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Central hubs prediction for bio networks by directed hypergraph - GA with validation to COVID-19 PPI

Sathyanarayanan Gopalakrishnan, Supriya Sridharan, Soumya Ranjan Nayak, Janmenjoy Nayak, Swaminathan Venkataraman

A Department of Mathematics, School of Arts, Science, Humanities and Education, SASTRA Deemed to be University, Thanjavur, India
B Amity School of Engineering and Technology, Amity University, Uttar Pradesh, Noida, India
C Department of Computer Science, Maharaja Sri Rama Chandra Bhanja Deo University, Baripada, Mayurbhanj, Odisha, 757003

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ABSTRACT

Network structures have attracted much interest and have been rigorously studied in the past two decades. Researchers used many mathematical tools to represent these networks, and in recent days, hypergraphs play a vital role in this analysis. This paper presents an efficient technique to find the influential nodes using centrality measure of weighted directed hypergraph. Genetic Algorithm is exploited for tuning the weights of the node in the weighted directed hypergraph through which the characterization of the strength of the nodes, such as strong and weak ties by statistical measurements (mean, standard deviation, and quartiles) is identified effectively. Also, the proposed work is applied to various biological networks for identification of influential nodes and results show the prominence the work over the existing measures. Furthermore, the technique has been applied to COVID-19 viral protein interactions. The proposed algorithm identifies some critical human proteins that belong to the enzymes TMPRSS2, ACE2, and AT-II, which have a considerable role in hosting COVID-19 viral proteins and causes for various types of diseases. Hence these proteins can be targeted in drug design for an effective therapeutic against COVID-19.

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1. Introduction

A relation that connects a group of two or more systems or people [18] forms a network. To assess a network, one may need information's such as quality of relationships, perception of co-operations, network collaborations between nodes. In recent times one of the computational concepts like the graph properties plays a significant role in analysing a network by exploring the accessibility of nodes [21]. Of which Multi-graph [3,17] can represent the complex relational data of a network and works well provided that the significant changes are made only to the existing graph analysis algorithms.

In general, since the network comprises nodes in n-ary relations, based on the literature so far, we could see Hypergraphs can handle n-ary relations more efficiently than graphs or multi-graphs. Berge [1] proposed this concept of hypergraph firstly as “a generalisation of graphs” which [3] further defined and derived the notion of the ‘directed’ hypergraph.

The hypergraphs [15,20] constructed from the shortest paths of the networks tend to leave out some influential nodes, which is very important in analysing the network. Granovetter [5] proposed a method to identify influential nodes by weak ties for information dissemination. To surmount the frailty for hypergraph construction, this paper constructs a directed hypergraph based on the
relationship between the data. Later, degree centrality measure is employed for finding the influential nodes.

Among various centrality measures like degree, betweenness, closeness, eccentricity, cross-click, network, random walk betweenness, page rank, leverage, eigenvector, subgraph, information and many, degree centrality have high impact in analysing any network. Also, it classifies the nodes as strong and weak ties from which weak tie is more influential so, this takes less number of nodes that are responsible for spreading of news. Hence, we use the degree centrality for predicting the influential nodes.

In this paper, initially the weight of the node is the degree centrality of a node that is, ... the number of hyperedges incidence with the node. Thus, the same is calculated for all network nodes and fed into the Genetic Algorithm (GA) for further optimisations. After which statistical measures like mean, standard deviation and quartiles are employed to classify the nodes as strong tie and weak tie.

The proposed work is applied to Protein-Protein Interaction (PPI) networks to obtain the influential proteins. Predicting protein function is always a stumbling block in computational biology research. These proteins of PPI network help in drug target recognition, identify the role of a protein or gene, develop successful methods for treating different diseases, and provide early detection of disorders.

Recently, many researchers aims to detect the COVID-19 through images of X-rays using the concept of Cascaded Recurrent Neural Network (CRNN) [12] and ultrasound X-rays by classifying them using Multi-layers Fusion [16]. Here, we aim to detect the influential nodes which gives a promising direction in the impact of current pandemic COVID-19 and in need of designing drugs. Drug design requires the knowledge of the functionality of the COVID-19 viral protein interacting with human proteins. For this purpose, we identified some of the critical human proteins using centrality measures of the hypergraph.

These proteins belong to the enzymes - TMPRSS2, ACE2, AT-II, protein sets - IL6, cytoplasmic, cytokine storm. Some of them may cause diseases like dease chronic obstructive pulmonary disease, lower respiratory infections, blood pressure, diabetes mellitus, stroke and tuberculosis. The resultant proteins play a considerable role in COVID-19 viral interactions.

The major contributions are a state-of-the-art representation of protein interaction networks by weighted directed hypergraph and identifying influential nodes using weak tie of a weighted directed hypergraph. The degree centralities and genetic algorithm are hybridized to optimize the weights of nodes. Finally, validation of the proposed method identifies influential COVID-19 proteins from protein interactions that can be used for drug design.

Section 2 deals with basic definitions. The proposed methodology is presented in Section 3. The results of the ten biological networks and their comparison with existing graph centrality measures are presented in Section 4. Our method has been validated with the real-time pandemic COVID-19 viral-protein interactions in Section 5. The paper is concluded with a summary in the final Section.

2. Preliminaries

Some preliminary concepts on hypergraph are recalled in this section.

Let $H = (V_H, E_H)$ be a hypergraph [1], where $V_H$ and $E_H$ are set of all nodes and hyperedges respectively. Moreover, $V_H = \{v_i : i = 1, \ldots, n\}$ and $E_H = \{E_j : j = 1, \ldots, m\}$, with every $E_j$ is a subset of the set $V_H$.

A hypergraph is a standard graph, when every hyperedge $E_i \in E_H$ satisfies $|E_i| \leq 2$ for $i = 1, 2, \ldots, m$.

A hypergraph is said to be a directed hypergraph ($H_{DC}$) [3], if every hyperarc $E_{H_{DC}} = (T(E_{H_{DC}}), H(E_{H_{DC}}))$ has a direction, where $T(E_{H_{DC}})$ is the tail of $E_H$ while $H(E_{H_{DC}})$ is its head.

If every node of a directed hypergraph has a weight associated with it, then the directed hypergraph is a weighted directed hypergraph ($H_{WDC}$).
The directed hyperedge or hyperarc $E_{\text{HDC}} = (T(E_{\text{HDC}}), H(E_{\text{HDC}}))$ is said to be a Backward hyper-arc [3], or B-arc, if $|H(E_{\text{HDC}})| = 1$. Similarly, the directed hyperedge or hyperarc $E_{\text{HDC}} = (T(E_{\text{HDC}}), H(E_{\text{HDC}}))$ is said to be a Forward hyperarc [3], or F-arc, if $|T(E_{\text{HDC}})| = 1$.

A directed hypergraph is said to be a B-graph (or B-hypergraph), whose hyperarcs are B-arcs. A directed hypergraph is said to be an F-graph (or F-hypergraph), if hyperarcs are F-arcs. A directed hypergraph is said to be a BF-graph (or BF-hypergraph), if hyperarcs are either B-arcs or F-arcs.

3. Proposed methodology

This section discusses the proposed technique for the identification of influential nodes in a network. It consists of following four predominant steps:

1) Construction of directed hypergraph.
2) Conversion of directed hypergraph into weighted directed hypergraph.
3) Optimizing the weights using Genetic Algorithm (GA).
4) Identifying influential nodes.

Algorithm 1 comprises the above four steps:

**Algorithm 1: DHHGA.**

INPUT: Network

OUTPUT: Strong and Weak Ties

Procedure: Construction of Directed Hypergraph (Network) (Algorithm 2)
Procedure: Conversion of $H_{\text{DC}}$ into $H_{\text{WDC}}$ (Algorithm 3)
Procedure: Genetic Algorithm ($w_j$) (Algorithm 4)
Procedure: Weighted Directed Hypergraph Degree Centrality [WDHDC] (Optimized $w_j$) (Algorithm 5)

**Algorithm 2: Construction of directed hypergraph.**

INPUT: Network

OUTPUT: Directed Hypergraph ($H_{\text{DC}}$)

for $i = 1$ to $n$
  if $v_i$ not in $T(E_{\text{HDC}})$ (by using theorem 1) then
    Construct $E_{\text{HDC}}$ of the directed hypergraph $H_{\text{DG}}$ with
    $T(E_{\text{HDC}}) = v_i$ and
    $H(E_{\text{HDC}}) = \{v_{i+1} : \text{if } v_i \text{ has a communication with } v_{i+1}\}$
  end if
end for
Return $H_{\text{DG}}$.

3.1. Construction of directed hypergraph

If there is a communication between $v_j$ to $v_{j+1}, j = 1, 2, \ldots, h \in \mathbb{N}$, then directed hyperedge $E_{\text{HDC}} = (T(E_{\text{HDC}}), H(E_{\text{HDC}}))$ is constructed where $T(E_{\text{HDC}}) = \{v_i\}$ and $H(E_{\text{HDC}}) = \{v_{j} : j = 1, 2, \ldots, h \in \mathbb{N}\}$.

**Definition 3.1 (Minimal hypergraph based on. B-hyperarc)** A directed hypergraph $H_{\text{M}}$ is said to be minimal hypergraph (directed hyperedges are in B-hyperarc form or F-hyperarc form) with $H_{\text{M}}$ as $k$, if there is no minimal hypergraph $H_{\text{M}_p}$ with $|H_{\text{M}_p}| = p < k = |H_{\text{M}}|$.

**Algorithm 3: Conversion of $H_{\text{DC}}$ into $H_{\text{WDC}}$.**

INPUT: $H_{\text{DC}}$ from Algorithm 2

OUTPUT: Weighted Directed Hypergraph $H_{\text{WDC}}$

1: $V_{\text{WDC}} = V_{\text{HDC}} \cup E_{\text{WDC}} = E_{\text{HDC}}$
2: for $i = 1$ to $n$
3:   for $j = 1$ to $m$
4:     if $v_i \in e_j$ then
5:       $w_j = w_j + 1$
6:     end if
7: end for
8: Append the weight of $v_i$ as $w_j$ in $H_{\text{WDC}}$
9: end for
10: Return $H_{\text{WDC}}$

In general, B-hypergraph has $|H(E_{\text{HDC}})| = 1$ for every hyperedge, and there is no repetition in head of the hyperedge.

Suppose there are two hyperedges $\{(v_i, \ldots, v_k), v_j\}$ and $\{(v_i, \ldots, v_k), v_j\}$ with same $H(E_{\text{BM}})$, then combine the hyperedges and regenerate it as a single hyperedge $\{(v_i, \ldots, v_k, v_{j+1}, \ldots, v_j)\}$.

Continue this until the heads of the hyperedges are distinct.

Let $H_{\text{BM}}$ be the head set in the minimal hypergraph $H_{\text{BM}}$. Now, add the head of each hyperedge $|E_{\text{BM}}|$ of $H_{\text{BM}}$ to the set $H_{\text{BM}}$. Thus,

$|H_{\text{BM}}| = b < n$,

since the heads in $H_{\text{BM}}$ are distinct and at most $|V_{\text{HDC}}|$.

Since the number of hyperedges is equal to the number of elements in the head set $H_{\text{BM}}$ by B-hypergraph construction,

$|E_{\text{BM}}| = |H_{\text{BM}}| = b < n$

and hence $|E_{\text{BM}}| = b < n$

Similar arguments holds for F and BF hypergraphs and thus we have Theorem 1.

**Theorem 1.** Let $H_{\text{DC}} = (V_{\text{HDC}}, E_{\text{HDC}})$ be a directed hypergraph with $|V_{\text{HDC}}| = n$, then there exists a minimal hypergraph $H_{\text{BM}} = (V_{\text{BM}}, E_{\text{BM}})$ such that every directed hyperedge $E_{\text{BM}}$ of $H_{\text{BM}}$ is B-hyperarc or $H_{\text{BM}}$ is a B-hypergraph. Also, there exist a minimal hypergraph $H_{\text{BM}} = (V_{\text{BM}}, E_{\text{BM}})$ such that every hyperedge $E_{\text{BM}}$ of $H_{\text{BM}}$ is F-hyperarc or $H_{\text{BM}}$ is an F-hypergraph.

3.2. Weighted node degree centrality (WNC)

**Definition 3.2.** The weights of the node incidence with the corresponding hyperedge is called as weighted node degree centrality [9,13]. It is given by

$$C^p_i(v_i) = \sum_{j=1}^{m} w_j, \quad (i = 1, 2, \ldots, n)$$

where $w_j$ takes the value 1 if $v_i$ is incident with $e_j$, 0 otherwise.

3.2.1. Construction of weighted node degree centrality

Initially, every vertex $v_i$ of a directed hypergraph is assigned with a weight as its degree centrality and it is presented in Algorithm 3.

Here, the weight $w_j$ is calculated as defined in Definition 3.2. These weights are tuned using the GA (Algorithm 4).
Algorithm 4: Genetic algorithm.

INPUT: Genetic Algorithm($w_i$)

OUTPUT: Best solution
1: $p_t \leftarrow 0$
2: Generate populations at random (population($p_t$))
3: Determine the fitness values of population($p_t$)
4: for $p_t = 0$ to $TC$ (Termination Condition [TC]) do
5: Choose the best individuals from the groups of population($p_t$) using Roulette Wheel Ranking Selection
6: Apply single-point crossover to the resultant population
7: Apply uniform mutation to the resultant population
8: Evaluate optimised fitness values
9: end for
10: Return best solution

3.3. GA weight optimization

GA is a search heuristic, which optimizes the solution of search problems [21]. Usually, GA is a population-based search technique used in computing, with each candidate represented as fixed-length binary string chromosomes. The Roulette wheel with ranking selection, one-point crossover and a uniform mutation are the components of GA in this work. The objective function of GA is,

$$(\text{objective function}) \ Y = \sum_{i=1}^{n} (x_i \ast w_i),$$

where $x_i$ is the initial weight of the node $v_i$, and $w_i$ (weight) is the parameter that is to be maximized.

Now, Roulette wheel and ranking selection [10] methods are combined to select the best individual from the groups (of individuals) formed out the population, for the objective function. The Roulette Wheel uses,

$$\bar{ab}_{ij} = \frac{\sum_{j=1}^{N} ab_{ij}}{N}$$

where $ab_{ij}$ represents the average fitness of the population for $i$th generation which varies from 1 to ngen. This value is used to place in the segment of roulette wheel, the bigger the value, the larger the segment and it is more probably to be selected.

$$cd_j = \frac{ab_{ij}}{\sum_{j=1}^{N} ab_{ij}}$$

where $cd_j$ represents the probability for selecting the $j$th individual and $ab_{ij}$ is the fitness value of the $j$th individual in the $i$th generation, and for ranking

$$p_{r_i} = \frac{r_{ij}}{r_{sum_i}}, \ r_{sum_i} = \sum_{j=1}^{N} r_{ij}$$

where $i$ varies from 1 to ngen (number of generations) and $j$ varies from 1 to $N$ (population size).

Pioneer technique used in the crossover is the single-point crossover, and it is given as,

$$(\text{Single-point crossover}) \ \text{crossover} = \text{Bas} \left( \frac{\text{offspring-size}}{2} \right)$$

where $\text{Bas}$ stand for Binary array of size.

We select a random gene from chromosome, lets say $x_i$ and assign a uniform random value to it.

(Uniformmutation)$x_i = U(a_i, b_i)$

where $i \in [1, n]$, $a_i$ and $b_i$ are random integer, $U(a_i, b_i) \in [a_i, b_i]$ is a uniform random number.

The fitness value [4] $F$ is calculated using normalized weighted sum evaluation function given by

$$(\text{Fitness})F = \sum_{j=1}^{N} w_f j - f_{\text{min}}$$

where $f_j$ is actual fitness value, $f_{\text{min}}$ is the worst fitness value, $f_{\text{max}}$ is the best fitness value, of $j$th individual.

Now, Algorithm 5 categorizes the nodes as strong ($ST_{HHDG}$) and

Algorithm 5: WDHDC.

INPUT: $W_{HHDG}$ from Algorithm 3

OUTPUT: Strong ($ST_{HHDG}$) and Weak ($WT_{HHDG}$) Tie nodes
1: $|W_{HHDG}| = n$ and $|E_{HHDG}| = m$, $ST_{HHDG} = \phi$ and $WT_{HHDG} = \phi$.
2: Calculate the Mean ($\bar{W}_M$) and Standard Deviation ($\sigma_{SD}$) of the Weights
3: for $i = 1$ to $n$ do
4: if $w_i > W_M + \sigma_{SD}$ then
5: $ST_{HHDG} = ST_{HHDG} \cup \{v_i\}$
6: else if $w_i < W_M - \sigma_{SD}$ then
7: $WT_{HHDG} = WT_{HHDG} \cup \{v_i\}$
8: end if
9: end for
10: Return the sets $WT_{HHDG}$ and $ST_{HHDG}$

weak ($WT_{HHDG}$) ties from the optimized weights of Algorithm 4.

The categories of ties based on their strength using mean and standard deviation is given as,

$C^d_w(v_i) = C^d_w(v_j) > W_M + \sigma_{SD}$, for strong ties.

$C^h_w(v_i) = C^h_w(v_j) < W_M - \sigma_{SD}$, for weak ties.

Here $W_M$ stands for the mean of the weights, and $W_{SD}$ stands for the weights’ standard deviation.

Similarly, the categorization of tie strength using quartile can also be defined as follows:

$C^d_q(v_i) = C^d_q(v_j) > W_{q_1} + W_{q_0}$, for strong ties.

$C^h_q(v_i) = C^h_q(v_j) < W_{q_1} - W_{q_0}$, for weak ties.

Here $W_{q_1}, W_{q_0}$ stands for 1st and 3rd quartile of the weights and $W_{q_0}$ stands for quartile deviation of the weights.

4. Implementation

The proposed technique is applied to the following ten biological networks [14] using Python 3.5 in Intel® Core™ i7-6700 Quad Core 3.4 GHz, 4.0 GHz system running in Ubuntu 16.4. (i) bio-WormNet-v3-benchmark, (ii) bio-DR-CX’s, (iii) bio-DM-CX’s, (iv) bio-HS-LC’s, (v) bio-HS-CX’s, (vi) bio-CE-CX’s, (vii) bio-grid-fission-yeast’s, (viii) bio-grid-yeast’s, (ix) bio-grid-human’s, (x) bio-dmela, where the networks (i)–(vi), are all a kind of WormNet network, with nodes as genes and edges as links between them and they are an integration’s of all data-type specific networks (CE-CX, CE-GN, CE-CT, CE-HT, CE-LC, CE-PG, DM-CX, DM-HT, DM-LC, DR-CX, HS-CX, HS-HT, HS-LC, SC-CC, SC-CX, SC-HT, SC-LC, SC-TS) through modified Bayesian integration. And for the remaining networks (vii)–(x), nodes are proteins and the edges are PPI.
Table 1
Range of influential nodes (Weak ties) using mean and SD, and quartiles.

| HWDG | N(HWDG) | M(HWDG) | Range of WT(HWDG) nodes by mean and SD | Range of WT(HWDG) nodes by quartiles |
|-------|---------|---------|---------------------------------------|--------------------------------------|
| bio-grid-fission-yeast's | 2031 | 2026 | [400, 450] | [470, 530] |
| bio-WormNet-v3-benchmark | 2445 | 2316 | [490, 540] | [550, 640] |
| bio-DR-CX's | 3289 | 3051 | [650, 720] | [750, 850] |
| bio-DM-CX's | 4040 | 3594 | [820, 890] | [930, 1020] |
| bio-HS-LC's | 4227 | 3391 | [850, 930] | [1000, 1050] |
| bio-HS-CX's | 4413 | 3975 | [900, 1000] | [1000, 1150] |
| bio-grid-yeast's | 6010 | 6008 | [1215, 1280] | [1430, 1440] |
| bio-dmela | 7399 | 6640 | [1500, 1600] | [1750, 1900] |
| bio-grid-human's | 9527 | 9536 | [1970, 2050] | [2300, 2390] |
| bio-CE-CX's | 16,347 | 14,692 | [3420, 3490] | [3900, 4150] |

Table 2
Comparison of influential nodes with other centrality measures.

| G | N(G) | M(G) | DC_G | CC_G | EC_G | HC_G |
|---|------|------|------|------|------|------|
| bio-grid-fission-yeast's | 2031 | 25,274 | 964 | 450 | 450 | 450 |
| bio-WormNet-v3-benchmark | 2445 | 78,736 | 2032 | 2295 | 2152 | 2197 |
| bio-DR-CX's | 3289 | 84,940 | 1478 | 1647 | 1344 | 1158 |
| bio-DM-CX's | 4040 | 112,688 | 1267 | 964 | 957 | 1060 |
| bio-HS-LC's | 4227 | 39,484 | 2815 | 1673 | 1753 | 1661 |
| bio-HS-CX's | 4413 | 108,818 | 1493 | 1044 | 1392 | 1037 |
| bio-grid-yeast's | 6010 | 313,890 | 3150 | 4791 | 5414 | 4791 |
| bio-dmela | 7399 | 25,571 | 4078 | 3681 | 6383 | 6370 |
| bio-grid-human's | 9527 | 62,364 | 6621 | 8029 | 8029 | 8029 |
| bio-CE-CX's | 16,347 | 762,822 | 7714 | 5081 | 7596 | 5047 |

Table 3
Comparison of influential proteins (Count) with our algorithm in the COVID-19 interaction data-set.

| Enzyme/disease | Total number of proteins in cleaned data-set | Number of proteins obtained using our algorithm |
|---------------|---------------------------------------------|------------------------------------------------|
| TMPRSS2       | 47                                          | 47                                             |
| ACE2          | 4                                           | 4                                              |
| AT-II         | 11                                          | 11                                             |
| Sudden cardiac attack | 10                              | 10                                             |
| IL6           | 33                                          | 33                                             |
| Cytoplasmic   | 1159                                        | 1159                                          |
| Cytokines     | 3                                           | 3                                              |
| Chronic obstructive pulmonary disease | 3                                     | 3                                              |
| Lower respiratory infections | 3                                   | 3                                              |
| Blood pressure | 35                                         | 35                                             |
| Diabetes mellitus | 35                                 | 35                                             |
| Stroke        | 23                                          | 23                                             |
| Tuberculosis  | 18                                          | 18                                             |

4.1. Results and discussion

The influential proteins (or) genes of above ten biological networks are identified through Algorithm 1 of weak ties and presented in the Table 1 with data: the number of nodes, number of directed hyperedges in HWDG, range of weak tie nodes using Mean, SD and quartile.

Various graph centrality measures like Degree Centrality (DC_G), Closeness Centrality (CC_G), Eigen Vector Centrality (EC_G) and Harmonic Centrality (HC_G) are compared with the proposed technique. Table 2 presents the influential nodes of the above explained ten biological networks.

The minimum number of influential nodes are to be derived which are responsible to maximize the influence to entire network. It is apparent from the values tabulated, our proposed work yields the minimum number of influential nodes both in mean, SD and quartile when comparing with the other centrality measures expect the bio-grid-fission-yeast's. In bio-grid-fission-yeast's network the number of the influential nodes using quartile is greater than the existing centralities.

Fig. 1 illustrates the count of edges of graph and hyperedges, it is apparent that number of hyperedges is much lesser than the number of edges of graph. Figs. 2 and 3 depicts the comparison of degree centralities of the proposed work based on mean-standard deviation, and quartiles-quartile deviation respectively, with the graph based centralities.

5. COVID-19 validation

In this section, we intend to validate our technique for COVID-19 protein-protein interaction. On Dec 8, 2019, the coronavirus (COVID-19) had identified in the seafood market in the Wuhan city of China. Coronavirus is one of a kind belonging to severe acute respiratory syndrome (SARS) virus. The world health organization (WHO) declared coronavirus as a pandemic.

Coronavirus (SARS-COV-2 or COVID-19) is one of the family members of Coronaviridae and order Nidovirales. This family contains two subfamilies, namely, Coronavirinae and Torovirinae. The Coronavirinae are classified into four categories:

- Alphacoronavirus - which consists of human coronavirus (HCOV)
- Betacoronavirus - which includes of human coronavirus (HCOV) with the SARS-COV-2 virus,
- Gammacoronavirus - which includes the viruses of bird and whales.
Fig. 1. Comparison of edge and hyperedge count.

Fig. 2. Comparison of degree centrality of graph with hypergraph (Using mean and SD).
• Deltacoronavirus - which consists of viruses which are isolated from birds and pigs.

The COVID-19 is Betacoronavirus together with the impact of viruses, namely, middle SARS viruses and pathogenic viruses. From the biological laboratory results [2,6,11,19] some crucial proteins have been identified, that plays a vital role in the protein-protein interactions(PPI’s) of COVID-19 with the human body. And, some of these essential proteins belong to the enzymes TMPRSS2 (Transmembrane protease, serine 2), ACE2 (Angiotensin - Converting Enzyme 2), and AT2 (Angiotensin II).

The COVID-19 protein-protein interactions (PPI’s) from [7] has been constructed as directed hypergraph. Here the nodes are the proteins and the directed hyperedge is constructed if there is an interaction between viral protein with human host proteins and human host protein with human proteins. Now, the directed hypergraph is transformed to weighted directed hypergraph by assigning the weights as the number of PPIs. These weights are tuned using GA and the classification of weak tie proteins is summarized in Table 3.

Proteins in TMPRSS2, ACE2, AT-II enzymes are 47, 4 and 11, respectively, in the cleaned SARS COVID II and human interactome data-set [8]. These proteins act as a major cause of various disease. We had also identified the proteins which cause the cytoplasmic, cytokine storm, chronic obstructive pulmonary disease, lower respiratory infections, blood pressure, diabetes mellitus, stroke, tuberculosis.

6. Conclusion

In this work, hypergraph is being exploited as a more powerful tool that reduces the complexity considerably compared to graphs as the weighted directed hypergraph of any network has fewer directed hyperedges. The influential nodes of the network are obtained by weak ties of degree centrality. The weights of the nodes are tuned using GA is employed by combining the Roulette wheel and ranking selection. The empirical results obtained from the computation show that proposed work perform better than other graph based centrality measures. Also, obtained critical proteins which play an influential role in COVID-19 viral interactions. These proteins may be a direct or indirect host of the COVID-19 viral protein and useful in drug design. For big data the elapsed time proliferates in identifying the influential nodes by the proposed technique. In the future, a suitable dimensionality reduction scheme will be introduced along with a congenial evolutionary algorithm to handle big data efficiently. Also, the expected protein interactome will be verified by protein docking based on the different mathematical modelling.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

[1] C. Berge, Hypergraphs North Holland mathematical library, 1989,
[2] B.J. De Witt, E.A. Garrison, H.C. Champion, P.J. Kadowitz, L-163,491 is a partial angiotensin at1 receptor agonist in the hindquarters vascular bed of the cat, Eur. J. Pharmacol. 404 (1-2) (2000) 213–219.

[3] G. Gallo, G. Longo, S. Pallottino, S. Nguyen, Directed hypergraphs and applications, Discrete Appl. Math. 42 (1993) 177–201, doi:10.1016/0166-218X(93)90045-P.

[4] M. Gen, R. Cheng, Genetic Algorithms and Engineering Optimization, vol. 7, John Wiley & Sons, 1999.

[5] M.S. Granovetter, The strength of weak ties, Am. J. Sociol. 78 (6) (1973) 1360–1380.

[6] M. Hoffmann, H. Kleine-Weber, S. Schroeder, N. Krüger, T. Herrler, S. Erichsen, T.S. Schieggens, G. Herrler, N.-H. Wu, A. Nitsche, et al., SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor, Cell 181 (2) (2020) 271–280.

[7] INTACT contributors, Coronavirus proteins interactions data-set, 2020a, https://www.ebi.ac.uk/intact/.

[8] INTACT contributors, Enzymes data-set, 2020b, https://www.uniprot.org/uniprot/?query=tmprss2(ace2/at-II)&sort=score.

[9] K. Kapoor, D. Sharma, J. Srivastava, Weighted node degree centrality for hypergraphs, in: 2013 IEEE 2nd Network Science Workshop (NSW), IEEE, 2013, pp. 152–155.

[10] R. Kumar, et al., Blending roulette wheel selection & rank selection in genetic algorithms, Int. J. Mach. Learn. Comput. 2 (4) (2012) 365–370.

[11] J. Lan, J. Ge, J. Yu, S. Shan, H. Zhou, S. Fan, Q. Zhang, X. Shi, Q. Wang, L. Zhang, et al., Structure of the SARS-CoV-2 spike receptor-binding domain bound to the ACE2 receptor, Nature 581 (7807) (2020) 215–220.

[12] G. Muhammad, M.S. Hussain, COVID-19 and non-COVID-19 classification using multi-layers fusion from lung ultrasound images, Inf. Fusion 72 (2021) 80–88.

[13] T. Opsahl, F. Agneessens, J. Skvoretz, Node centrality in weighted networks: generalizing degree and shortest paths, Soc. Netw. 32 (2010) 245–251, doi:10.1016/j.socnet.2010.03.006.

[14] R.A. Rossi, N.K. Ahmed, The network data repository with interactive graph analytics and visualization, 2015, http://networkrepository.com.

[15] S. Roy, B. Ravindran, Measuring network centrality using hypergraphs, in: Proceedings of the Second ACM IKDD Conference on Data Sciences, 2015, pp. 59–68.

[16] K. Shankar, E. Perumal, V.G. Díaz, P. Tiwari, D. Gupta, A.K.J. Saudagar, K. Muhammad, An optimal cascaded recurrent neural network for intelligent COVID-19 detection using chest X-ray images, Appl. Soft Comput. 113 (2021) 107878.

[17] R. Vagnetti, M.C. Pino, F. Masedu, S. Peretti, I. Le Donne, R. Rossi, M. Valenti, M. Mazza, Exploring the social cognition network in young adults with autism spectrum disorder using graph analysis, Brain Behav. 10 (3) (2020) e01524.

[18] Wikipedia contributors, Social network—Wikipedia, the free encyclopedia, 2004, [Online; accessed 22-February-2020], https://en.wikipedia.org/wiki/Socialnetwork.

[19] R. Yan, Y. Zhang, Y. Li, L. Xia, Y. Guo, Q. Zhou, Structural basis for the recognition of SARS-CoV-2 by full-length human ACE2, Science 367 (6485) (2020) 1444–1448.

[20] Y. Yoshida, Almost linear-time algorithms for adaptive betweenness centrality using hypergraph sketches, in: Proceedings of the 20th ACM SIGKDD International Conference on Knowledge Discovery and Data Mining, 2014, pp. 1416–1425.

[21] S. Zhang, S. Cui, Z. Ding, Hypergraph spectral analysis and processing in 3D point cloud, arXiv preprint arXiv:2001.02384 (2020).