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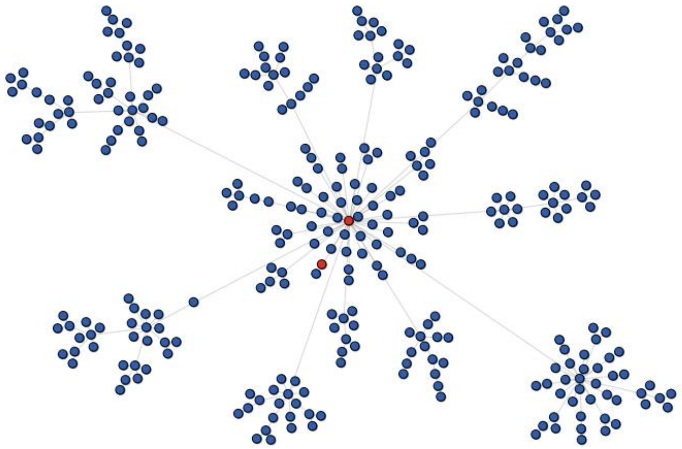
# Popular biological networks
## Protein-Protein Interaction networks

Sadegh Sulaimany



Biological network analysis course

# Agenda

- Protein
  - Protein review
  - Protein-Protein Interaction network introduction
  - PPI network construction
  - Detecting interactions
    - Experimental, Computational
  - Graph analysis of PPI
  - Protein complex detection
  - Some recent reviews
  - PPI databases

# Protein-Protein Interaction (PPI) network

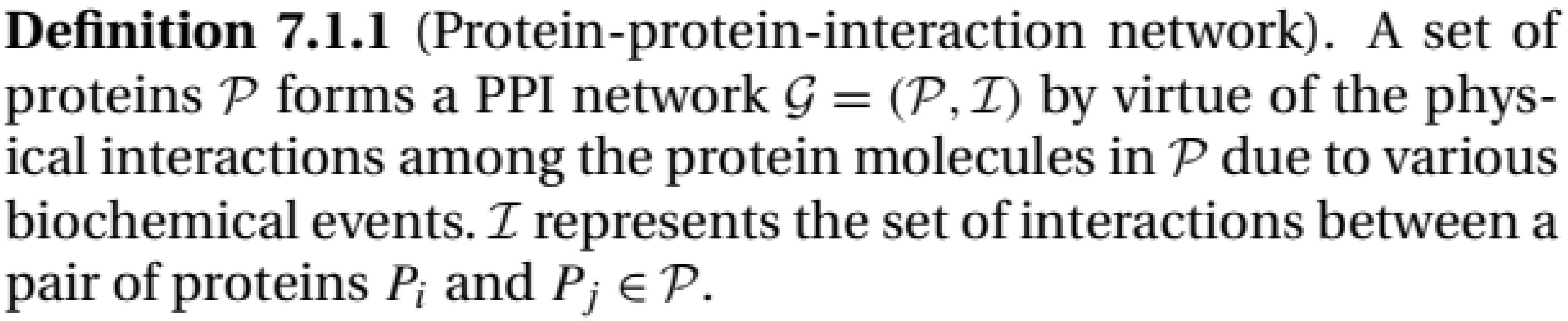
- Proteins
  - Main agents of biological functions
  - control molecular and cellular mechanisms
    - determine healthy and diseased states of organisms

  - they are not functional in isolated forms
    - they interact with each other and with other molecules
    - (e.g., DNA and RNA) to perform their functions.

  - So, study of proteins' interactions
    - is crucial to understand their role inside the cell

# Protein-Protein Interaction network

- PPI (Protein-Protein Interaction)



**Definition 7.1.1** (Protein-protein-interaction network). A set of proteins $\mathcal{P}$ forms a PPI network $\mathcal{G} = (\mathcal{P}, \mathcal{I})$ by virtue of the physical interactions among the protein molecules in $\mathcal{P}$ due to various biochemical events. $\mathcal{I}$ represents the set of interactions between a pair of proteins $P_i$ and $P_j \in \mathcal{P}$.

  - none protein-protein interactome has been completely identified
  - available protein-protein interaction networks are error-prone
    - experimental methods used to discover interactions may include false positives or there may unreveal some existing interactions

# Protein-Protein Interaction network

- Different methods to constructing PPI network
  - none of them is better than the others
  - each method has its own strengths and weaknesses
  - Goodness of a method
    - sensitivity

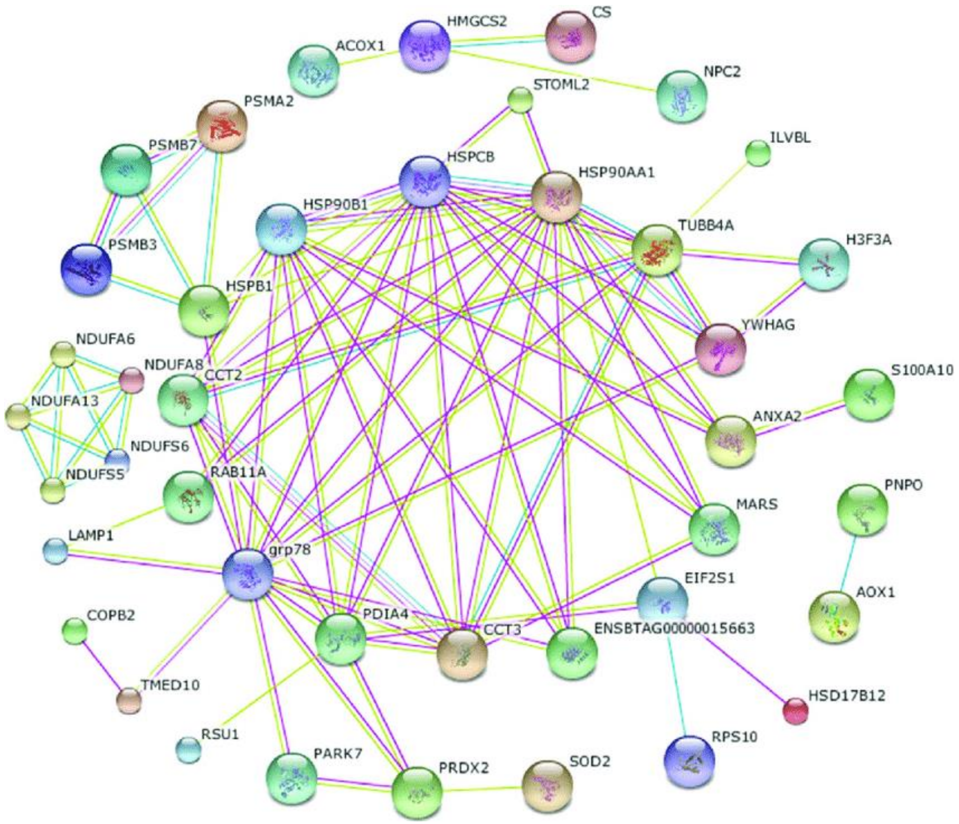
      (the ability of the method to discover many real interactions)
    - specificity

      (most of the interactions detected are real interactions)

  - associated a weight to PPI link
    - that takes into account the sensitivity and specificity of the method used to discover it

# PPI network

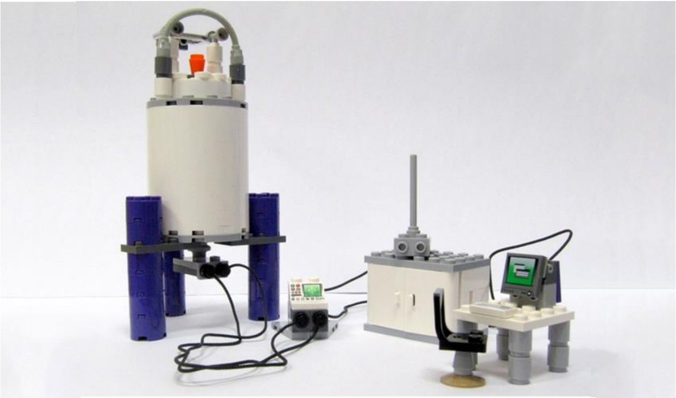
- Detect protein-protein interactions
  - Two main groups
    1. Experimental methods
    2. Computational methods



# PPI network

- Experimentally constructing the network
  1. Biophysically methods based on structural information
     - X-ray crystallography, NMR spectroscopy, fluorescence, atomic force microscopy

  2. High-throughput methods,
     - can be either direct or indirect
     - direct :Yeast two-hybrid (Y2H)
     - Indirect: Based on the use of other types of experimental data such as gene co-expression data.



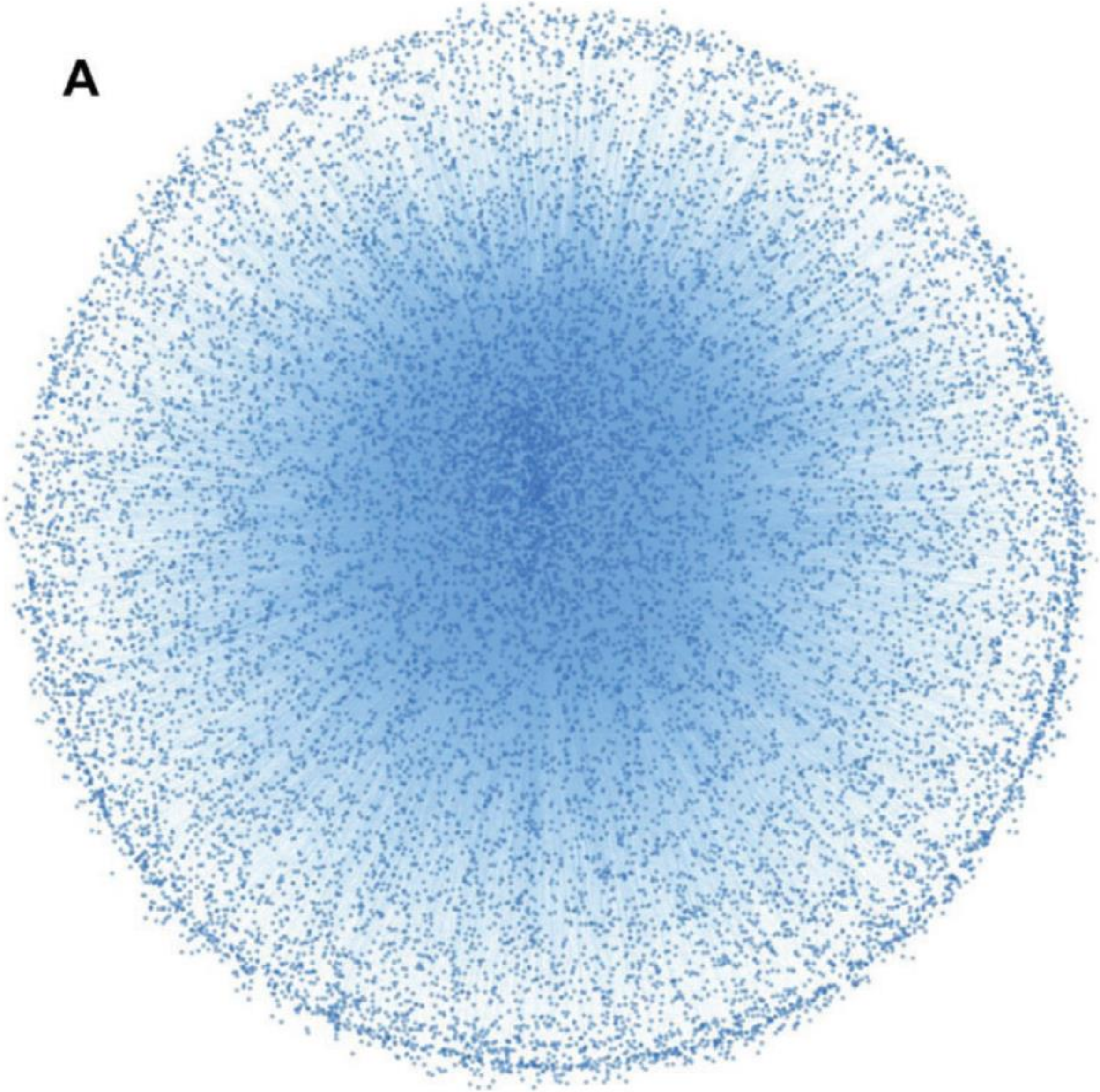
- Drawbacks
  - Expensive and Time consuming
  - Incomplete and Error-prone

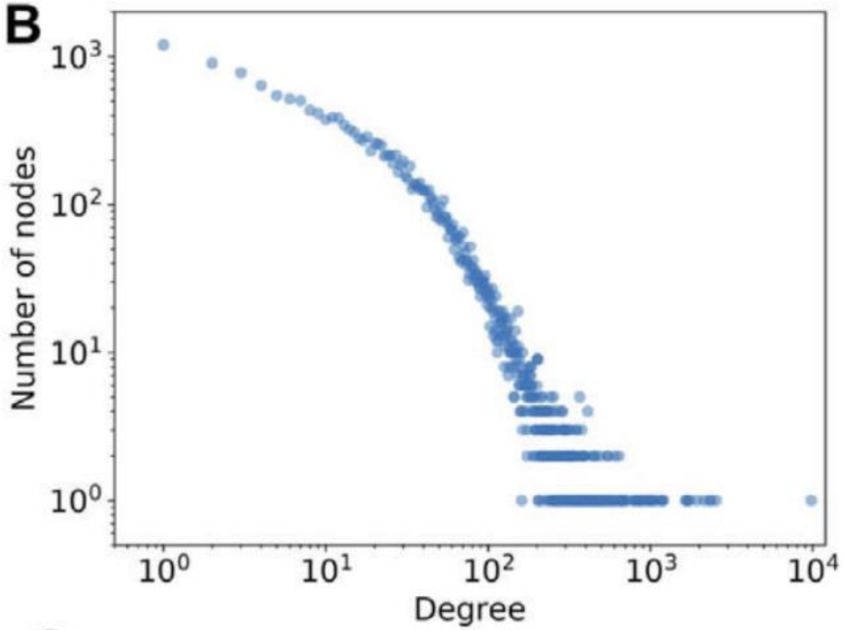
# PPI network

- Computational methods for PPI detection & Improvement
  - Fast and Cheap
    1. Empirical predictions
       - Use experimental data to infer new protein-protein interactions
    2. Theoretical predictions
       - Use some accepted assumptions to predict protein-protein interactions

    - Drawback: They may naturally propagate errors and inaccuracies

# PPI analysis – Short Example





**C**

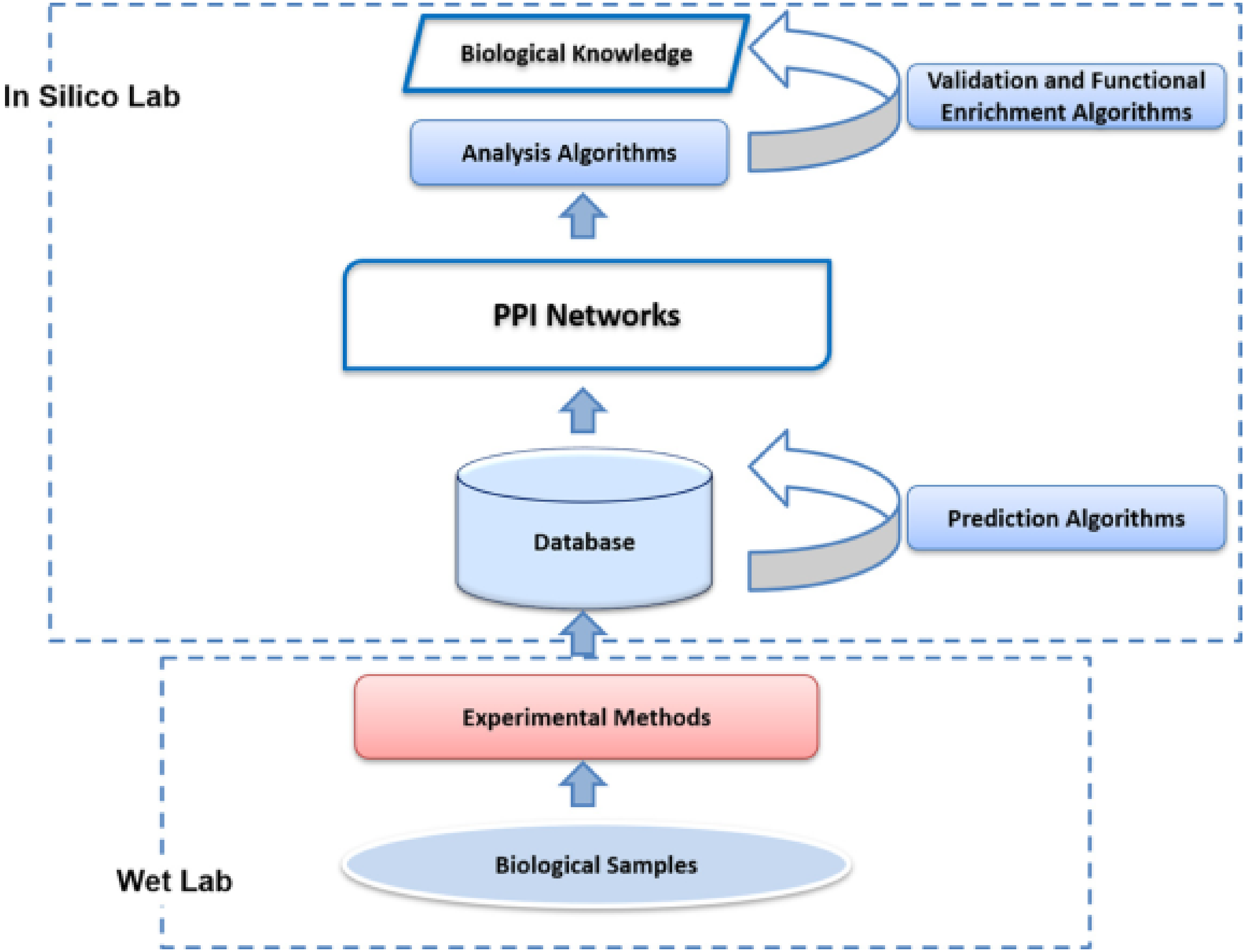
| | |
|---|---|
| Number of nodes | 17706 |
| Number of edges | 351444 |
| Network density | 0.002 |
| Degree (min-mean-max) | 1 - 39.7 - 9777 |
| Distance (min-mean-max) | 1 - 2.70 - 8 |

# Graph analysis of PPI network

- Independently from the species
  - protein-protein interaction networks are scale-free
    - some hub proteins have a central role participating in the majority of the interactions
    - while most proteins, that are not hubs, only participate to a small fraction of interactions

- Graph modeling
  - Simple, weighted or
  - hyper-graph
    - PPI are often obtained from protein complex detection and not really as binary interactions
    - each hyper-edge involves all proteins belonging to the same complex

# PPI big picture



# Some Applications

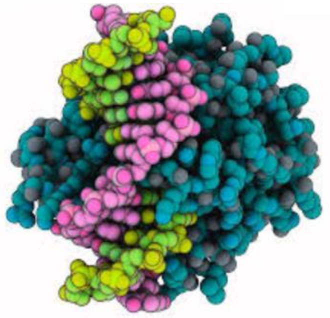
- Predicting the possible interaction
  - verifying them with experiment

- analyze structural properties

- Understanding disease beginning and progression mechanisms
- Discover novel protein function
- Identify functional modules and conserved interaction patterns
  - Biomarker identification
- Drug Design

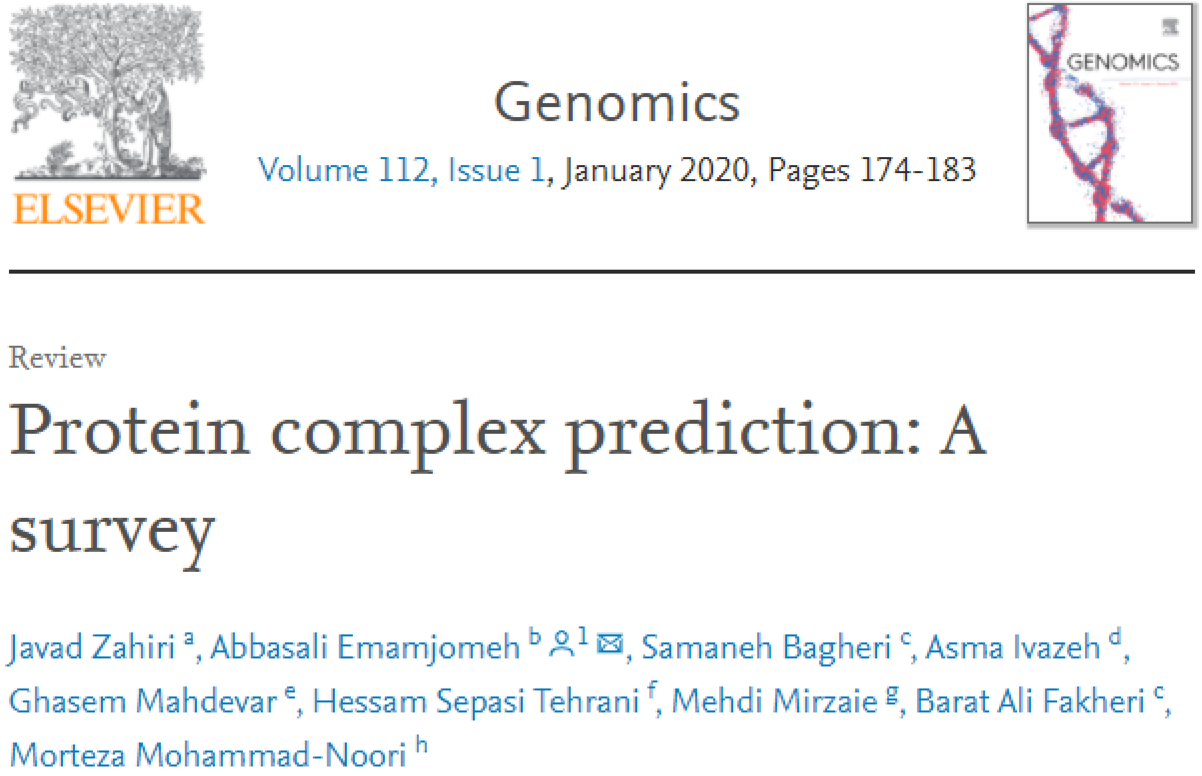
# Protein Complex Prediction

- Protein complex
  - a group of two or more associated proteins, which interact, sharing the same biological goal
    - Example
      - breast cancer protein 1 (BRCA1) is known to participate in multiple cellular processes by multiple protein complexes, such as in association with the BARD1 protein or with the proteins Rad50-Mre11-Nbs1



  - Starting from an interaction network
    - complexes may be identified by searching for small and highly interconnected regions
      - cliques
  - There are enormous algorithms for protein complex detection

# Some recent reviews



Genomics

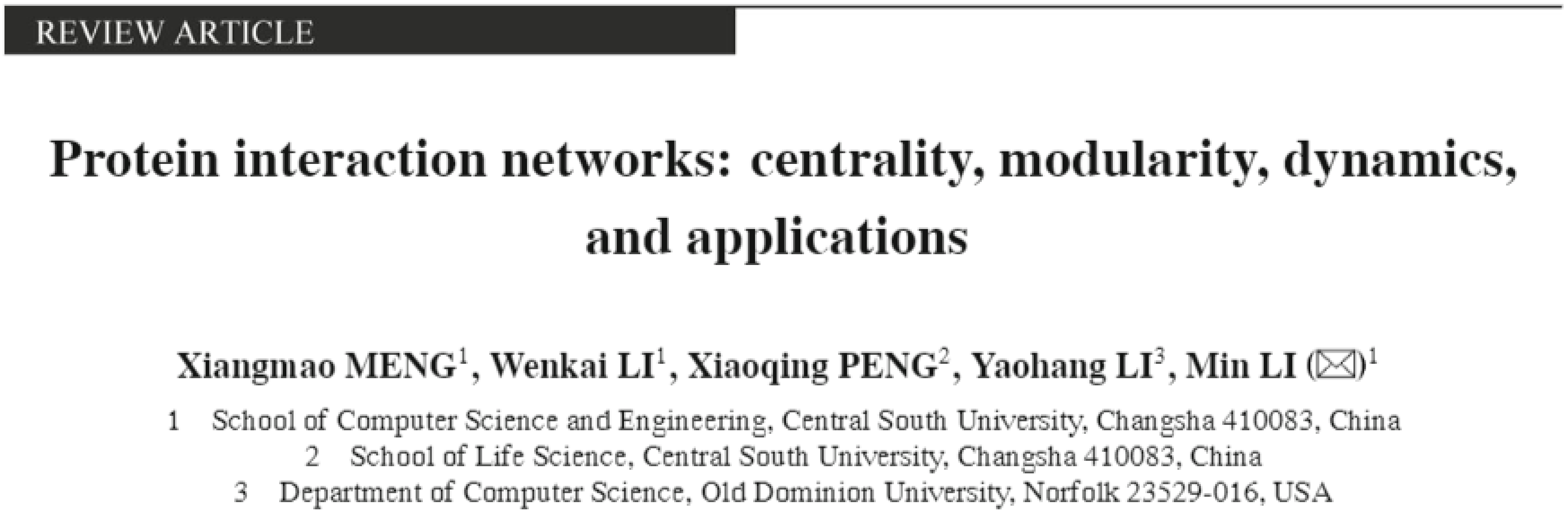
Volume 112, Issue 1, January 2020, Pages 174-183

Review

## Protein complex prediction: A survey

Javad Zahiri [a], Abbasali Emamjomeh [b] [1], Samaneh Bagheri [c], Asma Ivazeh [d], Ghasem Mahdevar [e], Hessam Sepasi Tehrani [f], Mehdi Mirzaie [g], Barat Ali Fakheri [c], Morteza Mohammad-Noori [h]

Front. Comput. Sci., 2021, 15(6): 156902
https://doi.org/10.1007/s11704-020-8179-0



REVIEW ARTICLE

## Protein interaction networks: centrality, modularity, dynamics, and applications

Xiangmao MENG[1], Wenkai LI[1], Xiaoqing PENG[2], Yaohang LI[3], Min LI (✉)[1]

1 School of Computer Science and Engineering, Central South University, Changsha 410083, China
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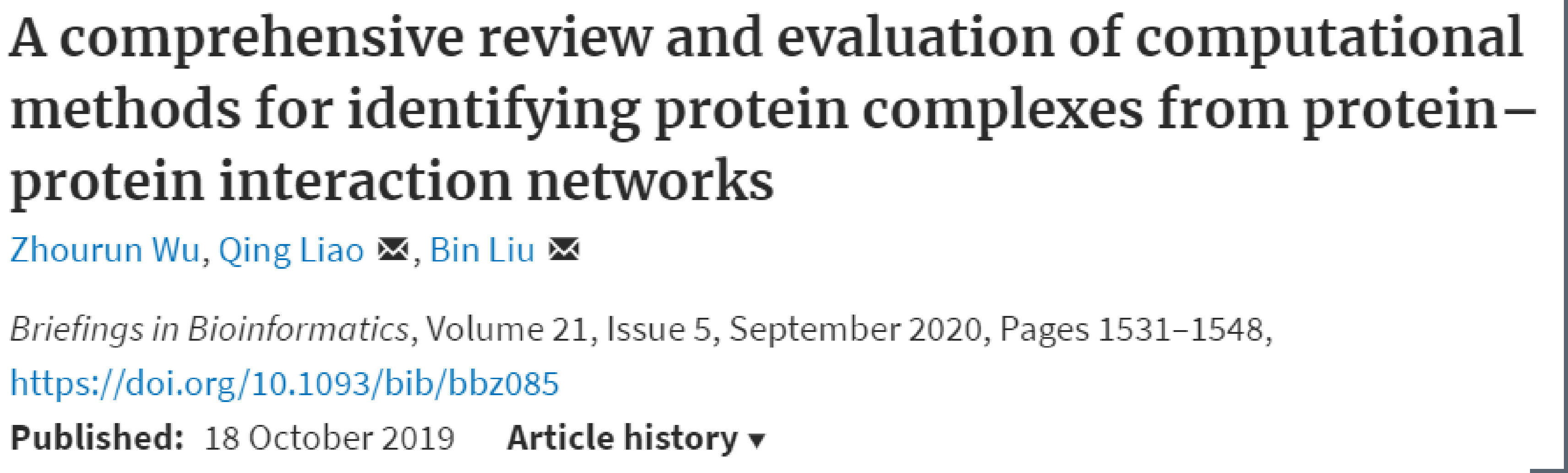
3 Department of Computer Science, Old Dominion University, Norfolk 23529-016, USA

# Some recent reviews papers on PPI



## A comprehensive review and evaluation of computational methods for identifying protein complexes from protein–protein interaction networks

Zhourun Wu, Qing Liao ✉, Bin Liu ✉

*Briefings in Bioinformatics*, Volume 21, Issue 5, September 2020, Pages 1531–1548, https://doi.org/10.1093/bib/bbz085

**Published:** 18 October 2019 **Article history ▾**

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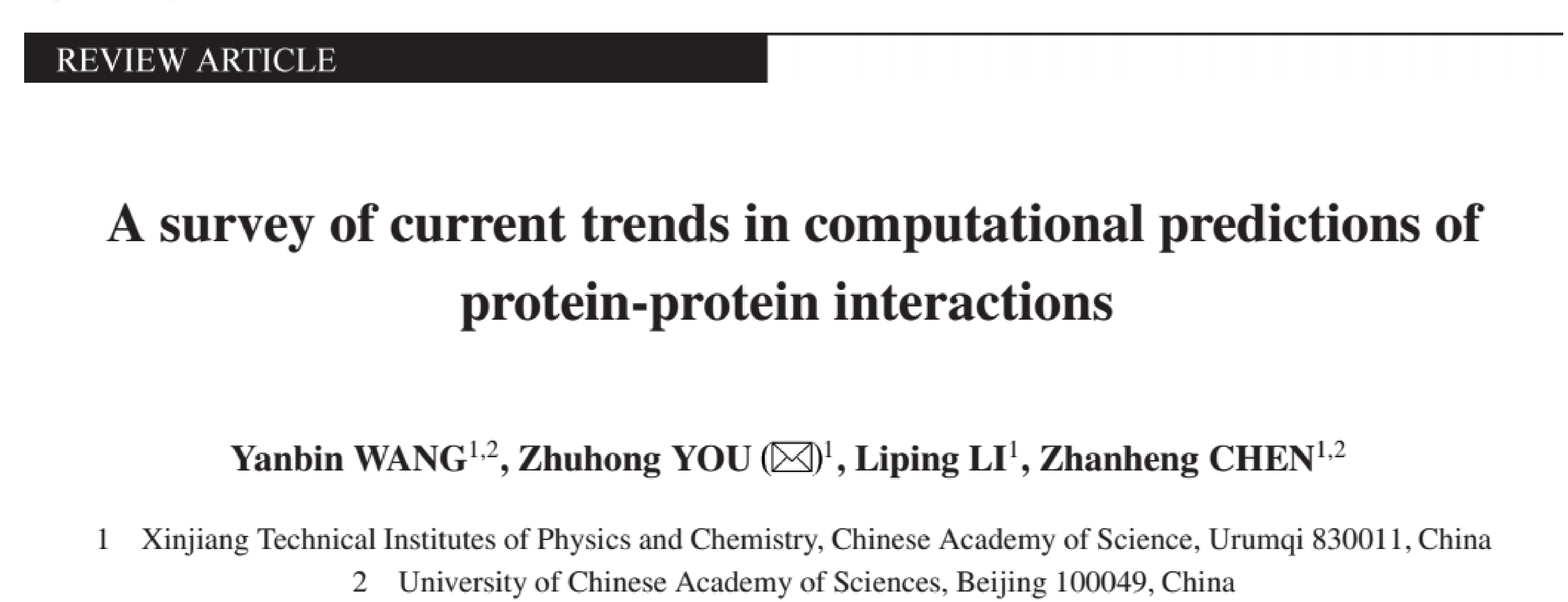
Front. Comput. Sci., 2020, 14(4): 144901
https://doi.org/10.1007/s11704-019-8232-z



REVIEW ARTICLE

## A survey of current trends in computational predictions of protein-protein interactions

**Yanbin WANG**[1,2], **Zhuhong YOU** (✉)[1], **Liping LI**[1], **Zhanheng CHEN**[1,2]

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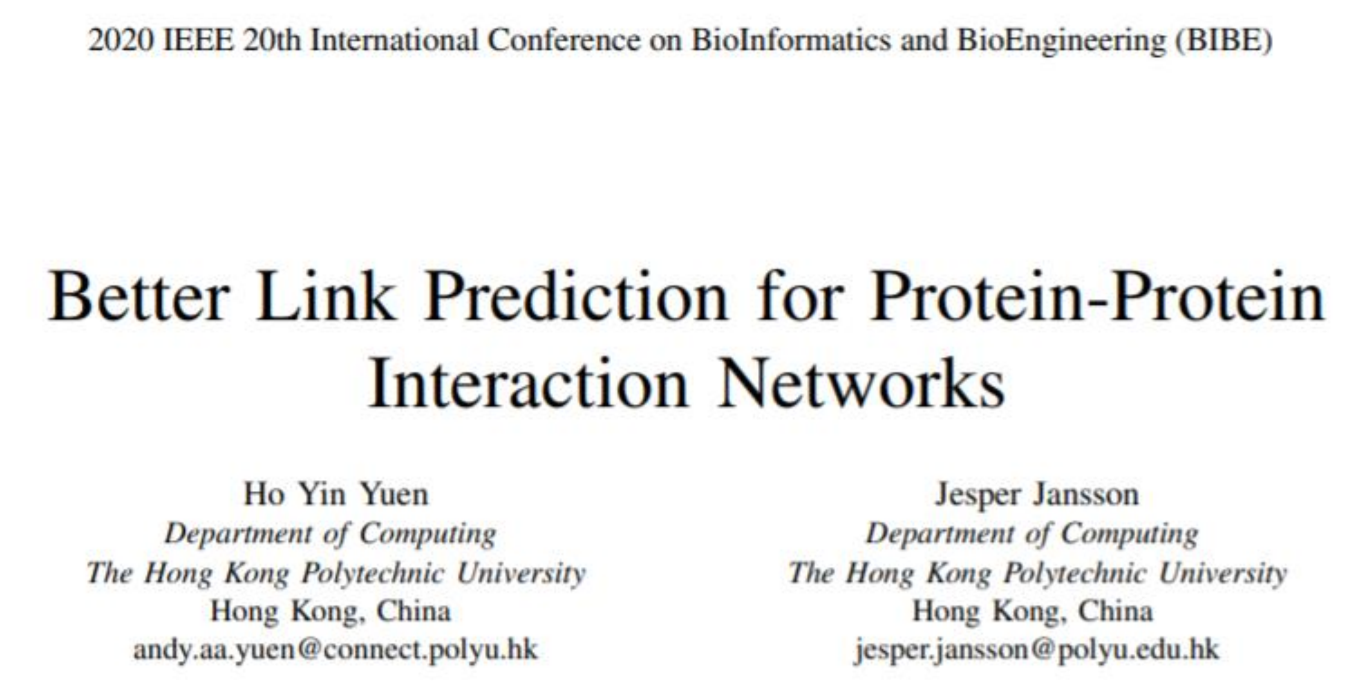
2 University of Chinese Academy of Sciences, Beijing 100049, China

# Some recent papers on PPI



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## Better Link Prediction for Protein-Protein Interaction Networks

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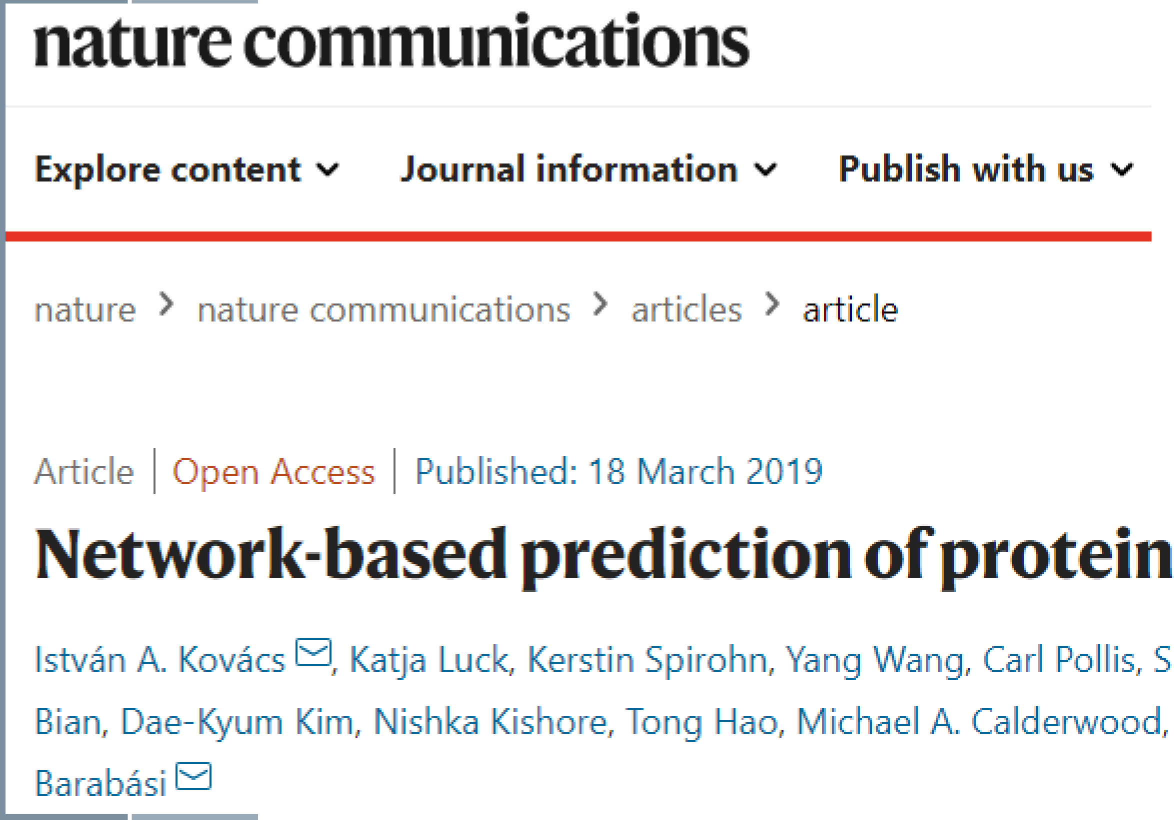


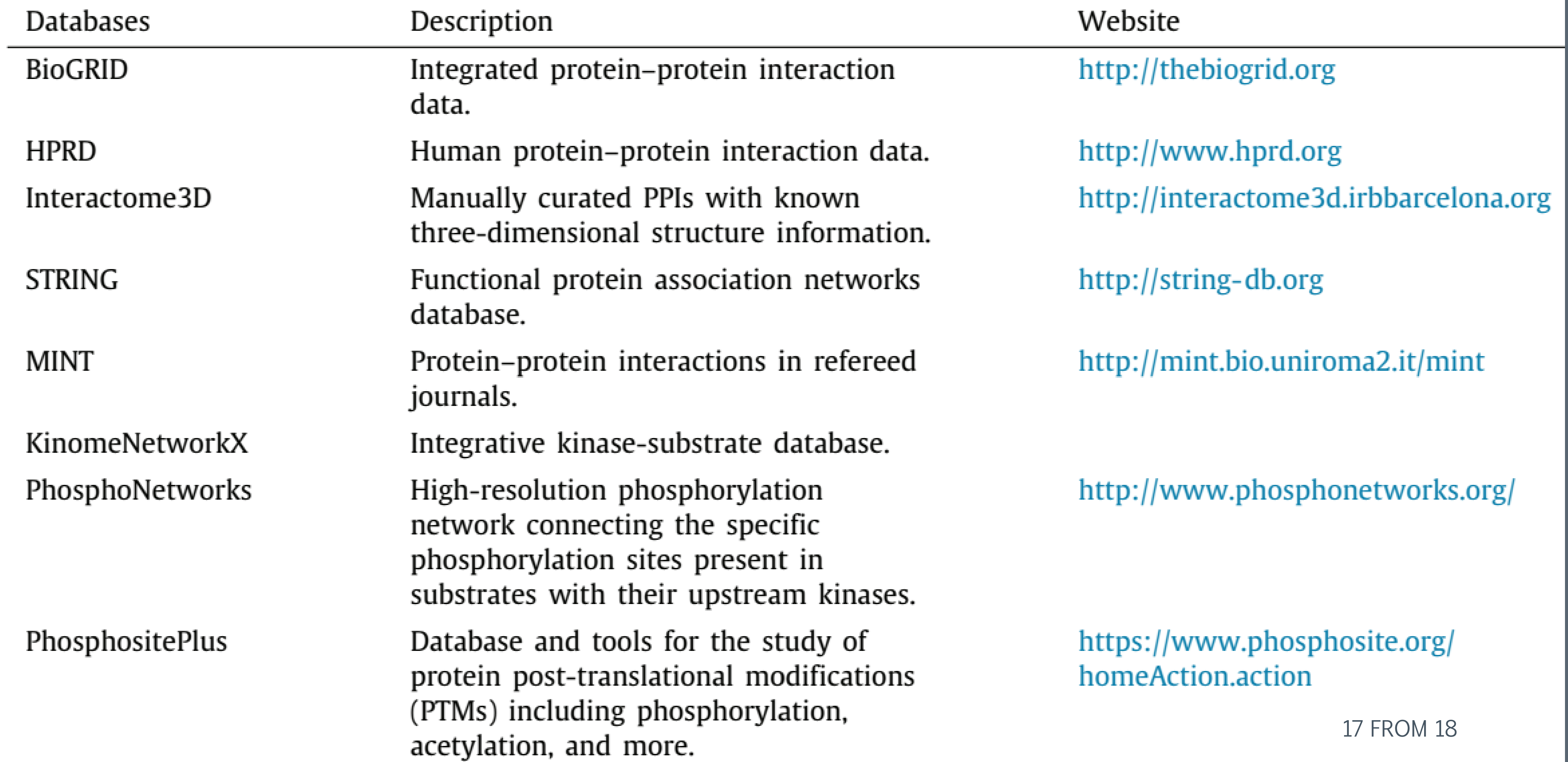
**nature communications**

Article | Open Access | Published: 18 March 2019

## Network-based prediction of protein interactions

István A. Kovács, Katja Luck, Kerstin Spirohn, Yang Wang, Carl Pollis, Sadie Schlabach, Wenting Bian, Dae-Kyum Kim, Nishka Kishore, Tong Hao, Michael A. Calderwood, Marc Vidal & Albert-László Barabási

# Resources



| Databases | Description | Website |
|---|---|---|
| BioGRID | Integrated protein–protein interaction data. | http://thebiogrid.org |
| HPRD | Human protein–protein interaction data. | http://www.hprd.org |
| Interactome3D | Manually curated PPIs with known three-dimensional structure information. | http://interactome3d.irbbarcelona.org |
| STRING | Functional protein association networks database. | http://string-db.org |
| MINT | Protein–protein interactions in refereed journals. | http://mint.bio.uniroma2.it/mint |
| KinomeNetworkX | Integrative kinase-substrate database. | |
| PhosphoNetworks | High-resolution phosphorylation network connecting the specific phosphorylation sites present in substrates with their upstream kinases. | http://www.phosphonetworks.org/ |
| PhosphositePlus | Database and tools for the study of protein post-translational modifications (PTMs) including phosphorylation, acetylation, and more. | https://www.phosphosite.org/homeAction.action |

# Question?

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