





# ABSTRACT

Biological systems are composed of highly complex networks and several algorithms have been designed to identify the most influential regulatory points within them. However, current methods do not address all the topological dimensions of a network or correct for inherent positional biases. We developed the Integrated Value of Influence (IVI), which integrates important most the network centrality measures in an unbiased way and captures all of the topological dimensions of a network to identify the most influential nodes. IVI is accessible on the Influential Software Package web portal at: https://influential.erc.monash.edu/IVI/

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# Identification of the most influential nodes involving all topological dimensions of a network

### INTRODUCTION

Network science has been used for the study of complex networks in almost all domains (1, 2). In all network analyses the topology of a network is analyzed using different centrality algorithms to identify the most influential nodes and get a deeper insight from the network (3). In this context, two major concepts are defined, hubness and spreading potential. While hub nodes have high connections with other nodes, the spreader nodes have the greatest impact on the flow of information throughout the network (4, 5). In a study published in Patterns, Cell Press, we for the first time demonstrated that nodes with a simultaneously large number of connections and high spreading potential are the most influential and vital nodes in a network (5). IVI is the synergistic product of integration of six network centrality measures.

#### IVI algorithm

- $\bullet$ measures, respectively, as follows.

most important centrality indices

The centrality measures were integrated using the Addition and Multiplication functions to synergize their effects and produce the IVI.

The Spreading and Hubness scores emerged as the product of four and two different centrality

 $Spreading_{score_i} = (NC'_i + CR'_i)(BC'_i + CI'_i)$ 

 $Hubness_{score_i} = DC'_i + LH'_{index_i}$ 

• The integration of Spreading and Hubness scores resulted in the IVI, which synergizes the effects of

 $IVI_i = (Hubness_{score_i})(Spreading_{score_i})$ 



**Fig. 1.** The positional bias of betweenness centrality and collective influence. This figure has been adapted from (5). BC and CI are positionally biased in the network and this bias is in contrast to the behavior of NC.



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Fig. 3. Performance of IVI in comparison with 14 other current methods in identification of the most influential nodes. This figu has been adapted from (5).

- IVI outperformed 12 other contemporary methods in detecting influential network nodes. Also, Spreading and Hubness scores, the components of the IVI formula, came up as the second and third ranked metrics, respectively.
- AUC: Area Under the Curve corresponding to receiver operating characteristic (ROC) analyses.

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#### CONCLUSIONS

•	IVI algorithm integrates six of the most important
	centrality measures in such a way that their strengths
	are synergized and positional biases are removed

- IVI algorithm outperforms other algorithms in identifying the most influential nodes
- IVI could be a beneficial tool for all future network analyses including systems biology studies

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