protein-protein interaction networks in the future.



(a) The full-scale human protein-protein interaction network [8]



(b) The separation degrees of 1000 random pairs of proteins

Figure 1: The separation degrees in the full-scale human protein-protein interaction network.

REFERENCES

- [1] “Six degrees of separation.” https://en.wikipedia.org/wiki/Six_degrees_of_separation.
- [2] R. J. Williams, E. L. Berlow, J. A. Dunne, A.-L. Barabási, and N. D. Martinez, “Two degrees of separation in complex food webs,” *Proceedings of the National Academy of Sciences*, vol. 99, no. 20, pp. 12913–12916, 2002.
- [3] D. J. Watts and S. H. Strogatz, “Collective dynamics of ‘small-world’ networks,” *nature*, vol. 393, no. 6684, p. 440, 1998.
- [4] M. E. Newman, “The structure of scientific collaboration networks,” *Proceedings of the national academy of sciences*, vol. 98, no. 2, pp. 404–409, 2001.
- [5] Y. Sun, P. N. Hameed, K. Verspoor, and S. Halgamuge, “A Physarum-inspired prize-collecting Steiner tree approach to identify subnetworks for drug repositioning,” *BMC Systems Biology*, vol. 10, no. S5, pp. 25–38, 2016.
- [6] T. Li, R. Wernersson, R. B. Hansen, H. Horn, J. Mercer, G. Slodkiewicz, C. T. Workman, O. Rigina, K. Rapacki, H. H. Stærfeldt, *et al.*, “A scored human protein–protein interaction network to catalyze genomic interpretation,” *Nature methods*, vol. 14, no. 1, p. 61, 2017.
- [7] D. Szklarczyk, A. Franceschini, S. Wyder, K. Forslund, D. Heller, J. Huerta-Cepas, M. Simonovic, A. Roth, A. Santos, K. P. Tsafou, *et al.*, “String v10: protein–protein interaction networks, integrated over the tree of life,” *Nucleic acids research*, vol. 43, no. D1, pp. D447–D452, 2014.
- [8] Y. Sun, C. Ma, and S. Halgamuge, “The node-weighted Steiner tree approach to identify elements of cancer-related signaling pathways,” *BMC Bioinformatics*, vol. 18, no. S16, pp. 1–13, 2017.