Supplementary Methods

Centrality Metrics

For any graph, G there is a corresponding adjacency matrix, A;

$$A = (a_{ij})$$

$$(a_{ij}) = \begin{cases} 1 & e_{ij} \in E(G) \\ 0 & e_{ij} \notin E(G) \end{cases}$$

Degree of centrality *(DCi)* is the number of direct links which can be calculated as in Eqn. 1[1].

$$DC_i = \sum_{j=1}^{N} a_{ij} \qquad (1)$$

where N is the number of nodes in the network.

Betweenness centrality (BC_i) of the node *i* is the total fractions of shortest paths that passese through node *i* (Eqn. 2)[2].

$$BC_i = \sum_{j \neq k \neq i} \frac{\sigma_{jk}(i)}{\sigma_{jk}} \qquad (2)$$

where $\sigma_{jk}(i)$ is the number of shortest paths between node *j* and *k* that passes through the node *i* and σ_{jk} is the total number of shortest paths between node *j* and *k.*

Eigenvector centrality (EC_i) of the node *i* is the i^{th} component of the principal eigenvector of the adjacency matrix A. Non-zero vectors which satisfies Eqn. 3 are called eigenvectors

$$Av = \lambda v \qquad (3)$$

where λ values satisfying the equation are called eigenvalues. Then EC can be calculates as in Eqn. 4.

$$EC_i = v_1(i) \qquad (4)$$

where v_1 is the first principal component, i.e. the eigenvector corresponding to the largest eigenvalue[3].

Subgraph centrality (SC_i) of the node *i* is the weighted sum of closed walks starting and ending at node *i*, where short walks have higher weights with respect to longer walks[4]. SC scores were calculated as in Eqn. 5.

$$SC_i = \sum_{j=1}^{N} \left[v_j(i)\right]^2 e^{\lambda_j} \qquad (5)$$

Network parameters

Network density can be defined as the ratio of number of links in a graph to number of maximum possible links (Eqn. 2)[1].

$$Network\_density = \frac{2\sum_{i=1}^{N}\sum_{j=1}^{N} a_{ij}}{N(N-1)} \qquad (2)$$

Network centralization is a measure of network compactness and it can be defined based on different centrality measures (Freeman 1978). In this work it was calculated by Cytoscape which bases on degree centrality (Eqn. 3)[1].

$$Network\_centralization \cong \frac{\max(DC) - mean(DC)}{N} \qquad (3)$$

Coefficient of variation of degree distribution is defined as network heterogeneity (Eqn. 4)[1].

$$Network\_heterogeneity = \frac{\sigma_{DC}}{mean(DC)} \qquad (4)$$

Characteristic path length (*cpl*) is the average of the shortest path lengths (*spl*) between all possible node couples (Eqn. 5)[5].

$$cpl = \frac{2\sum_{i=1}^{N}\sum_{j=1}^{N} spl_{ij}}{N(N-1)} \qquad (5)$$

Diameter is the longest shortest path between any pair of nodes. It gives the size of the largest connected part of the network (Eqn. 6)[4].

$$D = \max(spl_{ij}) \qquad (6)$$

Clustering coefficient of a node is the ratio of links among its neighbors to the maximum possible number of links among its neighbors. Clustering coefficient of a network is the average clustering coefficient of all nodes (Eqn. 7)[1].

$$CC = \frac{1}{N}\sum_{i=1}^{N} \frac{2l_i}{DC_i(DC_i - 1)} \qquad (7)$$

where l_i is the number of links among the connected nodes to the node *i.*

Assortativity coefficient is the slope of the line fitted to degree correlation distribution (Eqn. 8)[6].

$$r = \frac{1}{\sigma_q^2}\sum_{ij} ij(e_{ij} - q_i q_j) \qquad (8)$$

where e_{ij} is the probability of having a link between a node with degree *i* to another node with degree *j*, q_i is the probability to have a node with defree *i* and σ_q^2 is the variance of the degree distribution.

Efficiency is the sum of reciprocal of *spl* between all possible node couples in a network (Eqn. 9)[7].

$$\varepsilon = \sum_{i=1}^{N}\sum_{j=1}^{N} \frac{1}{spl_{ij}} \qquad (9)$$

In this work centralities and parameters were calculated by either network analyzer plug-in of Cytoscape[5] or MATLAB R2012a software.

References

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