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RESEARCH ARTICLE

Incoming, Outgoing Degree and Importance Analysis of Network Motifs

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Abstract: Exploring the features of network motifs as it provides different processing activities is significantly important. As network structure is applicable into different scientific and engineering fields, motifs (or significantly recurrent subgraphs) will clarify the different processing structures involved in the proposed organization. Herein, the indegree and outdegree of a motif are proposed as well as nodes' motif centrality and motif importance within the network. These concepts will help scientists to explore the most common and important activities within the network and classify the nodes functionality as related as well.
Keywords: Complex Network, Biological Motifs, Degree Centrality.

I. INTRODUCTION

Exploring the processing features as patterns of interaction among complex network entities and understand its interaction's methodologies are significantly important. This exploration influences scientists to build more efficient and effective therapies that help human kind curing from different diseases and increase treatment level with lower efforts [1, 2]. The determination of such interaction helps scientists in biology, medicine, bioinformatics, computer science, computational biology and many other "biology – related" discipline to have insights toward the determination of how do different diseases spread over these interactions and how to control that distribution using appropriate algorithms. Moreover, many engineering field try to imitate the features of biological organisms to its architectures as the last exhibit powerful and intelligent structures or so called "biological robustness" [3, 4].

However, by the word "interaction" it is referred to any kind of connection occurs among any two or more organisms. In general, exploring these interactions can go beyond that edge to any other connection (or relationship) among entities in different disciples. Interaction (or relationships among entities) can be presented as a network. In *graph theory*, a graph (or network) G = (N, E) is set of nodes N connected by set of edges E. Nodes may represent *human individuals, biological moleculars, computers* or *power supply units* and so on, each classification may have a relationship among its nodes such as *friendship, activating, communication, and transmitting* edges respectively [5]. These connections (edges) can be directed from one node to another (directed network), or an edge has no direction (undirected network). However, the specification of network orientation (directed or undirected) determined by the type and purpose of the network we are dealing with. Currently, we are interesting in direction oriented networks.

Networks are applicable to different real life structures, such as information network (such as world wide web, social networks, communication networks, citation network [6] .. etc), biological (biochemical and neural networks), ecological [7], power grid, roads traffics, airline traffics networks[8].. etc. Specifically in biology, scientists are very interesting in studying the patterns of interaction among different moleculars as in metabolic networks, and on the control mechanisms as in protein – protein interaction networks [9] and transcription regulatory networks [10].

In [11, 12], R. Milo presented subgraph (or motif) analysis as they recurrently appear in different complex network – more specifically in transcriptional regulatory networks. A motif is a set of nodes that appear in different networks with significant pattern of interactions. These motifs represent the different functionalities occurred within the network, as they implied different structures and properties. Critical to mention that a network consists of different set of motifs, and it is extremely significant to specify where diverse functionalities do distribute within network. With that, scientist will be able to cluster the network into several blocks, each block represent different functionality and know the sequence of interaction (based on specifying motifs' main entries and exits) which will lead to high impact on different fields as it provide the concept of understanding how do network work based on operational classification and flow. The specification of how do these motifs transferring knowledge or control would come from knowing the entries and exits of every block and the importance of that block to the entire network.

The rest of the paper will focus on the mathematical methodology used to conclude the indegree, outdegree of a motif and the importance of motif as well as nodes' motif centrality, conclusion and further researches to be conducted and the references used.

II. METHODOLOGY

Given a graph, G(V,E) where V represents set of vertices (or nodes) which are connected by set of edges E. Each node could represent any entity or object such as human individuals or articles or computers. Each edge represents the type of relationship that conducted between pair of vertices, such as friendship, citation or computer linking. However, every vertex has multiple features which play critically in specifying the underlying structure of the entire network. These features are conducted from the fact that each node is a part of complex organization of the graph such that relationships among them are the point of concern. One important and common feature of vertices is its degree. Degree of a vertex refers to the number of connections of involved vertex with its neighborhoods. Moreover, connection could be oriented from one vertex to another, such as friend request in Facebook or ReTweet in Twitter. These two types of degree are commonly referred as incoming degree and outgoing degree (or can be simply termed as indegree and outdegree). However, the mathematical representation of a graph could be specified by different approaches. If we denote an edge between vertex i and vertex j by (i,j) then the complete graph would be specified by a list of all edges between any pair of vertices. For example, the network in Fig. 1 has 10 vertices and edges set {(1,2),(1,3),(1,4),(1,5),(1,6),(1,7),(1,8),(6,9),(6,10),(7,8),(7,10)}. The edges set is referred to as *edge list* and usually used to store the network structure on computer. However, a better representation of a network is the *adjacency matrix*, see fig. 1.a. The adjacency matrix **A** is a two dimensions square array by the size of (N,N), N is number of nodes in the network and

$$A_{ij} = \begin{cases} 1 & if\ there\ is\ an\ edge\ from\ vertex\ i\ to\ vertex\ j \\ 0 & otherwise \end{cases}$$

In order to count the outgoing degree of each node, referred to as K_i^{out} we simply count the values of corresponding row, such that:

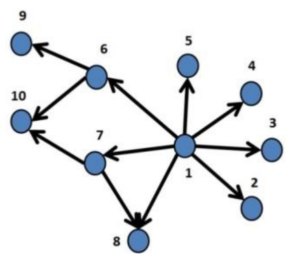
$$K_i^{out} = \sum_{j=1}^{N} A_{ij} \ldots\ldots (1)$$

And to count the incoming degree of a node, we can simply count summation of all values of the corresponding columns, such that:

$$K_i^{in} = \sum_{j=1}^{N} A_{ji} \dots \dots \dots (2)$$

Many other vertex features that exist can be found in [5]. However, the incoming and outgoing degree are considered to be the degree centrality of the specified node in directed network – fig. 1.a , while the degree of a vertex will represent the degree centrality of vertex in undirected network.

$$\begin{pmatrix} 1 & 1 & 1 & 1 & 1 & 1 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 1 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$



(a) (b)

Fig. 1: Directed Network of 10 vertices and 11 edges. **(a)** An adjacency matrix such that columns refer to vertices' j and rows refer to vertices'. **(b)** A graphic representation of the network.

TABLE I
INDEGREE AND OUTDEGREE OF NETWORK OF FIG. 1. VERTEX 1 HAS THE HIGHEST OUTDEGREE CENTRALITY WHICH REFERS TO EITHER ITS INFLUENCE OR CONTRIBUTION TO OTHER VERTEX FUNCTIONALITIES.

Vertex	Indegree	Outdegree
1	0	7
2	1	0
3	1	0
4	1	0
5	1	0
6	1	2
7	1	2
8	2	0
9	1	0
10	2	0

A. Motifs and Its Income and Outgo Degrees Measurement:

Network in general has been found to have "building blocks" [12], which reflect the architecture design of a network. Building blocks are simple *groups of nodes* or so called *motifs*. They apparently show up in most networks. However, studies depict that these motifs represent the core functionality of the entire network where each individual motif differs in functionality to others. The reason behind that difference is the way of unique interaction among its nodes. Motifs of our concern consist of three vertices other than others. There are 13 different unique patterns of interaction among these motifs. These patterns represent all possible interaction that could occur in any given three vertices motifs. See Fig 2.

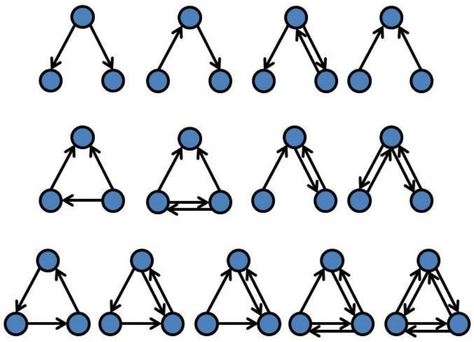


Fig. 2 Motifs' graphical representation using vertices and edges.

A motif can be mathematically defined as a M_{ijk} such that i, j and k referring to the index of motif's vertices in the adjacency matrix. The graphical and mathematical representation of the motifs is depicted in table (2). We only concentrate on the interaction as set of edges (edge - pair of vertices that fulfills the transition from one vertex to another) and on sequenced number of interaction in three vertices as provided for each motif. As been noticed, motifs are uniquely structured in term of that any motif functionality does not look the same as in others. However, it is remarkably important to notice that some motifs are recurrent in other motifs, i.e. motif 1 is occurring in motifs (3,5,6,8,10,11,12 and 13), motif 2 is occurring in motifs (3,5,6,7,8,9,10,11,12,13) and so on. Occurrence of a motif in another motif means that the structure of interaction of the first itself can be found in the second one among others. That is very important aspect which reflects the fact that motifs with low internal interaction have high appearance in motifs with high internal interaction than motifs with more internal edges. Motif 1 appears three times with three different representations in motif 13, fig. 3.

We can simply assume that the indegree and outdegree of a motif (fig. 4) is calculated as a summation of motif's nodes indegree and outdegree respectively:

$$M_{ijk}^{q,\ out} = \sum_{x=1}^{N} A_{ix} + \sum_{x=1}^{N} A_{jx} + \sum_{x=1}^{N} A_{kx} \dots\dots\dots\dots\dots (4)$$

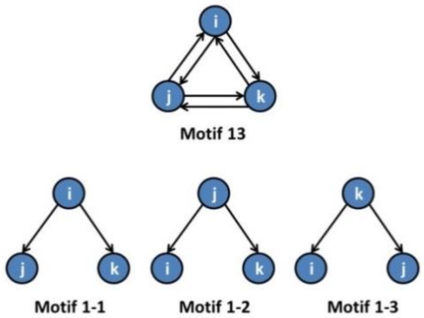


Fig. 3 The occurrence of three different downlinks (motif 1) of motif 13. Moreover, we can found all 12 first motifs extracted from motif 13.

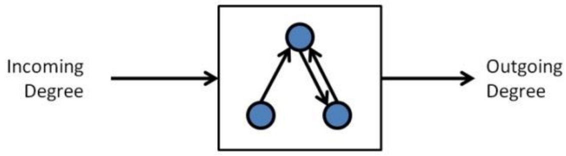


Fig. 4. Presenting sample motif with incoming and outgoing degrees.

$$M_{ijk}^{q,\ in} = \sum_{x=1}^{N} A_{xi} + \sum_{x=1}^{N} A_{xj} + \sum_{x=1}^{N} A_{xk} \ldots\ldots\ldots\ldots\ldots (3)$$

Such that $M_{ijk}^{q,\ in}, M_{ijk}^{q,\ out}$ refers to (indegree and outdegree of a) motif of type (number) q having vertices with indexes (i, j, k), N refers to number of nodes in given network. The values of $M_{ijk}^{q,\ in}, M_{ijk}^{q,\ out}$ will calculate all indegree and outdegree respectively to the three vertices including the internal edges itself. We have to normalize the values of $M_{ijk}^{q,\ in}, M_{ijk}^{q,\ out}$ by reducing the indegree and outdegree of motif internal edges as α – see table (2).

$$M_{ijk}^{q,\ in} = \sum_{x=1}^{N} A_{xi} + \sum_{x=1}^{N} A_{xj} + \sum_{x=1}^{N} A_{xk} - \alpha \ldots\ldots\ldots\ldots\ldots (5)$$

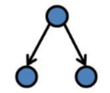
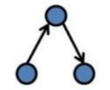
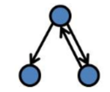
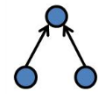
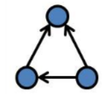
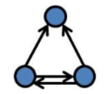
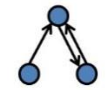
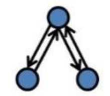
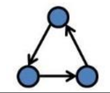
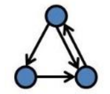
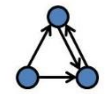
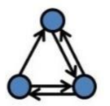
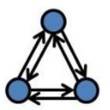
$$M_{ijk}^{q,\ out} = \sum_{x=1}^{N} A_{ix} + \sum_{x=1}^{N} A_{jx} + \sum_{x=1}^{N} A_{kx} - \alpha \ldots\ldots\ldots\ldots\ldots (6)$$

Precise calculation of 13 different motifs requires checking the resulted motifs against repeated format. In motif 1 for example, the structure (i, j, k) is the same as (i, k, j). This representation means that the father node *i* has two connections to nodes j, k.The precedence of children nodes is not important, i.e. the edges set of $\{(i, j), (i, k)\}$ as a motif 1 has same different formats since vertex i has two outgoing edges to both *j*, *k*. Herein, repeated motifs must be excluded although few set of motifs are applicable to that condition.

However, the use of the previous equations would not precisely reflect the ultimate degree of the motifs since we are dealing with the summation of nodes' degree (indegree, outdegree) regardless considering the series of moves that involve all nodes in a motif. If so, it will exclude the functionality of other internal nodes and so that we are ignoring the concept of motif in general. Consider a downlink motif $M_{ijk} = \{(i, j), (i, k)\}$, if only node *j* or node *k* have an indegree rather than node *i* then we will exclude the main role of node *i*. Another example is sequence motif $M_{ijk} = \{(i, j), (j, k)\}$, if node *j* have indegree rather than node *i* then we excluded the role of *i* in the motif.

Herein, it is critical to clearly specify where the motif starts its operations and how does it end. Basically, motifs received set of inputs and sent out set of outputs. The processing of internal action inside the different motifs would in turn have different explanations due to the different start node and end node.

TABLE II
MOTIFS' GRAPHICAL REPRESENTATION, INDEGREE AND OUTDEGREE DECREASE VALUES AND THE MATHEMATICAL REPRESENTATION FOR MOTIFS MATCHING IN ALGORITHM. SYMBOL i REFERS TO THE TOP NODE, SYMBOL j REFERS TO THE LEFT DOWN NODE AND SYMBOL k REFERS TO THE RIGHT DOWN NODE.

Motif Number	**Motif Figure**	**(α) Internal Edges**	**Motif mathematical representation (edges set of a motif)**
1		**-2**	$M_{ijk} = \{(i,j),(i,k)\}$
2		**-2**	$M_{ijk} = \{(i,j),(k,i)\}$
3		**-3**	$M_{ijk} = \{(i,j),(i,k),(k,i)\}$
4		**-2**	$M_{ijk} = \{(j,i),(k,i)\}$
5		**-3**	$M_{ijk} = \{(j,i),(k,i),(k,j)\}$
6		**-4**	$M_{ijk} = \{(j,i),(k,i),(j,k),(k,j)\}$
7		**-3**	$M_{ijk} = \{(j,i),(i,k),(k,i)\}$
8		**-4**	$M_{ijk} = \{(i,j),(j,i),(i,k),(k,i)\}$
9		**-3**	$M_{ijk} = \{(j,i),(i,k),(k,j)\}$
10		**-4**	$M_{ijk} = \{(j,i),(i,k),(k,i),(k,j)\}$
11		**-4**	$M_{ijk} = \{(j,i),(i,k),(k,i),(j,k)\}$
12		**-5**	$M_{ijk} = \{(j,i),(i,k),(k,i),(k,j),(j,k)\}$
13		**-6**	$M_{ijk} = \{(i,j),(j,i),(i,k),(k,i),(j,k),(k,j)\}$

A normalized version of indegree and outdegree of motifs can be proposed based on the node influence inside the motif and the concept of involving all *possible* nodes in interactions. In general, the incoming degree of a motif would go into the nodes that start or have high number of output to other connected nodes within the motif itself. Similarly, the outgoing degree of a motif would leave out of the nodes that end or have high number of inputs from other connected nodes within the motif. If more than one node fulfilled the condition then the indegree and outdegree of a motif would be calculated based on equal distribution of degrees to/from these nodes. If we measure the outdegree of a node to its indegree we will be able to measure the fraction of *processing* achieved by that node within the motif. Herein, a motif as a box would represent *processing unit* which received input(s) and have processing on it and would provide output(s). The input of the start node would be considered as the media by which the motif is activated to work. We depict in table (3) the fraction $F_{node} = \frac{Outdegree_{node}}{Indegree_{node}}$. The start node to be considered as input of a motif would be the node with the biggest value of F. The end node which to be considered as output of a motif would be the node with the lowest value of F. If two or three nodes have mutual value then the degree (in, out) would be calculated evenly.

TABLE III
THE START NODE (LABELLED WITH PINK) AND END NODE (LABELLED WITH GREEN) OF MOTIFS.

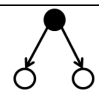
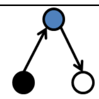
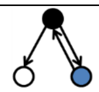
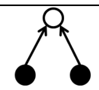
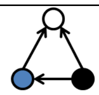
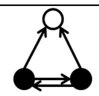
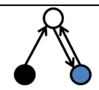
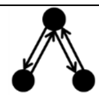
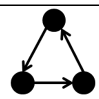
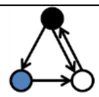
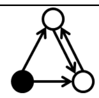
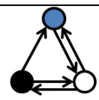
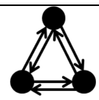
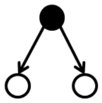
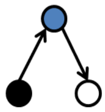
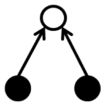
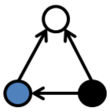
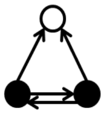
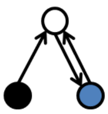
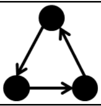
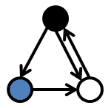
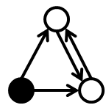
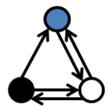
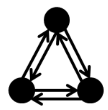
Seq	Nodes						$F = \frac{Outdegree}{indegree}$			Start Node; Internal Node; End Node
	i (Father)		*j(Left son)*		*k (Right son)*		F_i	F_j	F_k	
	In	Out	In	Out	In	Out				
1.	0	2	1	0	1	0	∞	0	0	
2.	1	1	0	1	1	0	1	∞	0	
3.	1	2	1	0	1	1	2	0	1	
4.	2	0	0	1	0	1	0	∞	∞	
5.	2	0	1	1	0	2	0	1	∞	
6.	2	0	1	2	1	2	0	2	2	
7.	2	1	0	1	1	1	0.5	∞	1	
8.	2	2	1	1	1	1	1	1	1	
9.	1	1	1	1	1	1	1	1	1	
10.	1	2	1	1	2	1	2	1	0.5	
11.	2	1	0	2	2	1	0.5	∞	0.5	
12.	2	1	1	2	2	2	0.5	2	1	
13.	2	2	2	2	2	2	1	1	1	

TABLE IV
THE DEGREE OF INCOMING AND OUTGOING OF 13 MOTIFS. NODES i, j, k REFER TO TOP, LEFT AND RIGHT NODES RESPECTIVELY.

Seq.	● Start Node ● Internal Node ○ End Node	**The indegree and outdegree of the motif**
1.		$M_{ijk}^{1,\ in} = \sum_{x=1}^{N} A_{xi}$ $M_{ijk}^{1,\ out} = \sum_{x=1}^{N} A_{jx} + \sum_{x=1}^{N} A_{kx}$
2.		$M_{ijk}^{2,\ in} = \sum_{x=1}^{N} A_{xj}$ $M_{ijk}^{2,\ out} = \sum_{x=1}^{N} A_{kx}$
3.		$M_{ijk}^{3,\ in} = \sum_{x=1}^{N} A_{xi}$ $M_{ijk}^{3,\ out} = \sum_{x=1}^{N} A_{jx}$
4.		$M_{ijk}^{4,\ in} = \sum_{x=1}^{N} A_{xj} + \sum_{x=1}^{N} A_{xk}$ $M_{ijk}^{4,\ out} = \sum_{x=1}^{N} A_{ix}$
5.		$M_{ijk}^{5,\ in} = \sum_{x=1}^{N} A_{xk}$ $M_{ijk}^{5,\ out} = \sum_{x=1}^{N} A_{ix}$
6.		$M_{ijk}^{6,\ in} = \sum_{x=1}^{N} A_{xj} + \sum_{x=1}^{N} A_{xk} - 2$ $M_{ijk}^{6,\ out} = \sum_{x=1}^{N} A_{ix}$
7.		$M_{ijk}^{7,\ in} = \sum_{x=1}^{N} A_{xj}$ $M_{ijk}^{7,\ out} = \sum_{x=1}^{N} A_{ix} - 1$
8.		$M_{ijk}^{8,\ in} = \sum_{x=1}^{N} A_{xi} + \sum_{x=1}^{N} A_{xj} + \sum_{x=1}^{N} A_{xk} - 4$ $M_{ijk}^{8,\ out} = \sum_{x=1}^{N} A_{ix} + \sum_{x=1}^{N} A_{jx} + \sum_{x=1}^{N} A_{kx} - 4$
9.		$M_{ijk}^{9,\ in} = \sum_{x=1}^{N} A_{xi} + \sum_{x=1}^{N} A_{xj} + \sum_{x=1}^{N} A_{xk} - 3$

		$M_{ijk}^{9,\ out} = \sum_{x=1}^{N} A_{ix} + \sum_{x=1}^{N} A_{jx} + \sum_{x=1}^{N} A_{kx} - 3$
10.		$M_{ijk}^{10,\ in} = \sum_{x=1}^{N} A_{xi} - 1$ $M_{ijk}^{10,\ out} = \sum_{x=1}^{N} A_{kx} - 1$
11.		$M_{ijk}^{11,\ in} = \sum_{x=1}^{N} A_{xj}$ $M_{ijk}^{11,\ out} = \sum_{x=1}^{N} A_{ix} + \sum_{x=1}^{N} A_{kx} - 2$
12.		$M_{ijk}^{12,\ in} = \sum_{x=1}^{N} A_{xj} - 1$ $M_{ijk}^{12,\ out} = \sum_{x=1}^{N} A_{kx} - 2$
13.		$M_{ijk}^{13,\ in} = \sum_{x=1}^{N} A_{xi} + \sum_{x=1}^{N} A_{xj} + \sum_{x=1}^{N} A_{xk} - 6$ $M_{ijk}^{13,\ out} = \sum_{x=1}^{N} A_{ix} + \sum_{x=1}^{N} A_{jx} + \sum_{x=1}^{N} A_{kx} - 6$

B. Measuring The Participation of Nodes Within Different Motifs:

Let M_n represent the number of motifs of type n such that $n = \{1,2,..,13\}$, M_n^x represent number of motifs of type n does node x participate in. The percentage of motifs does node x participate in of motifs of type *n* would be:

$$P(x,n) = \frac{M_n^x}{M_n} \ldots\ldots (7)$$

C. Measuring The Importance of a Motif Within a Network:

For a given motif M_{ijk}, $P(i,n), P(j,n), P(k,n)$ would represent the percentages of motif's nodes in the network as whole for type n motifs. Given that, the importance of motif M_{ijk} would represent the summation of its nodes' importance:

$$I_{M_{ijk}}^n = \sum_{x\ in\ M} P(x,n) \ldots\ldots (8)$$

The fraction $I_{M_{ijk}}^n$ represents the value of motif contribution to the network. The contribution of specified motif includes the contribution of its members in other motifs. This is very important aspect as each node contributes to many motifs and it is crucially required to count that too.

In the same way, we can measure the importance of given motif relatively to the average network's motifs importance as follow:

$$\bar{I}_{M_{ijk}}^n = \frac{I_{M_{ijk}}^n}{\frac{\sum_{m\ in\ M} I_m^n}{M_n}} \ldots\ldots (9)$$

A simplified version of motif importance recalled from (7) and (9) would be:

$$\bar{I}_{M_{ijk}}^n = \frac{M_n^x}{\sum_{m\ in\ M} I_m^n} \ldots\ldots (10)$$

III. CONCLUSIONS

In this research, an indegree and outdegree of a motif are specified, as well as measuring the nodes contribution to network's different motifs or so called node's motif centrality. The influence of measuring these factors will result in discovering the different processing features of nodes within the network individually and on set of 3 nodes motif. This means the following:

1- Specifying the two roles of nodes within the complex network: input and output of motifs. Measuring the basis start and end nodes within given motifs can help in compressing these motifs into node representation, decreasing the network representation to lower structure.
2- Specifying which nodes are playing critically in which motif (i.e. start, processing or internal and end node).
3- Nodes with high motif centrality have more contribution to network than other lower motif centrality.
4- Recognition of the nodes as they start and end specified motifs, this can help in clustering the network into groups of blocks depending on their functionality.

Measuring these two features is very important in many fields as it refers to the most and less dominating motif in the network, the important nodes with special activity within network. The specification of motifs indegree and outdegree provide new approach toward reading the activities flow in network.

A further research would be focused on compressing these motifs into fewer set of nodes in order to understand the features of ***m***otif ***a***s ***n***ode (MAN)'s interaction. The previous work of Vertex sharing Motif Network (VMN) [13] comes with exponential number of nodes which increase the complexity of analyzing the network. Additionally, the different centralities of given MANs need to be calculated to demonstrate the distribution features of different motifs within the complex network.

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