# Methods

## Essentiality prediction

The essentiality consensus of a protein in the protein - protein interaction network is most commonly predicted by centrality measures (Jalili et al. 2016). In this work we used The historicaly first centrality used for the prediction of the essential proteins is the degree centrality in the influential paper (Jeong et al. 2001) which introduced the **centrality - lethality rule**. The degree centrality (DC) of a node v is defined as :

where deg(v) is the number of neighbors of node v.

Degree centrality predicts that hubs are more likely to be essential than non - hubs. This is a simplified view because there are essential proteins that are not hubs. Another classification of proteins in respect to network topology is to examine whether they are *bottlenecks*. Bottlenecks are the nodes that are located between highly connected clusters and their importance is measured through betweenness centrality (BC) (Freeman 1979; Joy et al. 2005; Yu et al. 2007). Betweenness centrality (BC) of a node v is defined as:

## Gene ontology

Functional analysis

You can also write it inline: or use the $-signs to refer to a symbol, for example: is distance (m).

To refer to the equation in text, you can write: see equation . If you use the autoref command, it will automatically specify what kind of LaTeX object you are referring to, for example: see .

Freeman, Linton C. 1979. “Centrality in social networks conceptual clarification.” *Soc. Networks* 1 (3): 215–39. doi:[10.1016/0378-8733(78)90021-7](https://doi.org/10.1016/0378-8733(78)90021-7).

Jalili, Mahdi, Ali Salehzadeh-Yazdi, Shailendra Gupta, Olaf Wolkenhauer, Marjan Yaghmaie, Osbaldo Resendis-Antonio, and Kamran Alimoghaddam. 2016. “Evolution of Centrality Measurements for the Detection of Essential Proteins in Biological Networks.” *Front. Physiol.* 7 (August): 375. doi:[10.3389/fphys.2016.00375](https://doi.org/10.3389/fphys.2016.00375).

Jeong, H, S P Mason, a L Barabási, and Z N Oltvai. 2001. “Lethality and centrality in protein networks.” *Nature* 411 (6833): 41–42. doi:[10.1038/35075138](https://doi.org/10.1038/35075138).

Joy, Maliackal Poulo, Amy Brock, Donald E. Ingber, and Sui Huang. 2005. “High-betweenness proteins in the yeast protein interaction network.” *J. Biomed. Biotechnol.* 2005 (2): 96–103. doi:[10.1155/JBB.2005.96](https://doi.org/10.1155/JBB.2005.96).

Yu, Haiyuan, Philip M. Kim, Emmett Sprecher, Valery Trifonov, and Mark Gerstein. 2007. “The importance of bottlenecks in protein networks: Correlation with gene essentiality and expression dynamics.” *PLoS Comput. Biol.* 3 (4): 713–20. doi:[10.1371/journal.pcbi.0030059](https://doi.org/10.1371/journal.pcbi.0030059).