Original Research Article

Comparative Analysis of Gene Networks in Humans and Model Organisms for Aging Studies

ABSTRACT

Aging is the cause of the loss of vitality on a day-to-day basis, a risk factor for developing chronic diseases and ultimately leading to death. This inevitable biological process is yet to be completely understood. A hypothesis states that manipulation of aging process can enable maintain physiological function and perhaps prevents age related diseases. Currently, model organisms are being used in the investigation of the genetic and molecular mechanism of the aging process. In this study, the adequacy of the major model system, the fruit fly (Drosophila melanogaster) and the rodent mouse (Mus musculus), was analyzed using Jepetto software through comparison of all the genomes of the model organisms with all the genomes of human genome by network statistics of string interactions. The software mapped the gene set of humans and the two model organisms on an interaction network and computed the gene properties by network density, centrality nodes and clustering coefficient. Of all three genomes, the human gene network is the largest and dense with the highest number of neighbors. On the other hand, the mouse and drosophila network are relatively smaller and in terms of density, the former is less dense, and the latter is sparse. The average number of neighbors of both model organisms are similar and approximately 25% of the human network. In the distance/shortest path length between the nodes, there was a decreasing order of connectivity in drosophila to mouse to human. The node with the path length 2 exhibited the highest frequency in all the organisms. In between centrality distribution, the nodes of the human network were observed to be closer. On comparison, mouse network is closer while the drosophila network is widely spread. The information spread between the nodes is measured by the closeness centrality distribution plot and the human network found to have highest closeness centrality than the other two species. Neighborhood connectivity distribution. The network clustering coefficient of genes of drosophila was much more widespread than the other two species.

Keywords: Aging Jepetto software, Network Statistics, Drosophila, Mouse, Human,Closeness

1. INTRODUCTION

Globally the average age a human being can live up to was estimated as 73.2 years, with both sexes combined. This is a drastic increase, nearly doubled, from the 1950s expectancy rate of 47 years (United Nations Population Division estimate) [1]. The increase in the average living age of the humans can only be owed to the great breakthroughs in the medicinal field in the past 70 years such as the development of life saving vaccines for robust diseases, polio vaccine by Jonas Salk (1952)[2], measles vaccine by Maurice Ralph Hilleman (1964)[3]; organ transplant procedure, first human kidney transplant by Joseph Murray in 1954[4], in 1963 first liver transplant in human was performed by Thomas Starzl[5] and lung transplant by James Hardy[6]; development of therapeutic agents for treatments, first human recombinant insulin by Eli Lilly and Company in 1982[7], first human embryonic stem cell developed in 1988 by James Alexander Thomson[8]; development in disease diagnosis and surgical techniques, Thomas Fogarty's invention of balloon catheter in 1969[9], capsule endoscopy procedure by Tarun Mullick in 1985, intravascular stent procedure in 1988 by Julio Palmaz[10]. So far in the 21st century, the scientific research had achieved human genome sequencing, stem cell technology for organs growing in vitro, 3D printing technique for developing human parts and vaccines for novel viral diseases. Even with the

enormous innovations, the scientific community is still being unable to fully understand and control the one major cause for the inevitable death, i.e., age.

Aging is an irreversible biological process of life that results in the progressive decline in the function and performance of the organ systems over the life span [11]. Several theories have been proposed for the mechanism of the aging process, but none have been proven. According to Kirkwood, aging is triggered by the accumulation of damaging molecules inside the cells influenced by genetic control. This hypothesis proposed as the disposable soma theory. The cells have a system to repair the damage caused for cell status maintenance. This theory suggests that shortage of nutrients will lead the organisms to balance energy maintenance between germ cell lines and somatic cell lines [15]. Both exogenous and endogenous biochemical and biological stress can lead to the accumulation of those molecules. Damage can be caused by extrinsic sources such as UV irradiation and toxins or intrinsic sources such as reactive oxygen species and reactive nitrogen species. Throughout the course of life, the body will be in constant vulnerability and thus with increasing age, it is more prone to diseases and declining health [12]. An alternative to that of Kirkwood's theory was Programmed longevity theory and according to that, life has been programmed to maintain fitness during the healthy state of life[16]. The antagonistic pleiotropy theory proposed by George Williams suggests that aging may be a result of the natural selection that has led to the fixation of late-acting deleterious alleles in a population for it is advantageous in early part of life [14].

Although the medicinal innovations have been achieved to expand our life span, a major concern is the quality of that extended life. Old age is associated with diseases and chronic conditions such as arthritis, cardiovascular diseases, obesity, hypertension, diminution of cognitive function and also limitations of mobility and functions [13]. Maintaining the quality of life becomes very difficult in the aged community. But there are also instances where the individual over 80 years old may present with the physical and mental ability as same as in a much younger individual of about 20 years of age and vice versa [11]. This suggests that aging is a complex process and widely variable among individuals. Aging is influenced by factors such as genetic, lifestyle, socio-economic status and sex of each individual. A complete understanding of the aging mechanism can be gained only by intervening experiments and models systems.

Human aging takes place over decades hence cannot be studied in vivo using human subjects. Through observation, researchers are trying to understand human aging process along with their associated pathologies throughout their life span, while also comparing young and old individuals by cross sectional studies. Genetic studies of longevity can reveal information only at the molecular level. These types of studies cannot reveal a thorough understanding of human aging. Hence model organisms are necessary in gerontology.

Traditional biomedical model organisms include yeast, mice, rats, fruit flies, and roundworms. They have well established widespread resources, reagents and protocols that allow studies to be conducted in a faster and cheaper way.

The first and the foremost of the major model systems in the gerontology study of human aging process is the human cells. In vitro systems of human cells will be the most relevant model for the purpose of characterization of intrinsic cell factors of aging but the key aspects of aging like diseases and immune response, interactions among organs and tissues cannot be recapitulated [17]. Another argument against cellular models is that most cellular models of aging, such as replicative senescence, are based on measurements of cell proliferation which are not necessarily a measurement of vitality. Cancer, for instance, is derived from rapid, uncontrolled cellular proliferation. Other methods exist to measure aging in cells, such as stress resistance, but the relevance of these methods to organismal aging remains to be demonstrated. The second most used model is the unicellular organisms such as the yeast Saccharomyces cerevisiae. Yeast and mammalian genome have high similarities. The maintenance of these simple eukaryote models are relatively cheap and easy and also facilitate high throughput methodologies to be performed [18]. Two pathways exist in yeast for aging, the replicative life span and logical life span. The mediators in those cellular pathways have found to have orthologues in higher eukaryotes implying the conservation of mechanism from yeast to human. This makes Yeast an effective model in understanding human diseases [19]. The roundworm Caenorhabditis elegans is established as one of the model organisms of human aging in 1965. The nematode is relatively small in size (adults only reach up to 1.5 mm in length) has a generation time of 3-5 days and a life span of 2-3 weeks. The worm constitutes less than 1000 cells and 19000 genes, of which half of the percentage is found to be conserved in the human genome. This makes this organism ideal for understanding simple phenotypes and longevity [20]. For more than a century, the fruit fly Drosophila melanogaster had been the key model organism for ageing research. Apart from low-cost maintenance, the factor that makes it an ideal candidate for ageing research is their genome. The genome of the fly has a higher proportion of human equivalent ageing related disease genes. Genetic manipulation studies can be conducted in a larger population. Research in this model organism can shed light on ageing progression and the effects of environmental and genetic factors [21]. The commonly used mammalian model for understanding the aging process is mice. They had already been well established to test therapeutics. As the model organism, it is small and has short life cycles, no more than 4 years. It makes them inexpensive subjects for aging studies, and the ability to genetically manipulate them gives researchers ample opportunities to test their theories and unravel molecular and genetic mechanisms of aging. Research with lower

organisms and non-vertebrates can be advantageous to some extent but a mammalian model is unavoidable. Humans and mice have similar physiological functions and biological systems such as cardiovascular system and nervous system [22].

Model organisms had been widely used to understand the aging process for it is simpler than a human, easily maintained and affordable. Another advantage of those organisms is that series of rigorous research can be performed to understand and control aging process without ethical problems. The knowledge on the aging process that we have learned so far had been gained using those organisms. Their small size and easy maintenance enable employing large-scale genetic screens and functional genomics, that are not possible in humans or in other non-traditional model organisms. To give an example, thousands of genes and drugs can be screened for effects on worm lifespan, so lower model organisms are adequate for initial surveys.

The downside of model organisms, of course, is that it is nearly impossible to tell whether an organism is representative of human aging or not. It has been argued that similar mechanisms operate across many species while others have proposed that some aging mechanisms (called “public”) are common to all species while others are unique (“private”) of each species. Since the basic blocks of life are common to most known species, common pathways might be involved in aging across phylogeny. Could it be that the weakest pathway succumbing to senescence is the same in all organisms? Such hypothesis is hard to believe based on the huge diversity of aging phenotypes found in Nature, and certain animals appear to age for different causes than us. For example, the male Australian mouse (*Antechinus stuartii*) has a bizarre aging phenotype. The rapid death following reproduction observed in Antechinus and in other species is much different from the gradual waning of humans and so Antechinus is not a good model of human aging as different mechanisms are likely involved. The traditional biomedical model organisms all exhibit a gradual decline, but the question remains of whether they are accurate paradigms of human aging.

This review analyzed the adequacy of the major model organisms of human ageing, the fruit fly (Drosophila melanogaster) and the rodent mouse (Mus musculus), using JEPETTO software through comparison of all the genomes of the model organisms with all the genomes of human genome by network statistics of string interactions.

JEPETTO (Java Enrichment of Pathways Extended ToTopology) is an open source software which uses topological analysis and protein interaction networks for integrative analysis of human gene set such as finding connection between known cellular pathways and genes useful for specific functions. It is a plugin that enables a user to integrate their experiment derived genomic data for analysis such as network enrichment, expansion of pathways and topological matching by communication with previously published three web servers[23].

2. MATERIAL AND METHODS

A Cytoscape plugin analyzer was used for the analysis of the three gene sets of human, mice and fruit fly. The software used TopoGSA server to identify the topological relationship between the three gene sets.Two sets of parameters were analyzed by the software namely simple or local parameters and global parameters. Simple parameters include clustering coefficient, connected components, neighborhood connectivity, network density and diameter, number of nodes and average number of neighbors. The standard software tool and parameters used for the analysis.

Global parameters are pathways related, that included betweenness centrality, closeness centrality, neighborhood connectivity distribution, average clustering coefficient, node degree distribution, shared neighborhood distribution, stress centrality and topological coefficient).

3. RESULTS AND DISCUSSION

A node in a biological network corresponds to the genes, in some cases it is often proteins or metabolites while the physical relationship between those entities or their expression of gene regulation are represented as edges [24]. A cystoscope provides models of biological systems and enables the user to better understandvisualization, analysis and interpretation. Here, using Cystoscope software undirected network statistics were performed for the three genomes, human mouse and fruit fly. Undirected type statistics is more specific than the directed one for this type of analysis. The basic assumption of this statistics is that reciprocity exists between two nodes connected by edges. The statistics helps to identify whether relationships exist between the human network and the two commonly used most relevant model organisms of human aging mechanism, so that we can rely on the results obtained from them to take measures in the human systems for aging control and related pathologies.

SIMPLE OR LOCAL PARAMETERS

In the Cytoscape software, for every node in the network, a variety of local parameters were computed which are summarized in Table 1 and represented in Figure 1a, 1b and 1c.

The parameters computed are connected components, clustering coefficient, number of nodes, network density, diameter, centralization values, average number of neighbors, the shortest path and the analysis time.

Table 1: SUMMARY OF THE SIMPLE PARAMETERS OF HUMAN, MOUSE AND FRUIT FLY NETWORK

Parameter	Human	Mouse	Fruit fly
Clustering coefficient	0.529	0.498	0.421
Connected components	1	1	2
Network diameter	4	6	6
Network radius	2	3	1
Network centralization	0.550	0.511	0.283
Shortest paths	90902 (100%)	14042 (100%)	18908 (97%)
Characteristic path length	2.022	2.358	2.674
Avg. no. of neighbour	45.689	11.731	11.257
Number nodes	302	119	140
Network density	0.152	0.099	0.081
Network heterogeneity	0.797	0.991	0.976
Isolated nodes	0	0	0
Number of self loops	0	0	0
Multiedge node pairs	0	0	0
Analysis time (s)	0.529	0.223	0.083

Two nodes in an undirected network are connected if edges are present between them. If all the nodes within a network are pairwise connected, they form a connected component. The number of connected components is the representation of the strength of the network. The lower the value the stronger the connectivity. The connected component value of human and mouse is 1 while that of the fruit fly is 2. This represents that there is a stronger connectivity within the human and mouse network, but the connectivity is slightly lesser in that of the fruit fly network.

Clustering coefficient is a measure of the existing links connecting a node to every other node in the neighborhood. It is the ratio of the number of edges between the neighbors of a node to that of the maximum number of edges possible between the neighbors of a gene node. The value of this parameter will be between 0 and 1. The clustering co-efficient of the human network was integrated as 0.529 for a total of 302 nodes while for that of the mouse and fruit fly were 0.498 for a total of 119 nodes and 0.421 for a total of 140 nodes respectively. The value 0 means that no nodes are connected in the neighborhood and the value 1 means every node in the neighborhood is connected to every other node indicating that the neighborhood is complete. In other words, the clustering coefficient value closer to zero indicates lesser connections between the nodes in the neighborhood and value closer to 1 indicates higher number of connections between the nodes. Both mouse and fruit fly network exhibited better clustering coefficient for their total number of nodes. This signifies that in both the gene networks the communication between genes is well established.

In human networks each node has an average of 45.689 neighbors with a network diameter value of 4. In mouse network, each node has an average of 11.731 neighbors and the diameter value of 6 while each node in the fruit fly network has about 11.257 average neighbors and the network diameter is 6. The diameter of a network is the measure of the shortest path of two of the most distantly situated nodes, in fact, it is the longest path of a network from all the shortest paths that can be calculated. On the other hand, density of a network is the ratio between the number of edges in a network to the number of possible edges with respect to the number of nodes. Our genome analysis revealed the density of all the three networks as 0.152, 0.099 and 0.081 respectively for human, mouse and fruit fly network. On the basis of network diameter and density of network, when all three networks were compared, it is observed that the human network is the most dense followed by the mouse network which is not as dense as that of human while the fruit fly network was more sparse compared to the other two networks.

From the charts we see that the human genes form considerably a large network with higher density and huge no. of neighbors. This signifies the greater life extending capacity.

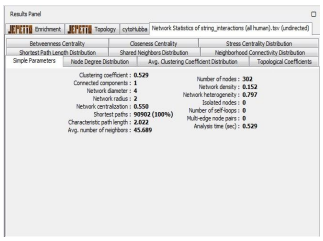


Figure 1a: All parameters for Human network

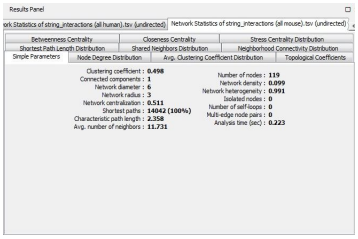


Figure 1b: All parameters for Mouse network

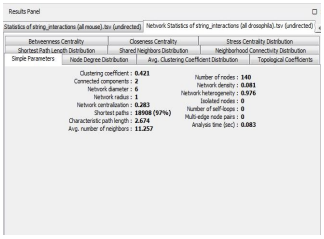


Figure 1c: All parameters for the Drosophila network

Figure 1a: All parameters for Human network Figure 1b: All parameters for Mouse network

Figure 1c: All parameters for the Drosophila network

GLOBAL PARAMETERS:SHORTEST PATH LENGTH DISTRIBUTION

The path length is the length of an edge connecting two nodes. The path in which two nodes can be connected using the least number of edges is known as the shortest path length. It is one way to conceptualize the rate of type 1 error in null hypothesis when conducting multiple comparisons.

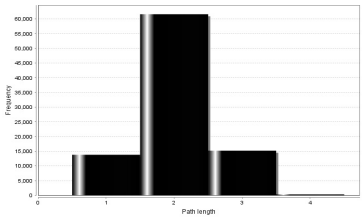


Figure 2a: Shortest Path length Distribution for Human

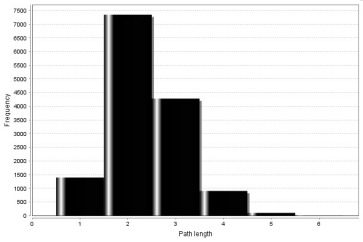


Figure 2b: Shortest Path length Distribution for Mouse

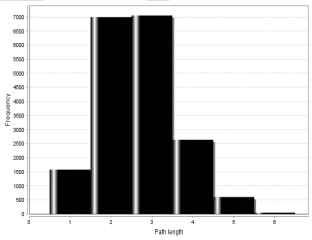


Figure 2c: Shortest Path length Distribution for Drosophila

Figure 2a: Shortest Path length Distribution for Human Figure 2b: Shortest Path length Distribution for Mouse Figure 2c: Shortest Path length Distribution for Drosophila

It shows that the nodes with path length 2 have the highest frequency than the remaining.

The shortest path length is the average length of the shortest path between n and any other node. If n is an isolated node, the value of this attribute is interpreted as zero. The length of a path is the number of edges forming it. There may be multiple paths connecting two given nodes. The shortest path length, also called distance, between two nodes n and m is denoted by L(n,m). The characteristic path length, also known as the average shortest path length, represents the expected distance between two nodes that are paired. The analysis revealed an average of 2.022, the shortest path length for human network while for mouse and fruit fly network the values are 2.353 and 2.674 respectively. The parameter establishes a decreasing order of connectivity in drosophila to mouse to human ascertaining the fact that even if the genome is simple but still the complexity may be more.

BETWEENNESS CENTRALITY

Betweenness centrality reflects the importance of the node based on the number of shortest paths that pass through each node

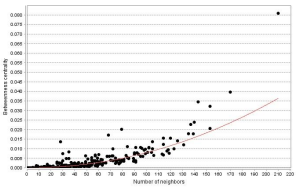


Figure 3a: Betweenness centrality distribution for the analysis of the Human network

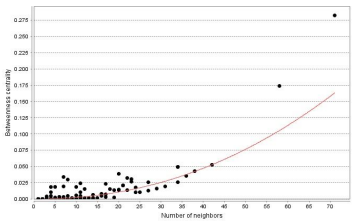


Figure 3b: Betweenness centrality distribution for the analysis of the Mouse network

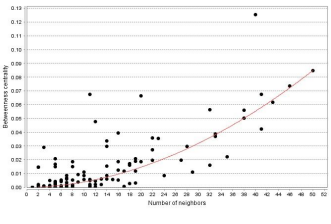


Figure 3c: Betweenness centrality distribution for the analysis of the Drosophila network

Figure 3a: Betweenness centrality distribution for the analysis of the Human network; Figure 3b: Betweenness centrality distribution for the analysis of the Mouse network; Figure 3c: Betweenness centrality distribution for the analysis of the Drosophila network

It represents the distribution graph of human mice and drosophila respectively; it can be observed that the nodes co-relate with the fitted line.

In general, betweenness centrality are not computed for all networks but for the networks that do not contain multiple edges. The normalized value, n, for a node is obtained by the division of number of node pairs

(N-1)(N-2)/2

Here N corresponds to the total number of nodes in the connected component that n belongs to. This gives the betweenness centrality of each node, a value in the range of 0 and 1. The betweenness centrality of a node reflects the amount of control that this node exerts over the interactions of other nodes in the network. This measure favors nodes that join communities (dense subnetworks), rather than nodes that lie inside a community.

The nodes of the drosophila species are more widespread than the other two species.

CLOSENESS CENTRALITY

Closeness centrality is a measure of how fast information spreads from a given node to other reachable nodes in the network. It computes the closeness centrality of all nodes and plots it against the number of neighbors. The closeness centrality of isolated nodes is equal to 0.

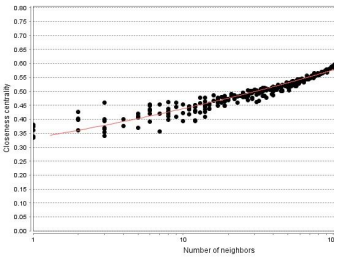


Figure 4a: Closeness centrality distribution for the analysis of the Human network

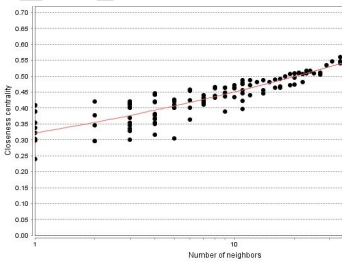


Figure 4b: Closeness centrality distribution for the analysis of the Mouse network

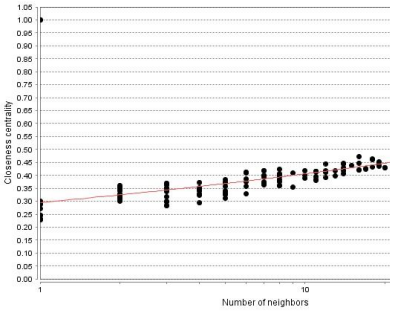


Figure 4c: Closeness centrality distribution for the analysis of the Drosophila network

Figure 4a: Closeness centrality distribution for the analysis of the Human network Figure 4b: Closeness centrality distribution for the analysis of the Mouse network Figure4c: Closeness centrality distribution for the analysis of the Drosophila network

Network Analyzer computes the closeness centrality of all nodes and plots it against the number of neighbors. The closeness centrality of isolated nodes is equal to 0.

Closeness centrality of a node tells fast information can spread from that node to other nodes within the reach. The CC of humans is highest and much clustered when compared to the more widespread two other species. Both mouse and drosophila network have similar closeness centrality.

NEIGHBORHOOD CONNECTIVITY DISTRIBUTION

The average neighborhood connectivity is the connectivity of a node to the number of its neighbors. The neighborhood connectivity of a node is defined as the average connectivity of all neighbors of that node. If the neighborhood connectivity distribution is a decreasing function, edges between low connected and highly connected nodes prevail in the network.

The drosophila network has more widespread neighborhood connectivity than the other two networks.

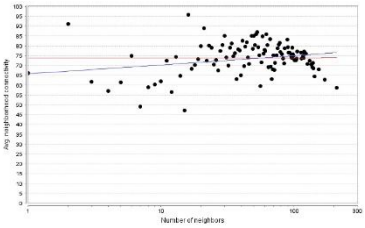


Figure 5a: Average neighborhood connectivity distribution for the analysis of the Human network

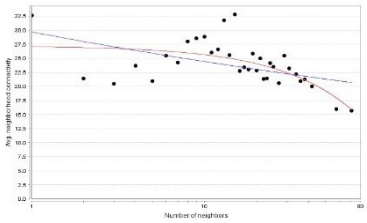


Figure 5b: Average neighborhood connectivity distribution for the analysis of the Mouse network

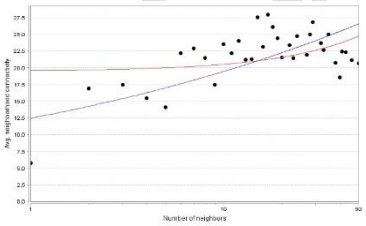
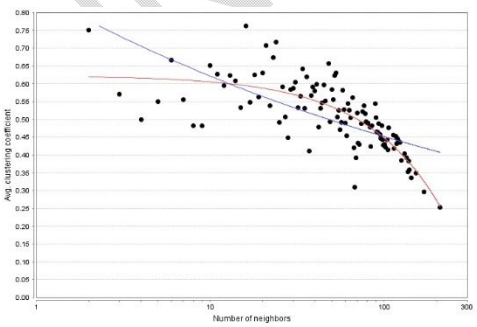


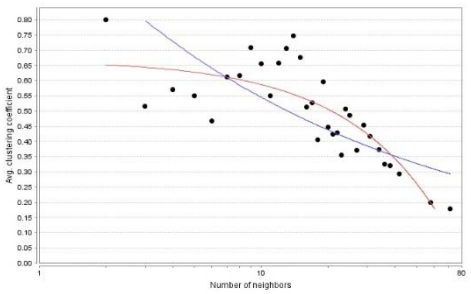
Figure 5c: Average neighborhood connectivity distribution for the analysis of the Drosophila network

Figure 5a: Average neighborhood connectivity distribution for the analysis of the Human network Figure 5b: Average neighborhood connectivity distribution for the analysis of the Mouse network Figure 5c: Average neighborhood connectivity distribution for the analysis of the Drosophila network

AVERAGE CLUSTERING CO-EFFICIENT

The network clustering coefficient is the average of the clustering coefficients for all nodes in the network, a measure of the number of connections among nodes in relation to the maximum number of connections in the neighborhood. Nodes with less than two neighbors are assumed to have a clustering coefficient of 0. A value of 1 means that the nodes are fully connected in a network. The human network in the Figure 6, is denser compared to other two networks with the maximum ratio of 0.8. The clustering coefficient of genes is much more widespread in drosophila when compared to the other two species.





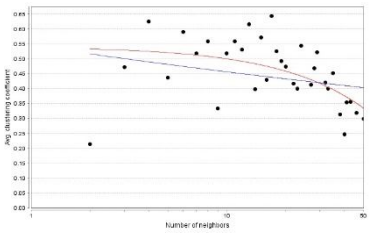


Figure 6a: Average Clustering Coefficient for the analysis of the Human network

Figure 6b: Average Clustering Coefficient for the analysis of the Mouse network

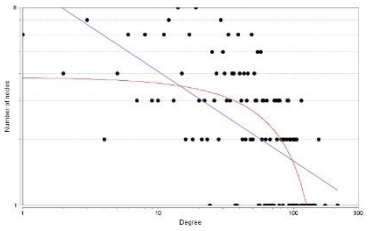
Figure 6c: Average Clustering Coefficient for the analysis of the Drosophila network

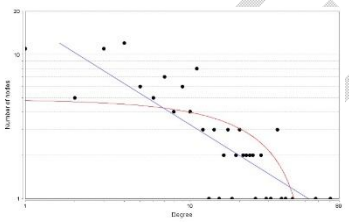
Figure 6a: Average Clustering Coefficient for the analysis of the Human network Figure 6b: Average Clustering Coefficient for the analysis of the Mouse networkFigure 6c: Average Clustering Coefficient for the analysis of the Drosophila network

NODE DEGREE DISTRIBUTION

In undirected networks, the node degree of a node n is the representation of the number of connections or number of edges linked to that n. A self-loop of a node is counted like two edges for the node degree. The node degree distribution gives the number of nodes with degree k for k = 0,1, In directed networks, the in-degree of a node n is the number of incoming edges, and the out-degree is the number of outgoing edges. Like undirected networks, there are an in-degree distribution and an out-degree distribution. The node degree distribution is to distinguish between random and scale-free network topologies.

In a network analysis, the degree distribution is the probability of the degrees of all the individual nodes over the network. The degree of the human network nodes are more (represented by the long tail), in other terms it can be depicted as the nodes are highly connected. There are more highly connected nodes in the graph of human network which are called hubs. In mouse network, the hubs are few and the degree of the nodes are less. The degree of the node distribution of the drosophila network is much less than the mouse network.





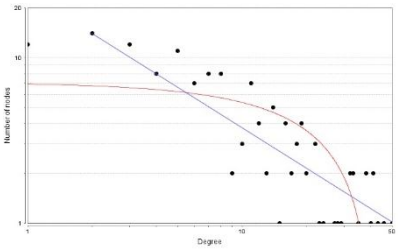


Figure 7a: Node Degree Distribution for the analysis of the Human network

Figure 7b: Node Degree Distribution for the analysis of the Mouse network

Figure 7c: Node Degree Distribution for the analysis of the Drosophila network

Figure 7a: Node Degree Distribution for the analysis of the Human network; Figure 7b: Node Degree Distribution for the analysis of the Mouse network; Figure 7c: Node Degree Distribution for the analysis of the Drosophila network

SHARED NEIGHBORHOOD DISTRIBUTION

The shared neighborhood connectivity, P(n,m) is the number of partners shared between the nodes n and m, that is, nodes that are neighbors of both n and m. The shared neighbors distribution gives the number of node pairs (n,m) with P(n,m) = k for k = 1,….

If a motif is over-represented in a network, this can be inferred from the shared neighbor's distribution. The graph represented in Figure 8 demonstrates that more motif overrepresented in the human aging genes. Even though both the drosophila and mouse network have a smaller number of shares neighbours and the frequency compared to the human network, they are similar to each other.

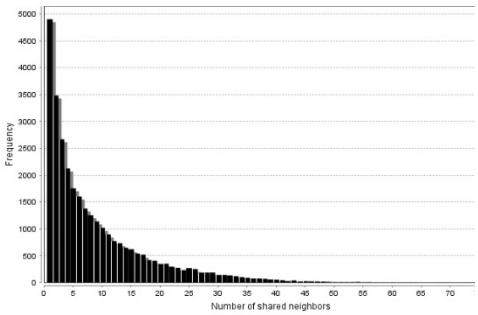


Figure 8a: Shared Neighborhood Distribution for the analysis of the Human network

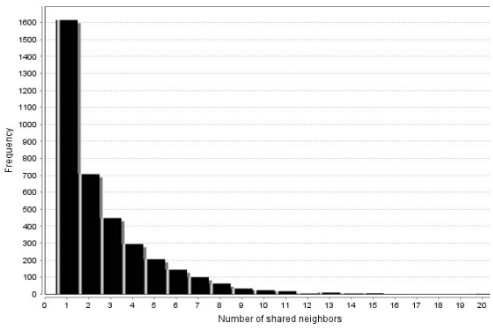


Figure 8b: Shared Neighborhood Distribution for the analysis of the Mouse network

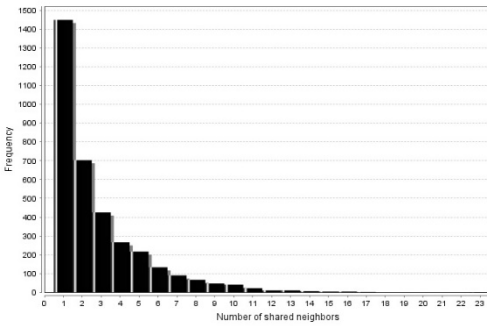


Figure 8c: Shared Neighborhood Distribution for the analysis of the Drosophila network

Figure 8a: Shared Neighborhood Distribution for the analysis of the Human network; Figure 8b: Shared Neighborhood Distribution for the analysis of the Mouse network; Figure 8c: Shared Neighborhood Distribution for the analysis of the Drosophila network

STRESS CENTRALITY

The stress of a node n is the number of shortest paths passing through n. A node has a high stress if it is traversed by a high number of shortest paths. This parameter is defined only for networks without multiple edges.

The stress centrality plot of all the three networks is plotted in figure 9. The stress distribution gives the number of nodes with stress s for different values of s. The values for the stress are grouped into bins whose size grows exponentially by a factor of 10. This is based on the count of the shortest paths that pass through the node and the potential of that node to control the flow (Shimbel, 1953). The centrality measurement revealed human gene network have the highest stress score followed by drosophila network and the mouse network.

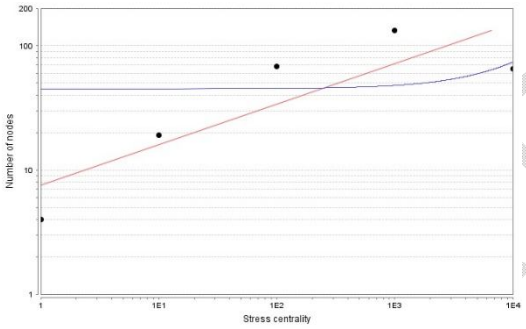


Figure 9a: Stress Centrality for the analysis of the Human network

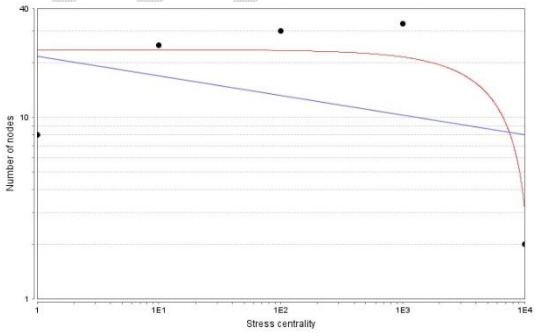


Figure 9b: Stress Centrality for the analysis of the Mouse network

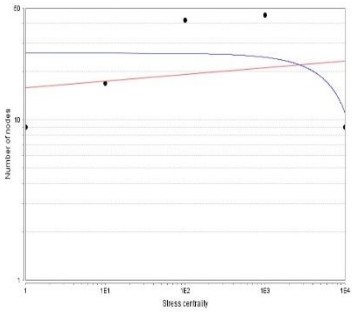


Figure 9c: Stress Centrality for the analysis of the Drosophila network

Figure 9a: Stress Centrality for the analysis of the Human network; Figure 9b: Stress Centrality for the analysis of the Mouse network Figure 9c: Stress Centrality for the analysis of the Drosophila network

TOPOLOGICAL COEFFICIENT

Topological coefficient is one of the global parameters computed by the Network Analyzer. A node sharing more than one neighbor with the other nodes is measured by the system and the topological coefficient is the relative measure for all nodes in the network i.e. the extent a node sharing neighbors with all other nodes in the network. The topological coefficient is a number between 0 and 1. A topological coefficient of zero is assigned to the node if that node only have one neighbor or none at all.

The topological coefficient and the average number of neighbors of individual nodes of the three networks are plotted in the figure 10. The red line indicates the average topological coefficient of all the nodes.

In the human network, the topological coefficient is a decreasing line with an increase in the number of neighbors. The maximum topological coefficient of a node was 0.75 and the minimum value was approximately 0.20. Some nodes with low number of neighbor's (less than 10 number of neighbors) have high topological coefficient. The nodes in the human network have up to 300 neighbors. Compared to human networks, the mouse and fruit fly are relatively small with the maximum numbers of neighbors nearby as 80 and 50 respectively. The topological coefficient of the two model species' gene networks was higher even though they had neighbours that were less than 30% of those of the human network. This means that the genes in those model organisms have relatively close communication.

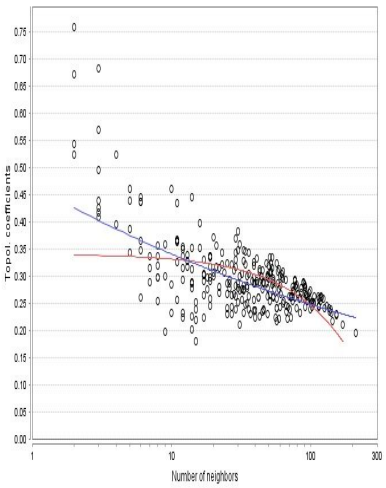


Figure 10a: Topological Coefficient for the analysis of the Human network

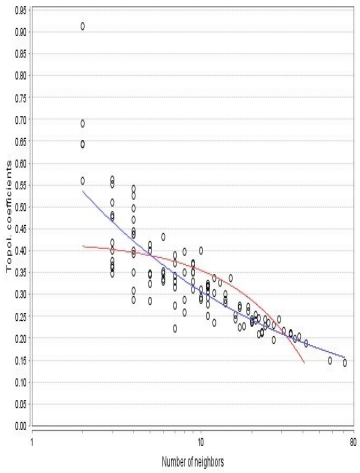


Figure 10b: Topological Coefficient for the analysis of the Mouse network

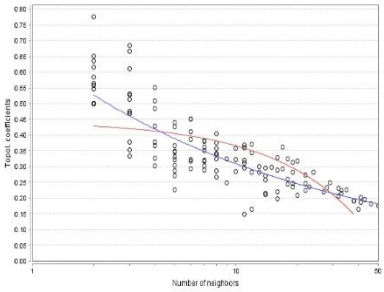


Figure 10c: Topological Coefficient for the analysis of the Drosophila network

Figure 10a: Topological Coefficient for the analysis of the Human network; Figure 10b: Topological Coefficient for the analysis of the Mouse network; Figure 10c: Topological Coefficient for the analysis of the Drosophila network

4. CONCLUSION

The scientific community is evolving each day to fulfill the requirements of the growing needs of society. Researchers of different disciplines are working in collaboration to support that process. One such field is network science that utilizes resources from mathematics, computer science, physics, statistics and sociology to study connections among different elements in a complex network. The field has applications in computer networks, social networks, telecommunication networks, cognitive and semantic networks and most importantly in biological networks.

In this study, the biological network method was used to understand the relations of the human network with the mouse and the fruit fly network. The mouse and the fruit fly are the major model systems for the human in gerontology research. Hence it is important to identify whether these organisms share similarities with humans so the reliability of the results obtained from them can be ensured. Thus, the adequacy of those model organisms is elucidated through the network interaction statistics analysis and the results revealed that the mouse network had the most similarities with the human network than the fruit fly model. The difference could be because humans and fruit fly belong to different classes of the animal kingdom and while humans and mice belong to the same Mammalia class. Even though the fruit fly network showed less similarities than the mouse network, it still has a complex genome so can still be utilized to study simple parameters of the human aging process while for most robust research mouse model should be utilized.

CONSENT (WHEREVER APPLICABLE)

No manuscripts will be peer-reviewed if a statement of patient consent is not presented during submission (wherever applicable).
This section is compulsory for medical journals. Other journals may require this section if found suitable. It should provide a statement to confirm that the patient has given their informed consent for the case report to be published. Journal editorial office may ask the copies of the consent documentation at any time.

Authors may use a form from their own institution or SDI Patient Consent Form 1.0. It is preferable that authors should send this form along with the submission. But if not already sent during submission, we may request to see a copy at any stages of pre and post publication.

If the person described in the case report has died, then consent for publication must be collected from their next of kin. If the individual described in the case report is a minor, or unable to provide consent, then consent must be sought from their parents or legal guardians.

Authors may use the following wordings for this section: "All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal."

ETHICAL APPROVAL

None to declare.

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