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Abstract

Motivation: Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text Text.
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Contact: name@bio.com
Supplementary information: Supplementary data are available at *Bioinformatics* online.

1 Introduction

In the post-genomic era, it is a crucial task for biomedical research to explore how different types of entities (such as disease, gene, phenotype, pathway et al) are related. A researcher often requires a exhaustive understanding of possible indirect associations between related entities, which is the key to reveal the deeper biological mechanism behind the related entities (Liekens *et al.*, 2011). The development of experimental and computational techniques allows to construct interacting network of biomedical entities using high-throughput data (Zhou *et al.*, 2014; Barabasi and Oltvai, 2004). Lots of networks including knowledge within or across domains are generated, like protein-protein interaction network (Szklarczyk *et al.*, 2014), disease-disease interaction network (Menche *et al.*, 2015), disease-drug interaction network (Hanlon *et al.*, 2015), integrated network (Peng *et al.*, 2017). Given the fact that experimentally exploring association between entities is high cost and time consuming, these networks enable the use of network-based computational approaches to querying and working with the data as well as revealing how different entities are related.

Based on the availability of biomedical networks, various tools have been proposed to identify the relations between biomedical entities. These tools can be loosely divided to two groups. One group is to predict whether two entities are related ignoring possible functional path between entities. Most methods in this group is based on the "guilt-by-association" assumption to predict disease-gene association (Wang *et al.*, 2011), protein-protein interaction (Baspinar *et al.*, 2014), drug-target interaction (Pahikkala *et al.*, 2014) and so on. The other group of tools is to find a map of relations linking given entities in a biological network (Liekens *et al.*, 2011). Different with predicting new relations between biological entities, these tools provide a way to explain how two entities are functionally related based on the given network. In this paper, we focus on the problem of exploring how two biological entities are functionally related.

Figure 1 shows that the above method Text Text Text Text Text Text Text Text Text Text Text Text. (**?**) wants to know about …… text follows.

$$\sum x + y = Z \tag{1}$$

2 Approach

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3 Methods

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- for bulleted list, use itemize
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Table 1. This is table caption

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row4	row4	row4	row4

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3.2 Test1

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4 Discussion

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5 Conclusion

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Acknowledgements

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Funding

This work has been supported by the... Text Text Text Text.

References

Barabasi, A.-L. and Oltvai, Z. N. (2004). Network biology: understanding the cell's functional organization. *Nature reviews genetics*, **5**(2), 101–113.

Baspinar, A., Cukuroglu, E., Nussinov, R., Keskin, O., and Gursoy, A. (2014). Prism: a web server and repository for prediction of protein–protein interactions and modeling their 3d complexes. *Nucleic acids research*, **42**(W1), W285–W289.

Hanlon, J. T., Semla, T. P., and Schmader, K. E. (2015). Alternative medications for medications in the use of high-risk medications in the elderly and potentially harmful drug–disease interactions in the elderly quality measures. *Journal of the American Geriatrics Society*, **63**(12), e8–e18.

Liekens, A. M., De Knijf, J., Daelemans, W., Goethals, B., De Rijk, P., and Del-Favero, J. (2011). Biograph: unsupervised biomedical knowledge discovery via automated hypothesis generation. *Genome biology*, **12**(6), R57.

Menche, J., Sharma, A., Kitsak, M., Ghiassian, S. D., Vidal, M., Loscalzo, J., and Barabási, A.-L. (2015). Uncovering disease-disease relationships through the incomplete interactome. *Science*, **347**(6224), 1257601.

Pahikkala, T., Airola, A., Pietilä, S., Shakyawar, S., Szwajda, A., Tang, J., and Aittokallio, T. (2014). Toward more realistic drug–target interaction predictions. *Briefings in bioinformatics*, page bbu010.

Peng, J., Bai, K., Shang, X., Wang, G., Xue, H., Jin, S., Cheng, L., Wang, Y., and Chen, J. (2017). Predicting disease-related genes using integrated biomedical networks. *BMC genomics*, **18**(1), 1043.

Szklarczyk, D., Franceschini, A., Wyder, S., Forslund, K., Heller, D., Huerta-Cepas, J., Simonovic, M., Roth, A., Santos, A., Tsafou, K. P., *et al.* (2014). String v10: protein–protein interaction networks, integrated over the tree of life. *Nucleic acids research*, page gku1003.

Wang, X., Gulbahce, N., and Yu, H. (2011). Network-based methods for human disease gene prediction. *Briefings in functional genomics*, **10**(5), 280–293.

Zhou, X., Menche, J., Barabási, A.-L., and Sharma, A. (2014). Human symptoms–disease network. *Nature communications*, **5**.